# Basic Research Needs for
Catalysis Science

Report of the Basic Energy Sciences Workshop on
Basic Research Needs for Catalysis Science to Transform Energy Technologies
May 8–10, 2017

Image courtesy of Argonne National Laboratory.

Basic Research Needs for
Catalysis Science
TO TRANSFORM ENERGY TECHNOLOGIES

Report from the U.S. Department of Energy, Office of Basic Energy Sciences Workshop May 8–10, 2017, in Gaithersburg, Maryland

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Abbreviations, Acronyms, and Initialisms

AFM	atomic force microscopy
AIMD	*ab initio* molecular dynamics
ALD	atomic layer deposition
ANN	artificial neural networks
APO	apoenzyme
APT	atom probe tomography
AP-XPS	ambient pressure X-ray photoelectron spectroscopy
ATP	adenosine triphosphate
BAS	Brønsted acid site
BEEF	Bayesian error estimation functional
BEP	Brønsted-Evans-Polanyi
BES	Basic Energy Sciences
BN	boron nitride
BODIPY	boron-dipyrromethene
BRN	Basic Research Needs
CAACs	cyclic (alkyl)(amino)carbenes
CCSD	couple cluster single double
CD	circular dichroism
CFD	computational fluid dynamics
CMD	concerted metalation-deprotonation
COF	covalent organic framework
CP2K	density functional based massively parallel and/or linear scaling codes
CPMD	density functional based massively parallel and/or linear scaling codes
CVD	chemical vapor deposition
DFT	density functional theory
DFT-QM/MM	density functional theory quantum mechanics/molecular mechanics
DME	dimethyl ether
DNN	deep neural network
DNP NMR	dynamic nuclear polarization nuclear magnetic resonance
DRIFTS	diffuse reflectance infrared fourier transform spectroscopy
ED	electroless deposition
EDS	energy dispersive X-ray spectroscopy
EELS	electron energy loss spectroscopy
ELM	extreme learning machine
ESM	electrochemical strain microscopy
ESP	electrostatic potential

E-TEM	environmental transmission electron microscope/microscopy
EXAFS	extended X-ray absorption fine structure
FCC	fluid catalytic cracking
FCEV	fuel cell electric vehicles
FLPs	Frustrated-Lewis Pairs
FF	force field
GCC	graphite-conjugated catalysts
GGA-DFT	generalized gradient approximation density functional theory
GRNN	general regression neural network
GVL	γ-valerolactone
GW	gigawatt
HAADF/STEM	high angle annular dark field scanning transmission electron microscopy
HER	hydrogen evolution reaction
HERFD	high-energy resolution fluorescence detected
HMF	5-hydroxymethylfurfural
3-HP	3-hydroxypropionic acid
HTL	hydrothermal liquefaction
IGPS	imidazole glycerol phosphate synthase
INS	inelastic neutron spectroscopy
IR	infrared
IR-SNOM	infrared scanning near-field optical microscopy
IWI	incipient wetness impregnation
LSR	linear scaling relationship
LT-STM	low temperature scanning tunneling microscopy
MAS	magic angle spinning
MB	molecular beam
MB-pol	many-body potential with polarization
MD	molecular dynamics
MD/MC	molecular dynamics/Monte Carlo
MMO	methane monooxygenase
MoD-QM/MM	moving-domain quantum mechanical/molecular mechanics
MOF	metal organic framework
MP2	second-order Møller-Plesset perturbation theory
MPn	higher order Møller-Plesset perturbation theory
MSW	municipal solid wastes
NADH	reduced form of nicotinamide adenine dinucleotide
NDO	neglect of differential overlap (semi-empirical quantum chemistry method)
NMR	nuclear magnetic resonance
NOMGAs	nitrogen-doped ordered mesoporous graphitic arrays
NP	nanoparticle

OEC	oxygen-evolving complex
OER	oxygen evolution reaction
ONETEP	density functional based massively parallel and/or linear scaling codes
ORR	oxygen reduction reaction
PAFs	porous aromatic frameworks
PD	photodeposition
PDF	pair distribution function
PEM	polymer electrolyte membrane
PFG NMR	pulsed-field gradient nuclear magnetic resonance
PGM	platinum group metal
PHASR	pulse-heated analysis of solid reactions
PI	process intensification
PMR	protonic membrane reformer
POPs	porous organic polymers
PRD	Priority Research Direction
PRFAR	N'-[(5'-phosphoribulosyl)formimino]-5-aminoimidazole-4-carboxamide ribonucleotide
PROX	preferential oxidation
PSW	plastic solid waste
Qbox	density functional based massively parallel and/or linear scaling codes
REAXFF	reactive force field
SAA	single atom alloy
SEA	strong electrostatic adsorption
SML	supervised machine learning
SMR	steam methane reforming
SMSI	strong metal-support interaction
SPMs	scanning probe microscopies
SSNMR	solid-state nuclear magnetic resonance
STEM	scanning transmission electron microscope/microscopy
STM	scanning tunneling microscope/microscopy
STXM	scanning transmission X-ray microscope/microscopy
TAP	temporal analysis reactor
TEM	transmission electron microscope/microscopy
TEMPO	2,2,6,6-tetramethylpiperidinyl-N-oxyl
TERS	tip enhanced Raman spectroscopy
TOF	turn-over frequency
TXM	transmission X-ray microscope/microscopy
UHV	ultra-high vacuum
UV	ultraviolet
XANES	X-ray absorption near-edge spectrum/spectroscopy
XAS	X-ray absorption spectroscopy

XEOL	X-ray excited optical luminescence
XRD	X-ray diffraction
ZIFs	zeolitic imidazolate frameworks

Executive Summary

Energy technologies affect virtually every aspect of life in modern societies—including transportation, utilities, agriculture, medicine, and the availability of a myriad of consumer products—and depend on human ability to accelerate and to guide chemical transformations. Controlling these transformations, which occur in the microscopic world of atoms and molecules, forms the basis of countless technologies such as production of fuels, fertilizers, plastics, pharmaceuticals and much more. At the very core of these chemical transformations are catalysts—specialized and often highly complex types of matter that allow chemical reactions to occur rapidly and produce specific products. Catalysts also have the remarkable ability to perform their tasks millions of times without themselves being consumed. The discovery of inexpensive and widely-deployable energy and chemical technologies, and their underpinning catalysis science, is critical to ensure the economic viability of U.S. energy and chemical industries.

Over the past decade, remarkable new tools have been discovered that allow the observation of catalytic transformations in exquisite detail, and assembly of novel and elaborate catalytic architectures with atomic precision. Furthermore, increasingly sophisticated theoretical and computational tools allow understanding of the essential details of the catalytic processes, and this overall progress has led to the discovery of catalysts with superior performance and the associated economic benefit. In the next decade and beyond, science promises to revolutionize how catalysts and catalytic processes are designed, to enable the introduction of new energy resources, to provide routes to sustainable synthesis of chemicals and other valuable materials, and to create novel approaches to chemical energy storage.

What might the future of catalysis-based technologies look like? Imagine:

- **Synthetic catalysts that match or exceed the speed and specificity of biological enzymes, but are far more stable under industrial operating conditions**

- **Catalysts that can activate when they are needed, adjust their activity to accommodate changes in reaction conditions, and repair themselves when they become deactivated**

- **Catalysts prepared from inexpensive crustal elements like iron and copper rather than rare and expensive elements like platinum and rhodium that must be imported from other countries**

- **Catalytic technologies that allow inexpensive and abundant shale gas and carbon dioxide, or even industrial, municipal and agricultural waste streams, to be readily converted into fuels, synthetic polymers and high-value chemicals**

- **Catalytic processes that utilize intermittent electricity generated from solar or wind energy and produce transportation fuels, or even chemicals that can be produced on-site to purify water**

- **Modular chemical reactors that integrate catalyzed chemical reactions with separation processes and allow distributed conversion of biomass into precursors for the production of synthetic polymers**

New catalytic processes with higher efficiencies, greater tolerance to diverse feedstocks, and longer catalyst lifetimes will require significant developments in our understanding and control of complex catalyst architectures and their dynamic evolution, and the ability to understand and control chemical transformation networks. These advances will require even more sophisticated and powerful characterization and analysis methods, precise synthesis techniques, multiscale theory and modeling, strategic use of the tools of data science, and integration of these activities across disciplines.

This report is the result of the Basic Energy Sciences Workshop on Basic Research Needs for Catalysis Science to Transform Energy Technologies that was held in May 2017, and was attended by more than 100 leading national and international scientific experts. The attendees were organized into four panels: 1. Diversified Energy Feedstocks and Carriers, 2. Novel Approaches to Energy Transformations, 3. Advanced Chemical Conversion Approaches, and 4. Crosscutting Capabilities and Challenges: Synthesis, Theory, and Characterization. The workshop identified five priority research directions (PRDs) that are aimed at harnessing complexity in catalysis to create next-generation energy technologies and realizing efficient catalytic processes to increase the diversity of resources for production of chemicals and energy:

Design catalysts beyond the binding site
Enzymes, Nature's catalysts, combine binding sites (localized regions that promote bond breaking/making in the reacting molecule) with precise positioning of nonreacting components that influence reaction barriers and control access to the binding site. Atomic-level, three-dimensional design of robust nonbiological catalysts that precisely positions both reacting and nonreacting components will enable fast and selective chemical transformations for energy applications under conditions currently not possible.

Understand and control the dynamic evolution of catalysts
Catalysts are inherently dynamic materials whose local and extended structures change continuously, beginning with assembly of the components into a catalytically active architecture and continuing as the catalyst interacts with reacting molecules. These changes impact the chemical and physical properties of the catalyst and hence have profound consequences for its performance and lifetime.

Manipulate reaction networks in complex environments to steer catalytic transformations selectively
Many emerging chemical feedstocks have diverse, variable compositions with potential for reaction through large numbers of interconnected pathways whose contributions depend on process conditions. Mastering these challenging chemical conversions requires integrating catalyst design to control reaction kinetics with strategies to direct nanoscale transport and separations.

Design catalysts for efficient electron-driven chemical transformations
Electrocatalytic systems interconvert chemical and electrical energy by harnessing the flow of electrons to form and break chemical bonds. Designing electrocatalytic systems with tailored electronic states and controlled interfacial environments will allow electrocatalysis with high selectivity and energy efficiency.

Drive new catalyst discoveries by coupling data science, theory, and experiment
The complex coupling of many variables that govern catalyst reactivity and evolution makes it challenging to determine relationships between catalyst structure/composition and performance. Data science can reveal important patterns in such high-dimensional data, providing insights for predicting performance, designing critical validation experiments, and discovering new catalysts.

Introduction

Catalysis is key to the production of fuels and chemicals—currently, over 80% of all chemical products and carbon-based energy carriers are made using catalysts in at least one of the processing steps. Estimates of the total value of fuels and chemicals derived from catalysts in the United States exceeded $900 billion/year in 2010.[1]

Catalysts increase chemical transformation rates (reactivity) without being consumed in the reaction and enhance the yield of desired products (selectivity) by controlling the relative rates of competing reactions. High catalytic reactivity and selectivity reduce the required energy input, the number of process steps, and unwanted byproducts in the overall catalytic conversion. New catalysts and catalytic processes will enable more efficient chemical transformations of raw materials and interconversion of the energy stored in chemical bonds with thermal and electrical energy.

THE SHIFTING LANDSCAPE OF RESOURCES PRESENTS NEW CHALLENGES FOR CATALYSIS

In the last decade, the overall feedstock mix used for the petroleum and chemical industry underwent qualitatively and quantitatively remarkable transformations. From a perceived shortage of fossil resources in the early years of the twenty-first century, it is now realized that modern technologies enable a wide availability of hydrocarbon resources.[2] From a situation in which the United States imported 64% of petroleum and natural gas liquids in 2005, the percentage dropped to 22% in 2017.[3] The increase in the volume of available crude oil and natural gas-derived liquids, accompanied by an overall shift to lighter hydrocarbons over these years, has led to a gradual replacement of heavier carbon-rich crude oil. This shift in resources is displacing naphtha with methane and light hydrocarbons present in natural gas as the primary feedstocks for chemical production. Methane itself is mostly converted to CO and H_2 (synthesis gas), from which chemicals are synthesized, while light alkanes are used as the source for ethene and propene (the two key building blocks for the petrochemical industry) via ethane steam cracking and propane dehydrogenation, respectively. This shift has enabled the U.S. chemical industry to become one of the lowest-cost producers within the decade (from 2005 to 2015).[4] However, this shift required adaptation of existing catalytic technologies, as well as development of new technologies and catalytic processes, to enable novel routes to chemicals that had been previously made from naphtha cracking.

In parallel, new technologies enabled harvesting a larger fraction of chemicals and energy carriers from renewable resources. These include bio-derived carbon resources (plant material) and electricity from solar and wind energy. Increased utilization of biomass and renewable electricity poses structurally different challenges. In contrast to methane and natural gas liquids, bio-derived resources are rich in oxygen and have a lower net hydrogen-to-carbon ratio. Their dispersed nature and temporally fluctuating availability demand the development of new technologies and catalytic processes. Biomass, for example, has such a high water content that it is not economical to transport it over large distances.[5] Since the carbon in bio-derived resources has to be preserved to be economic, reactions involved in their transformation into chemicals and fuels require hydrogen as the key reducing agent. Strongly fluctuating energy sources, such as wind and solar, require energy storage. Catalysis efficiently promotes conversion of the energy into chemical bonds, which is energy-dense and transportable. Renewable energy contributions in the United States increased from 4.5% to 9.9% between 2007 and 2015, and this changing landscape demands advances in thermal catalysis and electrocatalysis to accommodate the future.[6]

At present, the conversion of hydrocarbon feedstocks is handled in large chemical plants, combining a multitude of thermally well-integrated processes. For example, a modern mid-size refinery converts a broad mix of hydrocarbons with a total power of up to 15 GW; such high capacities are the consequence of the availability and the high energy density of crude oil and natural gas-derived liquids. The increasing availability and utilization of decentralized biomass, stranded natural gas, and electricity from wind and solar sources require processing at smaller scales. The downscaling of chemical conversions necessitates simpler processes, a minimum number of separation steps, and processes realized at lower temperatures to reduce potential heat losses.

OPPORTUNITIES FOR NEW CATALYSTS AND CATALYTIC PROCESSES

The critical importance of catalysis has motivated significant research efforts to better understand how catalysts operate and to use this knowledge to design and deploy more efficient catalysts and processes. As a consequence, catalyst functions are increasingly understood at molecular and atomic levels, with concomitant descriptions of behavior at the level of elementary steps and active bond making/breaking structures. Essential to this progress is the ability to synthesize catalysts with high precision, to characterize working catalysts under operating conditions, and to employ advanced theoretical and computational approaches to predict catalyst behavior. Progress in these areas has provided detailed insight into how reactions occur, and has led to increased appreciation of the intrinsic complexity of catalytic processes. Detailed understanding of elementary reactions has enabled advances in areas as diverse as high-temperature transformation of hydrocarbons, low-temperature conversion of highly functionalized bio-derived compounds, highly selective synthesis of complex molecules, and improved electrochemical processes. By integrating insight gained from studies of homogeneous, heterogeneous, and biological catalysts, the catalysis community is beginning to take advantage of the remarkably diverse capabilities of catalysts based on multifunctional molecular complexes, functionalized porous materials, and nano- and single-atom-stabilized structures.

Future research opportunities are related to (i) diversified energy feedstocks and carriers, (ii) novel approaches to energy transformations, and (iii) the translation of fundamental insight to advanced chemical approaches driven by multicomponent feedstocks of variable composition. Common to all these directions is the need to better understand how complex and multi-functional catalysts can be synthesized, to develop and implement novel spectroscopic methods which are able to monitor the state and evolution of the catalyst during reaction, and to advance theoretical methods to describe the interactions and transformations of substrates.

The emergence of new *energy feedstocks* requires the ability to transform naturally-occurring bio-polymers such as lignocellulose directly and selectively into target chemicals. It also necessitates selective conversion of light hydrocarbons such as methane, ethane and propane to high-value compounds and may require conversion of CO_2 from industrial emissions to methanol or more complex chemical platform molecules. These examples only highlight a very small portion of the challenges facing the field and the diversity of new catalytic transformations that have yet to be developed.

Traditionally, heat transfer has been the primary method to provide the required energy to overcome the activation barriers to enable and accelerate chemical reactions. Replacing heat with electric potential could lead to electron-driven interfacial reactions with the possibility for innovative, sustainable processes.

Translating the fundamental catalysis concepts into novel processes requires mastery of the challenges of intensifying process steps and the development of solutions that allow a more efficient operation. Such targets include, among others, the integration of reaction and separation, the incorporation of catalysts in micro-structured reactors, and cascade reactions. The ability to integrate complex feedstocks into novel processes requires understanding of complex reaction pathways and robust catalysts that are able to handle the molecular diversity present in the feed without participating in unwanted cross-reactivity.

MASTERING CHEMICAL COMPLEXITY IS THE KEY TO FUTURE PROGRESS

Progress in these challenging areas requires unprecedented insight into catalyzed reactions, as well as the ability to harness this knowledge to construct better catalysts. One central insight involves the realization that catalytic transformations encompass intricate rearrangements of reacting molecules and all the constituents of the catalytically active site. During these reactions, catalysts are dynamically changing on several time scales, from the initial synthesis to the active form, as well as from the initial turnover to the millions of subsequent ones. Controlling these changes requires understanding catalytic transformations and the interactions between reacting substrates and catalyst on the same time scales. Developing more sophisticated tools to monitor and manipulate these processes at the atomic and molecular scale requires continued refinement of experimental and theoretical methods.

NOBEL PRIZES MIRROR THE IMPORTANCE OF CATALYSIS IN CHEMISTRY OVER THE PAST CENTURY

The central role of catalysis for the chemical sciences is well documented in the history of Nobel prizes over the tenure of their existence—of the 177 scientists who have received awards as of 2017, twenty have been directly associated with chemical and interfacial catalysis. Several more (among them Carl Bosch and Ben Feringa) have been active in related fields. This is an impressive number, only rivaled up to now by organic chemistry. While the dedications speak for themselves, it is fascinating to observe how fundamental science has advanced industrial progress—from ammonia synthesis, to olefin polymerization, to metathesis of alkenes—enabling the efficient synthesis of diverse chemicals, materials, and pharmaceuticals. The catalysis community stands on the shoulders of giants.
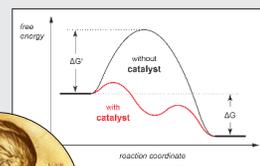

Figure I. Figure courtesy of Jon Darmon (Princeton University); image of Nobel medal courtesy of The Nobel Foundation, ©®The Nobel Foundation.

Select Passages from Nobel Citations over the Past Century Related to Catalysis

1909 Wilhelm Ostwald "…for his work on catalysis and for his investigations into the fundamental principles governing chemical equilibria and rates of reaction…"

1912 Paul Sabatier "…for his method of hydrogenating organic compounds in the presence of finely disintegrated metals…"

1918 Fritz Haber "…for the synthesis of ammonia from its elements…"

1932 Irving Langmuir "…for his discoveries and investigations in surface chemistry…"

1956 Cyril Norman Hinshelwood "…for researches into the mechanism of chemical reactions…"

1963 Karl Ziegler and Giulio Natta "…for their discoveries in the field of the chemistry and technology of high polymers…"

1973 Ernst Otto Fischer, and Geoffrey Wilkinson "…for their pioneering work, performed independently, on the chemistry of the organometallic, so called sandwich compounds…"

1994 George Olah "…for his contribution to carbocation chemistry…"

2001 William S. Knowles, Ryoji Noyori, and K. Barry Sharpless "…for their work on chirally catalyzed hydrogenation reactions and for his work on chirally catalyzed oxidation reactions, respectively."

2005 Yves Chauvin, Robert H. Grubbs, and Richard R. Schrock "…for the development of the metathesis method in organic synthesis…"

2007 Gerhard Ertl "…for his studies of chemical processes on solid surfaces…"

2010 Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki "…for palladium-catalyzed cross couplings in organic synthesis…"

Bringing about next-generation, efficient processes in large-scale production and new technologies to selectively convert emerging feedstocks in decentralized operations, requires transformative developments. For decentralized operations, milder reaction temperatures and pressures will be required, and the catalysts and catalytic pathways may take inspiration from Nature's effective low-temperature catalysts, enzymes. While enzymes themselves may be too sensitive for large-scale practical operations, functional models of enzymes can guide our design principles. Such novel catalysts will require advanced synthetic methodologies to be able to address complex three-dimensional anisotropic structures that create specific environments for the reacting molecules to undergo selective conversion with high rates.

SUMMARY

Advancing our understanding of and ability to control catalyzed reactions is essential to ensure the long-term economic viability of the energy and chemical industries. This report includes five priority research directions that provide details of the scientific challenges, as well as offering examples of areas for future research. It also includes four panel reports that summarize the current status and recent advances in catalysis research for energy applications, scientific challenges and opportunities for developing new catalytic processes required by the shifting landscape of energy resources, and the impact advances will have on energy-relevant technologies.

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PRD 1   Design Catalysts Beyond the Binding Site

Key question: How do we elucidate the cooperative interactions among the binding site, reacting molecules, and the surrounding environment to enable the design of catalyst structures that precisely control chemical reactions?

Summary: Enzymes, Nature's catalysts, combine binding sites (localized regions that promote bond breaking/making in the reacting molecule) with precise positioning of nonreacting components that influence reaction barriers and control access to the binding sites. Atomic-level, three-dimensional design of robust nonbiological catalysts that precisely positions both reacting and nonreacting components will enable fast and selective chemical transformations for energy applications under conditions currently not possible.

INTRODUCTION

At the molecular level, catalytic mechanisms involve direct interactions between reacting molecules and active sites which lead to the formation and/or cleavage of chemical bonds. These events occur at or very near where the reactants bind to the catalyst. As our ability to describe the precise nature of active sites advances, it is becoming clear that many other interactions, individually weaker than covalent binding but collectively significant, serve to orient reacting molecules and contribute to the energy landscape for the catalytic reaction, Figure 1.1. The effects can involve interactions between reacting and non-reacting molecules (including solvent molecules), or between reacting molecules and atoms located at specific distances from the binding site where they define void spaces. Well-known examples of such voids include the pockets or grooves in enzymes, and the pores in zeolites. Recently, many other possibilities have emerged, some of which are illustrated in Figure 1.2.[1] Consequently, the single

Figure 1.1. Schematic depiction of the extended environment around a binding site surrounded by atoms that comprise ancillary ligands, the solid support, co-reactants, ions, and solvent molecules. The ensemble forms the catalytic active site. Figure courtesy of Basic Research Needs for Catalysis Science 2017 Workshop Committee.

energetic descriptors that have been used successfully to create linear free-energy relationships to connect the composition and structure of active sites with their reactivity as catalysts are insufficient to predict the detailed kinetics of catalytic reactions. For this, it is necessary to explore diverse interactions beyond the binding site.[2,3] The spatial arrangement of additional directing groups, and of atoms that define the boundaries of confined spaces or voids adjacent to the binding site, can strongly influence catalytic behavior. Their presence can affect catalytic activity by (i) exerting electronic effects on the binding site, (ii) establishing the chemical potentials of reactants and intermediates by controlling diffusional access to the binding site; (iii) influencing the stabilities of specific transition states based on their size, shape, and polarity; and (iv) enabling kinetic coupling between different reactions, as well as the coupling of reactions with transport processes. The extended environment which constitutes the active site can also increase catalyst resilience towards deactivation, by restricting the access of poisons to the binding site.

Figure 1.2. Catalyst binding sites (green) illustrating confinement in various void spaces: A) metal nanoparticle in a zeolite pore; B) metal nanowire in a single-walled carbon nanotube; C) metal terrace covered by a graphene sheet.[1] Reprinted with permission from *Proceedings of the National Academy of Sciences of the United States of America*, Confined Catalysis Under Two-dimensional Materials, H. Li et al.

In principle, unique reactivity can emerge from the precise multi-scale positioning of specific structural motifs and functional groups with respect to the binding site. For example, the unique microenvironments present near enzyme binding sites allow alcohol dehydration to proceed at near-ambient conditions, while the same reaction catalyzed by hydronium ions in solution requires much higher temperatures. With their precise microporous structures, zeolites can mimic the confinement effects exhibited by enzymes, by lowering the free energy barriers for acid-catalyzed and other reactions. Catalyst systems containing multiple types of active sites may achieve higher or different selectivities compared to catalysts containing only one type of site. Thus, bimetallic hydrodeoxygenation catalysts that selectively cleave C−O bonds in oxygenates combine oxophilic metal sites (e.g., Re, W, Fe) to effect deoxygenation, with nearby noble metal sites that rapidly hydrogenate deoxygenated intermediates to stable products.[4,5] Bifunctional catalysts that combine two catalytic functions in a single active site can access unique pathways. For example, molecular heterobimetallic catalysts for olefin polymerization generate unique polymer microstructures that are unattainable using mixtures of the constituent mononuclear catalysts.[6] Supporting ligands can also endow catalytic sites with bifunctionality, as in the case of precisely-positioned peripheral sites that accept or deliver protons.[7]

Continued improvements in theoretical accuracy and more incisive spectroscopic and kinetic probes have helped to elucidate some of the kinetic effects of weak, concerted interactions between bound species and ligands or supports, resulting in preferential stabilization of certain transition states. In homogeneous catalysis, the design of ancillary ligand architectures allows steric constraints near the metal binding site to be tuned. For example, a high-valent iron catalyst achieved selective C−H bond amination by defining a reactive pocket with bulky adamantyl substituents (a steric effect), as well as via ligand control of spin state (an electronic effect).[8] Confinement effects in solid catalysts are typically associated with microporous materials, whose channels limit the access of certain reactants to intra-channel active sites. They may also retard the diffusion of some reaction intermediates and products away from the active sites. Specific transition states can be favored based on the size and shape of the confining voids, Figure 1.3. Certain catalytic reactions can also be influenced by the chemical properties and spatial arrangement of solvent molecules and co-adsorbates, whose presence alters the stability of transition states.
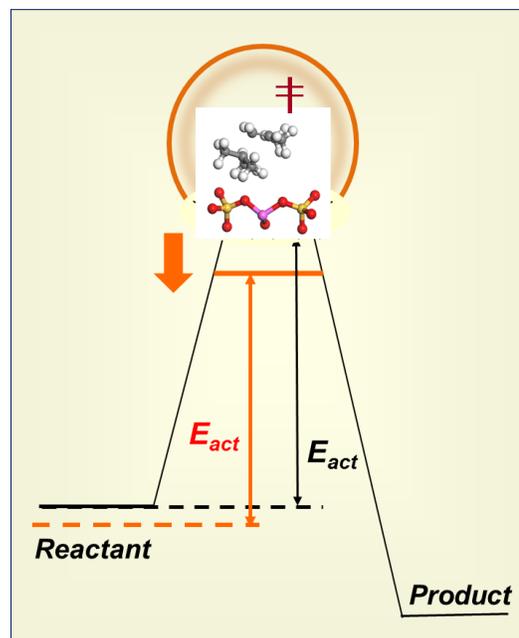
Figure 1.3. Confinement effect on the activation barrier for a catalytic reaction. Image courtesy of Enrique Iglesia (University of California – Berkeley).

SCIENTIFIC CHALLENGES

The optimal positioning of structural and functional motifs requires precise spatial control of multiple binding sites and of the shape, size, location and chemical properties of voids, ligands, and solvents. Experimental methods to design and synthesize active sites with specific extended architectures, which maintain the required organization of these weakly bound molecules during catalytic reactions, are not yet available. One challenge is to discover the underlying principles and most appropriate synthetic strategies for the deliberate construction of such extended reactive environments, in both molecular complexes and solid materials. For inorganic solids, this requires an understanding of the complex chemistry and hydrodynamics in dense phases during their assembly.

Recent advances in synthesis of complex structures have led to impressive increases in catalyst performance. For example, the exceptional catalytic activity and stability of a "yolk-shell" architecture was attributed to interfacial sites where the gold nanoparticle interacts with its amorphous sodium titanate support generated during the etching of a sacrificial silica layer (see Figure 1.4).[9] However, general methods to design and synthesize active sites at specific locations in their supramolecular surroundings do not yet exist. Such methods will require significant advances in our ability to position atoms, functional groups, and active site ensembles at precise locations within three-dimensional structures, where they can benefit most effectively from a given confining environment. Even in widely-used zeotype structures, installing heteroatoms at distinct positions in a given framework remains empirical, and the spectroscopic assessment of their location is attainable only for a few structures with a small number of crystallographically distinct sites. The preferential placement of active sites at desired locations within void structures has been possible only in limited cases so far,[10,11] and the placement of these sites at precise distances relative to other functional sites is seldom controlled.[12] The ability to decouple the effects of restricting molecular access to binding sites from the nature of the local confining voids that contain such sites remains a formidable challenge. Powerful new methods will be required to create interconnected spaces that vary systematically in size and shape. Those techniques, already used and developed empirically as structure-directing agents for zeolites, have led to the synthesis of only about 200 among the $>10^6$ structures that are theoretically achievable.

The interactions that give rise to essential and ubiquitous environmental effects in catalysis can be weak (e.g., hydrogen bonding, dispersion forces) and, in many cases, they involve concerted and/or cooperative interactions among multiple components in a catalytic system. These interactions involve large numbers of atoms, and they can be transmitted over much longer distances and time-scales than the chemical events that make and cleave bonds at or near the binding sites; consequently, they can be difficult to probe experimentally and to model computationally. It remains a challenge to describe quantitatively and *a priori* the details of the many weak interactions that provide enthalpic stabilization to molecules present in the active sites, at the entropic cost incurred by enforcing spatial organization. Current methods for characterizing the spatial relationships among various structural and functional motifs, with three-dimensional atomic arrangements including those creating void spaces, are often not sufficiently sensitive at intermediate length scales, between the local (<1 nm) and the distant (tens of nm).
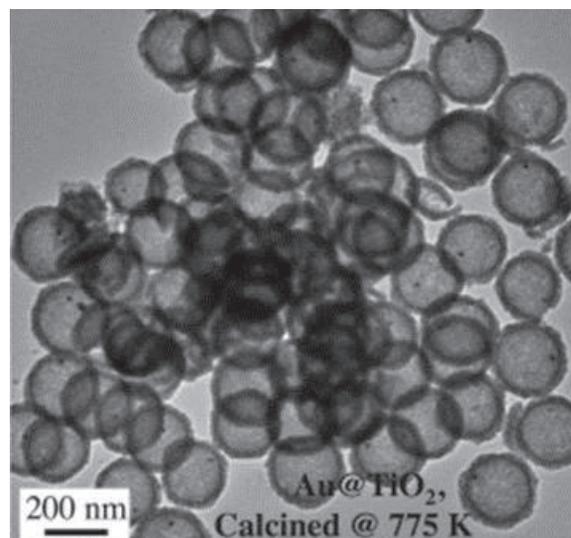
Figure 1.4. Individual Au nanoparticles encapsulated in voids within amorphous TiO_2 shells are exceptionally active for low temperature CO oxidation, which occurs at interfacial sites. From I. Lee, J. B. Joo, Y. Yin, and F. Zaera, "A Yolk@Shell Nanoarchitecture for Au/TiO_2 Catalysts," *Angew. Chem. Int. Ed.*, 50: 10208-10211. Copyright © 2011, Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

The effects of confinement on free energy barriers have been widely investigated, both theoretically and experimentally, for zeolite-catalyzed reactions conducted in the gas phase.[13] However, a similar level of understanding for reactions conducted in the liquid phase has yet to be achieved. Molecular organization in condensed phases has a profound influence on the interactions between the binding site and reactants, intermediates, and products present in its extended microenvironment. Understanding the consequences

of specific catalyst architectures will also require improved theory-based predictions of transition-state structures for kinetically-relevant steps, and transition-state formalisms that can be described in the context of thermodynamically non-ideal environments and with high charge densities, such as those present in condensed fluid media, and in dense adsorbed layers, Figure 1.5. A combination of molecular dynamics simulations and quantum mechanical calculations with rigorous kinetic analysis of experimental data is needed to provide insight into such systems.

The importance of solvents in determining catalytic reactivity and selectivity is well-documented and can even result in mechanistic changes,[14] but their effects are frequently recognized only *a posteriori*, via empirical observation and heuristics. The presence of a solvent can affect the stability of intermediates and transition states, and can modify the arrangement of


Figure 1.5. Molecular confinement in a dense adsorbate layer on a metal nanoparticle surface. Image courtesy of Enrique Iglesia (University of California – Berkeley).

ligands, ions, or coadsorbates around a binding center. Its functional groups and acid-base properties can alter the pKa in reacting molecules. In solid catalysts, dense adsorbed layers can act as two-dimensional solvating environments. The properties of the solvent (e.g., polarity, viscosity) at the interface may no longer be representative of its bulk properties. In both homogeneous and heterogeneous systems, the challenge is to understand how solvent effects are exerted to significantly change catalyst performance.

## SIDEBAR 1. ROLE OF COOPERATIVITY IN UPGRADING OF BIOMASS-DERIVED FEEDSTOCKS

The selective removal of oxygen is key to the upgrading of biomass-derived feedstocks to fuels and chemicals. In bifunctional carbon-supported Pt-Re catalysts for the hydrodeoxygenation of glycerol, the presence of Re promotes the rate of hydrogenolysis and changes the selectivity from 1,2-propanediol towards 1,3-propanediol. Even under H_2, the surface Re sites remain partially oxidized and

Sidebar Figure 1.1. A bimetallic Pt-Re catalyst performs tandem acid-catalyzed dehydration and hydrogenation much faster than a combination of a homogeneous Brønsted acid and a Pt hydrogenation catalyst. Reprinted with permission from *ACS Catalysis*, Evidence for the Bifunctional Nature of Pt–Re Catalysts for Selective Glycerol Hydrogenolysis, Falcone et al. Copyright © 2015, American Chemical Society.

are decorated with hydroxyl groups. These Re-OH sites are Brønsted acidic and catalyze dehydration of the secondary alcohol, via its protonation and tautomerization of the resulting carbenium ion to generate the aldehyde product.[17] This unsaturated intermediate is rapidly hydrogenated on adjacent, fully reduced Pt sites. In contrast, a combination of a supported Pt catalyst and a homogeneous Brønsted acid is much less effective, presumably because of the need for transport of the highly reactive intermediate between the two catalyst functions.

In heterogeneous catalysts based on multi-metallic ensembles, mixed oxides, and interstitial compounds such as carbides and nitrides, different types of active domains can create interfacial regions whose electronic and binding properties differ markedly from similar materials in which these domains lack atomic contact with each other (see Sidebar 1). Here, the challenges are to predict and control the nature of these interfaces in order to elicit the desired synergistic effects, and to develop synthetic methods to construct them. For both molecular and solid catalysts, characterizing interacting domains and their ability to communicate chemical information over distances greater than atomic dimensions (e.g., through proton or electron transfer, atomic or molecular diffusion) is difficult to achieve with the level of precision required for the purposeful design and predictive synthesis of novel compositions or materials. High-resolution methods capable of probing reacting systems must be further developed. For example, isolated Pt atoms dispersed in Cu were observed by STM, Figure 1.6, and their presence correlated with their ability to activate the C–H bonds in adsorbed methyl groups selectively without triggering coking.[15] Spectroscopic methods that can clearly distinguish between reactive species and spectators, for example, using frequency modulation,[16] are needed, while mechanistic studies must be able to account for the local gradients in chemical potential present in complex hydrodynamic environments.

Finally, while cooperativity is a common motif in enzyme catalysis, where it refers to conformational changes in a protein triggered by substrate binding at one subunit causing activation in other subunits,[18] translating the tremendous potential of cooperativity to non-biological catalysts will require tools to design and construct multisite cooperative catalyst systems that allow the emergence of new, mesoscale catalytic phenomena. The effectiveness of empirical/high-throughput testing strategies will be limited for such materials, because of the vast number of possible combinations of types of sites in synthetic materials, and of their spatial arrangements. Theoretical methods do not readily account for cooperative behavior in reaction cascades involving multiple functions, because many weak interactions acting in concert possess a very large number of degrees of freedom. Thus, the challenge is to develop alternate *in silico* strategies to predict catalyst architectures in which cooperativity can emerge.
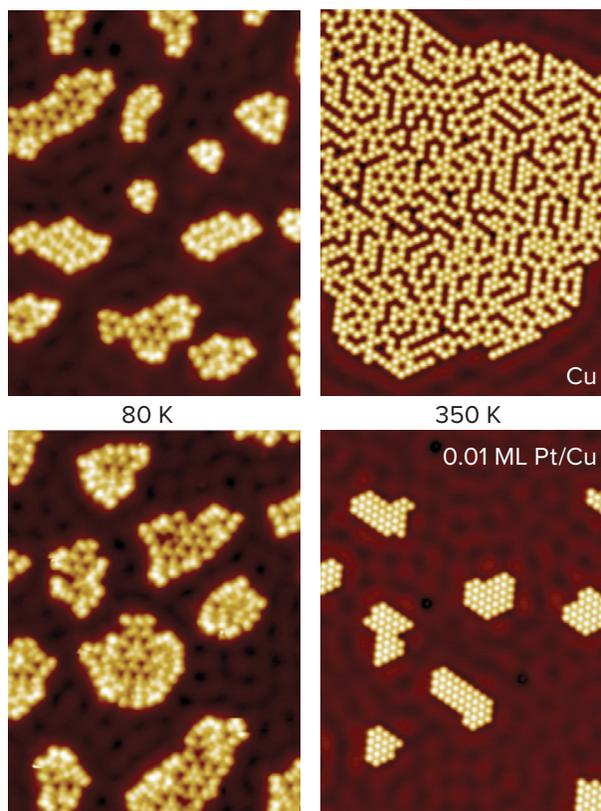
Figure 1.6. STM images, recorded at 5 K, show CH₃I adsorbed on Cu(111) and 0.01 ML Pt/Cu(111) surfaces (top and bottom rows, respectively), after annealing to 80 K (left, showing clusters of intact CH₃I molecules), and 350 K (right, dissociated iodine atoms appear as brighter protrusions, while methyl groups appear as darker protrusions). The loss of methyl groups from the Pt-containing surface is a consequence of C-H activation and formation of methane. Reprinted with permission from *Nature Chemistry*, 10, 325-332, 2018, Pt/Cu single-atom alloys as coke-resistant catalysts for efficient C–H activation, Marcinkowski et al. Copyright © 2018, Springer Nature.

FOCUS AREAS

Construct Multi-scale Catalyst Architectures with Spatial Precision

To orient and stabilize reacting molecules in next-generation catalyst systems, the interaction with a binding site will be controlled by multiple points of contact with various structural motifs, resembling enzyme-like behavior.[19] Creating the desired spatial arrangement of discrete architectural components will require a much higher level of control during catalyst synthesis than is typically used to create monofunctional binding sites. Specifically, synthetic protocols must be developed to allow positioning of similar and/or different types of interacting sites at prescribed distances and with specific orientations (see Sidebar 2). Such distances and orientations must encompass both the molecular and supramolecular length scales in order to induce precisely orchestrated, cooperative interactions adjacent to the binding site, as well as to allow for diffusion of intermediates between non-adjacent sites in tandem or cascade reactions. For example, pincer complexes with appended crown ether

substituents show hemilabile ligand coordination that modulates catalytic activity, based on solvent-induced cation binding.[20] These new catalyst designs may be an essential step in our ability to design catalysts that are not subject to linear scaling relationships. Such relationships link the affinities of reactants and intermediates for a particular binding center to the rates of elementary steps in a catalytic cycle, and thereby determine the relative rates of steps in a catalytic sequence; they also predict the maximum attainable rate for a given transformation occurring at a specified binding site. Exceeding this maximum rate, or breaking the scaling relation, will require the use of properties other than adsorption at an individual binding site.

SIDEBAR 2. BIO-INSPIRED DESIGN OF THE OUTER COORDINATION SPHERE FOR AN INORGANIC CATALYST

Certain heme-containing enzymes catalyze the reductions of nitrate and (per)chlorate efficiently by facilitating oxyanion binding using Coulombic interactions with positively charged amino acid residues, and extensive hydrogen-bonding networks to promote proton transfer and stabilize high valent metal-oxo intermediates. A cationic iron-based catalyst with an azafulvene-amine supporting ligand was designed with similar structural features to perform related reactions.[21] The oxyanions, which are difficult to activate because of their low binding affinities for transition metal ions, are oriented in the binding site by hydrogen-bonding interactions in the second coordination sphere, which facilitates deoxygenation by stabilizing the Fe(III)-oxo intermediate. Catalytic turnover was achieved by supplying protons and electrons to convert the oxo ligand to water and regenerate the Fe(II) site.
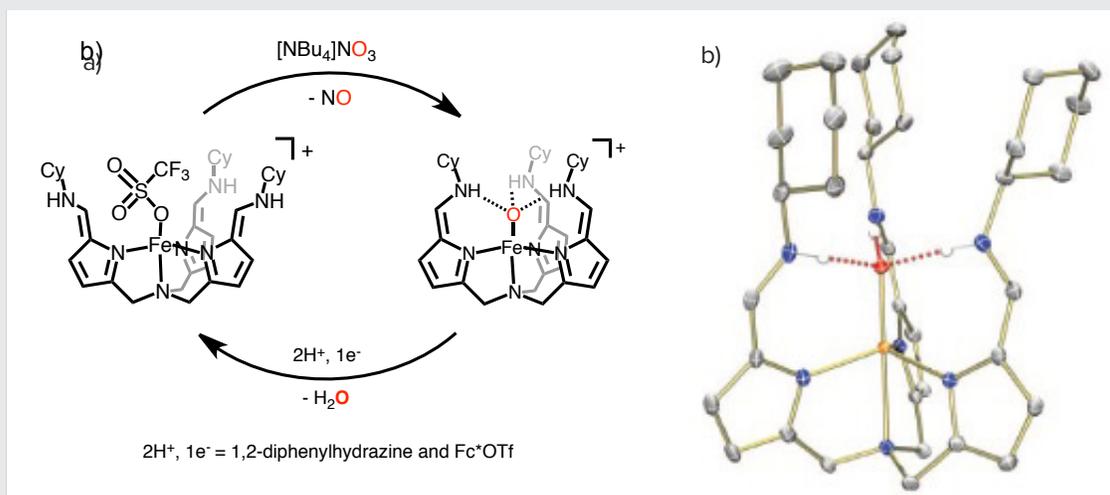
Sidebar Figure 1.2. Nitrate reduction mediated by a bio-inspired iron complex: a) formation of the Fe(III)-oxo intermediate; b) structural characterization of the cationic intermediate, showing its stabilization by outer-sphere hydrogen bonding. Image courtesy of Alison Fout (University of Illinois Urbana-Champaign).

Synthetic strategies to create specific three-dimensional ligand architectures and porous structures, as well as precisely located binding or grafting sites within such structures, are becoming feasible due to recent advances such as physicochemical characterization during synthesis and under reaction conditions, as well as more sophisticated computational models to describe the self-assembly process. The importance of such information is illustrated by the Pricat MFC gold-on-carbon catalyst, commercialized in 2015 to replace $HgCl_2$-based catalysts for acetylene hydrochlorination to vinyl chloride. Discovered in the 1980s, it was not until the catalyst was studied under working conditions using X-ray absorption spectroscopy that the active sites were shown to be atomically-dispersed Au cations, and not Au nanoparticles as previously believed. This finding completely changed our understanding of how these catalysts work, and will enable further design and optimization of Au-based catalysts.[22] Microporosity provides unique shape selectivity and confinement effects that can modify catalyst activity by affecting the enthalpy and entropy of transition states and intermediate products.[23] Structure-directing agents can impose specific connectivities,[24,25] create pores which stabilize specific transition states,[26] and locate active sites at specific locations within these catalytic materials.[10,11,27] Active sites can also be embedded in well-defined supramolecular cages, which may be soluble or part of an extended organic/inorganic solid, thereby creating microenvironments with tunable shapes and sizes where reactions can take place.[28] Both the local and

non-local structures around a catalyst binding site need to be assessed during synthesis, and under reaction conditions. There is potential for coupling computational and structural characterization methods with synthetic protocols to probe both weak and strong interactions within complex inorganic materials as they form. This is illustrated by the recent synthesis of a chiral zeolite, in which molecular models were used for the selection of synthetic routes and structure-directing moieties, and newly-developed electron microscopy imaging methods demonstrated the chirality of the structure.[29] The combination of these methods with powerful NMR tools for determining atomic connectivity in extended structures holds significant promise for the rational synthesis of new porous structures with interconnected channels of various dimensions.

New methods to create and exploit complex catalyst architectures must preserve the accessibility of the binding sites to reacting molecules. The effects of molecular diffusion to and from the active sites in catalytic materials, which create chemical potential gradients, must be clearly distinguished from local structural effects near the binding sites which confer transition-state specificity. A strategy that may be used to decouple these effects is the synthesis of hierarchically-structured materials, for example (i) generation of large, connecting channels within microporous crystals, via the synthesis of materials with bimodal distributions of pore sizes,[24] (ii) formation of single unit cell-thick supported zeolite sheets that can act as two-dimensional microporous structures,[30] (iii) delamination of crystalline materials to expose surface voids with hydroxyl groups that can be used to anchor active structures within partially confined pockets at accessible external surfaces,[31] and (iv) formation of cavities with functional groups or binding sites isolated from fluid media by mesoporous outer shells.[32] Experimental diffusion measurements using pulsed-field gradient nuclear magnetic resonance (PFG NMR) can be used to probe mass transfer limitations between the microporous and mesoporous domains.[33]

Optimize Weak Interactions to Stabilize Desired Transition States

Multi-point contacts involving a catalyst and molecules located at or near the binding site are analogous to the dynamic and adaptive reaction environments within enzyme pockets, which serve to guide reactions selectively along low standard free energy paths. The weak forces can include short-range van der Waals interactions, Coulombic interactions resulting from charged residues, hydrogen bonding, and solvation. For example, the rate of CO_2 hydrogenation catalyzed by an Ir pincer complex is greatly accelerated by the placement of a hydrogen bond donor in the ligand backbone.[34] When components of adsorbed intermediates and transition states interact with regions distant from the binding site, the arrangement of weakly-interacting molecules in the outer coordination sphere of the binding site become important. Multiple spectroscopies and theoretical approaches need to be combined to probe the local and extended structures of the catalyst under reaction conditions and over the different length scales of catalytic influence. Such methods will enable a more precise understanding of the organized structures formed around species adsorbed at the binding site, and the role of these interactions in stabilizing transition states. A potential direct outcome could be the ability to modulate catalyst activity without making changes directly to the binding site, but by manipulating its extended environment.[35] In the case of heterogeneous feedstocks, such an approach could enable rapid adaptation to changes in feedstock composition or quality, or to changes in the desired products.

One important aspect of liquid phase catalytic reactions that remains poorly-understood is the role of solvent reorganization. In enzyme-catalyzed reactions, the overall free energy barrier can be lowered by the pre-orientation of dipoles in the reaction pathway, despite the energy cost of reorganizing polar solvent molecules. As a result, enzymes accelerate reactions in polar solvents by virtue of their very polar active sites.[36] Similar effects may be at work in proton or hydride transfer reactions involving synthetic catalysts, when the charge distribution in the reactants and intermediates induces reorientation of solvent molecules and modifies reaction energetics. Density functional theory calculations using implicit solvent models miss important differences that can be identified only by quantum mechanical treatments involving explicit solvent molecules. The participation of solvent molecules is important in reactions involving charged species, such as the proton-coupled electron transfer oxidation of phenols,[37] and the oxidations of ethanol and glycerol to acids.[38] The local reaction environment within a solid inorganic framework can in principle be designed to promote reorganization of polar solvents during reaction. For example, in the presence of liquid water, the protons associated with the Brønsted acid sites (BAS) in zeolites are transferred to water clusters, and the resulting hydrated hydronium ions, $(H_2O)_n \cdot H_3O^+$,[39,40] have much higher catalytic activities inside the zeolite than the same ions in homogeneous solution.[13] Moreover, the extent of the rate enhancement can be varied experimentally by changing the structure and size of the confined space inside the zeolite.[41]

More accurate and reliable theoretical methods must be developed to describe the consequences of both molecular confinement and solvent effects in catalysis. Confinement within voids in supramolecular complexes or porous solids may dictate the course of a catalytic reaction by shifting the balance between enthalpic gains conferred by various interactions that lead to transition state stabilization, and entropic losses caused by confinement. Simulating these contributions correctly requires high-level wavefunction methods that can treat weak van der Waals interactions, Coulombic charge stabilization, and self-interaction energies accurately. Such effects can be captured through rigorous embedding schemes that contain high-level *ab initio* wavefunction methods, such as MP2, to determine the effects of the local environments, as well as more computationally-efficient methods such as density functional theory, to simulate the extended surroundings. Such methods have already been used to calculate adsorption energies as well as activation barriers for model reactions in zeolites, with accuracies within 2–4 kJ/mol.[42,43] Accurate simulations of entropic gains and losses along the reaction coordinate are critical, and they must account rigorously for the vibrational degrees of freedom of all confined molecules as well as the confining framework. This requires accurate sampling of a large number of statistical configurations and the use of *ab initio* molecular dynamics methods. Secondary and tertiary structures (also known as outer coordination sphere contributions) are responsible for energy focusing and dissipation in superstructures. In essence, small (free) energy differences may result in significant strain around the active sites, resulting in improved selectivity and rate enhancement. These energy requirements are mostly associated with the distribution of entropy ("entropy funnels" and changes in free energy landscapes). Hence, new methods to estimate these quantities reliably are essential, and will require close attention from theory.[44]

Design New Catalysts for Selective Transformations of Emerging Feedstocks

Converting small-molecule hydrocarbon feedstocks into value-added products selectively and efficiently will benefit from new catalyst architectures. For example, the direct use of shale gas to make liquid fuels and higher value chemicals without the involvement of synthesis gas will require the selective activation of the C–H bonds in light alkanes. Conventionally, oxidative addition is preceded by the formation of a metal-σ-complex, in which the C–H bond of an alkane acts as a ligand to a low-valent coordinatively-unsaturated metal center. However, such metal centers tend to react stoichiometrically and irreversibly with reactants, products, and impurities that are ubiquitous in alkane functionalization, such as water, O_2, other chalcogen- and halogen-containing molecules, and alkenes. New mechanistic discoveries and insights are needed to control the behavior of catalysts in the presence of these functionalizing reagents. A recently discovered concerted metalation-deprotonation reaction, in which the interaction of a C–H bond with a high-valent metal ion enhances its acidity thereby facilitating its subsequent deprotonation by a basic ligand, may be more widely compatible with the reagents typically used to functionalize alkanes.[45,46] Biological catalysts can also be adapted to catalyze non-biological reactions (see Sidebar 3) and along the way provide new insight into strategies for designing more selective catalytic pathways.

All but two of the top 16 organic chemicals produced via oxidation use either O_2 or air as the terminal oxidant, preferably without prior separation from air.[49] Natural gas and condensates are composed of saturated molecules that require oxidation to convert them to higher-value products (alcohols, alkenes, higher alkanes, arenes, carboxylic acids, and the like). A more precise understanding of O_2 activation pathways, specifically, the involvement of different kinds of reactive oxygen species, is crucial to enable the design of next-generation catalysts for selective aerobic oxidations, without the requirement for the use of costly, toxic, or corrosive oxidants, such as H_2O_2, Cl_2, O_3, or high-valent metal cations (all of which ultimately require O_2 as the terminal oxidant). The high selectivity achieved by metalloenzymes in aerobic oxidation reactions relies on timed and controlled binding of O_2 to the active site, leading to the formation of high valent metal-oxo intermediates.
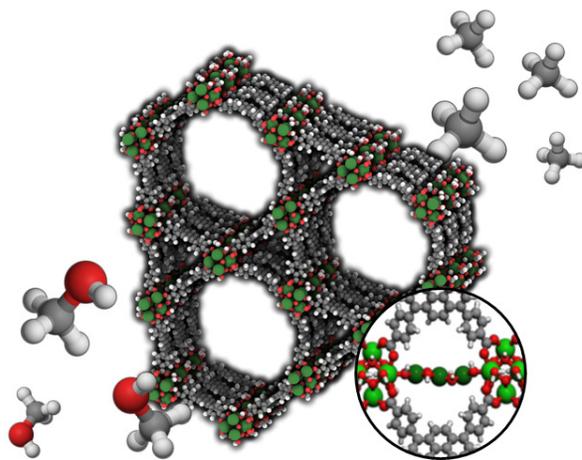

Figure 1.7. Trinuclear Cu-oxo clusters, prepared by atomic layer deposition of Cu(dmap)₂ and H₂O in the metal-organic framework NU-1000, catalyze the partial oxidation of methane to methanol, dimethyl ether and CO₂ under mild reaction conditions (150 °C, 1 bar). Image courtesy of Laura Gagliardi (University of Minnesota).

SIDEBAR 3. DIRECTED EVOLUTION OF BIOLOGICAL CATALYSTS FOR NON-BIOLOGICAL TRANSFORMATIONS

The manufacture of organosilanes is practiced commercially on large scales using a Pt-based catalyst, although recent work has shown that first-row transition metal complexes can achieve similar reactivity in alkene hydrosilylation.[47] While the reaction does not occur in Nature, a cytochrome c derived from *Rhodothermus marinus* achieves C-Si bond formation under mild conditions and with high chemo- and enantioselectivity via the heme-catalyzed reaction of silanes with carbenes derived from diazo compounds.[48] Using directed evolution to vary amino acid residues in close proximity to the binding site, the catalytic activity and selectivity were significantly enhanced, eventually achieving results superior even to those of traditional transition-metal catalysts. The enzyme tolerates a broad range of substituted hydrosilanes and functional groups, including alcohols and amines.

Sidebar Figure 1.3. Site-directed mutagenesis of the heme in the enzyme Rma cyt c leads to efficient catalysis of new C–Si bond formation from organosilanes and diazo compounds, via a metal carbene intermediate. From H. F. T. Klare and M. Oestreich, Teaching nature the unnatural, *Science* 354, Issue 6315, 2016, 970. DOI: 10.1126/science.aal1951. Copyright © 2016, AAAS. Reprinted with permission from AAAS.
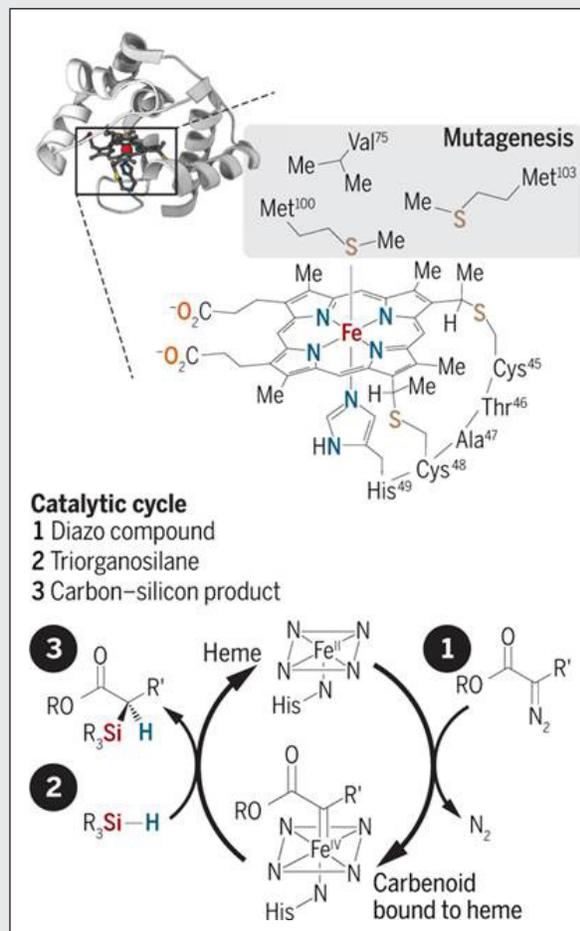
More generally, metal-O_2 interactions lead to a variety of highly reactive and often unselective oxygen species whose relative stabilities are influenced by the metal oxidation state as well as its local and extended coordination spheres (e.g., of a porous metal oxide framework, Figure 1.7).[50] Greater mastery of these interactions will be the basis for the development of new catalysts capable of highly selective oxidations.

Emerging feedstocks based on macromolecules, such as those present in biomass and synthetic polymers, will require new catalysts with the ability to cleave specific bonds in the presence of many others, some of which may be significantly weaker and therefore more reactive than the desired cleavage sites. The need for multiple, cooperative catalytic functions is also clear, since most reports involve unselective depolymerization, whether catalytic or not. Enzymes that catalyze the selective cleavage of biological macromolecules include proteases and cellulases, which target specific bonds using molecular recognition strategies. Designing catalysts for the large-scale conversion of biomass or synthetic polymers to fuels and chemicals will benefit from the use of similar strategies. Such catalysts will have to operate via different reaction pathways than those used to activate and transform small molecules[51] in order to achieve much better selectivities, and they are likely to require control of interactions at the active site as well as longer-range effects imposed by the catalyst environment at distances that are far removed from active sites.

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# PRD 2   Understand and Control the Dynamic Evolution of Catalysts

Key questions: How do we monitor and direct changes in catalysts during their life cycles and relate them to varying reactivity and selectivity? How do we design catalysts that adapt to varying feed composition and reaction conditions and ultimately can be reactivated?

Summary: Catalysts are inherently dynamic materials whose local and extended structures change continuously, beginning with assembly of the components into a catalytically active architecture and continuing as the catalyst interacts with reacting molecules. These changes impact the chemical and physical properties of the catalyst and hence have profound consequences for its performance and lifetime.

INTRODUCTION

Just as chameleons adapt to their surroundings through nanostructural changes in their skin that result in dramatic color changes,[1] catalysts can adopt new structures in response to their environments. Indeed, researchers have long realized that the as-synthesized catalytic material is rarely the same as the active material present under the chemical or electrical potential imposed by reactants, products, spectators, and electrodes, at the temperature and pressure in the reactor. Nature's catalysts, enzymes, do not have rigid structures, nor are they invariant: conformational changes are integral to their selective binding of certain reactants, as well as to the stabilization of desired transition states.[2] Dynamic behavior is also inherent in non-biological molecular catalysts, for which the dissociation and re-association of supporting ligands with accompanying geometric changes at the binding site are common steps in many homogeneous catalytic cycles, and pre-catalyst evolution to very different, active forms is well-documented.[3] Metal nanoparticles have considerable conformational lability.[4] Some of the many behaviors they are known to undergo are depicted in Figure 2.1.[5] Even the low-index surfaces of macroscopic single crystals can undergo dynamic restructuring under reaction conditions.[6,7]

Crystalline oxides can generate disordered phases once in the reactor. For example, crystalline $VOHPO_4 \cdot 0.5H_2O$, which catalyzes the oxidation of *n*-butane, transforms to a disordered phase during the reaction; the structural changes coincide with the appearance of the product, maleic anhydride.[8] Indeed, intrinsic adaptability of active sites is likely a necessary phenomenon for many types of catalysts. Flexibility, fluxionality, and hemilability of ancillary ligands are often associated with catalytic activity in molecular catalysts.[9,10] Relative to their crystalline counterparts, the greater flexibility of amorphous solid materials allows them to adapt more readily to changing chemical or electrical potentials to optimize the binding of reactants and intermediates.[11] Thus catalysts and electrocatalysts based on solids with less ordered structures may be more active than the corresponding ordered materials.[12,13] In nanocrystalline materials, disorder can also take the form of bulk and surface defects, which are often the key to catalytic activity, as in the well-studied $Cu/ZnO/Al_2O_3$ methanol synthesis catalyst.[14]
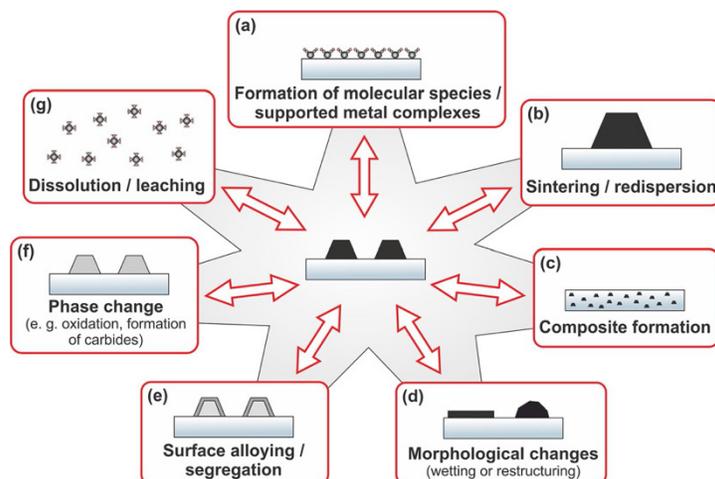
Figure 2.1. Examples of the dynamic behaviors in supported metal nanoparticle catalysts that can occur before, during, and after reaction. Reprinted with permission from Kalz et al., Future Challenges in Heterogeneous Catalysis: Understanding Catalysts under Dynamic Reaction Conditions, *ChemCatChem*, John Wiley and Sons, 2016. Copyright © 2017 Kalz et al.

Characterizing the active sites in dynamic materials is usually more difficult than describing the static structures of highly ordered catalysts. For a start, the relevant dynamic behavior occurs over a very wide range of time scales. It begins with the femtosecond motion of atoms within an enzyme, molecular complex, or nanocluster,[15] and extends to milliseconds, seconds or more for chemical phenomena such as molecular fluxionality, ligand exchange, surface segregation and reconstruction, and the migration of nanoparticles.[16] On even longer time scales, extending to many hours or days, physical changes in the morphology of a solid catalytic material may occur, components of the feed can be incorporated into the catalyst structure, and the material may undergo irreversible deactivation or regeneration, including phenomena such as Ostwald ripening, sintering, or cluster disintegration for nanoparticles.[17,18] Similarly, the length scales of important dynamic phenomena can range widely from interatomic distances (Ångstroms) for the rearrangement of atoms near the binding site of a catalyst, to hundreds of nanometers for the sintering and redispersion of nanoparticles, to micrometers and even larger for the macroscale attrition of catalyst pellets in a packed bed.

The intrinsically dynamic nature of catalytic materials has profound implications for the assessment of structure-function relationships, which are central to catalyst design. For example, the interaction of a metal nanoparticle with a support perturbs both the electronic and geometric structures of the nanoparticle, and generates unique interfacial sites that are often highly reactive. The nature and number of these interfacial sites vary as the nanoparticle structure evolves in time. Selectivity can also be affected by structural changes. Supported palladium catalysts become selective in the partial hydrogenation of alkynes only when a carbide phase is fully established. In its absence, a Pd hydride phase catalyzes unselective total hydrogenation.[19] The slow evolution of dispersed nanoparticles of iron and cobalt towards various carbide phases under reaction conditions causes dramatic changes in Fischer-Tropsch selectivity towards alkanes, alkenes, and alcohols.[20] The complex interactions between a molecular complex or a catalytically active phase and its adsorbates, solvent molecules and ions under reaction conditions also affect the structure and dynamic behavior at or near the binding site,[21-23] with important consequences for reactivity.[24] These effects and the resulting structures evolve in time, in part due to the metastability of the active sites as well as due to variations in the reaction conditions over the course of catalyst operation. Thus, the binding site, its surrounding scaffold, adsorbates and nearby species in solution or in the gas phase are all simultaneously in play.

Understanding the origins and consequences of dynamic catalyst behavior at an atomistic level is the first step towards synthesizing new catalysts that can adopt desired active site structures readily (and perhaps reversibly) under reaction conditions, and impede the adoption of undesired structures. This atomistic description includes the identity of the atoms at and near the binding site and their distribution in three-dimensional space, as described in Priority Research Direction 1, but further requires information about their absolute and relative mobilities as a function of the reactive environment. Structural changes can also be induced by purposeful alterations of reaction conditions in order to control activity, selectivity and stability. A deeper appreciation of the coupling of dynamic behavior with disorder, both transient and persistent, will enable catalysis science to advance beyond ideal systems and approach the true complexity of real working catalysts.

SCIENTIFIC CHALLENGES

It is essential to be able to describe dynamic structural behavior in order to construct meaningful structure-activity relations and inform computational models, but this information can be very challenging to obtain. In general, catalyst characterization techniques are most readily applied to highly uniform and stable materials, such as well-defined molecular catalysts with non-fluxional supporting ligands, and crystalline well-ordered solids. Such materials are often used as structural models for real working catalysts, precisely because they are straightforward to describe. However, many important catalysts are made of less well-defined materials, have abundant defects, or are even amorphous. Indeed, the well-defined materials are often pre-catalysts, evolving to less structurally uniform materials under reaction conditions. Modern atomic-resolution imaging techniques are severely challenged by disordered materials. Studies of static, long-range order in catalytic materials may give a misleading view of inherently dynamic systems (reflecting observational bias, colloquially called the "streetlight effect"). Even when the catalytic material is (at least, initially) uniform, the active sites are often a small fraction of all sites. Subtle structural differences between sites that activate and those that do not are often beyond the sensitivity of most spectroscopies to distinguish. The detection of minority sites and intermediates poses significant challenges for the sensitivity of characterization techniques, particularly in true *operando* conditions, when signals from spectator species can dominate observations.

Conventional catalyst characterization techniques designed to be compatible with the timescale of reactant conversion to products are poorly compatible with other time scales relevant to the dynamic behavior of catalytic molecules and materials, Figure 2.2.[25] For example, observations at the shortest (femtoseconds) times require the use of ultrafast triggers, such as very short laser pulses to generate excited electronic states, and ultrafast detection systems. Other processes, such as convection and diffusion of molecules towards and away from the binding sites, are slower but are still challenging to distinguish in bulk measurements that report temporally- and spatially-averaged behavior. Very slow changes (hours to weeks) can pose problems in terms of measurement stability. For some types of catalysts (such as vehicle emissions control catalysts) accelerated aging tests can reduce timescales significantly, but such experiments can involve assumptions that are difficult to test.
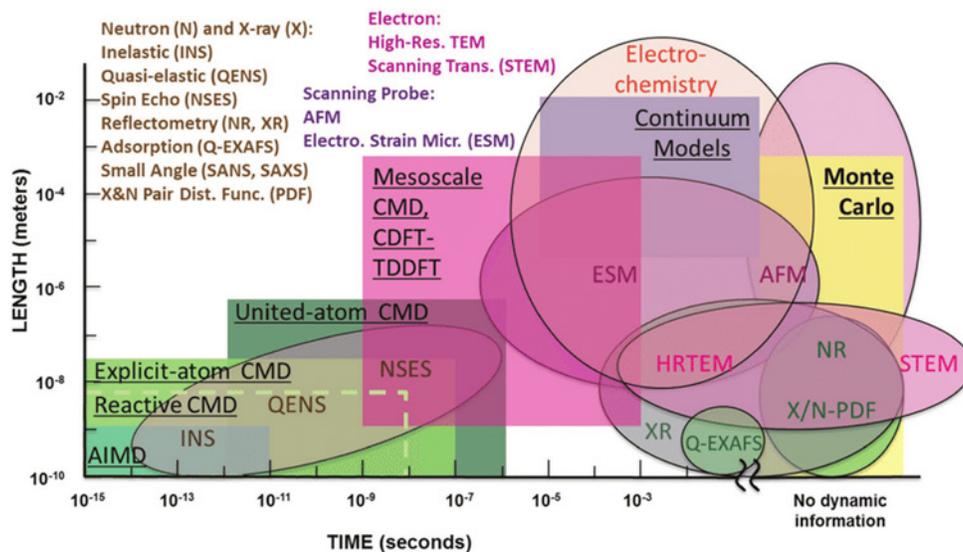

Figure 2.2. Schematic representation of the distribution of experimental and theoretical characterization techniques across different simulation time/length scales. Reprinted with permission from Zhan et al., Computational Insights into Materials and Interfaces for Capacitive Energy Storage, *Advanced Science*, John Wiley and Sons, 2017. Copyright © 2017 Zhan et al.

Although modern atomistic simulation capabilities are on the verge of being able to address the structures and dynamics of complex representations of catalytic systems in detail, including active sites, supports, extended coordination spheres and solvent effects, our ability to model reactivity in highly dynamic systems, such as those found at solid/liquid interfaces, or active sites in molecular catalysts with flexible coordination shells, remains underdeveloped. Current electronic structure methods can predict local structures and spectroscopic signatures along a reaction pathway with high accuracy ($\sim10^2$ atoms for post-HF methods) or intermediate accuracy ($\sim10^3$ atoms for DFT). In the first case, atomistic models usually include the binding site and possibly part of the support or a few solvent molecules, for which they provide reliable potential energies but no temperature effects.

In the second case, computational efficiency has reached a level that allows statistical sampling of ensembles of ~10^6 configurations, and simulation timescales of ~nanoseconds. Here, atomistic models may include large regions of the support as well as many solvent molecules, and can capture temperature effects. Better methods are needed to extend both length and time scales for realistic catalyst systems and their environments. Recent advances in enhanced sampling techniques are moving in this direction, but there are still many challenges associated with extending the length/time scales of the most accurate methods, and improving the reliability of the less accurate ones.

FOCUS AREAS

Describe Dynamic Phenomena in Atomistic Detail over Multiple Time and Length Scales

Identifying the dynamic assembly of atoms in the active site and understanding the processes that control its formation are essential first steps in efforts to directly synthesize the specific active site motifs. These motifs—the ensemble of active sites that form under operating conditions, rather than their precursors—are the true actors in catalysis. For example, the ZnCu alloy which is present in the reduced methanol synthesis catalyst becomes partially oxidized in the presence of CO_2, Figure 2.3.[26] Most characterization techniques report average properties of ensembles of catalyst components, allowing broad structure-activity relationships to be developed. There is now a pressing need to move beyond this simplistic picture so that selectivity/conversion can be clearly linked to specific active sites. New *operando* characterization methods must be discovered and developed to probe dynamic catalyst structures and behaviors in the presence of adsorbates, at the molecular scale, under operating conditions (see Sidebar 1). These methods should be able to discern subtle structural and chemical variations, including the effect of adsorbates at the atomic/molecular scale, and describe how these differences modulate the reactivities of particular types of sites.
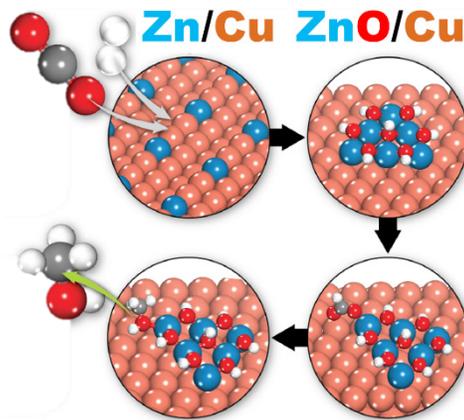
Figure 2.3. Concurrent with the onset of product formation in a methanol synthesis catalyst, *in situ* X-ray photoemission spectra suggest that a model ZnCu alloy catalyst generates ZnO regions supported on Cu nanoparticles.[26] Density functional and kinetic Monte Carlo computational studies showed that the structural transformation could be triggered by CO_2 dissociation at Zn sites. Image courtesy of Jose Rodriguez and Ping Liu (Brookhaven National Laboratory).

Advances in theoretical methods will need to handle more sophisticated models for catalysts rather than the traditional, atomistic models that represent idealized, static structures and their energies. Temperature/entropy effects are included by expanding harmonic partition functions about local minima. While this approach may suffice as a basis for rapid catalyst screening, its predictions can be unreliable, for example, when large numbers of atoms in the extended active site oscillate collectively and anharmonically at elevated temperatures. Solvent effects may fall into this category. They are conventionally described using continuum models, and occasionally with a small number of explicit solvent molecules interacting with the active site, but long-range, collective motions of the solvent are almost completely absent in such representations. Thus, future atomistic models must be extended representations of catalysts that include binding sites, flexible ligands, support and extended coordination shells, as well as defects and solvent molecules
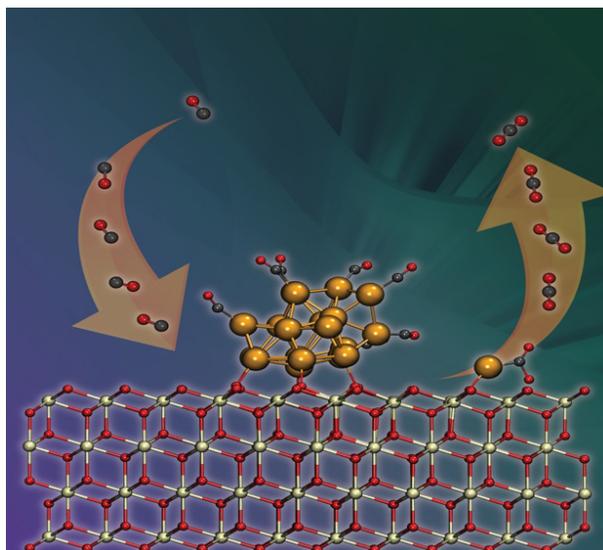
Figure 2.4. Redox reactions such as the oxidation of CO catalyzed by Au/CeO$_2$ involve transient formation of gold cations which detach from metal nanoparticles and are subsequently reintegrated back into the nanoparticles after reaction. Image courtesy of Roger Rousseau and Vassiliki-Alexandra Glezako (Pacific Northwest National Laboratory).

SIDEBAR 1. IMAGING DYNAMIC REORGANIZATION IN A SUPPORTED CATALYST

The much-studied strong metal support interaction (SMSI) is a classic example of a dynamic phenomenon in heterogeneous catalysis.[27] It involves gross changes in the morphology and accessibility of small nanoparticles supported on reducible oxides, such as titania. The SMSI effect is manifested in: (i) migration of the partially reduced oxide onto the metal nanoparticle, effectively blocking access to reactant molecules at the metal surface; (ii) dramatic alteration of the surface structure of

Sidebar Figure 2.1. *In situ* transmission electron microscopy (TEM) images of a Pd nanoparticle supported on TiO$_2$, recorded in the presence of different reactive atmospheres (left to right: O$_2$, H$_2$/O$_2$, H$_2$) at 500 °C, as well as computed representations of the Pd(111) surface corresponding to the same conditions (Pd: dark green; Ti: light gray; O: red). Reprinted with permission from *Nano Letters*, Dynamical Observation and Detailed Description of Catalysts under Strong Metal–Support Interaction, S. Zhang et al. Copyright © 2016, American Chemical Society.

the nanoparticle, for example, through changes in faceting; and (iii) creation of new interfacial sites at the three-phase boundary (gas-metal-support), which may promote the reaction and/or significantly change the mechanism. Recently, the dynamic behavior of Pd nanoparticles on TiO$_2$ under realistic reaction conditions was described using a combination of *in situ* ambient pressure scanning transmission electron microscopy (STEM) and computational analysis.[28] Under O$_2$, the TiO$_2$ support is stoichiometric and shows minimal interaction with the metal. However, in the presence of H$_2$, the reduced support migrates over the Pd surface where it induces a round-to-faceted reconstruction. This phenomenon results from the formation of epitaxial TiO$_x$ as either a mono- or bilayer covering the Pd(111) surface, depending on the oxygen chemical potential.

The ability to control the amount, type and location of the oxide phase present on the nanoparticle surface will make it possible to harness the SMSI effect by controlling access to the catalytically active surface, modifying its electronic properties, and creating new interfacial sites to promote desired reaction pathways such as in the reduction of CO$_2$ and in the conversion of methane.

present at or near the binding site. It will be critical to evaluate and understand the role of entropy in these systems, due to the large configurational space when dynamic fluctuations are present in any or all of these components. Modern computational methods, software and computer architectures are beginning to allow models which capture these effects and evaluate them routinely. Enhanced sampling methods, like hyper- and meta-dynamics[29,30] as well as replica exchange methods,[31] will enable realistic descriptions of dynamic behavior, and the extraction of free energies for reaction events that do not occur by pre-specified mechanisms. Eventually, theory should be able to identify both the species present under a given set of reaction conditions, as well as reaction mechanisms. Researchers are just beginning to exploit many of these new capabilities in catalysis science.[32-34] For example, the importance of the dynamic creation of active sites under reaction conditions and their essential role in catalysis was shown by *ab initio* molecular dynamics (AIMD) simulations of the catalytic mechanism for CO oxidation by ceria-supported gold clusters in which the mobility of individual gold atoms is critical, Figure 2.4.[35]

A hierarchically integrated array of simulation methods and tools is emerging that will further improve the accuracy of computational predictions by bridging information across very different time and length scales.[36] *Ab initio* molecular dynamics methods, as well as more scalable methods that treat electron correlation and long-range interactions, provide information about bond-breaking and bond-making, as well as interactions involving extended structures. Although their scalability has improved, the application of AIMD algorithms is still hampered by computational expense.[37] Recent advances in accelerated sampling techniques[38] will be able to describe dynamic behavior in extended catalytic systems and processes and provide free energy estimates for these phenomena. Reactive force fields for larger-scale simulations will be essential for describing events over longer times (nanoseconds to microseconds) and longer length scales (micrometers). Methods such as ReaxFF,[39] tight

binding DFT and semi-empirical electron structure,[40] MB-pol[41,42] and reactive FF using minimal bias methods[43] are also very promising for bridging time and length scales. However, they remain rather system-dependent and will require significant new effort in parameterization. Advances in this area may also come from machine learning and the construction of large computational databases, as discussed in Priority Research Direction 5.

Simulation of spectra and imaging of catalysts across a wide range of time and length scales will be important for validating theories, interpreting experiments and deriving the next generation of testable hypotheses with respect to structure-activity relations. Consequently, there is a need to develop new theories to predict spectra accurately for models containing relatively large numbers of atoms (10^2-10^3), matching the increasing sophistication of the measurements. Furthermore, theory must be able to account for dynamic behavior across multiple time scales. This is particularly true for multimodal spectroscopy and imaging approaches in which the structure and dynamics of a system are probed simultaneously on different time scales. Imaging techniques, such as TEM, STEM, atomic force microscopy (AFM), and electrochemical strain microscopy (ESM), require accurate description of time-dependent quantities (e.g., velocity-velocity autocorrelation function for nuclei, or time-dependent DFT for electrons) for large systems at the femto- to nanosecond timescales. For intermediate time scales (nano- to microseconds), techniques such as inelastic neutron scattering can report on collective oscillations, particularly in complex liquids, and would benefit directly from simulation of scattering factors based on classical MD models at long time/length scales. Techniques involving longer time scales (microseconds to seconds) can be handled using ensemble averages of spectra computed over either classical or AIMD trajectories. For example, spectral linewidths contain critical information about the local structures of active sites and their structural fluctuations. At the longest time scales (> seconds), dynamics are best formulated as kinetics in micro-kinetic models for reactive cross-sections, transient intermediates and catalyst degradation pathways. These models will benefit from methods for computing rate constants beyond simple transition state theory to compile reaction networks.

Design Catalyst Architectures for Dynamic Responsiveness

A deeper appreciation of the factors that determine the dynamic responses of catalysts to changing environments could lead to the development of catalysts that spontaneously adopt optimum structures for a given set of operating conditions, even detecting changes in reaction conditions and adapting to them. While synthetic methods for crystalline solids as "pre-catalysts" are reasonably well-developed, the factors which control the emergence of active (and sometimes amorphous) phases under reaction conditions are less well-understood. Identifying these active phases and understanding how to stabilize or destabilize them will inspire new synthetic efforts to make the phases directly, or to make precursors that can generate them more efficiently. For example, solid solution precursors can be designed to de-mix to the desired nanostructured composite phases under reaction conditions.[44] Another possible advance could involve using dynamic phenomena to induce changes in catalyst structures at different stages of a catalytic cycle, offering a way to circumvent the linear free energy "scaling" relations that limit the activity of a particular (i.e., static) catalyst structure.

Allosteric regulation is a type of large-scale dynamic behavior found in biological systems. It is a powerful mechanism for manipulating enzyme activity via the binding of a remote activator, coenzyme and/or deactivator (see Sidebar 2). Similar triggering mechanisms for synthetic catalysts have been explored, including photoswitching, ion/molecule binding and redox triggers that tune the reactivity of such catalysts, Figure 2.5.[45] A recent example involves the reversible association of a Lewis acid with a remote position on the supporting ligand, inducing a key reaction step, such as C–C coupling by reductive elimination, by changing the electrophilicity of the metal center.[46] A mechanically-induced distortion in a Pd(II) complex with a photoswitchable chiral bisphosphine caused changes in the enantioselectivity of C–C coupling reactions.[47] This type of regulation could be applied in catalysis to influence reactivity, couple proton and electron transfers, or protect the active site in a stable, unreactive resting state. For example, a conformational change could be used to convert the active site to a more reactive form during catalysis.[48] This behavior could be reminiscent of enzymes that extricate themselves from inactive oxidation states or inhibitory complexes, or enzymes that auto-activate. One consequence of self-repairing capability in synthetic catalysts would be extended productive lifetimes. For example, the self-healing of a heterogeneous OER electrocatalyst involves fast redeposition of solubilized cobalt onto the electrode surface during potential cycling in the presence of phosphate ions.[49] The key to this discovery was identifying conditions where the solubility equilibria favor the reassembly of the active phase of the catalyst.

SIDEBAR 2. CHARACTERIZATION OF ALLOSTERY IN CATALYTIC MECHANISMS USING NETWORK ANALYSIS

V-type allosteric enzymes have two distant binding sites: an active site which binds the substrate and is responsible for the catalytic reaction, and an allosteric site which binds an "effector" that triggers the catalytic reaction. Imidazole glycerol phosphate synthase (IGPS) catalyzes glutamine hydrolysis to ammonia. The rate of the catalytic reaction is enhanced by binding of the effector PRFAR (N'-[(5'-phosphoribulosyl) formimino]-5-aminoimidazole-4-carboxamide ribonucleotide) in the HisF subunit, at a distance of 25 Å from the glutamine-binding site in the HisH subunit. Motions of the amino acid residues were studied using solution NMR relaxation dispersion measurements, and correlations between motions in the activated and inactive enzymes were explored using community analysis of dynamical networks based on molecular dynamics simulations.[50] Motion in the PRFAR binding loop was found to be correlated to motion at the glutaminase active site.
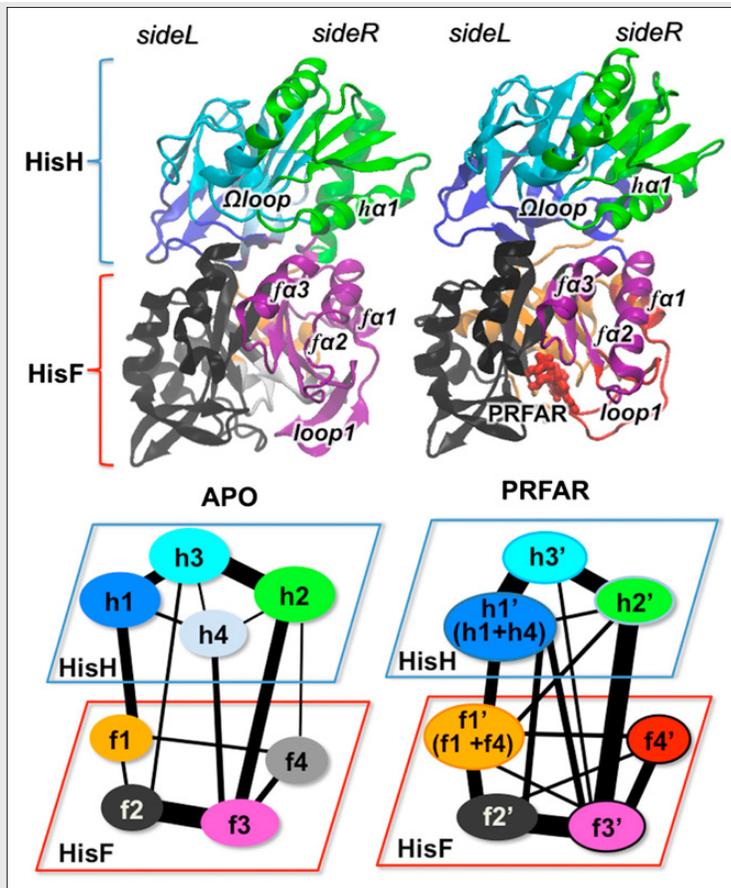
Sidebar Figure 2.2. Color-coded optimal community networks for the APO (left) and PRFAR-bound (right) IGPS complexes, with predominant contributions from HisH (h) and HisF (f) subunits. In the PRFAR network, the APO communities in parentheses are those that contribute the most to the newly-formed PRFAR communities. Reprinted with permission from *Proceedings of the National Academy of Sciences of the United States of America*, Allosteric Pathways in Imidazole Glycerol Phosphate Synthase, I. Rivalta et al. Copyright © 2012 National Academy of Sciences.

Many catalysts are metastable materials, readily undergoing structural changes under reaction conditions. Investigation of catalytic materials with very high thermodynamic stability will lead to more resilience, and perhaps faster adoption of such catalysts for highly distributed manufacturing applications, where the need for frequent catalyst regeneration or replacement is highly detrimental. For example, complex oxides based on extremely stable structures such as perovskites can accommodate a wide range of redox-active transition metal dopants. This concept was invoked to describe the behavior of a Pd-doped perovskite catalyst for automotive emission control, in which the catalytically active metal cycles between segregated nanoparticles and a solid solution.[51] The latter results in spontaneous redispersion of the metal as the redox atmosphere changes. The first doped perovskite materials were commercialized
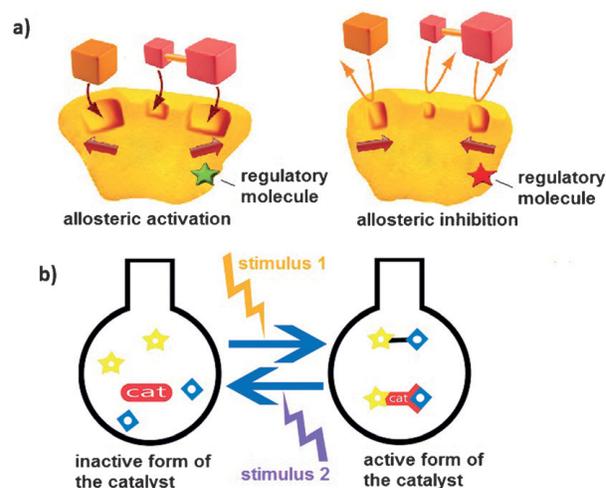

Figure 2.5. Analogy between the dynamic conformational changes in a) allosteric enzymes, and b) synthetic catalysts triggered by exposure to external stimuli. From M. Vlatković, B. S. L. Collins, B. L. Feringa, Dynamic Responsive Systems for Catalytic Function, *Chemistry A European Journal*, 2016, 22, 17080. Copyright © Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

as emissions control catalysts in 2002.[52] Exsolved nanoparticles are not necessarily the active sites in all such systems,[53] and the dissolution of the nanoparticles can be slow and incomplete.[54] An alternative explanation for their enhanced stability involves the formation of "socketed" metal nanoparticles in close contact with the oxide host, Figure 2.6.[55] Nevertheless, there is considerable potential to apply this concept of "geo-inspired" catalysts to other complex oxides, and to extend it to other catalytic reactions. Future efforts could seek to harness this property to prolong catalyst lifetime and, when necessary, to restore the catalyst to an original, pristine state.
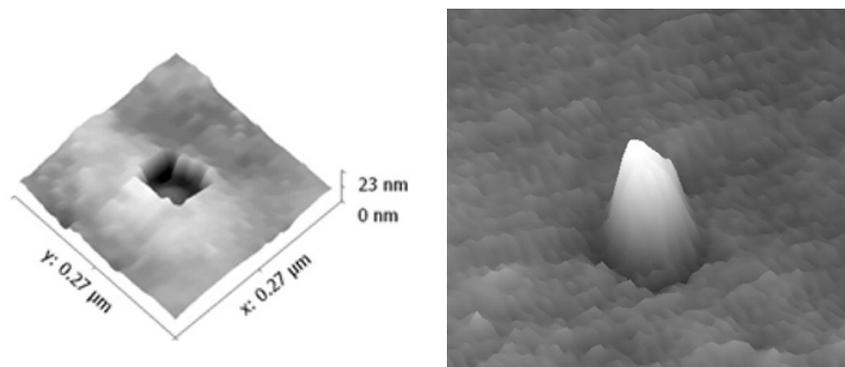
Figure 2.6. AFM images of La$_{0.4}$Sr$_{0.4}$Ti$_{0.97}$Ni$_{0.03}$O$_{3-\delta}$, showing a strain-induced pit formed during initial Ni(0) exsolution upon reduction in H$_2$ at 600 °C (left), and a "socketed" Ni(0) nanoparticle after further reduction in H$_2$ at 900 °C (right). Reprinted with permission from *Journal of Physical Chemistry Letters*, Evidence and Model for Strain Driven Release of Metal Nanocatalysts from Perovskites during Exsolution, T-S. Oh et al. Copyright © 2015, American Chemical Society.

SIDEBAR 3. SPATIO-TEMPORAL RESOLUTION OF INDIVIDUAL ACTIVE SITES

Variability in local catalyst environments and behaviors was investigated at the level of individual active sites and single turnovers using a fluorescence microscopy technique. Norbornene was labeled with a fluorescent probe molecule (BODIPY, shown in green), in order to detect the incorporation of single monomers into growing polymer chains by ring-opening metathesis polymerization catalyzed by individual molecular ruthenium carbene catalysts. When the active sites are deposited from solution onto a glass surface due to the insolubility of the polymer, their diffusion is slowed and their signals are detected.[66] Unlike other techniques that rely on ensemble averaging, only active catalyst sites produce signals. The high sensitivity measurements reveal how different regions of the growing polynorbornenes exhibit different catalytic activities.
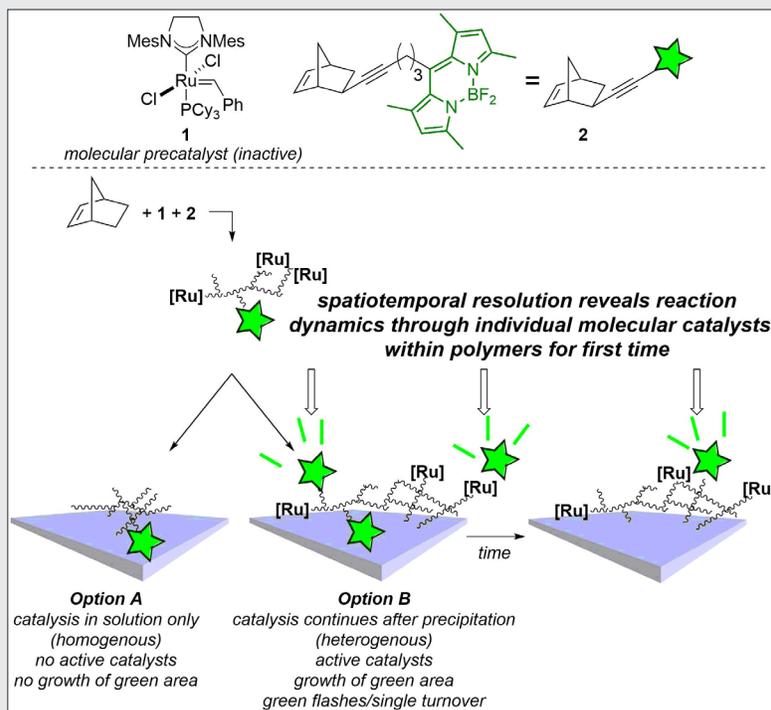
Sidebar Figure 2.3. Schematic representation of spatiotemporal resolution in an experiment to image individual monomer insertions for a molecular olefin metathesis catalyst. The wavy lines represent polymer chains. From Q. T. Easter, S. A. Blum, "Single Turnover at Molecular Polymerization Catalysts Reveals Spatiotemporally Resolved Reactions," *Angewandte Chemie International Edition,* 2017, 56, 13772. Copyright © Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

Extend Catalyst Life Cycles

The activation and deactivation of catalysts are often studied and discussed separately from activity measurements and promotion/inhibition phenomena, but all are coupled during their life cycles. The vast majority of fundamental investigations focus on the initial activity of a catalyst, covering just a few hours or sometimes days. However, activity and selectivity are influenced by changes in reactor conditions, catalyst aging, and the accumulation of (side) products. Some dispersed metal oxide catalysts, such as those used commercially for olefin polymerization and metathesis, are capable of spontaneous self-activation that transforms inactive, inorganic sites to organometallic active sites.[56,57] A detailed understanding of the mechanisms by which these active sites are generated[58] could lead to strategies to induce self-reactivation without interrupting catalyst operation, and eventually to the development of new catalysts with greatly extended lifetimes. Catalysts could also be designed to recover spontaneously from variations in feed composition and/or exposure to poisons that result in deactivation. For example, more efficient activation and regeneration of a supported molybdate catalyst for olefin metathesis were induced with simple physical treatment protocols.[59] Processes that lead to irreversible loss of activity in molecular catalysts, such as changes in metal oxidation state and nuclearity, or ligand oxidation, should be identified and mitigated by new ligand designs.[60,61]

Many factors can compromise catalyst stability. For example, in Fischer-Tropsch synthesis, a long list of causes for the gradual deactivation of cobalt catalysts has been proposed, including poisoning, re-oxidation of reduced cobalt active sites, formation of surface carbon species, carbidization, surface reconstruction, sintering of Co crystallites, metal-support solid-state reactions, and attrition.[62] Discontinuous processes have also been observed. This complexity implies that new methodologies for studying activation/deactivation/reactivation at the atomic/molecular levels are needed (see Sidebar 3). This knowledge will make it possible to control dynamic behavior by designing catalyst architectures that retard deactivation and facilitate reactivation.

As a first step, developing a detailed understanding of catalyst life cycles is required. The challenges will include replicating authentic process conditions (pressure, temperature, use of "real" feed with possible contaminants, flow dynamics, etc.) in the laboratory, and the extended times that may be required to observe deactivation (weeks or months). For example, a long-term study of the $Cu/ZnO/Al_2O_3$ methanol synthesis catalyst conducted over 5 months at 60 bar and 230 °C revealed that its deactivation is caused primarily by changes in the ZnO component, Figure 2.7.[63] More general accelerated catalyst aging protocols, already in use in a few areas of catalysis[64] and electrocatalysis,[65] are needed to mimic slow deactivation processes; at the same time, the underlying assumptions in such protocols need to be explored and verified.
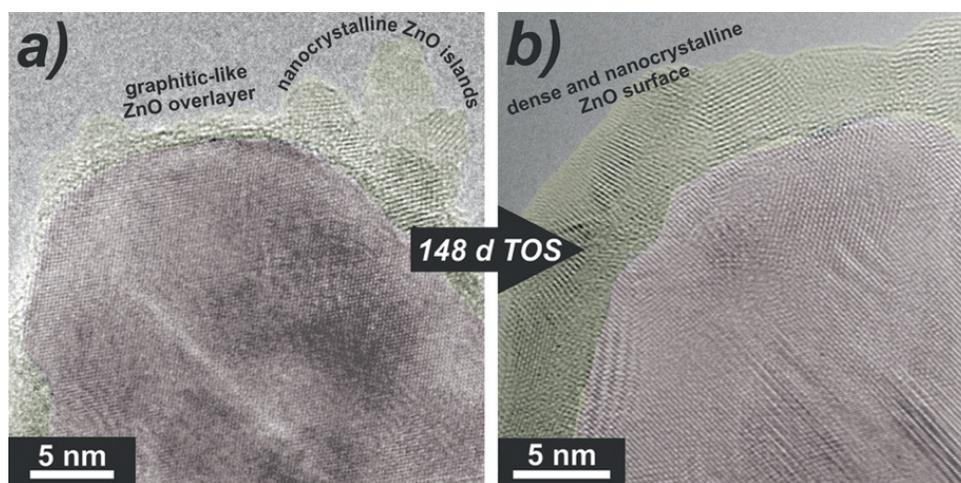
Figure 2.7. Structural changes in ZnO (yellow) dispersed on Cu nanoparticles (red), as observed by high resolution TEM, a) before, and b) after extended time-on-stream (TOS) in the presence of syn gas at 230 °C and 60 bar. From T. Lunkenbein, F. Girgsdies, Kandemir, N. Thomas, M. Behrens, R. Schlögl, E. Frei, "Bridging the Time Gap: A Copper/Zinc Oxide/Aluminum Oxide Catalyst for Methanol Synthesis Studied under Industrially Relevant Conditions and Time Scales," *Angewandte Chemie International Edition*, 2016, 55, 12708. Copyright © Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

Catalytic processes could be dramatically simplified, with considerable energy savings, by designing more robust catalysts and simplifying regeneration procedures. For example, the PtSn catalyst used for propane dehydrogenation is reactivated by coke removal, but the oxidative regeneration process changes the physical and electronic structure of the nanoparticles.[67] Redispersion of Pt-based refining catalysts by oxychlorination following a carbon burn requires the use of corrosion-resistant reactors, and an additional process to eliminate corrosive chlorine compounds in the vent gas.[68] For both processes, milder methods for removing deposits and/or redispersing active components that avoid high temperature calcinations or harsh reagents are highly desirable. Thus, studying activation/deactivation mechanisms and redispersion strategies is expected to generate new understanding that will guide designs to prolong catalyst lifetimes.

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# PRD 3 Manipulate Reaction Networks in Complex Environments to Steer Catalytic Transformations Selectively

Key questions: How do we control the kinetics of multiple reactions at all relevant length scales to direct reaction pathways in catalytic reaction cascades, especially for multicomponent mixtures? How do we understand and integrate interdependent steps that may occur over different time and energy domains?

Summary: Many emerging chemical feedstocks have diverse, variable compositions whose transformations involve interconnected reaction pathways that depend upon process conditions. Mastering these challenging chemical conversions requires integrating catalyst design to control reaction kinetics with strategies to direct nanoscale transport and separations.

INTRODUCTION

For simple catalytic processes involving just one or two reactants, it is possible to understand key steps in the mechanism, and their dependence on reaction conditions such as concentration, temperature, and pressure, by examining the effect of each reaction variable independently, and to obtain detailed information about intermediates and transition states using *ab initio* computational methods. This approach is much less effective in the case of more complex feeds. For example, catalytic converters necessarily deal with a mixture of CO_x, NO_x, unburned hydrocarbons and H_2O, all of which are present simultaneously, and which interact with one another in various ways depending on the temperature of the exhaust gas and the air-to-fuel ratio as these variables fluctuate over wide ranges during operation.[1] Similarly, crude oil fractions after distillation are multicomponent mixtures of hydrocarbons which are converted simultaneously in a series of interlinked refinery processes.[2] The general strategy of understanding complex chemistry through simplification has elucidated many of the principal chemical reactions, but often fails to predict overall kinetic behavior accurately. Consequently, catalyst evaluation must be performed with the complex mixtures themselves, often in relatively large-scale installations.

Rapid development of catalytic processes to efficiently use a broader range of non-traditional feedstocks will require new approaches. In particular, highly distributed energy sources, such as shale gas, shale oil, biomass, and waste organic materials, are often compositionally extremely variable, and will require flexible strategies to convert them to chemicals and fuels. For example, shale gas is a mixture of C_1–C_4 hydrocarbons, with significant amounts of CO_2, H_2O and H_2S, and its composition varies from well to well.[3] Lignocellulosic biomass and the pyrolysis or hydrothermal liquefied oils derived from it can change in both physical form and chemical composition depending on the source, the season, and the year.[4] The large variety of functional groups present in the mixture of oxygenated molecules after its deconstruction results in highly complex reaction networks, Figure 3.1.[5] Similarly, the mixtures present in organic waste materials, such as polymers, contain a broad range of large and small molecules to be converted.[6,7]
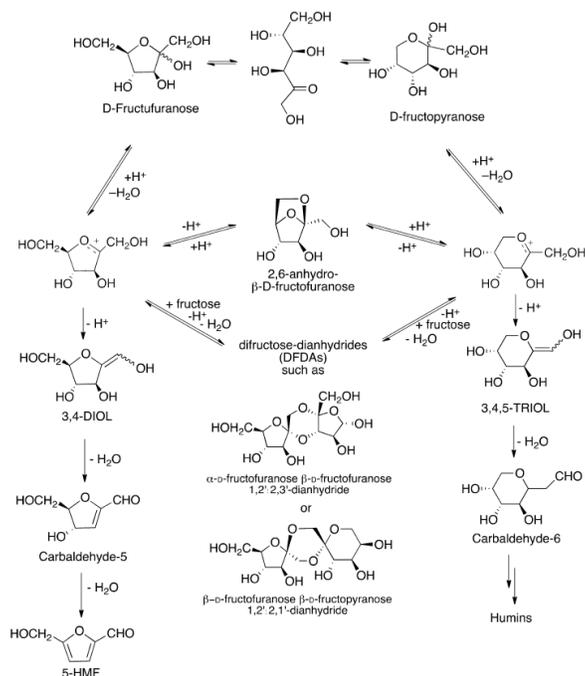
Figure 3.1. The molecular mechanism of acid-catalyzed dehydration of fructose to 5-(hydroxymethyl)-2-furfural (5-HMF) was mapped in a range of solvents using NMR techniques to identify reactive intermediates with ^{13}C and D isotopic labeling. Five fructose isomers are present, but only the furanose isomer leads to the desired 5-HMF; it is linked by reversible equilibria to the pyranose route, which leads to oligomeric humins, limiting the yield. Reprinted with permission from _Chemical Reviews_, Catalytic Conversion of Carbohydrates to Initial Platform Chemicals: Chemistry and Sustainability, L. T. Mika et al. Copyright 2018 American Chemical Society.

Designing catalytic processes for use with emerging energy feedstocks implies an ability to identify, control and optimize many reactions simultaneously, and to understand how reactants and intermediates participate in multiple, parallel kinetic pathways. The crossover may result in new catalytic chemistry, as well as products that differ from those obtained in conventional processing of simpler mixtures. For example, the shuttling of a growing polymer chain between two different active sites during ethylene/propylene copolymerization led to a new family of polyolefins with much improved mechanical toughness.[8] Other combinations of polymerization active sites produce branched polymers by generating oligomers _in situ_ at one site, then incorporating them into the main polymer chain at another site. The nature of the incorporation can be very sensitive to the spatial relationship between the two sites,[9] demonstrating the power of modulating the local concentration gradients of intermediates near the active sites (as described in Priority Research Direction 1). Promoting or impeding the transport of species between active sites in bifunctional catalysts is another method to change selectivities, by altering relative rates in reaction networks.[10] Even in conventional applications in existing refining and petrochemical installations, a more quantitative understanding of the complexity of reaction networks imposed by operating conditions as well as upstream and downstream operations will allow the development of new generations of more effective catalysts.

Complex reaction networks also include unproductive pathways. Suppressing these pathways obviously improves catalyst efficiency and may enhance selectivity, reducing the need for downstream separations. Such unwanted reactions can involve catalyst deactivation pathways. For example, computational analysis of the reaction landscape for hydroarylation identified an off-path pre-catalyst transformation that resulted in a considerably less active catalyst.[11] This information led to the design of an alternative molecular precursor that yielded a much more active catalyst. Similar insights could lead to the design of catalysts that can protect themselves from impurities or from developments during reaction conditions that lead to deactivation; switch catalytic activity on/off in response to transients in reactor operation; and repair themselves without active user intervention (as discussed in Priority Research Direction 2). Such properties could be extremely attractive, especially for catalytic processes related to decentralized production or additive manufacturing.

SCIENTIFIC CHALLENGES

Directing complex catalytic transformations is predicated on an understanding of both the individual elementary steps and all of the potential connections between them. The ultimate goal is the ability to direct reactions along specific pathways that can be selected depending on the desired product and the availability of feedstock. Identifying individual reactions and elementary steps, and extracting reliable kinetic parameters for individual active sites, become even more daunting for ensembles of such sites, in the presence of multiple reacting species, as well as solvent molecules, ions, and adventitious or inherent poisons. Thus, characterizing active sites and reactive intermediates in complex reaction environments presents many currently unsolved challenges, including phenomena which cannot be predicted by combining the results from simpler systems. In particular, model systems can fail to reproduce emergent behavior because of interactions involving various feedback loops, and the soft potential energy landscapes of highly coupled processes. It is also challenging to fully integrate the controlled delivery of electrical and light energy into chemical catalytic systems, and to understand how these impulses affect the rates of coupled thermal reactions (an issue discussed further in Priority Research Direction 4).

Significant progress in this area will require an ability to characterize active sites in the presence of realistically complex mixtures of reactants, intermediates, and products (i.e., using *operando* methods), as well as to undertake kinetic and mechanistic studies that map the complex transformation pathways of reacting molecules in the presence of multiple types of spectators under relevant conditions of temperature, pressure, concentration, etc. While characterization tools that enable molecular-level understanding of catalytic reactions are continuously improving, many experimental techniques are not yet fully compatible with true *operando* conditions, and therefore struggle to distinguish reaction intermediates from non-productive transient species by validating them kinetically. The challenge is to dramatically increase the sensitivity of these techniques, for example, to probe for highly reactive minority species present at interfaces, or to achieve much better time-resolution in order to observe short-lived intermediates that are largely undetectable with conventional spectroscopies. New methods are needed to characterize complex systems that include multicomponent and amorphous catalytic materials with non-periodic and/or dynamically changing structures, such as those described in Priority Research Direction 2.

When experimental approaches are accompanied by electronic structure calculations to assess reaction pathways, confirm spectroscopic assignments, and provide details concerning the structures and energies of transition states and fleeting intermediates, it will be possible to use the outcomes to construct powerful predictive microkinetic models for reaction network behavior as a function of changing input feeds, temperatures, or other variables. Modern machine learning methods, the focus of Priority Research Direction 5, will likely be critical in this effort. However, machine learning requires abundant and reliable experimental data. Generating the appropriate data, which are not yet available for many complex reactions, will be very challenging, and will require careful initial system selection. Combining machine learning with first-principles simulations may help to generate a substantial amount of reliable information "on the fly." This approach has benefitted from recent developments in graph-theoretic algorithms that can sample chemically plausible reactions efficiently with little user intervention. However, it remains a challenge to merge machine learning with quantum chemical calculations and microkinetic modeling.[12] As the number of elementary reactions in a network grows, the corresponding set of equations that must be solved in the microkinetic model becomes increasingly singular, stiff and ill-determined. Because rate constants for different elementary reactions can vary by many orders of magnitude, the concentrations or coverages of some intermediates can also vary over a very wide range. The problem becomes apparent for kinetic Monte Carlo approaches involving reaction steps close to equilibrium, which occur many times for every slow reaction step, thus necessitating very long sampling times. Current computational tools are not capable of handling such problems in a reasonable time or at an acceptable cost.

Understanding the detailed mechanism of a catalytic reaction is already a formidable task when it involves a single catalyst or family of closely related catalysts. In order to accelerate the discovery of new catalysts, we need to reliably identify and predict reaction networks for large numbers of catalyst candidates. Since each catalyst is a complex and dynamic material, and since reaction conditions include many interdependent variables, the phase space of all potentially useful catalytic materials and the appropriate reaction conditions for each is far too large to screen experimentally in an efficient manner, even using elegantly designed, high-

throughput, parallel experiments.[13] A central challenge is therefore to devise experimentally validated theories to limit the number of catalysts required for establishing an efficient design process, and to integrate these theories fully with chemical intuition and experimental screening. Such advances could enable the design of more sophisticated catalytic processes by allowing researchers to address more complex catalyst design criteria.

FOCUS AREAS

Design Reaction Cascades and Discover New Pathways in Complex Reaction Networks

Integrating multiple catalytic reactions into a single process can overcome equilibrium limitations, couple endothermic and exothermic processes to avoid the need for large temperature changes, and allow reactive intermediates to be converted efficiently to more stable products. Some recent successes include catalyst systems for alkane oxidative dehydrogenation,[14,15] alkane dehydroaromatization,[16] carbonyl-olefin metathesis,[17] direct olefin epoxidation with H_2/O_2 mixtures,[18] and cellulose depolymerization coupled with further upgrading of the monomeric sugars.[19,20] Controlling selective oxidation is a particularly attractive target for multiple catalytic reaction sequences, as described in Priority Research Direction 1. In the case of saturated alkanes, such as those found in shale gas, partial oxidation products are more reactive than the starting materials and are formed selectively at low conversion. The use of tandem or cascade strategies will allow higher conversions to stable products by converting reactive intermediates in subsequent, closely coupled steps, Figure 3.2.[21] Reaction sequences may even be integrated with separation steps, which might be incorporated in the form of selectively permeable membranes or catalytic distillation. Other opportunities include accessing new catalytic reaction pathways and outcomes using energy sources other than thermal, including electrochemical,[22] plasmonic,[23] or plasma.[24]
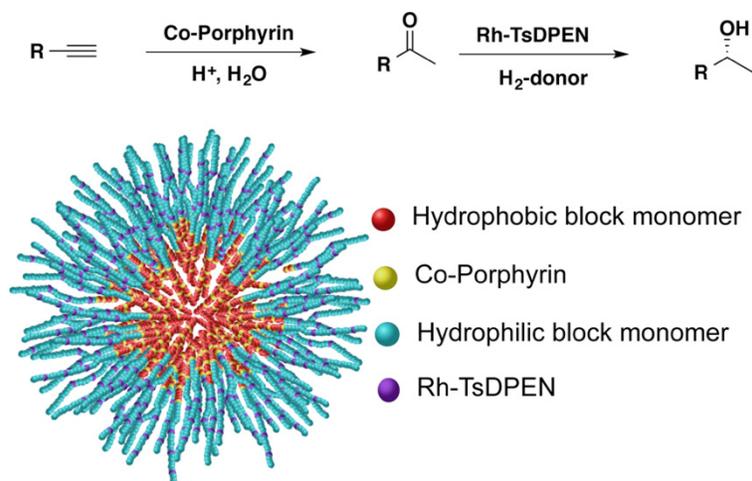

Figure 3.2. Incompatible catalytic transformations can be carried out in tandem using bio-inspired compartmentalization strategies. A covalently cross-linked micelle based on amphiphilic triblock copolymers of poly(2-oxazoline) was used to immobilize two distinct metal catalysts. A Co-porphyrin complex in the hydrophobic core catalyzes terminal alkyne hydration, while an asymmetric Rh catalyst in the hydrophilic shell catalyzes transfer hydrogenation of the ketone intermediates to chiral alcohols. Reprinted with permission from *Journal of the American Chemical Society*, Compartmentalization of Incompatible Catalytic Transformations for Tandem Catalysis, J. Lu et al. Copyright 2015 American Chemical Society.

Designing reaction networks introduces additional levels of complexity, including choices about the type, concentration/surface densities and relative spatial orientations of cooperating catalyst sites. For example, sequential or parallel reaction sequences in heterogeneous catalysis may benefit from occurring at adjacent sites within the same catalyst particle, or at sites located in different catalytic particles.[10] Molecular catalysts can be tethered together, or can operate independently in solution. Finally, it may be advantageous to combine different types of catalysts (e.g., homogeneous/heterogeneous, chemical/electrochemical, or biological/non-biological) to achieve new reaction outcomes that may be difficult or impossible with a single type of catalyst. For example, the tandem use of enzymes and chemical catalysts can take advantage of the general versatility of a chemical catalyst and combine it with the extremely high specificity of a biological catalyst, Figure 3.3.[25] This strategy may be particularly useful in the conversion of biomass-derived feedstocks. Recently, production of the commodity chemical acrylonitrile was achieved using a hybrid strategy that involves biological conversion of glucose followed by a chemical catalytic transformation (see Sidebar 1).

Figure 3.3. An organometallic metathesis catalyst and a P450 enzyme work cooperatively in a single reactor to promote dynamic isomerization of alkenes and selective epoxidation of the cross-metathesis products to produce internal epoxides regio- and enantio-selectively.[25] C. Denard, H. Huang, M. J. Bartlett, L. Lu, Y. Tan, H. Zhao, J. F. Hartwig, "Cooperative Tandem Catalysis by an Organometallic Complex, and a Metalloenzyme," *Angewandte Chemie International Edition* 2013, 53: 465-469. Copyright © 2014 Wiley VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

SIDEBAR 1. INTEGRATING BIOLOGICAL AND CHEMICAL CATALYSIS WITH SEPARATION FOR COMMODITY CHEMICAL PRODUCTION

Acrylonitrile is used on a large scale as a precursor to resins, polymers, acrylics, and carbon fibers. Currently, it is produced at a rate of 14 billion pounds annually from fossil-fuel-derived propylene. The process involves exothermic ammoxidation, which gives yields just over 80%, leads to the formation of toxic HCN as a by-product, and presents a process safety hazard because of the potential for a runaway reaction. Instead, acrylonitrile could be manufactured safely, renewably, and efficiently from 3-hydroxypropionic acid (3-HP) obtained from lignocellulosic glucose by microbial catalysis.[26] After conversion to the ethyl ester, the solid acid TiO_2 catalyzes the dehydration of ethyl 3-HP, then converts the resulting ethyl acrylate to acrylamide and ethanol in the presence of ammonia. Dehydration of acrylamide yields acrylonitrile.

An integrated process based on this chemistry was modeled at scale using a low-pH-tolerant microbial strain to produce 3-HP, followed by dewatering in a simulated moving bed with elution by ethanol. The ethyl acrylate can be separated from 3-HP by esterification/dehydration during reactive distillation in the presence of ethanol. Finally, ethyl acrylate is converted to acrylonitrile over TiO_2 in essentially quantitative amounts (98 ± 2%), without the need for O_2. However, continuous catalyst regeneration, for example, in a riser reactor, would be required to remove carbon deposits from the catalyst.

Sidebar Figure 3.1. Conceptual process diagram for production of renewable acrylonitrile from lignocellulosic sugars via a combination of biological and chemical catalytic upgrading coupled with separation and catalyst regeneration. From E. M. Karp et al., Renewable Acrylonitrile Production, *Science* 368, Issue 6368 (2017) 1307. DOI: 10.1126/science.aan1059. Reprinted with permission from AAAS.

Designing cooperative catalytic systems will require an ability to adjust active site densities and reaction conditions to optimize performance by kinetic matching of different key catalytic reactions, which in turn implies knowledge of the rates of contributing elementary steps. The analysis of reaction networks is therefore complementary to the design of new catalyst architectures at and beyond local binding sites, as described in Priority Research Direction 1. Monitoring the kinetics and dynamics of concomitant, complex reactions in real time and at specific active sites creates new demands for spectroscopic techniques in terms of temporal and spatial resolution. Kinetic measurements will need to incorporate both steady-state and transient studies and selective isotopic labeling to obtain kinetic parameters, identify rate-controlling steps, and map reaction trajectories.

As an example, consider biomass conversion to fuels and chemicals via catalytic upgrading. It involves a complex set of depolymerization reaction networks in which steps such as glycosidic and aryl ether bond cleavage can generate mixtures of hundreds of highly functional organic compounds. One experimental approach to dealing with this complexity is illustrated in recent studies of cellulose pyrolysis catalyzed by alkali and alkaline earth cations.[27,28] Reactions within the molten cellulose polymer are influenced by interactions with neighboring molecules, which can be disrupted by the catalyst. The overall course of the reaction is further complicated by interphase transport associated with diffusion and evaporation of volatile organic compounds. A new reactor design capable of applying millisecond thermal pulses to solid cellulose (and lignocellulose) made it possible to identify and independently characterize some of the individual reactions, among thousands of parallel reaction pathways, Figure 3.4.[29]
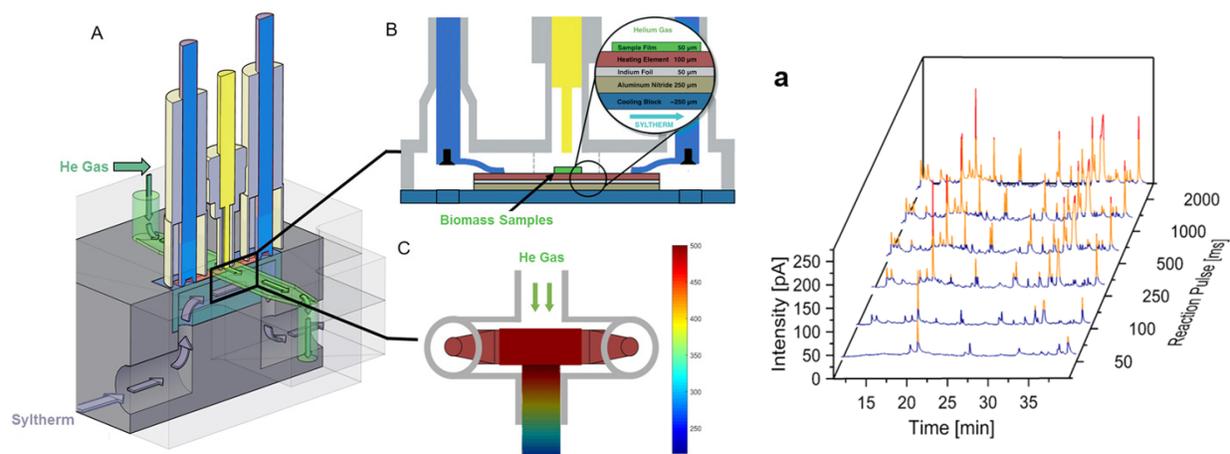

Figure 3.4. Schematic of a PHASR (pulse-heated analysis of solid reactions) reactor, in which solid biomass samples are placed on a heating element and vapor products are carried in a stream of He for analysis via GC-QCD/FID. The chromatograms show the evolution of individual chemical species from loblolly pine at 500 °C as a function of pulse time. Reprinted with permission from *ACS Sustainable Chemistry and Engineering*, Five Rules for Measuring Biomass Pyrolysis Rates: Pulse-Heated Analysis of Solid Reaction Kinetics of Lignocellulosic Biomass, S. Maduskar et al. Copyright 2018 American Chemical Society.

Develop More Powerful Tools to Describe Reaction Networks

As the cost of floating point calculations has decreased exponentially over the past few decades, the number of systems that can be analyzed atomistically in a typical computational study has increased correspondingly. At the same time, the accuracy of modern electronic structure theory approaches has improved dramatically; for example, they are much better able to describe the energetics of adsorption at surfaces. Consequently, computational chemistry now plays an important role in mechanistic studies of catalytic reactions. However, when reaction networks contain hundreds or thousands of reaction intermediates that undergo thousands of elementary reactions, it is no longer possible to rely primarily on human intuition to set up the calculations. As computational studies become larger and more complex, new computational methods will be needed that can operate in an automated fashion, using rule-based reaction generators that construct reaction networks using fundamental reactivity rules.[30] A framework to predict the rate-limiting steps in large reaction networks is shown in Sidebar 2, using the example of the conversion of syngas to hydrocarbons over a Rh(111) surface.[31]

SIDEBAR 2. ADDRESSING REACTION NETWORK COMPLEXITY THROUGH DFT AND MACHINE LEARNING

Catalytic reaction networks can exhibit enormous complexity, involving thousands of species and reactions. A computational framework was developed to predict the rate-limiting steps in large reaction networks such as those found in the conversion of syngas to hydrocarbons.[31] Adsorption energies, reaction energies, and transition state energies were computed on the fly for a Rh(111) surface using linear scaling relations and machine-learning regression methods. To improve model predictions, reactions most likely to be rate-determining are identified and studied with full-accuracy DFT. This step is critical for ensuring that the correct pathways are identified, yet allows a much larger reaction network to be considered. Use of uncertainty-aware DFT functionals (BEEF) facilitates the assessment of the likelihood that the reduced pathway is correct, considering known DFT errors.
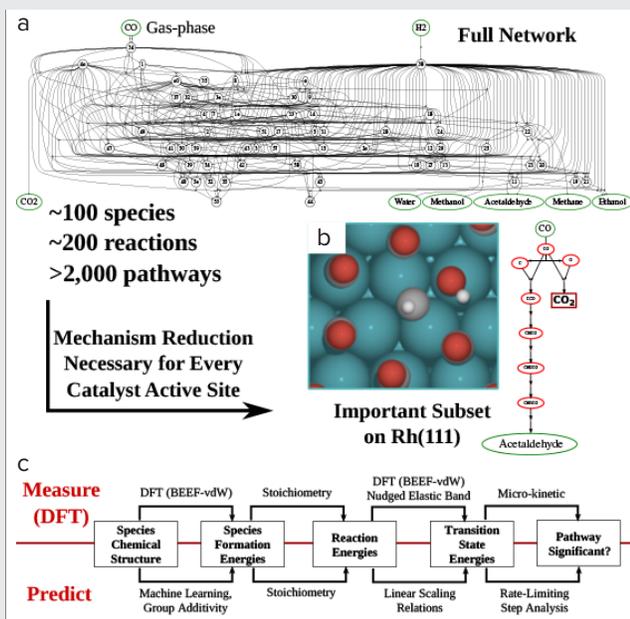
Sidebar Figure 3.2. Reduction of a catalytic reaction mechanism using predictive models: (a) full reaction network for the conversion of syngas to various C_1 and some C_2 products; (b) reduced mechanism for the reaction of syngas on Rh(111), leading to selective formation of acetaldehyde; (c) typical workflow to measure reaction properties using expensive DFT calculations (top), along with the predictive models (bottom). Reprinted with permission from *Nature Communications*, To Address Surface Reaction Network Complexity Using Scaling Relations Machine Learning and DFT Calculations, Z. W. Ulissi et al. Copyright © 2017, Springer Nature.

Theory-based methods may have an advantage over experimental approaches in the analysis of complex reaction networks, since the calculations are performed on "exactly characterized" systems. Theoretical methods, combined with data science approaches, could eventually be used in a hierarchical way to study millions or even billions of catalysts and intermediates. However, these studies will be relevant only if they can describe events representing real catalytic performance accurately. They will have to be validated and adjusted with experimental results obtained under realistic reaction conditions. Such measurements will require improved spectroscopic techniques, especially those capable of *operando* deployment, and those sensitive enough to detect reactive intermediates present at low concentrations. Surface-sensitive time-resolved techniques, such as advanced X-ray techniques available at national laboratory facilities, will also be important. To accelerate the collection and improve the analysis of spectroscopic data, the experiments must be more closely integrated with theoretical modeling of catalyst structures, and with advanced data science approaches.

In microkinetic simulations, rate constants for elementary steps are calculated with density functional theory, which uses exchange correlations that lead to discrepancies between computed and experimental data. Probabilistic analyses can illustrate uncertainties and quantify the errors and correlations in DFT-computed energies. For example, a recent study of the water-gas shift reaction catalyzed by Pt/TiO_2 was explored using different functionals, and a wide range of transition state and oxygen vacancy formation energies were obtained.[32] While the model captured experimental trends, errors in the computed reaction orders, TOF, and apparent activation barrier were significant, and dependent on the selected potential. Thus, model calculations even for simple reactions should be accompanied by an assessment of uncertainty to avoid misinterpretation. As the complexity of computational studies increases, computational and/or experimental errors in each adsorption energy and elementary rate constant the model uses are compounded.[33] Predictions about the activity or selectivity of a particular catalyst must be examined in light of the sensitivity of the model to the uncertainties in the data on which the model is based, by propagating these uncertainties through the kinetic model. The development of machine learning methods for analyzing complex reaction networks and for catalyst discovery could also facilitate our understanding of uncertainty in such studies. Indeed, machine learning methods based

on Bayesian statistics are well-suited to generate the most reliable models given the available data, and to simultaneously estimate the uncertainties in their predictions. In the example in Sidebar 2, the use of uncertainty-aware DFT functionals facilitated an assessment of the likelihood that the reduced pathway is correct.

Constructing and populating databases with computed stabilities for intermediates and energy barriers will allow these values to be used in the computational analysis of many different reaction networks that share similar intermediates. Such databases could combine computed and experimental data and could be used to enable tools that integrate calculations into the analysis of experimental data, as well as tools for the design of new experiments. As described in Priority Research Direction 5, these data could be used to train machine-learning-based models to predict binding and elementary reactions for catalyst compositions and morphologies that differ from those already studied, or for catalytic systems that have yet to be modeled in detail. Since these methods are typically millions of times faster than electronic structure calculations, such machine-learning-based algorithms might be used to explore even more complex reaction networks and catalyst structures. The underlying databases could also be used to generate model potentials, such as neural network potentials, thereby making thermodynamic correction sampling much more tractable compared to the use of full electronic structure theory calculations.

Adopt Holistic Approaches to the Design of Catalyst Systems

All catalytic processes include, in addition to the catalytic reaction, nanoscale transport of reactants and energy to the binding sites, and products and energy away from the binding sites. In this sense, the functioning of a chemical catalytic system can be compared to the operation of a cell, whose complex metabolic networks are intrinsically coupled to intracellular and transmembrane transport and separation processes. Especially for complex reactions, effective catalyst design must be integrated with consideration of the process within which the catalyst will operate, including broad operability under variable conditions such as gradients in concentration and temperature, as appropriate. For example, when intermittent disruptions or variability in feedstock are expected, robust catalysts should continue to promote the desired chemistry selectively without irreversible loss of activity. Catalytic processes are usually operated in conjunction with one or more separations, both upstream and downstream from the catalyst, and sometimes within the catalytic reactor itself. Holistic catalyst design will also account for integration with secondary (non-catalytic) functionality, such as with membranes or absorbents or, in the case of photon-driven electrocatalytic processes, light absorption. An example of the integration of catalytic steam methane reforming with H_2 removal and compression is shown in Sidebar 3. Inherent in this approach is the need to optimize performance for all steps of the integrated process. For example, a catalytic reaction may require a temperature very different from the optimum temperature for the separation to which it is coupled. In such cases, it will be critical to identify what real gains are possible from integration, and if necessary to redesign parts of the system or to look for alternative strategies to achieve the desired goal.
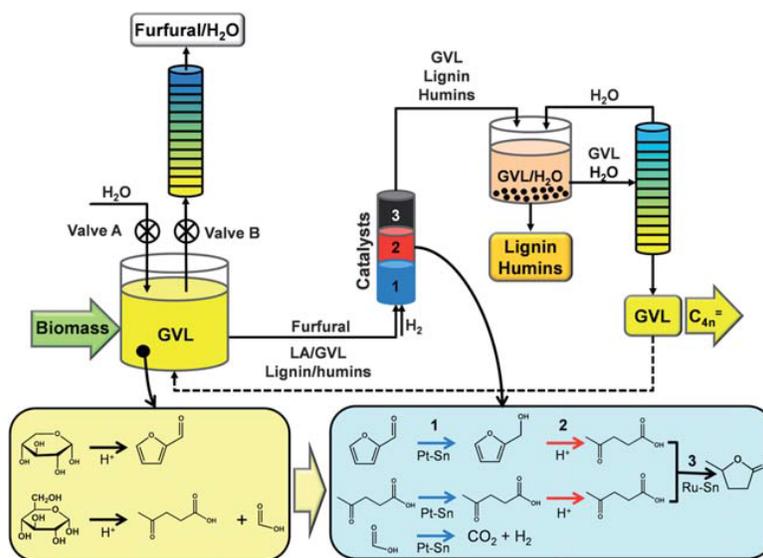

Figure 3.5. Schematic representation of the integrated conversion of both the hemicellulose and cellulose portions of lignocellulosic biomass to furfural and γ-valerolactone (GVL), using a portion of the GVL as a solvent and the remainder for conversion to butene oligomers. From *Energy and Environmental Science*, Integrated Conversion of Hemicellulose and Cellulose from Lignocellulosic Biomass, D. M. Alonso et al. Copyright © 2013 The Royal Society of Chemistry. Reproduced by permission of The Royal Society of Chemistry.

## SIDEBAR 3. INTEGRATION OF STEAM METHANE REFORMING WITH H_2 REMOVAL VIA A PROTON-CONDUCTING MEMBRANE

Large-scale production of H_2 is practiced by combining steam methane reforming with the water-gas shift reaction, followed by separation and compression. On a much smaller scale, a protonic membrane reformer (PMR) can produce high-purity H_2 from methane in a single step with minimal energy loss.[35] A proton-conducting solid electrolyte based on $BaZrO_3$ is deposited as a dense film on a porous Ni composite electrode, which also functions as the reforming catalyst. At 800 °C, 99% of the H_2 is removed from methane, and simultaneously compressed electrochemically up to 50 bar. The entire system is thermally balanced, owing to the coupling of thermal and electrochemical processes.
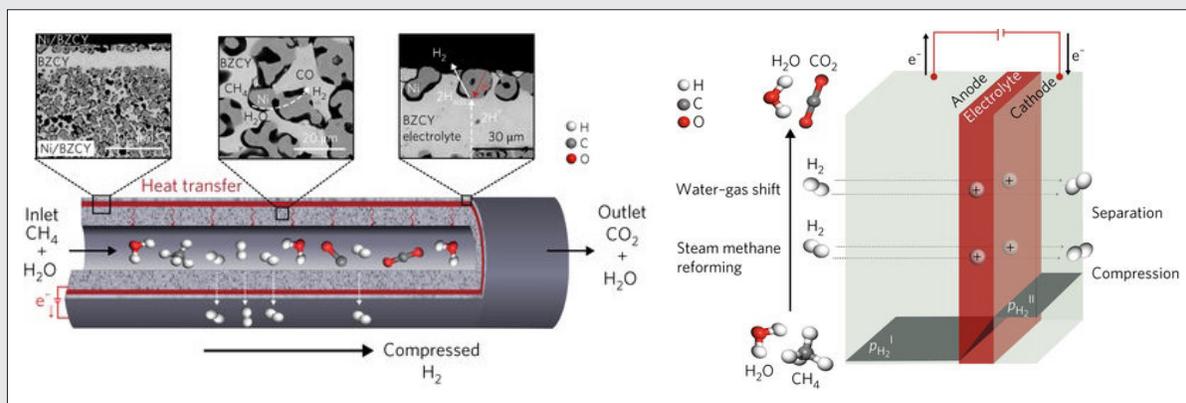
Sidebar Figure 3.3. Left: Protonic membrane reformer for production of compressed H_2. Methane is converted to CO and H_2, and CO is converted to CO_2, over the Ni catalyst located inside the ceramic tube. The H_2 is transported to the outside of the tube as protons, so that the outlet composition is principally CO_2 and H_2O. The heat for the endothermic reaction is supplied by the galvanic operation of the electrochemical cell. Right: Schematic representation of the PMR: H_2 migrates from the anode side to the cathode side, where it is directly compressed as a result of the applied voltage. Reprinted with permission from *Nature Energy*, 2, 923931, 2017, Thermo-Electrochemical Production of Compressed Hydrogen from Methane with Near-Zero Energy Loss, Malerød-Fjeld et al. Copyright © 2017, Springer Nature.

In some cases, the resulting catalytic processes will be more efficient, and have unique selectivities, compared to more traditional approaches. The example in Figure 3.5 shows how pretreatment steps are eliminated in the design of an integrated catalytic process to convert the various components of lignocellulosic biomass while generating its own solvent.[34]

Differences in solubility can be used to control reactions by introducing transport limitations, as well as via separation of reactants, intermediates, and products. For example, biomass-derived compounds show contrasting water and oil solubilities, depending on their oxygen content. By tailoring the hydrophobic and hydrophilic properties of a catalyst surface, it is possible to locate active sites in different regions of aqueous/organic mixtures, or at their interfaces, thus controlling the relative reactivities of different components in the mixture via their solubilities. Although the rates of many reactions are not controlled by solubility but rather by the chemical potential of the reactant in the equilibrated vapor phase, solubilities do play a significant role in mass transfer rates. Therefore, selectivity can be controlled by regulating the rates of mass transfer through the different phases. Reaction intermediates and/or deactivation precursors may thereby be excluded from the phase in which the active sites are located. For example, catalyst stability was significantly improved for glucose isomerization catalyzed by a hydrophobized zeolite in combination with fructose dehydration catalyzed by functionalized carbon nanotubes in a water/oil emulsion. The biphasic system also favors continuous separation of the 5-hydroxymethylfurfural (HMF) product into the organic phase, increasing selectivity to HMF-derived products and inhibiting HMF polymerization in the aqueous phase, Figure 3.6.[36] Finally, understanding catalyst poisoning and developing robust catalysts that can adapt to changing reaction conditions is important. For example, catalysts that are required to operate either for extended periods or transiently in the presence of hot water must be sufficiently hydrolytically stable, or hydrophobic enough to avoid contact with water.[36-39] Alternatively, the dynamic behavior of catalysts can be harnessed to incorporate self-repair as a functionality (see Priority Research Direction 2).
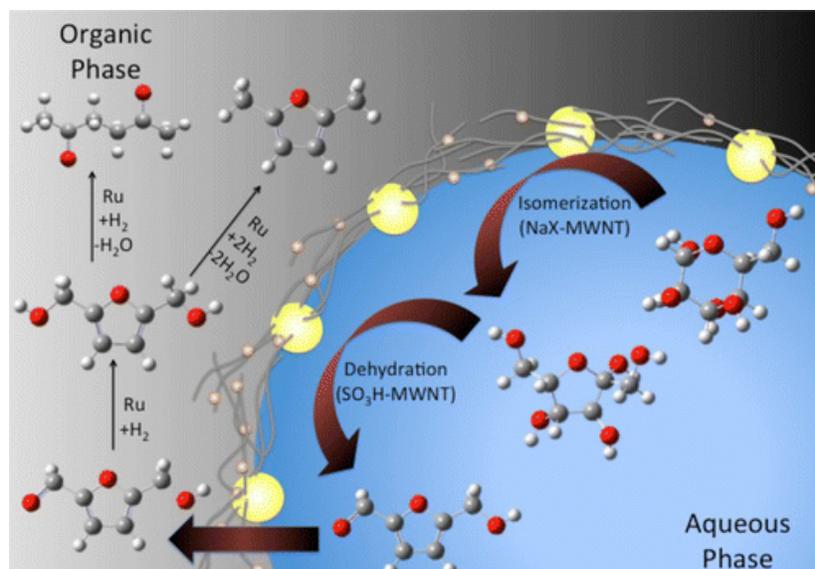
Figure 3.6. A water/oil emulsion is stabilized by hydrophobic carbon nanotube/zeolite hybrids, which in turn catalyze glucose conversion for improved yields of HMF-derived products and enhanced catalyst stability. Reprinted with permission from *ACS Catalysis*, Carbon Nanotube/Zeolite Hybrid Catalysts for Glucose Conversion in Water/Oil Emulsions, J. Faria et al. Copyright 2015 American Chemical Society.

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PRD 4 Design Catalysts for Efficient Electron-driven Chemical Transformations

Key questions: How do we design selective, efficient electron-driven chemical processes at electrically conducting interfaces and use mechanistic understanding of those processes to discover new electrocatalytic systems with high energy efficiencies?

Summary: Electrocatalytic systems interconvert chemical and electrical energy by harnessing the flow of electrons to form and break chemical bonds. Designing electrocatalytic systems with tailored electronic states and controlled interfacial environments will allow electrocatalysis with high selectivity and energy efficiency.

INTRODUCTION

Many chemical transformations that are usually conducted at elevated temperatures and pressures can, in principle, be accomplished under much milder conditions, via electron-driven and photon-assisted electron-driven pathways. Varying the chemical potential of electrons over several volts using a power supply such as a battery or a solar cell is a powerful and versatile way to modify the energy landscape for the chemical reactions that occur at an electrode-electrolyte interface. A similar level of control cannot be achieved in current thermochemical technologies by simply changing reaction conditions. Using a broad range of temperatures and pressures while varying the chemical potential of electrons can provide additional control over the rates of electrochemical reactions, relative to purely chemical transformations. Light absorption represents yet another means to change the outcomes of electron-driven reactions, by creating electronic excited states.

The pressing need for facile interconversion of electrical and chemical energy is a consequence of the increasingly important contributions of renewable energies (e.g., solar and wind) to the U.S. power grid, forcing us to confront their highly variable nature. New electrocatalytic processes could play a central role in increasing the efficient use of these energy resources, by allowing for storage of electrical energy in the form of chemical bonds during periods of excess energy production.[1] An intriguing prospect is the use of electricity to convert abundant, low energy raw materials such as H_2O, N_2, and CO_2 for use as fuels or important industrial chemicals such as H_2, NH_3 and hydrocarbons. The reverse processes (e.g., H_2 oxidation in a fuel cell) can provide electrical energy on demand. An additional, appealing feature of direct photon-driven processes is the possibility of creating off-grid, integrated systems using sunlight, with lower capital costs for producing fuels and chemicals on-demand relative to technologies that produce the renewable electricity and perform electrolysis reactions separately.[2]

In the case of H_2, the current global rate of production is over 65 billion kg/year (approximately 9 kg/year/person) and rising.[3] Nearly all of it is derived from fossil resources, predominantly by steam methane reforming. An electrocatalytic process that generates H_2 by reducing water using renewable electricity is potentially a sustainable means of energy storage, and could also supply a key industrial chemical at-scale. In the future, this H_2 could serve as an important energy carrier. Similarly, electrochemical and/or (photo)electrochemical processes could reduce CO_2 to C-based fuels and chemicals, generating many of the key energy carriers and basic chemicals in use today, including gasoline, ethanol, and precursors for commodity polymers such as polyethylene, at gigaton/year scales. An electrochemical pathway that uses renewable electricity to reduce N_2 could lower the enormous global carbon footprint for the production of NH_3, which is currently manufactured via the conventional, century-old Haber-Bosch catalytic process at a rate of approximately 150 billion kg/year. The major use of this NH_3 is in fertilizer production, however, it could also be used as a fuel in internal combustion engines, in direct ammonia fuel cells, or by catalytically decomposing NH_3 to yield H_2. A sustainable

electrocatalytic process for NH_3 production would enable its use as an energy carrier. Furthermore, the development of better electrocatalysts for the oxidation of fuels such as H_2 and NH_3 could potentially accelerate the market penetration of fuel cell electric vehicles (FCEVs) into the transportation sector.[3] Finally, discovering efficient and stable electrocatalysts for water oxidation is critically important for all of these energy conversion technologies, since it is likely to be key in generating the electrons and protons necessary for the (photo)electrochemical production of fuels and chemicals.

A better fundamental understanding of both electron- and photon-assisted electron-driven chemical transformations will accelerate the development of effective catalysts for many of these reactions. New catalysts for the large-scale (photo)electrochemical production of fuels and chemicals must be stable, have a high density of active sites, and be readily separated from products and solvents. Although such characteristics are most likely to be achieved using insoluble electrocatalysts, there is nevertheless a strong motivation to understand (photo)electrocatalytic processes of all types, in order to identify and exploit common underlying principles. The next generation of electron-driven processes will be based on architecturally complex catalysts designed using powerful new theoretical approaches and prepared using sophisticated new methods of catalyst synthesis (Figure 4.1).[4] Electrochemical reactions will be controlled at the level of their elementary steps, including the precision delivery (or removal) of electrons and protons. A deeper understanding of the factors that determine activity and selectivity will emerge from experimental and computational investigations of reaction mechanisms, including the use of advanced spectroscopic techniques to identify reactive intermediates.
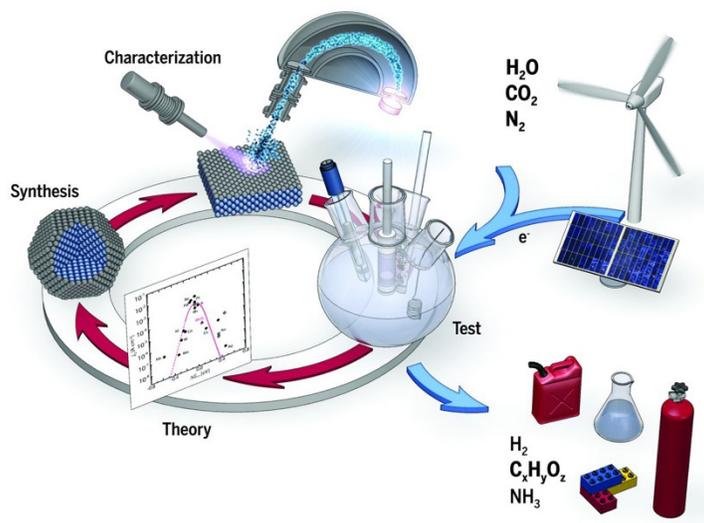
Figure 4.1. The design of new electrocatalytic processes for the production of value-added chemicals and fuels will emerge from concerted insight into catalyst synthesis, characterization, and evaluation, all of which are informed and interpreted by theory. From Seh et al., Combining theory and experiment in electrolysis: Insights into materials design, *Science*, Vol. 355 (6321):eaad4998. DOI: 10.1126/science.aad4998. Copyright © 2016, AAAS. Reprinted with permission from AAAS.

SCIENTIFIC CHALLENGES

New catalysts for electron-driven chemical transformations are needed to improve the performance of electrochemical cells, both galvanic and electrolytic, including cells in which light is used as an energy input. In some cells, the interfacial reactions have intrinsically fast kinetics already. However, in many of the cells of greatest relevance to current or future energy technologies, the half-reactions occurring at the anode and/or cathode exhibit large kinetic barriers. The reasons for the high barriers are relatively well understood from a theoretical perspective. They arise primarily from the difficulty in optimizing a single catalyst structure/composition for all elementary steps in processes that involve multiple electron and proton transfers. In all such multi-step processes, there is generally at least one high energy transition state or intermediate whose formation limits the rate. One challenge is to design catalysts for these transformations that achieve the precise delivery of electrons and protons but avoid such high energy species, and thereby lower kinetic barriers. When

undesirable side-reactions occur at potentials similar to those for the desired transformation, they lower the chemical selectivity and energy efficiency. A related challenge is therefore the design of electrocatalysts which do not promote other half-reactions simultaneously at either the anode or cathode. While issues of activity and selectivity are, of course, common to both thermal catalytic and electrocatalytic processes, a challenge unique to energy-efficient electrocatalytic transformations is the need to achieve rapid reaction at low overpotentials, that is, near the position of thermodynamic equilibrium.

In many electrochemical cells (with the notable exception of those involving mediators), electron-driven chemical transformations take place within a few nanometers of an electrode surface. Inevitably, therefore, electrocatalysis involves reactions at electrified solid/solution interfaces. A fundamental challenge is to understand how the properties of these interfaces influence catalysis. Furthermore, in complete electrochemical systems, the current/potential characteristics which determine cell performance can also be affected (and are sometimes dominated) by ion transport. In efficient cells, such transport occurs at rates at least commensurate with the electron-driven chemical transformations. This is generally accomplished by using electrolytes with high ionic strengths and/or very high or very low pH values, especially for cells that must operate at high current densities in order to minimize their capital cost. It is challenging to design robust electrocatalysts whose stabilities are not severely compromised by these operating requirements. The importance of geometric factors such as the shape and porosity of the electrodes, which can affect the uniformity of current distribution, the need for immediate separation of products, and possible requirements for optical transparency in photon-driven electrocatalysis, present additional challenges for the fabrication of electrocatalysts. For photon-driven electrochemical transformations using broad-band light sources (e.g., sunlight), careful calibration of the spectral distribution is critical for making meaningful efficiency comparisons. (Photo)electrocatalytic reactions that generate multiple, soluble products present analytical challenges associated with measuring product distributions (i.e., selectivities) in electrolytes accurately, as a function of applied potential, and in real time.

A major challenge for the field of electrocatalysis is the consistent assessment of catalyst performance, without interference from complicating factors that can mask the effect of the catalyst on the intrinsic rate of an electron-driven chemical transformation. Differences in rates between good catalysts and poor ones can be as large as ten orders of magnitude. Unfortunately, electrochemical measurements of catalyst performance rarely provide a direct probe of the intrinsic activity/selectivity of the electrocatalytic material or molecule. Instead, they are extrinsic measurements which are convoluted with factors such as the configuration of the electrochemical cell, conductivity, mass transport, electric field effects, electrode roughness, catalyst loading and accessibility. While corrections can be made for some of these factors (e.g., IR losses from cell resistance), others have yet to be accounted for. These complications impede accurate comparisons of electrocatalysts, even when they are otherwise similar, and especially when the attempted comparison involves vastly different catalyst types (i.e., heterogeneous, homogeneous, and biological).

Methods for translating the aggregate extrinsic properties of a specific electrode/cell into intrinsic activity/ selectivity/durability parameters for the catalyst are not yet well-developed. Comparison of electrocatalysts can only be performed in a meaningful way if tests are conducted under precisely controlled (and described) conditions, including all concentrations, temperature, and pressure. Reporting either rates or overpotentials alone, without the other as a necessary counterpart, is uninformative for any class of electrocatalyst. For soluble electrocatalysts, the maximum observable turnover frequency can be extrapolated to the turnover frequency at zero overpotential in order to compare catalyst performance using a single metric. The result is a new benchmarking tool called the catalytic Tafel plot, illustrated in Figure 4.2.[5] However, experimental conditions must still be carefully controlled to avoid biasing the measurement in favor of a particular catalyst. For heterogeneous catalysts, the development of quantitative structure/function correlations is hindered by a lack of accurate, universal methods for measuring electroactive surface areas in diverse materials. This challenge also impedes comparisons of dissimilar materials, such as those based on Earth-abundant elements as potential replacements for existing precious metal catalysts. Even in the absence of significant changes in catalyst structure, variations in the diffusional characteristics and morphologies of electrodes can lead to dramatic changes in selectivity, for example, in the 2-electron vs. 4-electron reduction of O_2, or in the reduction of CO_2. Consequently, prospects for new catalyst development depend on the emergence of standardized methods and the widespread community adoption of benchmarking protocols.[6]
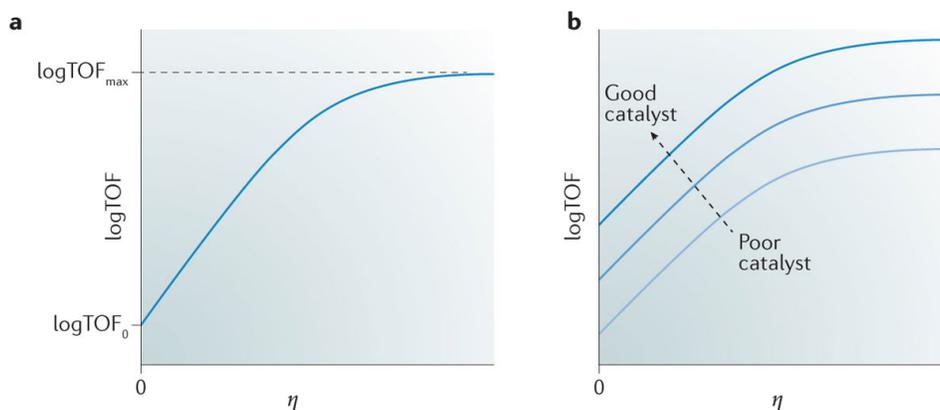
Figure 4.2. Catalytic Tafel plots for benchmarking the performance of homogeneous electrocatalysts, showing (a) extrapolation of turnover frequency (TOF) to zero overpotential (η), and (b) direct catalyst comparisons, with better performance indicated by a lower overpotential for a given TOF. Reprinted with permission from *Nature Reviews Chemistry*, 1, 0087 2017, Towards an intelligent design of molecular electrocatalysts, C. Costentin et al. Copyright © 2015, Springer Nature.

FOCUS AREAS

Design Catalyst Architectures for Reactions at Electrified Solid/Liquid Interfaces

It is important to assess how different structural motifs relate to electrocatalytic performance, and to be able to control the formation and evolution of active site structures with atomic-level precision. Electrocatalytic surface structures are inherently challenging to control, and we must learn how to synthesize them with a high degree of order and fidelity, recognizing that minority defect sites (steps, for instance) may dominate their catalytic activity.[7] The possibility of surface reconstruction under reaction conditions must also be recognized. Thus the design, synthesis, and study of next-generation catalysts for electron-driven chemical transformations will build on many of the innovations already identified in Priority Research Directions 1 and 2.

The structures of electrocatalysts beyond their binding sites, including interfacial structures that form in the complex reaction medium, can influence rates, overpotentials, and selectivities. Extensive prior studies have explored the effects of modifying the first coordination spheres of molecular electrocatalysts, but the importance of second or outer coordination sphere effects is now increasingly acknowledged. Solvents can play a variety of roles, both direct and indirect. They include binding to the catalyst, altering the stability of intermediates, and causing changes in the overall energy landscape.[8] The ions in the electrolyte can influence the outcomes of electrocatalytic transformations,[9] and must be better understood. The effects include those resulting from changes in the dielectric response of the medium, differential stabilization of reactant and transition states, as well as mesoscale phenomena spanning multiple time scales that are governed by subtle free energy fluctuations at the catalyst/solvent interface.[10] Creating confined spaces with molecular dimensions, for example, those found in microporous electrocatalytic materials, can alter the bonding in reaction intermediates and access more energetically favorable pathways for chemical transformations. Efficient electrocatalysis depends on a precise coupling of proton transfer with electron transfer events to maintain charge neutrality, avoid high-energy intermediates and circumvent large kinetic barriers. Controlling proton-coupled electron transfer reactions therefore requires an understanding of the thermodynamics of proton delivery and removal. In some cases, proton relays located in the catalyst architecture can be effective, aided by an understanding of the kinetics and thermodynamics of sites to and from which the proton transfers occur (see Sidebar 1). A better understanding of the design principles for redox enzymes, such as conformational changes, hydrogen-bonding interactions, and proton shuttling, is likely to lead to new ideas to improve the performance of synthetic analogs.

The design of new architectures for electrocatalysts also involves distinct issues related to their exposure to electrochemical environments (e.g., electrified solid-liquid and solid-ionomer interfaces). Traditional descriptions of catalytic current flow obtained from voltammograms, e.g., Tafel slopes, can provide important insight into electrocatalytic reaction mechanisms. However, more general methods for characterizing catalyst surface areas, diffusional gradients, and current/voltage inhomogeneities in complex electrodes are needed in order to make quantitative comparisons that can inform systematic catalyst design. While *ex situ* characterization of a pristine electrocatalyst is often a necessary starting point, the observation of a catalyst *in situ* under an applied

SIDEBAR 1. SYNTHETIC ELECTROCATALYSTS THAT TURN OVER FASTER THAN ENZYMES

Identifying key site requirements and mechanistic features in high-performing systems can provide guidelines for designing new catalysts. For some of the reactions of interest in large-scale energy conversion, enzymes represent a a class of remarkably efficient catalysts. Although Nature has a considerable head start (by a few billion years), researchers have recently made significant progress in preparing biologically-inspired catalysts that emulate key features of these enzymes, such as the local structures and/or behaviors of the active sites. This approach has led to improved synthetic catalysts as well as an increasingly detailed understanding of how enzymes function.

Hydrogenases are enzymes that produce or oxidize H_2. For one class of hydrogenases, a critical feature is the presence of an organic base, close to the active metal center, which functions as a "proton relay" by shuttling protons to and from the binding site at the metal. This knowledge inspired the synthesis of molecular metal catalysts whose ligands bear pendant amines.[11] In 2011, a nickel-containing electrocatalyst with such proximal amines was reported to produce H_2 with a turnover frequency greater than 100,000 per second.[12] This rate is about ten times faster than that of a natural di-iron hydrogenase enzyme. Further improvements emulating other features found in natural enzymes have resulted in circa 100-fold rate increases.[13]

Sidebar Figure 4.1. Electrocatalytic production of H_2 using a synthetic inorganic catalyst is accelerated by incorporation of pendant amines that function as proton relays.[11] From *Chemical Communications*, Production of H_2 at Fast Rates Using a Nickel Electrocatalyst in Water-acetonitrile Solutions, W. A. Hoffert et al. Copyright © 2013, The Royal Society of Chemistry. Reproduced by permission of The Royal Society of Chemistry.

These examples demonstrate that catalysts prepared in the laboratory can operate at rates that are comparable to or faster than those found in Nature. Similarly, researchers studying water oxidation have recently designed molecular catalysts that turn over more rapidly than the oxygen-evolving complex of Photosystem II.[14,15] In both cases, *faster* is not necessarily *better*, because the synthetic catalysts operate with much lower energy conversion efficiencies than the corresponding enzymes. Surpassing the overall performance of the biological catalysts with robust synthetic analogs will be the focus of further design improvements.

electrode potential and with current flowing is critical to understanding the nature of the active states. Advanced characterization techniques (where possible, implemented simultaneously with real-time product detection, i.e., *operando* conditions) will accelerate the linking of structures to their reactivity. New imaging and spectroscopy techniques will allow us to map charge states, and to visualize 3D changes in the electrode surface. For example, very short-range chemical forces at surfaces can be detected by non-contact AFM.[16] Developing sensitive multimodal and time-resolved spectroscopies will be critical to identify, and thereby control, reactive intermediates in complex systems. In photoelectrochemical systems, the photochemical generation of charge carriers and their transport to the solid-electrolyte interface can affect the subsequent electron transfer rates and, potentially, improve selectivity.[17] Photons can also be absorbed by reaction intermediates, whose excited vibrational states are thereby primed for chemical transformation. Understanding these and related phenomena induced by photons will ultimately lead to new ideas for improved catalytic activity and selectivity.

Characterizing and quantifying many of these subtle, and often complex, interactions will require the use of powerful new theoretical tools. More accurate free energy computations, which include the effect of the electrolyte and the influence of extended structures beyond the binding sites, are needed in order to use the full power of theory to design catalyst architectures.[18,19] The treatment of entropy and dynamic fluctuations will

be important here, as described in Priority Research Direction 2. For heterogeneous electrocatalysts, the effect of the support on electrocatalyst performance can be significant, and must be considered. Better modeling of double layer structure and dynamics will be necessary for making predictions of rates.[20,21] Theoretical descriptions of transient catalytic species and their spectral signatures will aid in experimental design and data interpretation.[22] In addition, computations that explicitly model strong electric fields, the complex solvent environment, and the ionic composition of electrode-electrolyte interfaces are critical to provide accurate comparisons between theory and experiment. It is also important to account for the stability of the electrocatalyst in the development of design principles.

Although multi-electron, multi-proton transformations involve a complex series of elementary steps, there are often relatively simple correlations between the reaction energies of various elementary steps and their rates.[23] These "scaling relations" have made it possible to rationalize trends in catalyst composition and to guide the design of new catalysts,[19,24] by identifying a few, readily available descriptors of rate and/or selectivity.[25] They also highlight the compromises that are necessary in optimizing rates for the different elementary reaction steps in a catalytic reaction network, and they dictate the limits of such optimization. A critical priority for future theoretical research in this area is to discover new catalyst materials and architectures that are capable of essentially "breaking" these scaling relations,[26] thereby overcoming fundamental limitations for the rates of electrocatalytic processes.

### Explore New Concepts for Electrified Interfaces and Electron/Proton Delivery

Most (photo)electrochemical systems used in energy technologies contain interfaces between metallic or semiconductor electrodes and ion or electron conductors. The system components are conventionally arranged in a parallel-plate or similar configuration in order to couple electron transfer reactions at the interface with mass transfer processes involving reactants/products/ions, as well as with solar radiation in the case of photoelectrochemical systems. These types of interfaces and configurations may impose constraints on electrocatalyst development that inhibit innovation in system design, as Priority Research Direction 3 anticipates. For example, the catalyst in a photoelectrochemical system must be located near the solid-liquid interface to allow for efficient electron transfer, but cannot block or absorb incident light. For molecular electrocatalysts dissolved in the electrolyte, the fraction of catalyst molecules that are sufficiently close to the electrode surface (and therefore electrochemically active) at any given time is small, limiting the observed current. The activity of heterogeneous electrocatalysts is constrained by the ability of a given surface to stabilize all intermediates and transition states efficiently. Therefore, future research efforts should include the design and characterization of new types of electrified interfaces and arrangements of system components. Some examples include combinations of molecular and heterogeneous electrocatalysts, and mediated electrolysis.

Molecular electrocatalysts have discrete electronic states that pin their redox potential at specific values that may not be well-matched to a desired catalytic transformation, resulting in low overall energy efficiency. This restriction does not apply to metals due to their continuum of closely-spaced band states, but heterogeneous electrocatalysts are intrinsically less tunable by synthetic methods than molecular systems. In principle, the desirable features of both molecular and heterogeneous catalysts can be combined by electronic coupling of molecular reaction centers to the band states of a metallic or semiconductor electrode. Numerous methods have been developed for appending molecular catalysts to electrode surfaces,[27] but they often rely on saturated linkers (e.g., aliphatic hydrocarbon chains) that provide poor electronic coupling between the molecular unit and the electrode surface. An alternative strategy involves the use of conjugated aromatic linkages,[28] as illustrated in Sidebar 2 for a graphitic carbon electrode conjugated to a molecular Re-based catalyst.[29]

Mitochondrial respiration and other forms of energy transduction in biology achieve the transport of redox equivalents via mediators, consisting of redox-active proteins (e.g., cytochrome c) or small molecules (e.g., NADH, ubiquinone). Similar strategies could facilitate the interconversion of electrical and chemical energy in non-biological systems, by combining soluble, redox-active species with molecular or heterogeneous catalysts. Such systems have been called "chemically regenerative redox fuel cells", and they bear some resemblance to redox flow batteries. The redox mediators transport electrons (and possibly also protons) between the electrode and components present in the bulk solution.[31] Such mediated electrolysis processes may be important in chemical transformations that are too slow to occur within the diffusion layer of an electrode; that exhibit slow kinetics at the electrode resulting in a high overpotential (such as those found in O_2 or N_2 reduction); or that involve reactions of macromolecular chemical feedstocks, such as lignin or cellulose. There is a need to identify

SIDEBAR 2. MAKING MOLECULAR ELECTROCATALYSTS BEHAVE LIKE METALS

The active sites in heterogeneous electrocatalysts commonly used for energy conversion reactions are inherently dynamic and hard to identify, much less characterize and modify strategically. It can be difficult to extract significant molecular-level understanding for these materials, and to tune their activity or selectivity through synthetic modifications. A new class of electrocatalysts incorporates highly tunable molecular active sites into heterogeneous graphite surfaces. For example, reaction of *fac*-Re(5,6-diamino-1,10-phenanthroline)$(CO)_3$Cl at *o*-quinone edge defects generates a hybrid electrocatalyst.[30] The CO_2 reduction activity of the surface-bound Re sites is higher than that of the corresponding molecular Re complex in solution, while maintaining high selectivity for CO relative to H_2 production.
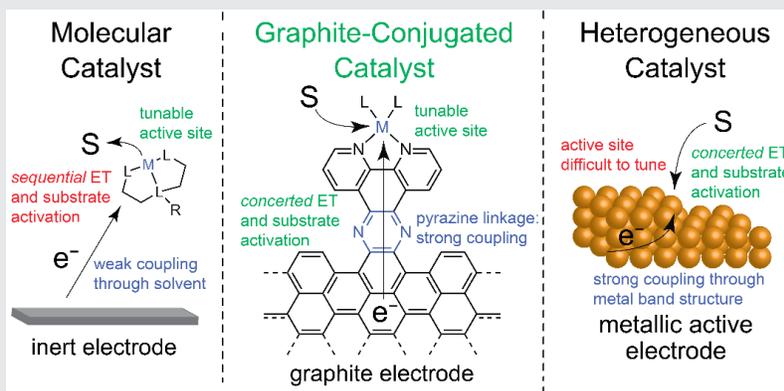
Sidebar Figure 4.2. Molecular catalysts (left) possess tunable active sites but impose severe electron transfer (ET) barriers, while heterogeneous catalysts (right) enable facile ET, but are difficult to tune at the molecular level. Graphite-conjugated catalysts (center) combine concerted ET with molecularly tunable active sites. S represents the reaction substrate. Reprinted with permission from *Journal of the American Chemical Society*, Strong Electronic Coupling of Molecular Sites to Graphitic Electrodes via Pyrazine Conjugation, M. N. Jackson et al. Copyright 2018 American Chemical Society.

The strong electronic coupling, created by the conjugated pyrazine linkage between the molecular active sites and the electrode, allows these graphite-conjugated catalysts (GCC) to behave like metal sites. The appended surface sites thereby acquire the fast electron transfer properties of metals, while the molecular nature of the active sites and their high degree of uniformity make them highly tunable and enable mechanistic investigations. New synthetic approaches for promoting band-molecule coupling across diverse material and molecule classes will allow chemically-modified electrodes to integrate the attractive features of both molecular and heterogeneous electrocatalysts.

robust, low-cost mediators with appropriate redox potentials to achieve the desired energy transductions at high rates without large overpotentials. Key mediator properties, such as fast electrochemical kinetics and mass-transport behavior, and low susceptibility to membrane crossover, must be assessed. In many cases, redox mediators are themselves catalytically inert. Thus, mediated electrolysis often requires a separate molecular or heterogeneous catalyst. Charge transfer rates between the mediator and the terminal catalyst must be much better understood, particularly for proton-coupled mediators, in order to maximize opportunities for cooperative catalytic phenomena.

Develop Efficient, Scalable Electrocatalysts for Energy-Relevant Half-Reactions

Electrocatalytic systems interconvert chemical and electrical energy by harnessing the flow of electrons to form and break chemical bonds. Electrocatalyst research focused on energy-relevant half-reactions should be cognizant of the scale and operating conditions which the corresponding processes are likely to require. In many cases relevant to energy technologies, the important bond formation and cleavage events occur in the forward- and reverse-directions of a single half-reaction. For some of these half-reactions, such as H_2 evolution/oxidation and O_2 evolution/reduction, research is needed to improve existing electrocatalysts, design better ones, and make them significantly less expensive. For some other half-reactions, such as CO_2 or N_2 reduction and selective hydrocarbon oxidations, effective catalysts are virtually unknown at present, have poor selectivity, and/or are unstable. Finally, electrochemical transformations such as the production and use of H_2O_2 or C–N bond-making/bond-breaking reactions have been much less explored, but could become energy-relevant if they can be conducted efficiently on large scales.

Currently, the best catalysts for H_2 evolution and oxidation are Pt and the hydrogenase enzymes. They are capable of evolving H_2 (and oxidizing H_2) with fast rates *and* at low overpotentials. However, neither catalyst is

SIDEBAR 3. HETEROGENEOUS ELECTROCATALYSTS WITH EARTH-ABUNDANT ELEMENTS

There has been considerable progress in the development of highly active and stable electrocatalysts based on Earth-abundant elements, such as those designed using layered molybdenum sulfides. Their overall activity in the hydrogen evolution reaction (HER) depends on (1) the turnover frequency of the active sites, (2) the total number of active sites, and (3) the electrical accessibility of these sites. For MoS_2-based electrocatalysts, HER occurs at edge sites where sulfur atoms are undercoordinated, and the hydrogen binding energy is close to zero.[32] Interestingly, the turnover frequencies are similar for

Sidebar Figure 4.3. Various nanostructured electrocatalyst materials for HER, based on MoS_2. Reprinted with permission from *ACS Catalysis*, Catalyzing the Hydrogen Evolution Reaction (HER) with Molybdenum Sulfide Nanomaterials, J. D. Benck et al. Copyright 2014 American Chemical Society.

all of the crystalline, amorphous, and molecular cluster forms explored thus far, including nanoparticles, nanowires, nanoclusters, mesoporous structures, and thin vertical films.[33] The overall activity is determined predominantly by the total number of edge sites, which can be increased by nanostructuring.[34] Thus electrocatalytic activity can be optimized by synthesis strategies that maximize perimeter length.

likely to scale to the terawatt level needed for large-scale energy storage; hence efficient catalysts consisting entirely or largely of Earth-abundant elements will likely be required (see Sidebar 3). Some non-precious metal-based molecular catalysts and solid-state systems can achieve extraordinarily high rates for H_2 evolution, albeit at much higher overpotentials.[4] However, catalyst stability must be improved substantially during long-term operation, as well as catalyst resistance to strongly acidic or basic electrolytes. Pt and hydrogenase are among a small number of catalysts that carry out H_2 evolution and oxidation reversibly. Since the pathways for the forward and reverse reactions need not be the microscopic reverse of each other in multi-electron electrochemical reactions, it is not necessarily the case that a good H_2 evolution catalyst is also a good H_2 oxidation catalyst. Developing electrocatalysts to oxidize H_2 efficiently will enable large-scale processes that transform the chemical energy in H_2 to electricity. For molecular electrocatalysts, the reaction of H_2 with the metal site is often the step that must be accelerated. For heterogeneous electrocatalysts, controlling the dynamic behavior of the surface under reaction conditions may be the key to designing more efficient systems. A deeper understanding of the reaction mechanisms will enable the design of improved catalysts.

Oxygen reduction to water balances the oxidative reaction in many fuel cells. Pt-based nanomaterials are currently the best O_2 reduction electrocatalysts at near-ambient temperatures, but their high overpotentials lead to significant losses in efficiency. Although Pt-alloys often show better catalytic performance than pure Pt, further advances will likely require new materials and approaches.[4] Compared to Pt-based nanomaterials, molecular catalysts used in combination with chemical mediators also exhibit large overpotentials, and face additional challenges due to low numbers of active sites.[35,36] New catalyst systems and approaches are needed to provide higher densities of active sites, achieve faster reaction rates at low overpotentials, and operate in a stable manner in either acidic or basic environments. Further investigation of the use of chemical mediators may lead to better results for challenging reduction reactions. An alternative to difficult and energy-intensive OER in water electrolyzers involves the oxidation of organic compounds (e.g., derived from biomass) at much lower overpotentials, with the potential benefit of generating valuable coproducts in addition to H_2.[37,38] A similar strategy has been described for coupling electrochemical CO_2 reduction to alcohol oxidation.[39] The choice of coproduct will be critical for large-scale energy applications.

Currently, the best catalysts for water oxidation, also known as the oxygen evolution reaction (OER), are the enzymes in the oxygen-evolving complex (OEC) of Photosystem II, and heterogeneous oxides (e.g., IrO_x in acid, or $FeNiO_x$ in base). The latter require overpotentials of approximately 0.3 V or greater to achieve even modest current densities,[6] thus more active catalysts are urgently needed. Catalyst stability must also be improved, especially in strongly acidic or basic electrolytes. Even heterogeneous catalysts often corrode under such harsh operating conditions. For molecular catalysts, the ligands must also be able to withstand strongly oxidizing surroundings, and the catalysts must retain their molecular identities under reaction conditions. Indeed, a major

issue for research is ascertaining whether the actual catalyst is a molecular species, or a heterogeneous phase formed from decomposition under the reaction conditions.

The electrocatalytic conversion of CO_2 to hydrocarbons is a complex process requiring multiple reducing equivalents. For example, the reduction of CO_2 to CH_4 requires the addition of eight electrons and eight protons, even without the additional complication of C–C bond formation. Although some enzymes and synthetic molecular systems can accomplish this transformation with high selectivity, they typically require separate catalysts for each of the four consecutive two-electron reduction steps. Most molecular electrocatalysts make primarily two-electron reduction products (i.e., CO and/or formate), which can then be reduced further.[40] Heterogeneous catalysts are known which can convert CO_2 into interesting molecules beyond CO and formate, including methane, ethane, ethylene, ethanol, propanol, and acetone, among many others.[4] However, the required overpotentials are very large, and the range of products is generally very broad. Improved understanding of the mechanisms that lead to kinetic branching[41] and that determine the populations of the surface intermediates[42] are essential for enabling the systematic design of more selective CO_2 reduction catalysts. In addition to improved activity and selectivity, catalysts with much better stability are needed. Similar issues are encountered in the selective electrochemical reduction of N_2 to NH_3, particularly in suppressing the kinetically facile evolution of H_2 via the reduction of protons or water. Formation of H_2 as an undesired byproduct is problematic for all known molecular and heterogeneous catalysts for the electrochemical reduction of N_2. While much has been learned using chemical reducing agents in combination with acids, new electrocatalytic materials that favor N_2 protonation due to slow H_2 evolution kinetics are required.[17] Similar to the case of CO_2 reduction, there is also a tremendous need to discover catalysts that can achieve high selectivity and fast reaction rates at low overpotentials.

In the selective oxidation of hydrocarbons, for example, methane to methanol, and ethane to ethanol, electrochemical processes operating at near-ambient conditions may be able to achieve the high selectivities that have long eluded thermal catalytic approaches. However, electrocatalysts that exhibit reasonable activity, selectivity, and stability have yet to be discovered for these reactions. Similarly, the electrochemical oxidation of NH_3 used as a fuel will require new catalysts which do not yet exist. While the thermal process to convert ammonia to N_2 and H_2 is fairly well-understood,[43] the corresponding electrochemical decomposition of ammonia is much less studied. For example, the primary steps in removal of electrons or protons (possibly as proton-coupled electron transfers) must be identified and the thermodynamic parameters for such reactions, including the key step involving formation of the N–N bond, must be determined. Greater mechanistic understanding will facilitate catalyst development in all of these areas.

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PRD 5 Drive New Catalyst Discoveries by Coupling Data Science, Theory, and Experiment

Key questions: How do we augment hypothesis-based catalyst discovery with data science tools, including machine and deep learning, to extract new knowledge from highly diverse datasets? How can we use this approach to predict effective combinations of catalytic functions, structural components, reaction environments, and reaction mechanisms for complex systems?

Summary: The complex coupling of many variables that govern catalyst reactivity and evolution make it challenging to determine relationships between catalyst structure/composition and performance. Data science can reveal important patterns in such high-dimensional data, providing insights for predicting performance, designing critical validation experiments, and discovering new catalysts.

INTRODUCTION

Complex catalytic phenomena traditionally are made more tractable by the careful choice of model systems, as well as by separate study of the individual components of a catalytic system/process. In this reductionist approach, the behavior of catalysts is represented by defining a small number of descriptors, which express activity, selectivity, and stability; and the design of the next generation of catalysts is based on an assessment of these descriptors. Some of the outcomes of this general strategy include many effective catalyst synthesis protocols, increasingly detailed structural characterization of reacting systems, and insight into catalytic mechanisms arising from the combination of experiment, simulation, and theory. The research approach has also generated exceedingly large amounts of information. At this time, a deeper understanding of catalysis is impeded by our limited ability to perceive and describe relationships present in this vast data trove. Consequently, two of the next logical steps towards improving our understanding of catalyst performance and advancing catalyst design are to begin to use the methods of modern data science to extract new correlations from the data sets, and to infuse them with physical and chemical meaning.

The reductionist approach to understanding catalysis arises naturally from traditions in the physical sciences, where complex behavior is explained using a minimal set of fundamental principles. Although theory and experiment have successfully explained many individual observations in catalysis, the full complexity and dynamic behavior of reacting systems during operation have not yet been harnessed. At the same time, breakthroughs in materials synthesis, characterization, imaging, and theoretical/computational sciences in the past decade have contributed to a massive increase in the amount of available relevant information, as well as in the rate new information is generated. Much of this wealth of data relates to just a few, relatively simple catalytic reactions, such as ammonia synthesis, electrochemical proton reduction to H_2 or the water-gas shift reaction. Nevertheless, reliable simulated adsorption energies and energy barriers, in combination with detailed experimental characterization and careful measurements of catalyst performance, have made new insight possible, for example, into the nature of minority active sites,[1] leading to predictions of highly effective new catalyst compositions and structures.[2,3] Design strategies for families of heterogeneous electrocatalysts have been developed via the descriptor-based approach to rationalize catalyst performance.[4] For example, the performance of members of a family of molecular electrocatalysts for H_2 evolution and oxidation, O_2 reduction, and CO conversion can now be predicted *in silico* by correlating free energy maps with molecular thermodynamic properties.[5] Nevertheless, this powerful strategy still does not capture all of the complexity present in realistic catalyst systems. Some of the issues arise from the presence of multiple, competing reactions, and the corresponding difficulty in assessing kinetic parameters for individual pathways; the importance of support, solvent and coverage effects, which are generally not independent of each other; and the dynamic

evolution of catalysts under operating conditions. Furthermore, cooperative phenomena may emerge only in complex systems. Thus catalysis science could benefit from methods that facilitate a comprehensive conceptualization of enormous amounts of catalyst data.

As the first four Priority Research Directions in this report show, advancing our understanding of the intrinsic complexity of catalysts and catalytic reactions requires more complete descriptions of: (i) the interplay between local (i.e., inner coordination sphere) geometric and electronic effects and semi-local (i.e., outer-coordination sphere) influences, including the many interactions between active sites, their supporting ligands and/or solid supports, and molecular species in the reaction medium; (ii) minority (i.e., rare) active species distinct from majority-dormant or spectator species; (iii) active site diversity, and the reaction pathways available to them; and (iv) dynamic behavior of the active sites over multiple length and time scales. Better models must reflect this complexity, yet still remain robust and simple enough to predict improved catalyst formulations. Through data mining of both small and large datasets, the robust fitting of flexible models to multivariable data, automatic feature selection, and systematic uncertainty quantification, data science can contribute to closing the gap between information and understanding. Early examples demonstrated the ability of unsupervised machine learning to extract new descriptors for effective heterogeneous oxidation catalysts,[6] and to generate structure-function relationships for such catalysts from high-throughput screening data.[7]

Machine learning and deep learning can reveal subtle correlations in data to drive new discoveries (see Sidebar 1 for definitions).[8] Machine learning also has the potential to greatly expand the computational toolbox for generating predictive knowledge about catalysts from large datasets. Thus data science can offer a more integrated approach to mastering catalyst complexity, by extracting meaningful correlations from many different types of measurements and theory, by filling in gaps caused by missing data, and by leading to more encompassing theories that can guide simulations towards new solutions. Recent advances involve algorithms that thrive on data complexity, integrate disparate data types, and make unbiased use of experimental data, including the failed experiments that are typically less valued by researchers. Thus we are on the verge of being able to formulate and evaluate scientific hypotheses that encompass much more of the intrinsic complexity of realistic catalytic systems.

Finally, while catalysis science has much to gain by augmenting fundamental descriptor-based models with data science algorithms, we must also recognize that all-encompassing catalysis data models will not emerge from this approach any time soon. For example, experimental molecular electrocatalysis occupies a synthesis and operating parameter space that likely does not overlap sufficiently with that of membrane electrode assemblies to enable data-driven identification of all underlying fundamental relationships. Furthermore, caution is warranted when data science methods are applied without sufficient regard for the underlying scientific basis of the problem. Appropriate balance between training algorithms and training datasets is critical. Indeed, the outcomes of data science algorithms depend critically on the breadth and quality of data, and scientific challenges related to experimental needs that will allow the description of catalytic phenomena in atomistic detail over all pertinent parameter space; this topic was a focus area of Priority Research Direction 2. Finally, successful integration of data science with experiment and theory will rely on careful selection of initial catalysis problems that are amenable to data science methods, so that the resulting families of data models can be interconnected hierarchically as the field advances.

SCIENTIFIC CHALLENGES

A central question in catalysis science is how to incorporate the appropriate level of complexity into models for catalytic systems, as in, how to couple the dynamic reaction chemistry, structural configurations, and electronic states of multiple catalyst components across different length and time scales, yet maintain sufficient simplicity to generate useful structure-function correlations. The challenge begins with providing guidance for the synthesis of new catalysts. While it is possible to target desired catalyst structures using chemical understanding and intuition, it is not yet possible to devise reliable synthetic strategies for entirely new architectures and active sites. In contrast to the well-developed methodologies of organic synthesis, it remains unclear how to approach the synthesis of inorganic catalyst materials in a systematic way. The design and assembly of all of the components of such a catalyst system, at the binding sites and beyond, requires simultaneous control over multiple reaction variables and a large number of parallel and consecutive reaction steps. Yet we usually do not know how these variables and reactions, both individually and in combination, contribute to the key properties

SIDEBAR 1. MACHINE LEARNING DEFINITIONS FOR CATALYSIS SCIENCE

Machine learning originated in the field of computer science. Its goal is to enable computers to learn from experience, in order to bypass complicated algorithms and avoid extensive computations. Initially, it was applied to games like checkers or chess, allowing computers to master the game by providing only a set of rules and a (not necessarily complete) set of parameters.[9] As computers become more powerful, there are new opportunities to incorporate the algorithms into other fields of science, and to use the resulting knowledge to

Image courtesy of Argonne National Laboratory.

accelerate progress with less expense (with respect to time, money, or other resources) via a 'quick win' or 'fast fail' process. Machine learning techniques have become widespread in fields such as genomics, drug design, engineering, particle physics, and more. Since many of its terms are not yet widely used in catalysis science, this brief guide provides some key definitions and distinguishing characteristics.
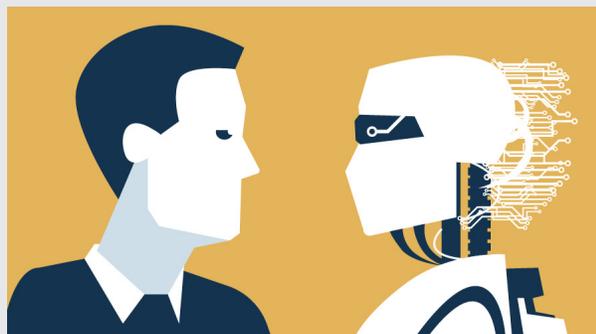
Machine learning algorithms implement statistical learning theory to parse data, learn from it, and make informed decisions based on what has been learned. It is an artificial intelligence (AI) process, in which "learning" is achieved by identifying a network of relationships within a data collection. *Deep learning* is a subset of machine learning, in which an algorithm improves itself and is capable of learning by using its own "computing brain". This process resembles (at least superficially) how a human brain perceives a phenomenon, thinks about it, then draws a conclusion. Other variations of machine learning include *unsupervised*[11] and *correlative*[12] *learning.* In the former, the underlying algorithms rely on correlations drawn from a dataset by inferring a function that connects the data (the "unlabeled" response). The latter relies on neuron-like responses from similar patterns that help the learning process to converge faster. All of the above variations are computationally intensive, and rely on large data sets to identify weak, but significant, correlations. These approaches to voluminous data sets face four 'V' challenges: *volume (the amount of data), variety (differences in the data), velocity (speed to obtain or access the data), and veracity (reliability of the data).* A large data collection is essential so that data analytics can reveal otherwise hidden trends and connections, supply missing data or identify anomalies,[13] and reduce computational costs relative to more conventional approaches.[14]

of the catalytic material. For example, in a typical solution-phase synthesis of colloidal metal nanoparticles, the chemical components include metal-containing reagents, solvents, and ligands/surfactants that modulate growth and stabilize or destabilize intermediates and products. Adventitious impurities and poorly characterized or even unknown intermediates that form transiently during the synthesis can also influence the reaction pathways and the ultimate catalyst structures. Additional details on synthesis are explored in this report by Panel 4 and in the U.S. Department of Energy (DOE), Office of Science, Basic Energy Science (BES) report, *Basic Research Needs for Synthesis Science for Energy Relevant Technology May 2016.*[15]

The complexity of an operating catalytic system implies that any single experimental tool or methodology is incapable of describing all of its diversity and dynamic behavior. Multiple, distinct experimental approaches, each sensitive to a particular part or property of the system, are generally required. For example, X-ray absorption spectroscopy and pair distribution function (PDF) analysis of X-ray or neutron scattering probe the average local structures of catalytic sites, while IR and NMR spectroscopies can reveal the speciation of reacting molecules. Electron microscopy images reveal atomic-level changes in morphology, while X-ray absorption and emission yield information about electronic states. The results from each type of analysis are typically combined in *ad hoc* ways. For example, a small series of catalysts may be compared to infer how systematic variation in specific parameters (such as composition, size, structure, state, etc.) impact catalytic performance. Such series, as well as carefully-designed model systems, can help us to discern structure-function relationships. Insights are consequently constrained by the small numbers of samples. A very large number of different materials and/or series must be explored in order to elucidate the many, intersecting relationships between different parameters,

MACHINE LEARNING DEFINITIONS FOR CATALYSIS SCIENCE (CONTINUED)

Data analytics

Machine/deep learning techniques rely on Artificial Neural Networks (ANN). Based on non-linear fitting algorithms, these ANNs can be very powerful because of their adaptive structures, relatively easy training, and tunable training parameters. Different types of ANN algorithms include the back-propagation neural network (BPNN), the general regression neural network (GRNN), the extreme learning machine (ELM), and most recently, the deep neural network (DNN), which has become very popular with the data science community due to its high learning capacity. A recent review summarizes how neural networks may be used in catalysis science.[16] For example, they have helped to identify the best catalysts for specific reactions (such as the photocatalytic degradation of 17α-ethynylestradiol by TiO_2),[17] to connect structure to function (e.g., in the optimization of a Cu-Zn-Al-Sc mixed oxide for methanol synthesis),[18] and to identify missing or new reaction steps and intermediates (e.g., finding new global minima for isomers of Au clusters).[19]

Applications of machine learning to catalysis science are still at a nascent stage. There are two main (and very significant) hurdles: (a) the lack of large amounts of data, either experimental or computational, in readily available (i.e., machine readable) form; (b) the large number of variables associated with problems in catalysis, coupled with not-so-clear correlations between these variables and catalyst properties that are necessary to train neural networks. In the past decade, both difficulties have been partially overcome by the development of new experimental and theoretical techniques that have expanded the amount of available data, as well as new computer architectures for better data storage, access and statistical analysis, but there is clearly much more to do.

Data interpolation

Digital inpainting and compressive sensing techniques are both essentially interpolation techniques that allow us to obtain missing information. *Digital inpainting* can generate a small portion of missing data, using background information.[20] As the name implies, it has historically been used to restore images. In catalysis, it can be used to augment incomplete data sets. *Compressive sensing* (also called compressed sensing, compressive sampling, and sparse sampling) refers to signal processing that helps to acquire and reconstruct missing signals, or data.[21,22] The underlying principle is that sparse (i.e., subsampled) data can be recovered through optimization. In addition, given information about the sparsity of the data/signal, signals may be reconstructed after intentionally recording even less data (hence the term compressive sampling). For example, if acquiring a high resolution electron microscopy image could damage a fragile catalyst material, then a lower resolution image can be acquired and its resolution subsequently improved. In a similar fashion, these techniques could also be used to recover sparse data in a collection of experimental or theoretical data such as missing structures, or reaction steps, and they can be applied to image and *in situ* structure recognition.

but there are limits to our ability to recognize patterns and find functional correlations in the data. The challenge is to systematize both the information and its interpretation. Since catalysis data is typically very heterogeneous, it will be challenging to assemble this information, to create interfaces that make the data sets available for computational analysis, and to train the algorithms by gradually increasing the complexity of the catalyst systems. The robustness of this approach and its ability to lead to more encompassing theories that can guide simulations to other solutions will also depend critically on the breadth of the series of catalysts explored. Initially, the most difficult aspect of training the models is expected to be the scarcity of usable data and their uneven (or unknown) reliability. Even after integrating the enormous amounts of existing information on catalysis, the field is expected to be data-starved compared to other emerging applications of machine learning in the near future.

For theoretical simulations of catalysts at the atomic scale, central challenges are the need to compute accurate energies, and to sample enough configurations/dynamical time steps to obtain accurate free energies. Traditionally, this has meant undertaking a large number of computationally intensive electronic structure simulations, which scale poorly with system size/complexity. In addition, it can be challenging to identify reasonable atomic-scale structural models to simulate, and to decide which reaction pathways to include. The number of possible configurations and reactions increases very rapidly with the complexity of the catalyst and the reactants/products. Furthermore, local catalyst structure and gross morphology often change with

exposure to the reactive environment, due to intrinsic metastability as well as fluctuations in the environment. Typically, the structures of interfaces that have been identified as most stable are assumed to be most relevant in catalysis. They are often calculated using unrealistically simple conditions (e.g. without a support or solvent). It can be difficult to correlate the properties of such models with experimental results, particularly for *in situ* measurements. Conclusions drawn from these simulations, such as the relative viabilities of computed mechanisms, may be overly simplified, ambiguous, or even incorrect. It is also extremely challenging to model accurately the effect of solvents at complex interfaces, including at solid surfaces, in confined spaces, and within enzymes. Currently available techniques do not reach the level of statistical mechanical sampling required for convergence, and therefore for accurate estimation of free energies. This issue also highlights the need for improved theoretical treatments of entropic contributions.

RESEARCH DIRECTIONS
Discover New Correlations within Large Datasets

Any individual study of a given catalytic process or system explores a relatively narrow combination of catalyst formulations, catalyst properties, and reaction conditions. A much broader parameter space can be explored by compiling results and insights from many distinct, and (preferably) diverse studies. Combining multiple studies using data science will, in principle, allow us to: (i) identify the existence of gaps in our knowledge about catalyst performance; (ii) extract important information only available in the larger dataset; and (iii) use this information to guide efficient new experimental and theoretical efforts. Achieving each of these goals will require new infrastructure to generate, assemble and connect different types of available data, to extract useful information from it, and to identify functional relationships in multi-dimensional spaces. New methods must be developed to harmonize and integrate data, and to input and extract the needed data efficiently. Only then will machine learning algorithms be able to mine these massive datasets to find new relationships.

To exploit the benefits of data-driven approaches, individual tools and procedures will need to be integrated with the databases, and conventions must be established for storing and sharing the relevant data and metadata (i.e., the relationships between data),[24,25] including the locations of null (missing or unknown) data that are critical for model testing. The metadata linking different observations are key to being able to define experiments in ways that contribute to a broader understanding of problems in catalysis. For example, the metadata needed to establish decision trees for "synthesizability" of catalytic materials are very different from the metadata needed to perform sparse sampling of spectra or images, or to accelerate atomic-scale simulations of catalysts and reactions. A key aspect is establishing and optimizing different domain/approach-specific metadata conventions, so that they provide a basis for creating the descriptive features used in decision-making, image reconstruction, materials selection, classification or machine learning regression.

High throughput methods in theory and experiment can play critical roles in ensuring that a larger fraction of catalyst synthesis efforts is directed towards structures that are more likely to be accessible/synthesizable, or which are likely to generate the most new insight. For example, traditional catalyst synthesis is optimized to maximize the number of active sites based on detailed studies that lead to a hypothesis about the nature and origin of the active sites, followed by a series of experiments aimed at varying their abundance. In contrast, high throughput mapping of catalyst activity and properties over a broad range of synthesis parameters could enable data-driven prediction of optimal synthesis parameters. Furthermore, integration of synthesis models with complementary data models that establish relationships between synthesis parameters and resulting structures/ morphologies could result in strategies for data-driven identification of active sites. More generally, high throughput studies will help to address data scarcity issues in catalyst science.

Key goals in catalyst characterization and testing for the next decade are the generation of better images and/ or improved spectra in shorter sampling times, with less interference between the measurement method and the material being studied. The application of data science tools also has the potential to enhance insights from the use of individual research methodologies applied to a given catalyst system, by expanding the limits of time resolution and sensitivity.[26,27] For example, intelligent sampling methods can overcome a longstanding challenge that limits the effectiveness of scanning transmission electron microscopy (STEM) in catalysis research (see Figure 5.1). During the measurement, the electron beam can significantly alter the catalyst structure and/ or reaction being observed. The electron dose, and hence the perturbation, can be minimized by using sparse or subsampling approaches based on Bayesian statistics, in which the measurement strategy is optimized

through machine learning. In this way, the same level of detail can be derived from fewer observations, resulting in a lower integrated dose, and improving the fidelity of the observation. Similarly, for data intensive methods such as spectroscopic imaging, ptychographic (scanning diffraction microscopic) imaging and *operando* arrays of measurements, intelligent sampling methods can reduce data requirements by several orders of magnitude, potentially yielding increased speed and time-resolution without loss in resolution or quality, or by increasing the sensitivity/resolution of the measurement at a given data acquisition rate. Such advances will allow researchers to undertake smarter experiments, study dynamic and transient phenomena (as described in Priority Research Direction 2) in much greater detail, and use finite resources (such as those available only at large scientific user facilities) much more efficiently. New instruments must be designed to create machine-readable data that can be readily ingested by data science algorithms, and that in turn can be controlled by signals from those algorithms to allow for tight coupling between the results that emerge from the analysis and decisions about the next set of measurements.
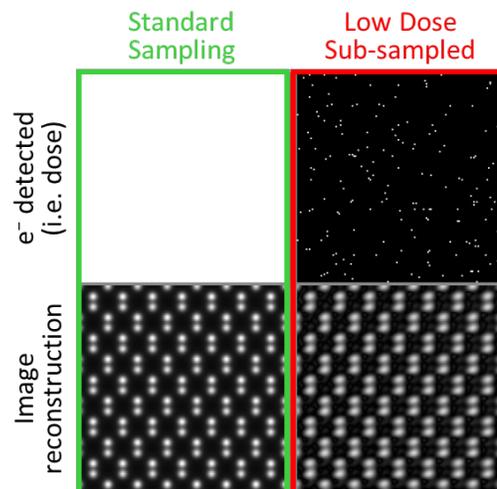
Figure 5.1. Representative reconstructions of atomically resolved image of GaAs. In the top row, white pixels represent locations where >1 electrons were detected. Image courtesy of Nigel Browning (Pacific Northwest National Laboratory).

Couple Disparate Datasets to Identify Emergent and Mesoscale Phenomena
Individually, the various types of information (spectroscopy, imaging, reactivity, theory, and simulation) about catalytic systems describe the complexity of real catalyst systems only partially. Furthermore, many spectroscopy measurements are performed on model catalysts *in situ* or even *ex situ*, rather than on real catalysts under *operando* conditions. Similarly, theoretical models often neglect particle size effects, support effects, etc. However, combining all of the individually inadequate measurements and calculations could allow us to formulate new hypotheses about structure-function relationships. This approach will also lead to the discovery of phenomena which are manifested as a result of the full system complexity. For example, species that act as catalyst promoters or poisons may be present only transiently, under operating conditions.[26,28] Data science approaches will therefore aid in identifying and describing the emergent and mesoscale phenomena that were the focus of Priority Research Direction 1, such as the roles of "spectator" species or support and/or solvent effects.[29] Coupling disparate types of data will be facilitated by integrating synthesis, characterization, and modeling in multi-modal experiments,[30] such that disparate data are collected from simultaneous measurements on the same system. This approach is illustrated in Figure 5.2. The ultimate goal is a more effective, versatile, and scalable integration of different observations, without making compromises (or allowing for better compromises) between different techniques used to make observations on the same sample.

SIDEBAR 2. SOLVING THE STRUCTURES OF CATALYTIC NANOPARTICLES USING MACHINE LEARNING

Tracking the structures of catalysts as they evolve under reaction conditions is a challenge, due to the paucity of experimental techniques that can measure the number of metal atoms and the distance between them with high precision, in real time. A supervised machine learning (SML) method deciphered the three-dimensional structure of Pt nanoparticle catalysts on-the-fly from X-ray absorption near-edge spectra (XANES).[26] The method was trained using a dataset consisting of *ab initio* XANES simulations. Application of the method to the *operando* spectra of nanocatalysts revealed previously "hidden" relationships between their geometries and subtle features in the XANES. The technique can be used to monitor the evolution of nanoparticle structure in time and in response to changes in reaction conditions, and to potentially correlate these changes with catalytic activity and selectivity.
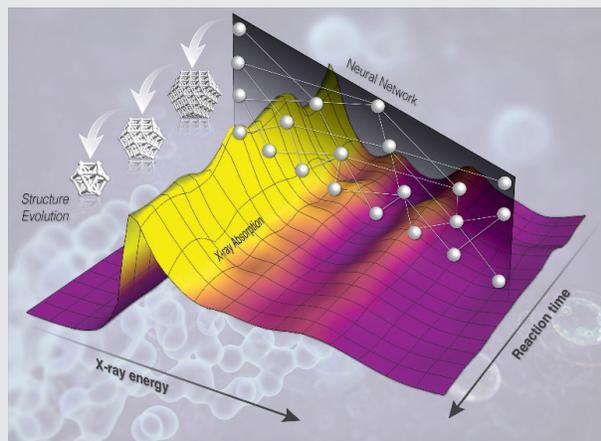
Sidebar Figure 5.1. A supervised machine learning (SML) method enabled fast, "on-the-fly" determination of the three-dimensional structure of Pt nanoparticles. The colored curves are synchrotron X-ray absorption spectra collected in real time. The neural network (white circles and lines) converts the spectra into geometric information (average nanoparticle size, shape, and morphology), giving a structural model corresponding to each spectrum. Figure courtesy of Anatoly Frenkel (Stony Brook University).
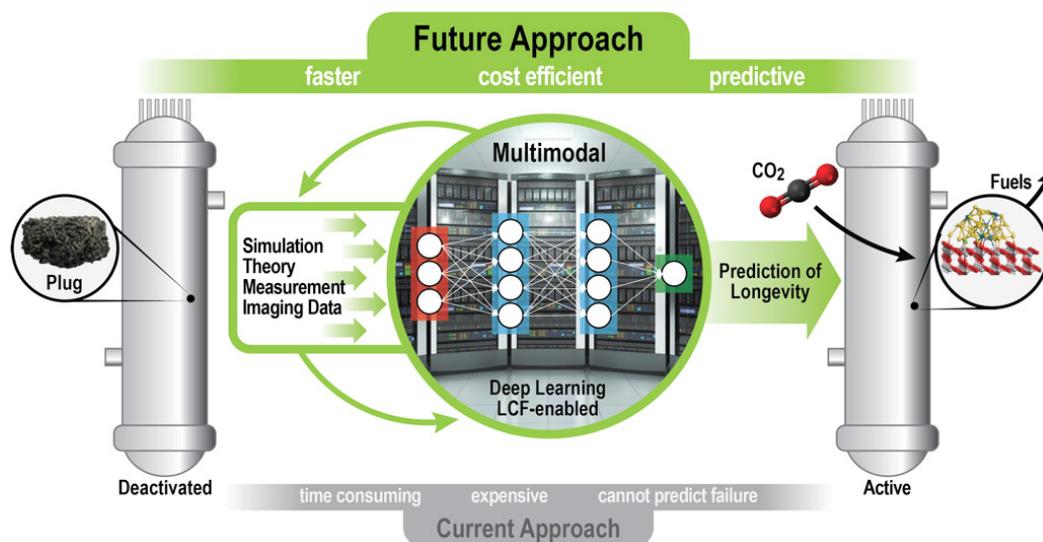
Figure 5.2. Multi-model data science enabled by Leadership Class Facilities (LCF-enabled) and illustrated here for the catalytic hydrogenation of CO$_2$. It can be used to integrate disparate observations and provide enhanced predictive models for catalyst dynamic behavior including activation and deactivation, leading to robust and long-lived, low-temperature and pressure catalytic conversions. Image courtesy of Pacific Northwest National Laboratory.

A promising path to achieve this type of integration is to couple data acquisition with analysis in real time, rather than conducting analyses after the conclusion of the experiments. The benefits of such an approach could be particularly important for high-throughput catalyst synthesis and characterization, including performance testing, by allowing data analysis to be conducted with machine learning models and optimization tools such as genetic algorithms. The result could be automated self-optimization of the synthesis of novel catalyst targets. As databases of computed physical and chemical properties of molecules and materials expand and simulations become faster, the approach could be extended to include fingerprints based on theoretical simulations present only in databases or, even calculated "on the fly" as illustrated in Sidebar 2.

In principle, merging disparate data from a wide variety of sources through machine learning-integrated algorithms could also facilitate data-mining and feature extraction to discover new relations between catalyst functionality, characterization, and simulations. Obviously, this expectation assumes that large and meaningful databases can be assembled. Similar tools could be applied to accelerate the synthesis of completely new catalysts. For example, integration of an automated microfluidic nanoparticle synthesis platform with a suite of on-line characterization tools would enable real-time monitoring of nanoparticle size, shape, dispersity, and reactivity, as the input variables are systematically modified. This approach would generate immediate feedback used to modulate the synthesis conditions. In turn, such processes will generate large amounts of data, for which machine-learning could be used to correlate reaction variables with synthesis pathways and efficiently identify parameters needed to achieve targeted catalyst structures.

Integrate Data Science, Experiment and Theory to Predict New Catalysts and Reactions

Data science approaches will complement the indispensable hypothesis-driven approach that allows researchers to formulate and rigorously test concepts in catalysis. One new frontier is text mining for catalyst synthesis conditions: recent examples have emerged for materials closely related to catalysis.[31,32] Other possibilities include the prediction of electronic and steric properties for organometallic active sites,[33] parameterization of ancillary ligand effects,[34] and descriptor-based parameterization of transition states.[35] Integration of high throughput screening with data science approaches can lead to the discovery of entirely new catalysts and catalytic reactions (see Sidebar 3).

SIDEBAR 3. A DATA-RICH PLATFORM FOR DISCOVERING NEW CATALYSTS AND CATALYTIC REACTIONS

An automated reaction discovery system was designed and implemented for the discovery of new catalytic reactions and, simultaneously, effective catalysts for these novel transformations, using high throughput screening.[36] Automated analysis of the reaction outcomes is facilitated by using reactants with substituents chosen to give unique mass spectral fingerprints. In control experiments, the system identified the products of known reactions. It then identified two classes of new reactions: a two-component alkyne hydroallylation of an alkyne, and a three-component alkyne diarylation. The platform is uniquely well-suited for experiments requiring complex mixtures of potential reactants.
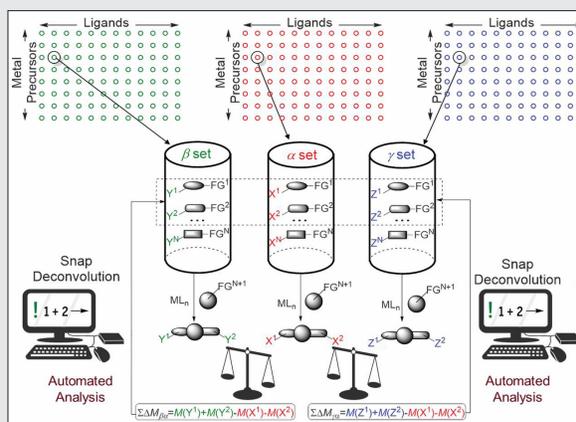

Sidebar Figure 5.2. The work flow for snap deconvolution involves three sets of reactions in 96 well plates with one catalyst combination per well and 3 × 15 reactants containing three sets of marker substituents with distinct masses. After chromatographic separation, masses are analyzed to identify differences that correspond to unique combinations of reactants combining in new reactions. From K. Troshin and J. F. Hartwig, Snap Deconvolution: An Informatics Approach to High-throughput Discovery of Catalytic Reactions, *Science* 357, Issue 6347 (2017) 175. DOI: 10.1126/science. aan1568. Copyright © 2017, AAAS. Reprinted with permission from AAAS.

Theory and simulation have become indispensable tools in catalysis science, applied to atomistic modeling of reactivity, kinetics and transport. Linear free energy relationships have helped to identify simple reactivity descriptors,[37,38] and correlations between them have provided guidance on the critical independent parameters that control catalyst performance. Cheminformatics techniques, as precursors to modern data science, have led to foundational concepts such as energy scaling relationships.[39,40] Data science can allow us to extract the correlations which underlie structure-function relationships in catalysis, using existing information. In the next decade, hybrid approaches will emerge in which high performance simulations and data science complement each other. Machine learning is already helping to create better DFT functionals,[41] and to extend their use to compute free energies (see Sidebar 4).

## SIDEBAR 4. COMBINING DFT AND NEURAL NETWORK POTENTIALS TO COMPUTE BINDING ENERGIES

The binding of reactants and intermediates to catalyst surfaces is a key step in their activation for reaction. Adsorbate free energies are therefore fundamental quantities in the microkinetic modeling of catalytic reactions. DFT-based approaches provide access to only the 0 K components of the free energies, while approximate models are typically used to describe finite-temperature contributions that require assessment of coverage-dependent configurations. The reliability of several popular approximations (harmonic oscillator, hindered translator, or two-dimensional ideal gas) was benchmarked against free energies extracted from exact quantum mechanical solutions for translational energy states accessible to monoatomic adsorbates such as H, C, N, O, and S on the Pt(100) and Au(100) surfaces.[42] The approach can ultimately be extended to the calculation of accurate free energies for arbitrary adsorbate potential energy surfaces (PESs) at moderate computational cost, by combining DFT and neural network potential energy sampling.
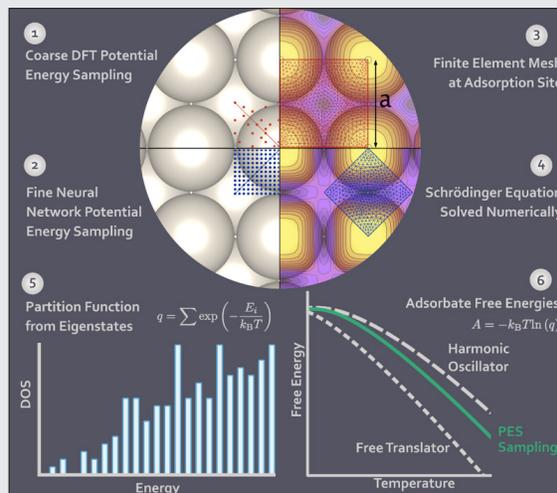
Sidebar Figure 5.3. Protocol for computing full adsorbate potential energy surfaces. Adapted with permission from *ACS Catalysis*, Benchmark First-Principles Calculations of Adsorbate Free Energies, A. Bajpai et al. Copyright © 2018, American Chemical Society.

Figure 5.3 illustrates how data science could be used to bridge areas of traditional catalysis inquiry across scales. For example, deep learning approaches can be used to: (i) estimate thermodynamic data with accuracies similar to those obtained from quantum chemistry calculations,[43] via database mining; (ii) represent energy surfaces in molecular dynamics/Monte Carlo (MD/MC) simulations, in lieu of classical potentials;[44,45] and (iii) generate microkinetic models that can be solved for a large number of equations over longer time and length scales than traditional methods.[46,47] At the same time, rapid growth in atomistic simulation software and high-end platforms will enable the application of electronic structure methods to systems with up to 10^3 atoms, and millions of configurations; considerable growth in capabilities is anticipated over the next decade.[48] Finally, while current models often neglect cooperative and dynamic effects that arise in systems with multiple reactants, products and active sites; at high temperatures and pressures; and in the presence of solvents or confinement effects; these features can in principle be incorporated into data science models. Such models would need to be trained using enormous amounts of data, assuming appropriate databases exist.
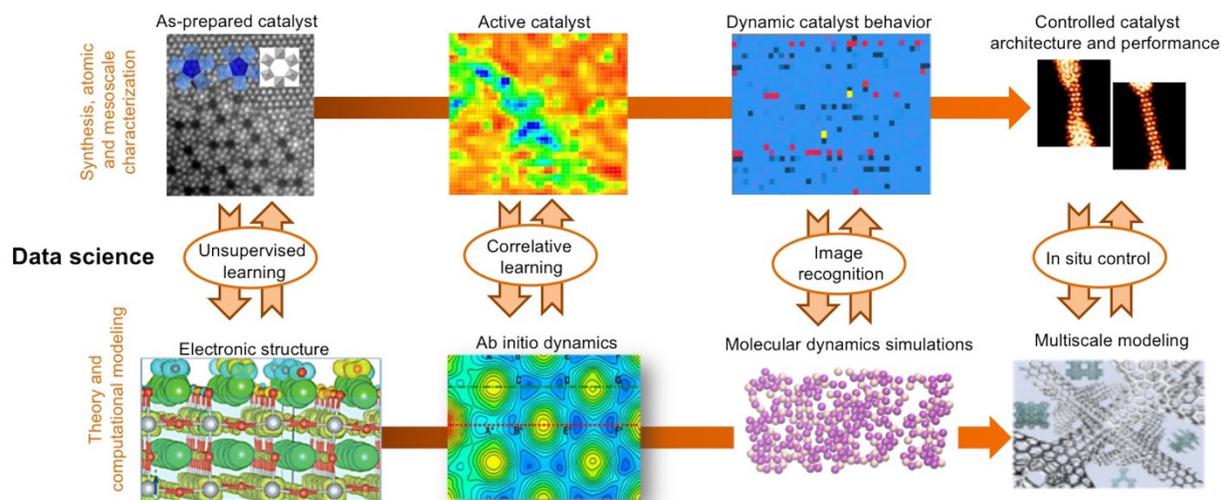
Figure 5.3. Schematic representation of how data science bridges experiment, theory, and simulation across multiple size and time scales. Image provided by Olga Ovchinnikova (Oak Ridge National Laboratory).

Ultimately, we expect data science to generate not just interpolations but robust predictions for new catalysts. *It is critical to reflect on how to integrate data science with hypothesis-driven research so data science can inform us about the depth of our knowledge for a given catalytic system and identify gaps in our understanding.* The use of deep learning with uncertainty quantification is also likely to be important to identify where to deploy advanced simulations most effectively to fill knowledge gaps and correct erroneous predictions based on existing models/data (as described in Priority Research Direction 3). Advances in both data science and high-performance computing will lead to more complex models and catalytic phenomena, allowing new levels of hypothesis-driven research enabled by versions of machine learning grounded firmly in physics and chemistry.

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Workshop Panel Reports

The *Basic Research Needs for Catalysis Science to Transform Energy Technologies* workshop was structured around four panels, which focused on the following topics:

PANEL 1: DIVERSIFIED ENERGY FEEDSTOCKS AND CARRIERS

PANEL 2: NOVEL APPROACHES TO ENERGY TRANSFORMATIONS

PANEL 3: ADVANCED CHEMICAL CONVERSION APPROACHES

**PANEL 4: CROSSCUTTING CAPABILITIES AND CHALLENGES:
         SYNTHESIS, THEORY, AND CHARACTERIZATION**

Each panel produced a report focused on the status of the field, scientific challenges and opportunities, and possible impacts. The reports presented here formed the basis for identifying the five Priority Research Directions (PRDs).

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Panel 1 Diversified Energy Feedstocks and Carriers

The landscape of resources available in the United States today is changing. Efficient and effective use of emerging feedstocks, such as shale gas, biomass, and waste streams, for the synthesis of fuels and chemicals provides numerous opportunities to diversify and protect our national energy supply chain. The transformation of methane to methanol, higher alkanes or olefins, highlights the potential of shale gas as a chemical feedstock that could overcome certain technical barriers associated with use of synthesis gas as an intermediate. Biomass can be converted into platform molecules that are precursors to fuels and high-value chemicals. Chemical transformations of high energy-content wastes, such as hydrocarbon polymers, could provide new routes to fuels and chemicals enabled by advances in catalysis. Concurrently, there have been significant advances in strategies for synthesizing increasingly complex catalytic architectures, for observing these architectures using spectroscopic and crystallographic tools, and for describing structure, function and electronic properties using theoretical approaches that can be deployed to tackle significant hurdles in utilizing these resources efficiently.

CURRENT STATUS AND RECENT ADVANCES
A New Landscape for Feedstocks

The emergence of shale gas as a principal carbon source, the development of cellulosic ethanol processes and related conversion of biorenewable feedstocks, and the emergence of wind and solar energy as major components of the energy landscape, are having significant economic consequences for the fuels and petrochemicals markets and for the energy independence of the United States and of the world at large. These shifts in feedstock access and costs require a concomitant shift in how we frame the fundamental scientific challenges and needs in the catalysis field towards strategies that are likely to bring the greatest societal impact.
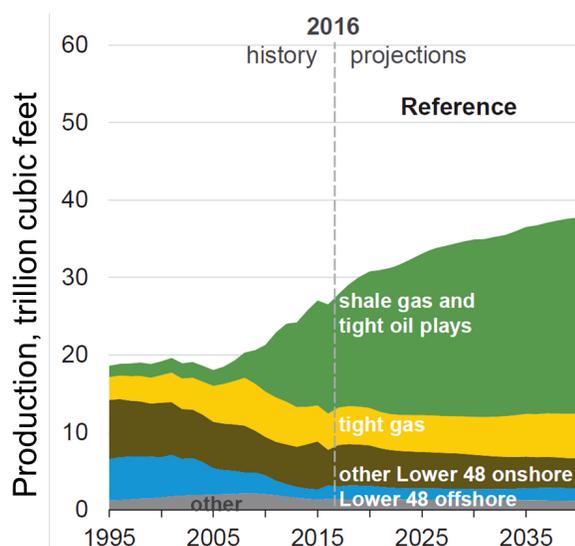

Figure 1.1. Historic and projected dry natural gas production in the United States. Source: U.S. Energy Information Administration, Annual Energy Outlook 2017 Projections to 2050.

The U.S. energy economy has relied significantly on crude oil in the past, with material but limited contributions from natural gas to power generation, transportation fuels, and chemicals. More recently, the widespread deployment of hydraulic fracturing and horizontal drilling technologies has led to the emergence of natural gas as the most significant energy source in the United States, followed by crude oil and natural gas condensates.[1] Together, these sources provide ~60% of energy usage in the United States. Since 2007, shale gas production has increased from less than two trillion cubic feet energy equivalent to nine trillion per year, equivalent to nearly 30% of total natural gas production, with future projections rising far above this level (Figure 1.1). Shale gas's light composition (C_1–C_3) is distinct from the broader range of hydrocarbons obtained from petroleum refining, making ethylene abundant but creating new challenges to the petrochemical supply chain.

Biomass-derived fuel production has concomitantly increased from about 720 TBtu/yr in 2006 to 2260 TBtu/yr in 2016.[1] Ethanol fuel production continues to be dominated by conventional starch-based ethanol, but there has been a noticeable increase over the past five years in production of advanced biofuels, such as cellulosic biofuel (Figure 1.2). Such advanced biofuels employ technologies that allow the deconstruction and conversion of woody crops and agricultural residues and waste, instead of carbohydrates and vegetable oils derived from arable crops like corn and sugar cane. Concurrently, the field has come to understand the potential and the formidable challenges inherent in the commercial practice of lignocellulosic biomass conversion to fuels and chemicals. The current approaches are based on the concept of an integrated biorefinery, in analogy with those that have driven the improvements and the integration of crude oil refineries over the last century. Such strategies seek to intensify process integration and to produce complex product streams that address diverse market needs at the scale required for significant impact on the use of energy and petrochemicals by their intended markets. For example, one strategy uses a biomass-derived γ-valerolactone (GVL) solvent to produce: (i) a high-purity cellulose product; (ii) furfural, a valuable platform chemical from hemicellulose, which can be used to produce value-added chemicals; and (iii) a solid lignin product that preserves the functional linkages of lignin in the native biomass feedstock and can also be developed into specialty chemicals (Sidebar 1).[2] The recent history in this area illustrates the formidable challenges inherent in such approaches because of the diverse chemical structure of the biomass constituents (i.e., cellulose, hemicellulose, and lignin) and the large volumes of solvents and solids involved in handling biomass-derived streams.

The energy content of municipal solid wastes (MSWs), including plastic wastes, provides potential for a more efficient use of national resources. The high energy content of plastic solid wastes (PSWs) could be recovered through selective conversions to higher value materials that make use of their highly catenated carbon-rich structures. Catalytic approaches to selective carbon-carbon bond cleavages can produce liquid hydrocarbons that drop into downstream petrochemical processes. Alternatively, some organic wastes may be transformed into smaller molecules, often as synthesis gas streams, that can then be converted in subsequent processes after purification and adjustments to their H_2/CO ratios. These waste streams are often mixed with biomass or crude oil during processing to provide outlet streams with higher energy content. MSW-based streams, in contrast with those from dedicated manufacturing facilities, pose inherent challenges brought forth by their diverse and fluctuating chemical contents and states of matter (e.g., liquid-solid ratios, volatility) and by the requirements that they be collected and separated into chemically compatible components. Such challenges inspire innovative and holistic approaches to the entire waste-handling infrastructure and discovery of new catalytic methods for chemical conversions, either involving homogenization via synthesis gas or CH_4 intermediates, through new catalytic separations, or by direct selective conversion into chemicals or fuels.
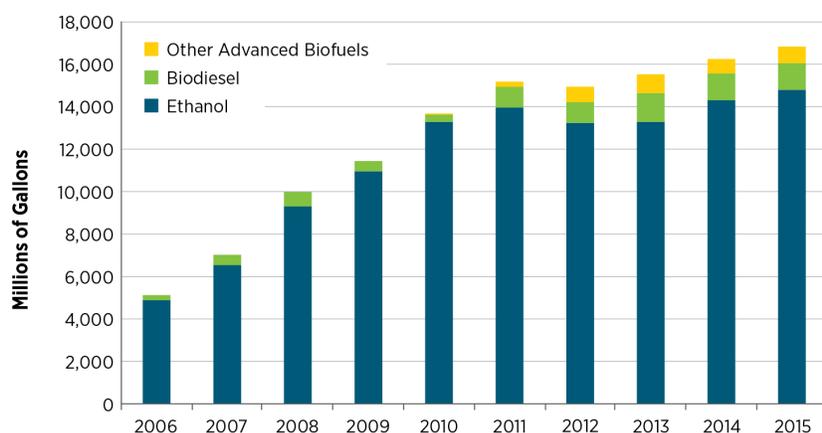
Figure 1.2. Recent trends in the production of ethanol, biodiesel, and other advanced biofuels (including biogas, cellulosic diesel, cellulosic ethanol, imported sugarcane ethanol and other advanced ethanol, naphtha, renewable diesel, renewable gasoline, renewable heating oil, renewable compressed natural gas, and renewable liquefied natural gas). Reprinted with permission from the National Renewable Energy Laboratory. Full report available at https://www.nrel.gov/docs/fy17osti/66995.pdf.

Each of these emerging feedstock resources represents a distinct challenge to catalysis science. In a general sense, natural gas and biomass represent extremes in functional group content and typical oxidation state of carbon in the feedstocks, and specifically in catenation, oxygen content and the prevalence of unsaturated moieties. Natural gas contains small, highly reduced molecules (methane, ethane, propane). As a result, its conversion to liquid fuels or chemicals requires functionalization of saturated molecules. Such processes, which involve carbon-carbon bond formation, are typically endothermic, whereas thermodynamically favorable oxidative processes pose considerable kinetic challenges. In contrast, biomass feedstocks contain hydroxyl-rich sugar-based cellulose and hemicellulose and aromatic-rich

SIDEBAR 1. LIGNOCELLULOSIC BIOMASS OFFERS AN OPPORTUNITY TO REPLACE CRUDE OIL AS A SOURCE OF CHEMICALS

Lignocellulosic biomass can be fractionated into its main components to replace petroleum-derived chemicals used in daily life. In order to accomplish this with high energy and material efficiencies, it is important to achieve direct conversion of the complex biomass molecules into target products, while forming few or no byproducts. Selective bond breaking and forming reactions are required. Chemical catalysis has achieved reasonable degrees of chemoselectivity, such as selective hydrogenation of C–C vs C=C and C=C vs. C=O, and selective activation of allylic and other C–H bonds and secondary vs. primary C–H bonds. However, there are few examples of regioselectivity, which is the ability to distinguish bonds by their locations in a molecule and not by their chemical differences.

Sidebar Figure 1.1. Reprinted with permission of Alonso et al., **"Increasing the Revenue from Lignocellulosic Biomass: Maximizing Feedstock Utilization,"** *Science Advances*, **2017. Copyright © 2017 Alonso et al.**

Chemical catalysis can take lessons from enzymes, where there are many examples of regioselectivity. For example, α-hydroxylase CYP52 oxidizes the terminal carbon to carboxylate, ω–hydroxylase CYP102 oxidizes a subterminal carbon, and 12-hydroxylase selectively reacts at the C12 position. Incorporating such regioselective functionalities into abiotic systems will enable efficient upgrading of biomass molecules.

lignin functionalities. These streams require the net removal of O atoms and the formation of specific backbones and functionalities in order to address the energy density and volatility requirements for their use as fuels or in the synthesis of petrochemicals. In such cases, choices must be made as to whether, how, and where along process schemes to remove O-atoms and form C–C bonds, and whether the most effective reagents are H_2 generated on purpose (for processes such as hydrodeoxygenation, and C–O hydrogenolysis) or the carbon atoms (decarbonylation, decarboxylation) or hydrogen atoms (dehydration) already present in the biomass-derived feedstocks. Multicomponent MSW faces similar challenges, and even single-component streams require new catalytic methods for conversion to valuable products. The economic choices among these alternate strategies are specific to location and context, while the basic research needs must provide the enabling fundamental science that addresses the most effective catalytic choices for each specific deployment, as well as the limits of each strategy for each type of biomass feedstock.

Additional information on energy feedstocks can be found in the Technical Perspectives Resource Document that accompanies this report, under Topic 1, "Diversified Energy Feedstocks and Carriers."

SCIENTIFIC CHALLENGES AND OPPORTUNITIES
Conversion of Biomass and Biomass-Derived Products

A practical strategy in the efficient use of biomass is to convert it into platform molecules that can be subsequently processed into fuels and high-value chemicals. There are four classes of platform molecules that can be obtained in the initial chemical processing of biomass: (i) carbohydrates, (ii) polyols, (iii) carbohydrate or polyol dehydration products, and (iv) lignin monomers.[3] Examples of platform molecules include furfural, hydroxymethylfurfural, levulinic acid, gamma-valerolactone, 2,5-furandicarboxylic acid, and levoglucosenone. Numerous studies have been devoted to the production and downstream conversion of these molecules. Whereas the earlier focus has been on conversion of hemicellulose and cellulose, recent emphasis has moved into the conversion of lignocellulose.

Direct conversions of lignocellulose and related biomass to targeted products have advantages over multistep, energy- and resource-intensive deconstruction and reconstruction processes. However, such direct conversion routes place formidable demands on chemoselectivity and regioselectivity, and do so in very complex hydrodynamic environments, in terms of selecting reactants and transforming them into specific products. Achieving such selectivity requires the following:

☐ Understanding the mechanisms that control the reactivity of specific chemical bonds and protection of the specific functionalities that must be retained in products,

☐ Controlling the highly non-linear and complex mechanisms by which the diverse molecules (and the impurities) present in these mixtures interact with each other and with active sites, and

☐ Using transition-state formalisms that describe chemical dynamics in thermodynamically non-ideal and dense reacting media.

Biological catalysts provide some of the guidance needed to address these challenges. For example, the Δ^9 desaturase enzyme selectively catalyzes the oxidation of the carbon atom at a very specific location (the C9 position) in long unsaturated oxygen-containing molecules, while one of its mutants oxidizes the same substrate at the C4 position.[4] Similarly, acyl CoA dehydrogenase shows remarkable regioselectivity in β-oxidation of a fatty acid,[5] but can be genetically engineered to oxidize the terminal carbon selectively to produce α,ω-diacids.[6] Whereas oleate hydratase converts oleic acid to 10-hydroxyoctadecanoic acid (10-hydroxystearic acid) by adding an OH to the C10 position and a proton to the C9 position, 12-hydroxylase converts oleic acid to ricinoleic acid by selectively hydroxylating the 12-position of oleic acid, and Δ^{12}-desaturase converts oleic acid to linoleic acid by creating a C−C double bond between C12 and C13.[7] These enzymes achieve their selectivity through precise orientation of the substrate (reactant), sometimes involving amino acid residues situated well beyond atomic distances from the substrate binding site.[8]

Understanding the interactions between reacting molecules and the catalytic active sites that form the basis for such high selectivities and translating them to non-biological catalytic systems would offer unprecedented and selective chemical transformations. For example, achieving the one-step, high-yield conversion of glucose to 1,6-dialcohol or diacid could provide an alternate route for the production of nylon, while the effective conversion of glycerol to propenol intermediates ultimately oxidized to acrolein could provide a novel strategy to synthesize acrylates from renewable sources.

Such unique enzymatic specificity has not been fully transferred into non-biological systems, in spite of promising advances. The selective activation of C_6 moieties in biomass-derived molecules allows retro-aldol reactions to selectively cleave specific C−C bonds and to insert oxygen, thus accessing small molecules in higher yields and lower temperatures than possible previously.[9-11] A Ni(II) complex catalyzes sequence-discriminating hydrolysis of amide bonds next to serine or threonine functions in a polypeptide (Figure 1.3),[12] and regioselective oxidations of polyols, such as glycerol or carbohydrates, may be realized with a palladium(II) neocuproine catalyst and O_2.[13-14]

These abiotic examples are encouraging. Extension to other types of reactions and the generalization of these concepts are essential for enabling their deployments in high-intensity chemical processes that are relevant to the needs and low profit margins in fuels and large-scale petrochemical syntheses. They require a more fundamental understanding of the relationship between chemical interactions and reaction dynamics, as well as synthetic expertise. It is essential to couple structural information about biological molecules, accurate modeling of molecular interactions and energetics of chemical transformation, atomic-level structural characterization of abiotic systems, and atomically precise synthesis.
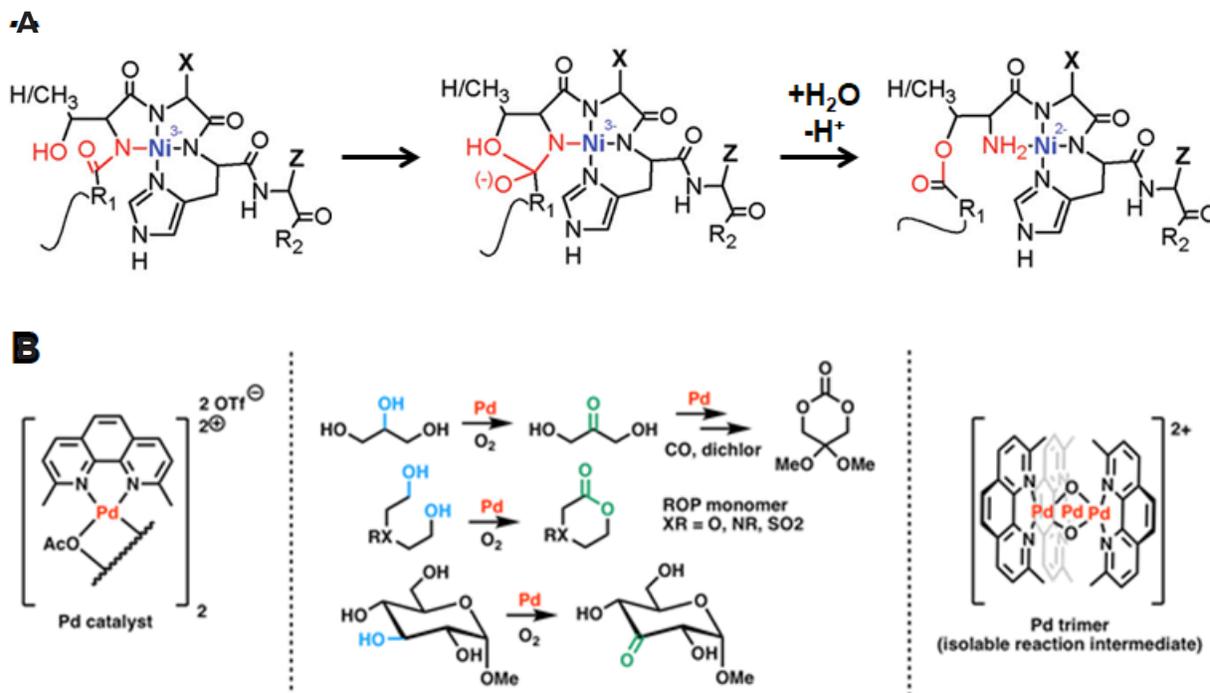
Figure 1.3. Examples of catalytic reactions demonstrating high regioselectivity. A) Ni(II)-catalyzed peptide hydrolysis of the R1-Ser/Thr bond in R1-(S/T)XHZ-R2 peptide sequences;[12] Reprinted with permission from *Inorganic Chemistry*, **July 2010, Sequence-Specific Ni(II)-Dependent Peptide Bond Hydrolysis for Protein Engineering: Reaction Conditions and Molecular Mechanism, Kopera et al. Copyright 2010, American Chemical Society. B) Oxidation of polyols to α-hydroxy ketones with air/O_2 using a cationic Pd neocuproine catalyst.[13,15] Reprinted with permission from** *Journal of the American Chemical Society*, **Oct. 2015, Catalytic Role of Multinuclear Palladium–Oxygen Intermediates in Aerobic Oxidation Followed by Hydrogen Peroxide Disproportionation, Ingram et al. Copyright 2015, American Chemical Society.**

Conversion of Shale Gas and Related Products

The need for high selectivity is essential for conversion strategies for more effective uses of natural gas components, including stranded gas. Current processes in practice are mediated by synthesis gas as the chemical intermediate to convert methane to chemicals and fuels; these strategies rely on reforming processes to form synthesis gas with the H_2/CO stoichiometry required for specific products. Synthesis gas processes are capital-intensive and suffer from energy inefficiencies brought forth by process integration and heat transfer requirements; they also benefit from economies of scale that require access to large methane supplies, making them ill-suited for small-scale deployment.[16] Direct conversion of methane to methanol, higher alkanes, or olefins would overcome these barriers. However, the challenges for these selective conversions are well known. The desired products are chemically more reactive than methane and react faster at lower temperatures than the saturated alkane reactants, thus leading to low yields of desired products. For example, methanol can be formed readily from methane, but preventing further reaction of methanol to undesirable products is difficult. In general, the challenge is how to cause the catalysts to activate the more stable bond without subsequent conversion of a weaker bond in the product. One strategy is to design catalytic centers that preferentially interact with the reagent compared to the product. This requires accurate modeling of interactions of products and reactants with the active site and its surroundings, and the emerging capability to synthesize the intended structures for such purposes.

As in the case of biomass feedstocks, examples from biological catalysts provide guiding principles; e.g., methane monoxygenases (MMO), present in bacteria, metabolize methane as a carbon source, selectively oxidizing methane to methanol. One type of monooxygenase (soluble MMO) uses a carboxylate bridged di-iron site to oxidize methane, and another (particulate MMO) contains one or more Cu centers (Figure 1.4).[17,18] MMOs and their homologs can also selectively oxidize diverse substrates, including propylene to propylene oxide. Catalysis by these enzymes requires selective access to active centers by methane and oxygen, the activation of O_2 to a form that would form one and only one C–O bond with the alkane, the rapid release of the methanol product, and the delivery of protons and electrons at appropriate points in the reaction cycle.

$$CH_4 + O_2 + 2e^- + 2H^+ \rightarrow CH_3OH + H_2O$$
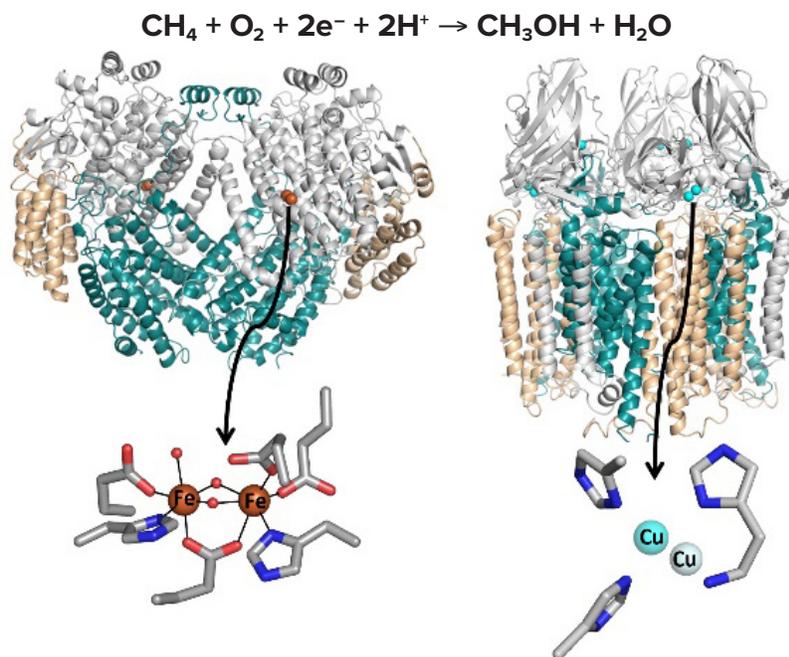
Figure 1.4. Biological methane oxidation reaction and structures of the iron- and copper-containing MMOs.[19] Understanding how the structures enable preferential methane binding and conversion to methanol, while preventing further oxidation, could lead to design of abiotic systems to achieve highly selective methane oxidation. Reprinted with permission from *Biochemistry*, March 2015, Enzymatic Oxidation of Methane, Sirajuddin et al. Copyright 2015, American Chemical Society.

The selective conversion of small hydrocarbons would impact many industrial processes and enhance the penetration of gas-derived condensates into the petrochemical and fuel markets. An attractive route for these transformations is oxidative functionalization. Many current processes, however, use oxidants other than O_2, which are more costly and often corrosive and which must ultimately be produced from oxygen via ancillary processes, leading to significant capital and operating costs as a result of process complexity and energy/atom inefficiencies. For example, the fifth largest chemical in production by mass (propylene oxide, nine billion kg in 2011) uses Cl_2, ROOH or H_2O_2 as alternate oxidants. In contrast, ethylene oxide can be produced via direct oxidation of ethylene with oxygen, but direct epoxidation with O_2 has not been achieved in practice for larger olefins that contain much more reactive allylic C–H bonds. It remains unclear how alternate oxidants circumvent the inherent hurdles associated with C–H bonds of different reactivity, another example of the incomplete knowledge about the differences in reactivity between hydroxy radical (HO•) and a metal-superoxo (M–OO•). Nature can provide guidance with the enzyme epoxidase. The monooxygenase enzyme squalene epoxidase catalyzes the insertion of an oxygen atom into the linear squalene molecule instead of its allylic C–H bonds to form 2,3-oxidosqualene, using O_2, NADH or NADPH and FAD.[20] A detailed understanding of the mechanism of this reaction could offer insight for developing strategies for abiotic catalysts.

While direct epoxidation of allylic hydrocarbons with molecular O_2 has not been demonstrated with practical selectivities, selective epoxidation of propene is feasible using molecular oxygen in the presence of a sacrificial reductant, such as H_2[21,22] or CO/H_2O,[23-25] but epoxidation selectivities are much lower without these sacrificial reductants.[26] A proposed mechanism involves the *in situ* generation of an alternate oxidant (H_2O_2, ROOH, or M–OOH). Although these routes circumvent the need to generate the oxidant separately, low efficiencies in sacrificial reductant utilization limit their commercialization potential. Understanding the reactions of O_2 and peroxide could lead to more selective catalysts that distinguish the sacrificial reductant from the reactant.

Oxidation of alcohols using homogeneous Cu-based catalysts, such as Cu/TEMPO (TEMPO=2,2,6,6-tetramethylpiperidinyl-N-oxyl), has demonstrated chemoselectivity. These catalysts can mediate the oxidation of primary hydroxyls in preference to secondary hydroxyls, and alcohol in the presence of sulfur/nitrogen-containing groups, for example.[27,28] The primary catalyst is the nitroxyl ligand, while the Cu center (or other transition metals such as Ru and Fe) functions to oxidize the hydroxylammonium species to nitroxyl. Although significant progress has been made with respect to functionalizing alcohols, selective oxidation of hydrocarbons remains a challenge. For saturated hydrocarbons, oxidation via free radical mechanisms remains the dominant pathway, and there have been few advances in controlling selectivity, especially regioselectivity.

In some cases, enzymes are able to achieve regio- and stereoselectivities much higher than available non-biological catalysts by using inexpensive reagents (e.g., O_2). However, biological processes typically operate at low substrate concentrations and, consequently, lack the volumetric efficiency and process intensities typical of large-scale chemical processes, thus incurring high costs associated with downstream separations. The field

of biocatalysis could benefit from development of methodologies to improve volumetric efficiency, as well as by extending the scope of possible processes through strategies that seek to couple biocatalysis with non-biological catalysis to create new multi-step processes and alternatives to cofactors and coenzymes.

Conversions of Hydrocarbon Polymers

The top five commodity polymers (polyethylene, polypropylene, polystyrene, polyvinyl chloride and polyethylene terephthalate) are made almost exclusively from fossil-fuel-based hydrocarbons. Their production currently consumes the equivalent of 6-8% of domestically produced oil and natural gas. From this, 300 million tons of plastic waste are generated worldwide each year. Three-fourths of all plastics are manufactured for short-term uses, such as packaging and disposable consumer products, and intermediate-term uses, such as textiles and electronic goods. Unlike recyclable glass or aluminum, recycling of many polymers is limited because their properties degrade. Chemical conversion to smaller molecules may be accomplished by pyrolysis or gasification, either through catalytic means or through thermal processes.[29]

Catalytic hydrocracking reactions may also be applied to depolymerization to fuel-sized hydrocarbon products. Early-metal hydride catalysts supported on silica, such as zirconium hydrides, are catalysts for C–C bond hydrogenolysis of polyethylene.[30] Alternatively, alkane metathesis combining polyethylene and petroleum ether provides waxes and liquid hydrocarbon products. This process involves a tandem, multi-catalytic sequence involving transfer dehydrogenation, olefin metathesis, and transfer hydrogenation to give a statistical distribution of hydrocarbon products.[31]

ADVANCES IN CATALYSIS AND RELATED SCIENCES

The last decade has seen significant advances in strategies for synthesizing increasingly complex catalyst architectures that achieve more precise control of atomic connectivity and of the outer-sphere environment around the binding sites. There have also been very significant advances in observing these architectures using spectroscopic and crystallographic tools, and in describing structure, function, and electronic properties using theoretical approaches. Taken together, these advances have enabled the more precise elucidation of what structures are required for catalytic function and the development of the synthetic protocols best suited for the assembly of such structures. A few illustrative advances are described briefly below.

Single Metal Atoms – The definitive identification of the presence and catalytic relevance of single metal atoms dispersed onto supports was recently achieved. These advances suggest that single metal atoms are stabilized at surface defects of supports, such as oxides[32] and carbon nitrides.[33] There are conflicting reports about the intrinsic reactivities of these single metal atoms, which have been found to be less[33,34] or more active[35] than metal nanoparticles or crystallites. Their higher reactivity for water-gas-shift reactions is well-documented,[35-37] and in some cases, such as acetylene hydrochlorination,[38] is uniquely high. The atoms in the host surface defects are not distributed symmetrically around the metal atoms or ions, thus offering opportunities to generate unique properties that cannot be obtained using metal centers in coordination complexes. There are related opportunities to tune the catalytic properties of these single metal atoms by controlling the type (chemical composition, stoichiometry, atom location) of surface defects. Devising methods to generate a high density of these defects, to characterize them, and to understand their chemical and thermodynamic properties and stabilities will be an important enabler of continuing advances in these strategies.

Main Group Element Catalysts – Main group element-based catalysts include boranes, phosphines, urea-based hydrogen-bonding structures, imidazolium salts, and frustrated Lewis acid-base pairs that act in concert to catalyze hydrogenation reactions. In these molecules, the acid and base moieties are separated by distances appropriate for the concerted stabilization of appropriate transition states (e.g., heterolytic H_2 activation), but too great for their mutual neutralization.[39,40] Although these catalysts are far less active in hydrogenations than traditional transition metal catalysts, their precise atom positions and the organic backbone that positions the acid and base functions offer opportunities to introduce more diverse functionalities at specific locations to confer cooperative effects for other catalytic transformations. More generally, metal-free catalysts have received renewed interest because of their ability to catalyze enantioselective reactions[41,42] and reactions of CO_2 with epoxides to form cyclic carbonates,[43] as well as to function effectively in a heterogenized form.[44] Organocatalysts can be synthesized with well-defined structures and conformations and their properties can be predicted by computation using first-principle methods.[45,46]

Biological Catalyst Mimics – Acid-base and multiple hydrogen bond cooperativity at the active site are hallmark features of specificity and activity for biological catalysts. This concept has been successfully introduced into both homogeneous and heterogeneous synthetic catalysts. For example, basic sites on the ligands of a metal complex have been designed to cooperate with the metal center in homogenous catalysts in order to activate and transfer hydrogen atoms, thus allowing the reduction of very challenging substrates such as esters, acids, amides, carbonates and even CO_2.[47,48] Concerted metalation-deprotonation (CMD) has emerged as an effective mode of C–H bond activation.[49] In such reactions, an electron pair on a ligand accepts the proton and a new M–C bond is formed. CMD has been used to functionalize C–H bonds of small molecules and for late-stage modification of C–H bonds in the synthesis of pharmaceuticals and fine chemicals.[50]

Catalysts with Multiple Functionalities – New synthetic capabilities have enabled the construction of active centers with multiple functionalities. For example, acid-base pairs can be formed on solid surfaces without mutual annihilation to effect enhanced reactivity in aldol condensation and cellulose-to-HMF conversion[51] owing to acid-base cooperativity.[52] In a related development, the activity of an amine group in a silica cage environment can be systematically tuned through the effect of polar or nonpolar groups separated by a few Ångstroms.[53] In homogeneous catalysis, multiple functionalities provide new strategies for conversions of hydrocarbons. For example, tandem processes that incorporate catalysts for alkane dehydrogenation and olefin metathesis have been developed.[54]

Confinement Effects – Theory and experiments have combined to shed light on the mechanistic details of confinement effects on the stability of transition states in heterogeneous catalysts with voids and channels of molecular dimensions. For acid-catalyzed reactions on zeolites, the effect of the void structure has been described in terms of structure-dependent charge reorganization (covalent) and electrostatic (ionic) interaction on the deprotonation energy of the acidic proton and the van der Waals contacts between the transition state and the void walls,[55,56] as well as by considerations of the balancing of activation entropies and enthalpies upon confinement.[57-59] The ability of a confined space to stabilize metal cations of uncommon oxidation states is also potentially useful and largely unexploited.[60]

Interfacial Perimeter Sites – There is now strong evidence that the metal-support oxide interfacial perimeter sites are catalytically relevant. For low-temperature CO oxidation, these sites permit CO adsorbed on the TiO_2 support to migrate and react with O_2 bound at gold particle surfaces or Au-support interfaces.[61] The presence of these sites is also shown to be necessary for the selective oxidation of propane to acetone,[62] for 2-propanol decomposition, and for acetic acid oxidation.[63] Another system illustrating the importance of such interfacial sites is found in biomass conversion where RhRe-based catalysts are used for the selective hydrogenolysis of cyclic ethers to produce α,ω-diols, as in the conversion of hydroxymethyltetrahydropyran to 1,6-hexanediol. Reactivity trends and results from DFT calculations suggest that hydroxyl groups on Re atoms associated with rhodium are acidic, owing to the strong binding of oxygen atoms by rhenium, and that these groups are likely responsible for proton donation leading to the formation of ion transition states.[64] The dependence of the catalytic properties of these sites on their structure and chemical composition remains uncertain, and the detailed reaction mechanisms and their involvement in other reactions have not yet been explored.

Unconventional Catalyst Materials – Pristine graphene structures possess unique electronic, optical, thermal, chemical, and mechanical properties quite distinct from other forms of carbon. Its high electronic conductivity has led graphene to be studied as a support in metal electrocatalysts.[65] Graphene oxide is the partially oxidized form of graphene, where oxidation introduces carboxylate, epoxy, and hydroxy groups. Thus, graphene oxide is an organocatalyst, and has been shown to be active for various mild oxidation and coupling reactions.[66] The extended two-dimensional structure of graphene and graphene oxide, the interphase between insulating graphene oxide and conducting graphene present in a reduced graphene oxide, and the radical-like character of carbon atoms at vacancy defects of graphene and reduced graphene oxide are potential sites with interesting chemical and catalytic properties that have yet to be examined in detail.

Other unconventional catalytic materials include carbon nitride (γ-C_3N_4), boron nitride (BN), metal organic frameworks (MOFs), and covalent organic frameworks (COFs). BN is structurally analogous to graphene and shows similar electronic and mechanical properties. Both materials have been explored as catalyst supports for thermal, photo-, and electro-catalytic reactions. MOF and COF[67] materials are new, well-defined three-dimensional structures that could extend the structural and compositional diversity of ordered microporous solids beyond zeolites. Their role in catalysis, especially as catalyst supports, is beginning to be explored,[68-70] but significant hurdles, imposed by the stability and reactivity of the organic linkages, remain a challenge under the conditions required for many catalytic reactions involved in the synthesis and conversion of large-scale petrochemicals and energy carriers.

Some less conventional catalysts have found applications in reactions relevant to biomass conversion. For example, metal phosphides are active for heteroatom removal in hydrodeoxygenation,[71] hydrodenitrogenation and hydrodesulfurization,[72-74] and hydrogenolysis of oxygenates.[75] Metal carbides are also active for hydrodeoxygenation of oxygenates[76,77] and for reforming of CH_4 with CO_2.[78] It is noteworthy that among metal surfaces, metal carbides deviate from the scaling relationship between binding energies of carbon-binding and oxygen-binding of adsorbates,[79] presumably because of their bifunctional nature, conferred by their M–C linkages.

Oxidation Catalysts – Significant progress has also been made toward understanding the catalytic mechanisms of methane oxidation enzymes, as noted above. The molecular basis for coupling the orderly delivery of protons, electrons, and substrates to the soluble methane monooxygenase iron active site has been elucidated[80] and the structure of the key oxidizing species in this enzyme has been identified by advanced time-resolved spectroscopic methods.[18] The active site of particulate methane monooxygenase has been identified[81] and this enzyme has been deployed in a prototype 3D-printed bioreactor.[82] The mechanism of reversible enzymatic methane formation has also been determined.[83] Beyond known enzymes, an explosion in genomic data is facilitating the discovery of enzymes with new catalytic sites.[84,85]

Progress has also been made in the development of new processes for the partial oxidation of light alkanes. Copper-exchanged zeolites exhibit remarkable reactivity for the selective conversion of methane to methoxy groups that can form methanol via subsequent hydrolysis in chemical looping strategies, but much remains to be learned about these catalysts, although the Cu sites in Cu-ZSM-5 seem to bear some resemblance to those in particulate methane monooxygenase.[86] New iridium catalysts for the borylation of light alkanes have also been developed.[87,88] In addition, main-group elements have demonstrated oxidation of methane, ethane and propane, in some cases with both high conversion and high selectivity.[89-92]

New Reactor Concepts – Tandem and cascade catalysis processes have emerged as promising strategies in homogeneous and heterogeneous catalysis. Multiple catalysts (homogeneous, heterogeneous or their mixtures) have been used in combination to accomplish sequential transformations. For example, tandem catalyst systems for alkane metathesis combine a homogeneous alkane dehydrogenation/hydrogenation catalyst with a homogeneous or heterogeneous olefin metathesis catalyst to modify the chain length of the linear alkanes formed.[54,93] A reported cascade catalytic system uses three catalysts working in concert to convert CO_2 first to formic acid, then to formate ester, and finally to methanol via hydrogenation.[94] Yet another tandem system uses two homogeneous catalysts to convert ethanol to n-butanol with unprecedented selectivity.[95] Such tandem and cascade systems are challenging to develop, as the different catalysts must not interfere with one another and must all be stable and active under the same reaction conditions.

Characterization, Computation and Synthetic Capabilities – In the past ten years, advances in characterization tools with much improved time and spatial resolution and chemical and structural sensitivity have enabled unprecedented visualization of catalytic systems. In spite of these advances, it is still not possible to characterize an active site in a heterogeneous catalyst with atomic details under reaction pressure or in a liquid medium and to distinguish such sites from spectator structures. It is also not yet feasible to gain structural information or to experimentally quantify the nature and strength of interactions beyond the second coordination sphere, especially for the complex structures typical of catalytic solids. Such information, especially if collected at reaction conditions, is essential for detailed descriptions and for the full utilization and improvement of advanced catalytic materials. There have also been rapid advances in computational capabilities, including speed, algorithms for parallel processing, storage memory, and software, all of which combined have impacted

not only achievable accuracy, but also the system size and complexity of the catalytic systems that can be described with first-principle computations.[96-100] These advances also affect our ability to collect, analyze, and mine experimental data. Computation-directed catalyst synthesis is another highly promising approach. There are some initial successes, especially in the case of zeolite structures,[101] but much remains to be done to make this a standard strategy for catalyst synthesis. A more detailed description and discussion can be found in Panel Report 4, Crosscutting Capabilities and Challenges: Synthesis, Theory, and Characterization.

POTENTIAL FOR ENERGY-RELEVANT TECHNOLOGIES

Achieving precision in selectivity so as to minimize the energy penalties, atom inefficiencies, and process complexity associated with reactant and product purification remains a key feature to enable innovative catalyst technologies for fuels and chemicals production with lower capital and energy intensities than those in current practice. Some of the broad challenges for selectivity control include the preferential activation of strong bonds in the presence of weaker bonds and the control of the energetics of specific pathways in order to avoid undesirable steps in multi-step reactions (e.g., over-oxidation or unintended polymerization). One of the key goals remains to be able to achieve significant kinetic differentiation among competing pathways for any substrate, whether molecularly simple or complex.

Achieving the selective functionalization and the selective depolymerization of biomass-derived materials through the cleavage of specific chemical moieties in their structure in order to extract small intermediates and platform molecules would greatly enhance the commercial attractiveness of biomass as a feedstock for fuels and chemicals.

More broadly, the selective conversion of small hydrocarbons, made abundant and less costly by the emergence of shale gas, can impact many industrial processes, as well as the penetration of gas-derived condensates into the petrochemical and fuel markets. In many instances, the most attractive value-adding route is oxidative functionalization, which circumvents the thermodynamic hurdles of non-oxidative routes. As with the selective activation of methane, high yields of selective products are essential to minimize energy demand in product purification. Current commercial selective oxidation processes focus on the production of relatively stable products, such as acrolein and maleic anhydride, which typically contain stronger C–H bonds than their respective precursor reactants. Many more fuel chemicals, solvents, and monomers formed from the reaction of light alkanes with O_2 await discovery by selective catalytic processes.

In summary, achieving chemoselectivity and regioselectivity will enable highly desirable but currently inaccessible processes for the synthesis of fuels, energy carriers, and large-scale chemical intermediates and products, such as the following:

☐ Use of air, instead of high-purity dioxygen or costly derivative oxidants, to decrease the energy and capital intensity of downstream separations; and use of impurity-resistant catalysts to avoid the cost of contaminant removal from feedstocks;

☐ More effective conversion strategies for hydrocarbons to high-value compounds, such as partial methane oxidation to methanol or aromatics, selective olefin oxidations (e.g., aerobic propylene oxidation), new selectivities for arene alkenylation and alkylation, and selective oligomerization or alkylation of small hydrocarbons to fuels and other new uses (for example, higher α-olefins and polyunsaturated chains);

☐ Conversion of carbon dioxide to fuels (e.g., methanol) or high-value chemicals (e.g., acrylic acid or other carboxylic acids) and selective reduction of dinitrogen to hydrazine; and

☐ Selective oxidation of alkanes at specific positions and selective reduction of polyols, with oxygen removal at desired locations, as versatile petroleum- or bio-based routes to important chemical intermediates.

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Panel 2 Novel Approaches to Energy Transformations

New, high-performance catalysts for electron-driven interfacial reactions have the potential to create innovative processes that produce fuels and chemicals in a more sustainable manner. Furthermore, the increasing availability of intermittent electricity has led to the need to store "off-peak" electricity more effectively through synthesis and utilization of energy-rich chemicals. Realizing these opportunities will require the design of catalysts with substantially improved performance (activity, selectivity, and durability), but which avoid or minimize the use of scarce precious metals. Over the last decade, many novel examples of heterogeneous, molecular and biologically derived electrocatalysts have been reported, and there have been important discoveries related to understanding their performance as a result of advances in theory and characterization tools. Key challenges for future research include understanding the evolution of catalysts and their local environment; developing the ability to control energies of intermediates, reaction barriers, and competing pathways; designing integrated catalyst systems, assemblies, and materials; and utilizing semiconductor-catalyst hybrids and bio-derived components.

CURRENT STATUS AND RECENT ADVANCES

Opportunities for Utilization of Electricity for Manufacturing of Fuels and Chemicals

Approximately 10% of today's global electricity production goes to the world's electrochemical industries.[1] Prime examples include the chlor-alkali process, which produces >50 billion kg/yr of NaOH and Cl_2 (each) as well as aluminum electrorefining, the conventional process employed across the globe to produce >15 billion kg/yr of aluminum metal from its ore.[1] Producing fuels or chemicals beyond NaOH, Cl_2, and Al by deploying industrial electrochemical processes faces challenges such as low electrical energy efficiency and chemical selectivity (typically measured as Faradaic efficiency, the percentage of reacted electrons going to the desired product), which impose capital and operational costs. The design, development and deployment of high-performance electrocatalysts, photocatalysts and biocatalysts have the potential to surmount these barriers, leading to disruptive chemical processes that can produce, in a more sustainable manner, the same types of fuels and chemicals that society relies on every day.

Furthermore, electrical energy sources in the United States have significantly shifted in the past decade as renewable energy sources (wind, solar, bioenergy) have increasingly penetrated the electricity generation market. Current costs for renewable electricity are competitive with conventional electricity production in favorable locations, enabling new opportunities to employ this intermittent form of electricity for chemical manufacturing. A central requirement for realizing these opportunities is preparing catalysts that can perform the needed chemical transformations with the desired selectivity, efficiency, reaction rate, and durability (Figure 2.1).

Equally important to the advancement of new electrochemical processes is the ability to utilize the energy in chemical bonds to produce electricity in devices such as fuel cells and redox flow batteries. A critical challenge is reducing our reliance on platinum group metals as electrocatalysts, as such metals are scarce and susceptible to poisoning by carbon-based species including carbon monoxide (CO). Another challenge, particularly in the oxidation of ethanol and higher alcohols, is the difficulty of breaking the C–C bond at low overpotential and mild temperature and pressure.
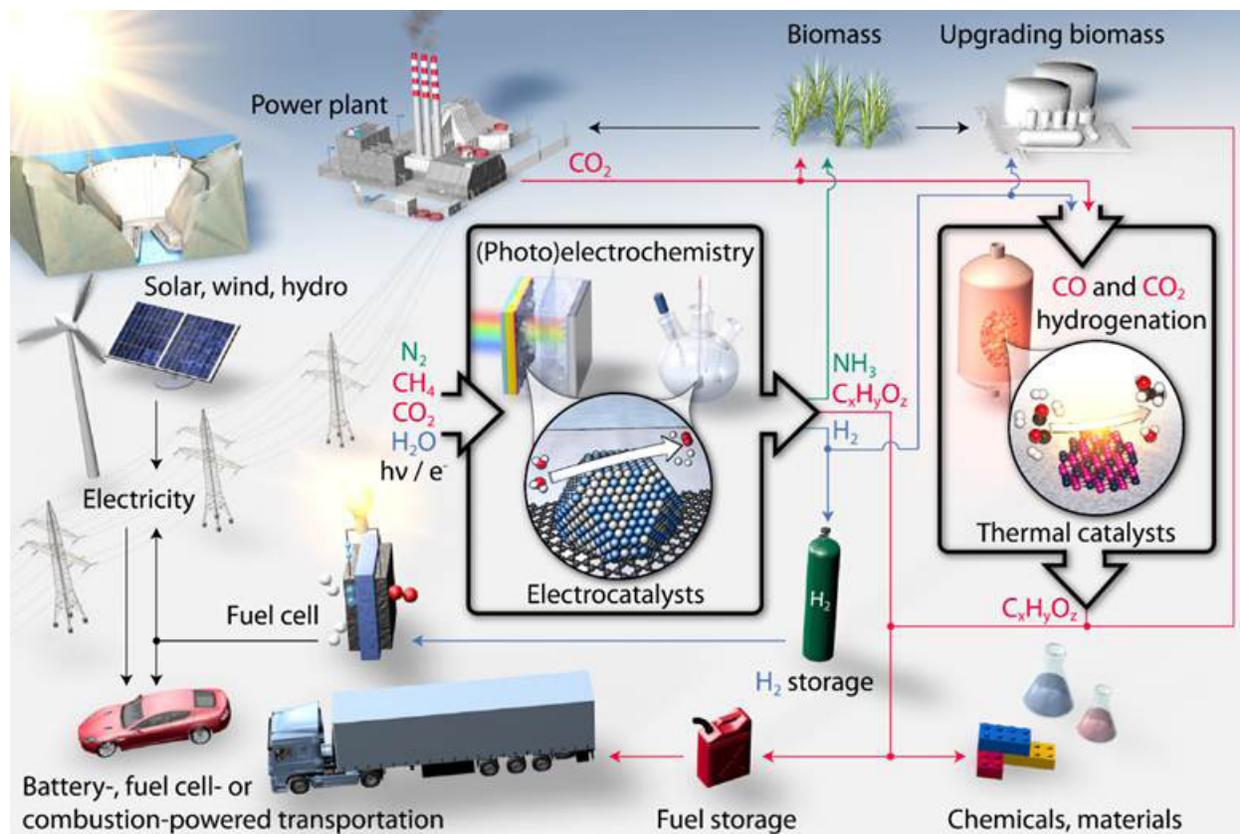
Figure 2.1. Producing fuels and chemicals from abundant, sustainable reactants (e.g., N_2, H_2O, CO_2) using non-fossil energy sources. From Z.-W. Seh, J. Kibsgaard, C. F. Dickens, I. Chorkendorff, J. K. Nørskov, and T. F. Jaramillo, Combining theory and experiment in electrocatalysis: Insights into materials design, Science 355 (6321) eaad4998, DOI: 10.1126/science.aad4998. Reprinted with permission from AAAS.

A prominent example of an electrochemical process that has the potential to make a large impact is water electrolysis for hydrogen (H_2) production. H_2 is produced globally at a massive scale of approximately 65 billion kg/year, which represents ~9 kg/person/year averaged across the globe. Most of the H_2 is used to produce fertilizer, needed to feed billions of people worldwide, and for petroleum upgrading to produce gasoline, diesel, and jet fuel. Almost all H_2 produced across the planet is derived from fossil feedstocks, with natural gas as the primary source. A new process to produce inexpensive, carbon-neutral H_2 from water electrolysis would serve two major purposes: (1) to use renewable electricity during peak production, which would allow for greater market penetration of renewables, and (2) to open up new markets for this sustainable chemical feedstock and fuel to achieve an even broader impact than it currently does. Building upon these purposes, production of H_2 by electrocatalysis using "excess" or off-peak renewable electricity enables production of fuels and chemicals from this renewable feedstock. For example, polymer electrolyte membrane (PEM) water electrolysis, coupled to wind or solar electricity, can produce H_2 with a much lower carbon footprint than can the conventional fossil-based process of steam methane reforming (SMR).[3]

SCIENTIFIC CHALLENGES AND OPPORTUNITIES
Cross-disciplinary Research and Advanced Characterization Tools
Realizing the potential opportunities described above will require catalysts with substantially improved performance (activity, selectivity, and durability) while avoiding or minimizing the use of scarce, expensive precious metals. The need for cross-disciplinary research in catalyst development is an important, recurring theme. Stronger connections should be established among researchers developing solid-state catalysts, molecular catalysts, and biocatalysts, creating deeper linkages between the fields of electrocatalysis, photocatalysis, thermal catalysis, and biological catalysis (enzymes). For instance, electrocatalysis and photocatalysis often involve intermediate steps that are thermally-driven rather than directly electron- or photon-driven. Therefore, to optimize catalysts for a multi-step reaction pathway may require knowledge that cuts across areas that are often viewed as distinct. Leveraging knowledge from homogeneous catalysis that involves

SIDEBAR 1. RESOLVING THE DYNAMICS OF CATALYSIS

Catalysis is at the heart of chemical transformations that convert energy from alternative forms such as electricity and light into storable fuels, such as H_2, alcohols, or higher-energy hydrocarbons. Accessing such storable fuels from alternative sources would greatly facilitate their use, by providing a way to store and release that energy on demand. Critical to efficient catalysis is the speed and selectivity with which bonds of reactant molecules are broken and re-configured into the higher-energy-storing fuel. While these transformations are expected to proceed dynamically and in a sequence of steps, catalysis has been traditionally investigated in a fashion where only one rate, the speed at which products evolve, is monitored. Yet, in order to truly tailor the efficiency of fuel evolution, an understanding of the full sequence of reactions is required. To meet this challenge, catalysts should be investigated while catalysis is occurring and in a manner that deconstructs the critical bond breaking and making steps.
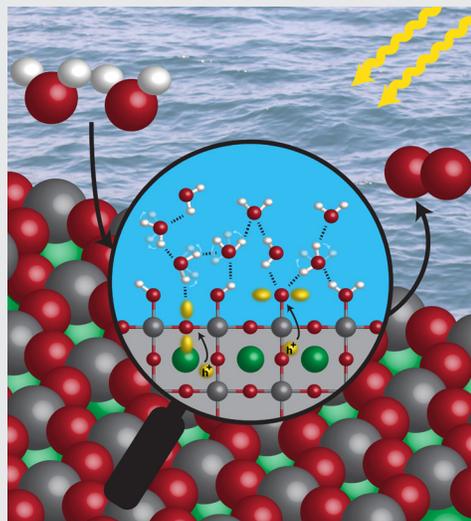
Sidebar Figure 2.1. Image courtesy of Tanja Cuk (University of Colorado – Boulder).

Obtaining such dynamic snapshots of catalysis necessitates cutting-edge advances that allow for diverse and time-resolved probes of the catalyst/reactant interface during operation. Recently, such advances include *in situ* sample cells that encase this interface, such that catalysis can proceed at the operating conditions of temperature, pressure, and applied voltage while being investigated by penetrating light beams. Important to obtaining a full picture of the reaction is the use of a wide range of light frequencies to investigate the different actors involved, including the atoms in the catalytic material, the vibrations of reactant molecules near the surface, and charges trapped at the interface. This means that light beams which span the spectrum from low-frequency infrared through visible/UV and up to high-frequency X-rays are important. Finally, critical to observing and quantifying the individual steps is the ability to initiate the catalysis with a pulsed excitation of light or charge, such that the steps can be separated in time.

Sidebar Figure 2.1 shows an intermediate step of the water-splitting reaction that transforms H_2O into H_2 and O_2 that was recently observed by infrared and visible light on a catalytic surface. The charge separated from the pulsed light excitation traps at the interface to create new species (yellow clouds), called catalytic intermediates, which break the bonds of adsorbed -OH and H_2O.[4] At later times, scientists anticipate that these intermediates initiate the formation of a chemical bond between two oxygen atoms. The goal of this and analogous work is to resolve catalysis dynamically, which is invaluable for determining the fundamental limits of catalytic activity. Furthermore, identifying the factors involved in each step will provide insight into how to exploit fundamental limits in both catalyst design and energy conversion architectures.

the precise design and modulation of catalytically active sites could aid in the design of electrode surfaces to provide new breakthroughs in control of reactions. Bio-inspired synthetic catalysts strive to incorporate features of enzymes, applying specific lessons from studies of biochemical conversions, such as incorporating specific functional groups found in many enzyme active sites (e.g., Brønsted acids and bases).

Tools for characterizing and modeling catalytic reactions should be applied across disciplines, including high-resolution microscopy techniques, *operando* measurements, and increasingly powerful theory for predicting performance and stability. Increased collaboration is needed among scientists and engineers focused on fundamental problems, as well as their connection to device developers. These collaborative efforts will inform the development of tools, methods, and approaches to address real-world problems, drive the understanding of complex structures and interactions, and enable mechanistic understanding of catalyst performance. The availability of powerful characterization tools, such as those for *operando* characterization, greatly aid in identifying and understanding the active form of a catalyst. The generation of new tools and increased availability of existing methods provide opportunities for better characterization of catalytic intermediates than previously possible (see Sidebars 1 and 2).

SIDEBAR 2. TRANSLATING SCIENTIFIC DISCOVERY INTO APPLICATION

A key obstacle to innovation is how to shorten the timeline from materials discovery to commercial implementation, which can often take 15–20 years. Understanding the challenges and science involved in translating materials to extended three-dimensional structures is essential to accelerate progress, and requires early collaboration between fundamental and applied scientists in academia and industry. For example, catalyst discovery typically begins with making very small amounts of new materials and testing them in highly simplified formats. A common screening tool is shown in Sidebar Figure 2.2 (top), where catalyst powder is well-dispersed on the electrode disk, so that each particle is easily accessible for reaction. This technique can provide consistent comparisons between materials, but throughput is very low, and real systems have many more variables and interactions that need to be understood. This test also usually lasts only minutes and therefore provides information on initial performance but not durability.

In a real device, binders and other additives are mixed with the catalyst to make it work in the application for long periods of time. The resulting electrode is much more dense, complex, and porous, and extends over an area hundreds of times larger than at the screening level (see Sidebar Figure 2.2, bottom). Packing the catalyst closer keeps adjacent components smaller and minimizes the two-dimensional area, which makes the process more economical; however, all the catalyst surface must retain fluid access. Understanding how these complex layers form, how to control them at scale, and how they change over time are fundamental science challenges, which require collaboration between universities, DOE national laboratories, and applied scientists, and resources such as microscopy and other tools to characterize these systems before and after testing.
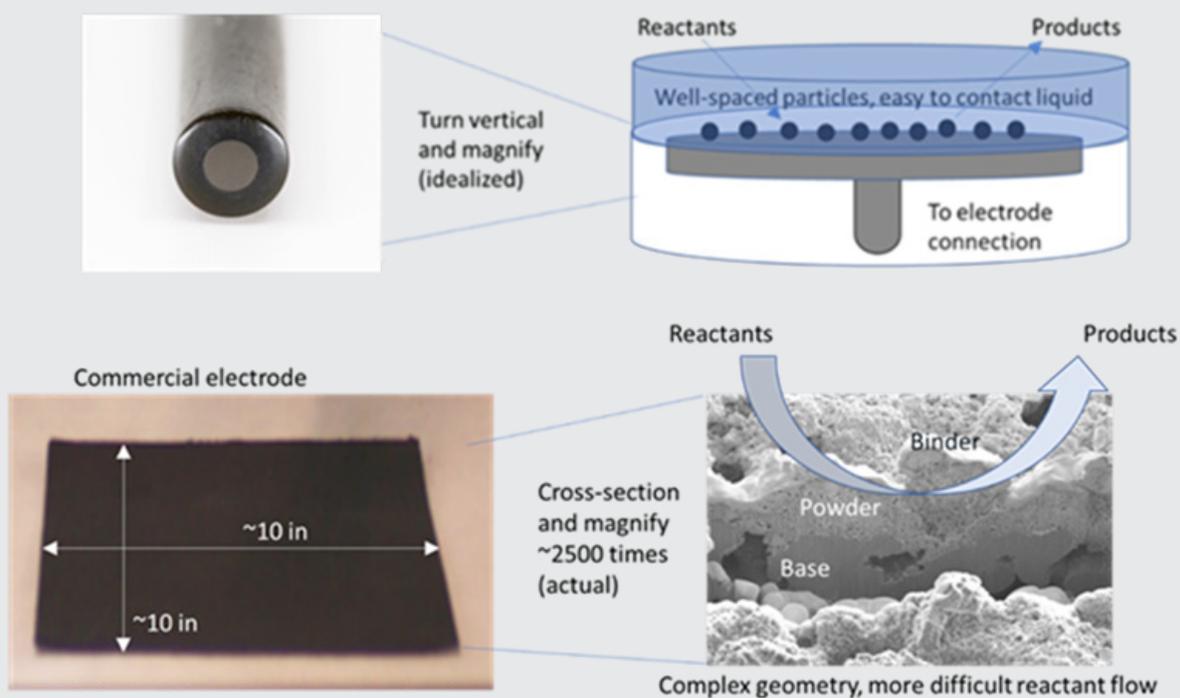
Sidebar Figure 2.2. Image of electrode (upper left) and sketch of magnified electrode face up (upper right). Example of a commercial electrode (lower left), with compact and complex geometry (lower right). Image upper left courtesy of Jon Darmon, Princeton University; upper right and bottom left and right, courtesy of Kathy Ayers, Proton Onsight, Wallingford, Connecticut (2018).

Understanding Structural Evolution of the Catalyst and Its Local Environment

The ability of a catalyst to accelerate reactions by lowering activation barriers is often correlated to its intrinsic structural flexibility under the conditions of the reaction. Thus the rational design of improved catalysts for energy-relevant reactions must begin with an accurate picture of the structure of the catalyst's resting state, from which bond transformations proceed. Catalysts involved in electrochemical or photochemical processes are confronted with the additional complexity of changes in chemical structure and reactivity because of rapid changes in energy input. This applied energy input is necessary to drive the desired reaction, but can dramatically alter the structure of the catalyst and/or its environment, with concomitant changes in catalytic performance.

Recent advances in synthetic methods allow us to control the structure of catalyst active sites with atomic precision in heterogeneous and homogeneous systems, and site-directed mutagenesis can accomplish the same goal in the active sites of biological catalysts. However, our understanding of how catalysts work under catalytic conditions is often limited, particularly under conditions that are subject to large excursions from chemical equilibrium. For example, metallic copper surfaces can catalyze the conversion of CO_2 to hydrocarbons.[5] Interestingly, thick Cu_2O films which are reduced under the conditions of catalysis can provide enhancements.[6] For the OER, $SrIrO_3$ catalysts show improvement versus IrO_2, enabled by a transformation of the as-synthesized material to a thin surface film of IrO_x on top of $SrIrO_3$.[7] Analogous chemical changes occur in molecular systems, including ligand association/dissociation as well as changes in the oxidation state of the metal center. In biology, enzyme activation from a pre-catalytic state is well known, and inactivation (particularly by O_2) is commonly observed. Changes in the local environment of the active site can also occur, including solvent properties, pH, ion concentration, and electric field, which collectively define the equilibrium population of intermediates, spectator species and promoters. As a specific example, during electrocatalysis, the large electric field across the surface-solvent interface can augment the population of adsorbed species at the surface, the local concentration of ions, and the structure of the solvent.

The systematic development and application of improved catalysts requires methods for reproducing and comparing key performance metrics across diverse catalysts. This goal can be advanced by developing general benchmarking protocols[8] to enable meaningful comparison of catalytic performance and stability across samples from different research groups, as well as between molecular and heterogeneous catalyst systems. While these comparisons provide an excellent starting point, ultimately the evolving nature of the catalyst active site from its as-synthesized form frequently complicates the comparison of catalytic performance of disparate materials. For example, surface restructuring of a catalyst may increase its effective area, rather than augment its intrinsic activity, leading to ambiguity in comparing disparate materials. In the most general terms, typical measurements of catalytic activity represent the convolution of individual factors; analyzing and understanding the influence of these factors is essential for developing meaningful structure-performance correlations that will guide design of improved catalysts.

Recent advances in kinetic methods, imaging and *operando* spectroscopy, including time-resolved crystallography, provide the basis for tracking changes in the catalyst and environment, as well as the critical capability of observing and determining the time evolution of transient intermediates. High-resolution electron microscopy probes surface features on nanoscale surface catalysts with atomic precision. Likewise, time-resolved and surface-sensitive spectroscopies spanning the electromagnetic spectrum from high-energy X-rays to low-energy infrared light provide the opportunity to characterize the evolution of catalytic materials with unprecedented detail. Time-resolved crystallographic methods, particularly involving the femtosecond resolution of sources found at DOE user facilities, provide similar capabilities. All these methodologies need to be applied more broadly to understand catalyst evolution across catalyst composition, reactive environment, and applied energy input. In addition, these established methods must be complemented by the development of new techniques that increase spatial and temporal resolution, surface specificity, and general applicability.

Surface- and tip-enhanced Raman spectroscopy provide localized chemical sensitivity for observing small quantities of catalyst structures and adsorbates to elucidate reaction mechanisms.[9] Scanning electrochemical microscopy allows for direct quantification and time-resolved evolution of surface active sites needed to map reaction pathways in liquid-phase media.[10] Environmental electron microscopy techniques can determine how the catalyst particle size, distribution, and migration evolve as reactions proceed for extended times.[11] All of the

understanding gained through advances in experimental methods should be coupled with advanced theoretical and computational methods that continue to be developed as well, providing unique insight into catalyst-solvent interfaces, the nature of intermediates and transition states, and self-healing of catalysts.

Leveraging these experimental, theoretical and computational methods will allow direct measurement of salient features that define effective energy conversion catalysts. For example, spectroscopic methods can provide direct insight into the binding energetics of reactive intermediates, and these thermochemical parameters can be used to validate theoretical methods. Similarly, direct probes of the evolution of catalysts permit mechanistic models of catalyst activation and degradation, providing rational approaches to enhancing catalyst activity and durability. Elucidating the mechanisms by which supports stabilize or destabilize catalysts against degradation will provide a basis for designing improved catalyst-support interactions.

Understanding Reaction Mechanisms In Electrochemical and Photocatalytic Reactions

Progress in the past decade has led to advances in our ability to synchronize catalytic events and capture and experimentally assess catalytic intermediates. These developments provide profound mechanistic insights into the function of biological, homogeneous and heterogeneous catalysts. Furthermore, they lay the groundwork for probing complete catalytic cycles and discovering new aspects of reaction mechanisms. For example, early intermediates of catalytic reactions have been identified spectroscopically on heterogeneous transition metal oxide surfaces that evolve O_2,[12-14] in homogeneous catalysts for CO_2 reduction to CO,[15] and for forming the hydride on hydrogenase.[16] With sufficiently fast time-resolved probes, intermediates can be detected at the time scale of charge transfer[4,15] and their decay can be followed on time scales relevant to bond-forming and -breaking events.[4,16]

Our ability to probe the contribution of the active-site environment in complex materials, synthetic catalysts, and enzymes has advanced to the point where the individual chemical determinants of catalysis can be delineated and manipulated. For example, at the transition metal oxide/aqueous interface, the role of water dynamics is especially important in OER chemistry. The formation of surface-bound radicals from charge carriers is rate-limited by solvent dynamics,[4] and the radical's vibrations couple to water librations (hindered rotations). These experiments begin to probe the "solvation environment" relevant to an electrode/electrolyte interface (often termed the electric double layer). These advances and others set the stage for identifying the sequence of intermediates within the catalytic cycle, and for resolving the time-dependence of reactive species reaching transition states that lead to chemical bonds that store energy.

Control of Energies of Intermediates, Reaction Barriers, and Competing Pathways

The central role of a catalyst is to alter the free-energy landscape of a reaction (Figure 2.2). The free energy of the transition state(s) ultimately dictates reaction rates and chemoselectivity, but catalytic performance can be seriously compromised when intermediates are bound either too strongly (orange line and dot) or too weakly (red line and dot). This principle, introduced by Sabatier, can be illustrated in an activity volcano plot of catalytic rate versus the binding energy of the key intermediate(s)/transition states (Figure 2.2, right panel). A powerful approach to optimizing catalysts is to bring the energy of the key intermediates (green line and dot) close to the energy of reactants and products – in other words, to remove large hills or valleys in the free-energy landscape. The energies of these intermediates would then be correlated with physico-chemical properties of the catalyst (e.g., hydricity, reduction potential, *d*-band center), providing a pathway for optimization. This optimization is, however, insufficient to guarantee efficient catalysis because the kinetic barrier for accessing the key intermediate may remain high (blue line and dot). Thus, in addition to controlling intermediate energetics, efficient catalysis also requires facile kinetics for each individual reaction step, i.e., lowering the barrier to reaction by stabilizing the transition state(s). These challenges are compounded for reactions that involve multiple intermediates because, in many cases, the energy difference between two or more intermediates remains constant over a large range of similar catalysts, leading to a "scaling relationship" between the binding energetics of key intermediates, limiting the maximum efficiency of the transformation. Thus, the design requirements mentioned above should be complemented by strategies for circumventing these scaling relations.
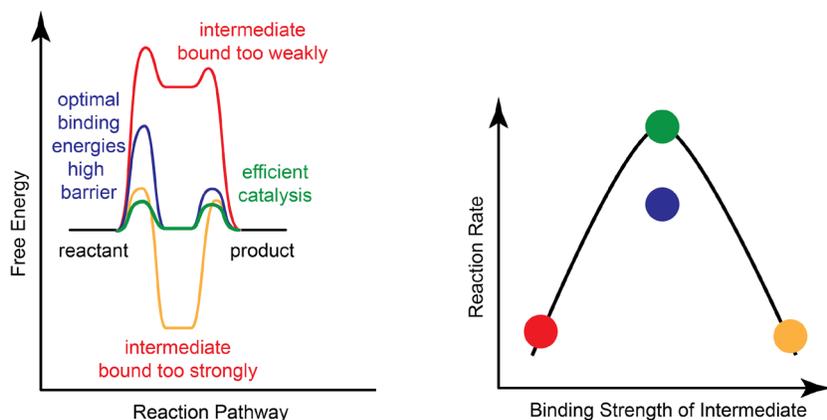
Figure 2.2. Catalytic performance can be greatly impacted by the relative free energies of intermediates on a reaction profile, thereby necessitating the ability to understand and control the stabilities of catalytic intermediates. Image courtesy of Yogesh Surendranath (Massachusetts Institute of Technology).

Utilizing the above analysis requires some knowledge of the free energy landscape for the reaction. Mechanistic insights identify key intermediates and rate-limiting reaction steps of the desired transformation. This knowledge, combined with insight into the transition state structure, could enable a systematic lowering of the reaction barrier without requiring increased driving force.

The local environment can have a large influence upon catalysis. For example, incorporating a facile route for proton transfer can circumvent highly unstable intermediates that form upon electron transfer. As further advances improve catalytic rates, molecular dynamics will play a larger role in enhancing activity,[17] and provide further clues on how to improve catalytic rates (Figure 2.3).

In reactions involving multiple pathways that are close in energy, product selectivity becomes an issue. Secondary interactions can also influence product selectivity by adjusting the energetics of a particular pathway relative to other routes. Among these interactions are hydrogen bonding, electrostatics, and oriented delivery of reactants to the substrate. The local environment also provides a route to disrupting correlated scaling relationships, or where two intermediate energies can contribute to catalytic activity and cannot be optimized independently at a single site. The reduction of CO_2 to CO is inversely dependent on the CO_2 and CO binding energy.[18] A cooperative interaction that disproportionately affects one binding energy over another can break the correlation of energies. The [NiFe] CO dehydrogenase performs reduction of CO_2 to CO efficiently, selectively, and reversibly.[19] Insight into how it achieves selectivity comes from studies indicating that the active site utilizes a second metal site to cooperatively bind CO_2, an interaction unavailable to CO.[20]

Figure 2.3. Dramatically improved catalytic performance can be achieved by understanding how to break linear scaling relationships between catalytic rates and overpotentials, such as through the use of complex ligand dynamics and mesoscale solvent effects. From A. J. P. Cardenas, B. Ginovska, N. Kumar, J. Hou, S. Raugei, M. L. Helm, A. M. Appel, R. M. Bullock, M. O'Hagan, Controlling Proton Delivery through Catalyst Structural Dynamics, *Angewandte Chemie International Edition*, 2016, 55, 13509-13513. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

Achieving high selectivity using heterogeneous metal catalysts relies on mapping the geometric and energy landscape of binding modes—both the reactant and intermediates—to the metal surface. Although calculating scaling relations on specific surfaces is tractable by DFT, surveying surfaces with 2-D defects, adatoms, and surface impurities common to synthesized materials remains a challenge. Approaches to include the coordination number of key intermediates as a function of surface facets, edges, and kinks are emerging.[21] However, much work remains to be done to successfully predict the rates of catalytic transformations with realistic catalysts. Rather, experiments often take cues from known homogeneous catalysts, with the goal of embedding reactive

sites into a matrix to retain the requisite geometry and electronic structure. For example, Au nanoparticles encapsulated in a polyamidoamine dendrimer matrix catalyze diastereoselective cyclopropanation.[22]

Designing Integrated Catalyst Systems, Assemblies, and Materials

The readily accessible surfaces of known materials frequently exhibit poor activity for the energy transformations that are critical to existing and emerging renewable energy technologies. Discovering catalysts that overcome these limitations will likely require an ability to access a broader surface structure space where electronic properties, adsorbate binding energies, coordination geometries, and the architecture of multi-functional sites can be adjusted precisely. Despite substantial advances in the methodology for materials synthesis in the past decade, there is limited ability to translate desirable surface properties or specific surface structures into rational syntheses that expose these surfaces and stabilize them under catalytic conditions. Innovative approaches to materials synthesis oriented to controlling surface properties, combined with a deeper understanding of the mechanisms by which surfaces evolve both during synthesis and under catalyst operating conditions, promise to unveil new catalysts that will enhance understanding and expand technological abilities.

In some cases, a specific surface site on a particular material is known experimentally or predicted from theory to be highly active, and the challenge is to design the bulk structure of catalyst particles to maximize the coverage of this surface site under operating conditions. For example, edge sites of MoS_2 have been identified as the catalytically active sites for H^+ reduction in acidic media, but edges are minority sites on bulk MoS_2 structures. By designing a double gyroid MoS_2 bicontinuous network—a porous material with highly curved surfaces—researchers engineered MoS_2 with a high surface coverage of edge sites, and observed a concomitant increase in catalytic activity per surface area.[23] In general, however, controlling the density of steps and edges across diverse materials remains challenging, particularly for metals, which have highly mobile surface atoms under operating conditions. Advances in colloidal nanoparticle synthesis have provided access to polyhedral nanostructures that in principle expose high-index facets with large step or edge densities. However, these structures are prone to evolve their morphology or adopt low-index surfaces under prolonged electrocatalytic operation.

In other cases, it is desirable to modulate the electronic structure of a surface by altering the subsurface structure. For example, researchers have shown that creating core-shell catalysts composed of Pt group monolayers on metal alloy or metal carbide cores alters the *d*-band energy of the Pt surface, which changes the adsorbate binding energy for critical electrocatalytic intermediates. These perturbations have enhanced activity for O_2 reduction and methanol oxidation in acidic media, among other examples.[24]

For many reactions, however, surfaces that are sufficiently active for practical applications have yet to be identified. A prime example is the electrocatalytic reduction of CO_2 to produce multi-carbon oxygenates and hydrocarbons. In these cases, the ability to access persistent high-energy surfaces across a broad range of materials is critical for uncovering new catalyst lead structures and breaking through efficiency limits of existing technologies. Advances in materials chemistry have enabled the synthesis of non-equilibrium structures with high-energy surfaces that may have desirable catalytic properties. Examples include polyhedral nanoparticles that expose high-index facets, core-shell structures, metastable alloys, and nanocomposites. However, the operational conditions of energy conversion often convert metastable catalysts into more stable structures with surfaces that are substantially less active. These conversions result from the inherent mobility of atoms at surfaces as well as adsorbate- or potential-induced migrations, even at ambient temperatures. A central challenge to achieving the catalyst performance necessary to maximize the use of renewable sources is how to design materials such that highly active surfaces are kinetically blocked from rearrangement to more stable, but less active, surfaces. Addressing this challenge requires expanding the synthetic methodologies of catalyst synthesis and improving our understanding of the mechanisms of catalyst restructuring during operation to design materials that resist these pathways.

Molecular catalysts offer the advantage of being able to tune systematically the electronic and steric characteristics of the ligands, to assess the impact on the catalytic reaction, and then to use that information in an iterative approach to improve catalyst performance. Heterogeneous catalysts offer advantages of ease of separation of products from the catalyst, and often more robust tolerance to higher temperatures, but are much

less amenable to systematic modification of the active site. Considerable effort has focused on attachment of molecular complexes to surfaces, covalently or otherwise, providing surface-immobilized catalysts.[25] Some of those approaches have been successful, but in many cases the surface-immobilized complex does not exhibit activity comparable to that observed under homogeneous conditions. Under highly oxidizing conditions, many molecules that are catalysts when not attached to a surface decompose to form less active or inactive catalysts once attached. In most efforts, the chemistry of the linkage between the molecular unit and the solid electrode is electronically insulating, introducing a tunneling barrier to electron flow to the reactive center. In this situation, the electronic states of the molecular center remain isolated from the energy bands of the electrode, leading, in the best case, to comparable activity for the surface appended unit relative to the isolated molecule. An attractive alternative approach is to exploit the native surface chemistry of the electrode to synthesize discrete molecular centers that are strongly coupled to the metallic electrode surface (Figure 2.4).[26] This approach is distinct from most prior efforts toward molecularly well-defined interfaces because it seeks to promote electrocatalytic reactivity by exploiting synergistic electronic interactions between the molecular center and the band states of the solid electrode. The strongly coupled molecular centers in the resultant modified surfaces display remarkably enhanced catalytic activity and durability relative to the molecular species under homogenous conditions. New research opportunities exist for exploiting band-molecule coupling in a systematic way across a wide range of materials to design high-performance electrocatalysts at the molecular level.
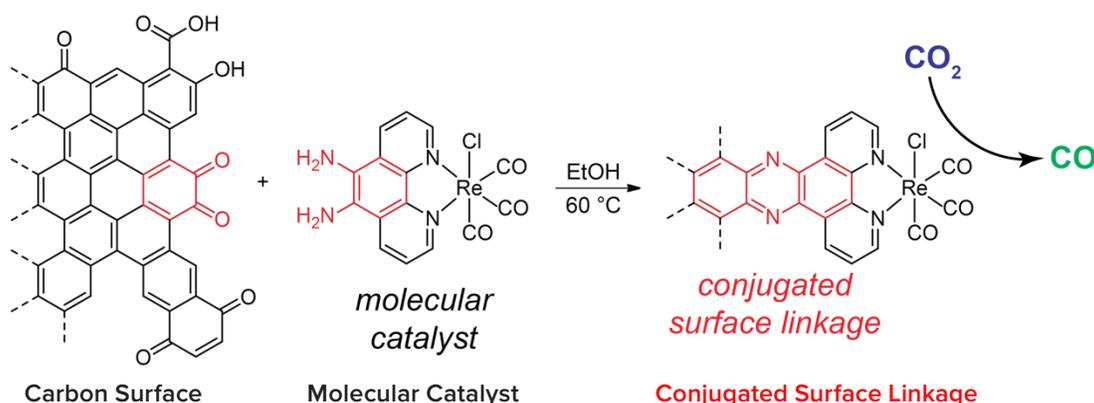
Figure 2.4. Molecular catalysts can be attached to carbon surfaces through conjugated aromatic linkages by condensing phenylenediamine units with native surface groups, generating functional electrodes for the reduction of CO_2 to CO. Reprinted with permission from *Journal of the American Chemical Society*, Feb. 2016, Graphite-Conjugated Rhenium Catalysts for Carbon Dioxide Reduction, S. Oh et al. Copyright 2016, American Chemical Society.

Computational design of solid catalysts has succeeded in creating tailor-made catalytically active surfaces for selected metal catalysts and binary oxides.[27] However, new research opportunities exist to expand this work to compositionally complex materials (ternary and higher order phases, materials that explicitly account for defects, metastable phases, etc.). These efforts are needed both computationally and experimentally. On the experimental side, methods for transforming nanostructures under equilibrium conditions abound, and include using molecular containers, nanostructure templating, developing core-shell architectures, and multicomponent restitution to prevent sintering. However, research efforts to probe how nanostructures transform under non-equilibrium conditions (e.g. in an electric field) are needed.

Hybrid systems consisting of catalysts (heterogeneous/molecular/biological) coupled to light absorbers/sensitizers/electrodes provide opportunities to couple highly selective catalysts with photoabsorbers to use photogenerated electron-hole pairs for oxidation-reduction catalysis directly. These systems should retain the intrinsic catalytic activity and should not significantly affect light absorption, and the interface should promote facile electron transfer. More work can also be done to improve the robustness of these interactions through sustained catalysis, especially for reactions that evolve gases that may mechanically disrupt the surface. It would be even more advantageous if the surface also had protective effects under electrolytic conditions, as stability is a concern in photoelectrochemical cells.[28]

SIDEBAR 3. PHOTOLYTICALLY DRIVEN NITROGEN FIXATION

The reduction of dinitrogen (N_2) to ammonia (NH_3) is an attractive way to store renewably generated electrons; it is a reaction vital to support life. However, the current methods for N_2 reduction demand tremendous energy input, primarily derived from fossil fuels in the industrially used Haber-Bosch process or ATP in the biological process. There are no known catalysts that can accomplish this reaction at scale with energy provided by light. Biological nitrogen fixation is catalyzed by nitrogenase in a reaction that involves a specific iron-sulfur protein as electron donor and the consumption of two equivalents of ATP per electron.

A bio-hybrid system has recently been developed that involves nitrogenase immobilized on CdS nanorods. The system fixes nitrogen using photolytically generated electrons from the nanorods.[36] When illuminated, the enzyme turns over at near-physiological rates with a turnover number in excess of 10^4. In addition to providing a model system for development of distributed ammonia production as an alternative to large, capital-intensive Haber-Bosch production plants, the bio-hybrids enable scientific studies of the mechanism of one of the most energy-demanding and difficult chemical reactions. Photochemically driven reactions offer exquisite control of the electrons (i.e., energy and flux) required by nitrogenase for chemical activation of the N≡N bond. Combining light control of electron transfer with biophysical methods offers a new approach to dissecting the mechanistic details of N_2 reduction by nitrogenase, which was not previously possible. Establishing the mechanistic principles that biochemistry uses for electron-driven reactions (or redox reactions) will enable advances in the design of synthetic catalysts for utilization of emerging energy resources such as solar (photochemical) energy, wind energy, and electrical (electrochemical) energy.
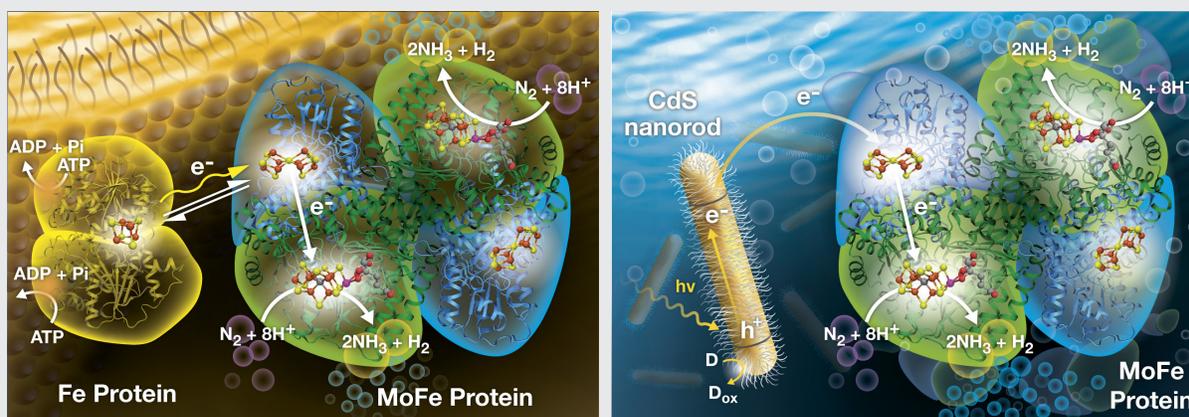
Sidebar Figure 2.3. Biological (left) and photobiohybrid (right) processes for the reduction of N_2 to ammonia by nitrogenase. The biological process requires Fe protein and ATP-dependent electron transfer to MoFe protein for catalysis to occur. In the biohybrid, a nanoparticle (CdS) replaces the Fe protein and ATP, and couples light harvesting to drive electron transfer to the MoFe protein for ammonia production. From Brown et al., Light-driven dinitrogen reduction catalyzed by CdS: Nitrogenase MoFe protein biohybrid, 2016, *Science* 352, Issue 6284 (2016) 448. DOI: 10.1126/science.aaf2091. Copyright © 2016, AAAS. Reprinted with permission from AAAS.

Utilization of Semiconductor-Catalyst Hybrids and Bio-Derived Components

A recent perspective[29] identifies a critical opportunity in using semiconductor quantum dots as colloidal photocatalysts. The state of the art focuses on manipulating surface coverage of the substrate by altering the ligand exchange chemistry and tuning the surface charge. These directions accomplish rapid delivery of redox equivalents as well as maximize the catalytically active surface area. Matching the rates of electron and hole scavenging is often accomplished by adding sacrificial agents. Accordingly, a critical research need is to build the quantum dot surface with atomic precision in order to adsorb substrates in the correct geometry for rapid charge transfer. In this manner, common test reactions, such as dye mineralization, can give way to selective organic transformations.

For the oxygen evolution reaction, there are examples of catalysts working in tandem with semiconductors to accelerate rates. Since the previous Catalysis BRN Workshop in 2007, there have been several realizations of water-splitting concepts using this design.[30-32] One critical question that remains within the field of OER is "What role do ionic species that comprise the electrolyte play in lowering the overpotential/ influencing the reaction mechanism?" For example, the borate versus phosphate salts of Co- and Ni- based catalysts show differing

Tafel slopes,[33] suggesting that the pathway of OER is altered. Moreover, even in strong base, Li^+, Na^+, and K^+ hydroxides show different rates of OER at the same ionic strength.[34]

Bio-hybrid designs offer opportunities for photo- or electrochemically driven CO_2 and N_2 reduction that exploit concepts from both biological and chemical catalysis. The integration of synthetic biology and chemistry approaches provides opportunities to achieve designs for complexity and selectivity in catalysis that exceed limitations found in Nature. For example, advances in our understanding of metalloenzyme structure and function suggest new ways to improve synthetic catalysts, frequently embedded within protein hosts.[35] Furthermore, CdS-nitrogenase hybrids have been developed that perform efficient light-driven ammonia production, by exploiting the light-driven multielectron reducing capacity of CdS nanorods to circumvent the need for an ATP cofactor in the biological nitrogen fixation reaction (see Sidebar 3).[36]

Biological organisms have evolved to exploit virtually every redox gradient available in their natural environment. Microbes produce an array of enzymes that catalyze oxidation-reduction reactions with exquisite reactivity for key energy-conversion transformations, including hydrogen production/oxidation, reduction of N_2 and CO_2, and many organic transformations. Importantly, biocatalysts combine unparalleled selectivity with high catalytic rates and turnover frequencies. They also serve as inspiration for the design of new homogeneous and heterogeneous catalysts. There is a need to determine how features of active sites and their interactions with the protein scaffold tune the reactivity of the catalyst. Many enzymes function naturally as photo- or electrocatalysts, and can be employed as such in the presence of appropriate photosensitizers, redox mediators, or electrodes. To date, fuel cells and fuel production applications have been developed that employ either isolated enzymes or intact microbes, but wide-scale utilization will require altering enzyme specificity and improving stability under photo- or electrochemical conditions, including development of improved methods for the immobilization, isolation, and stabilization of enzymes.

Understanding how complex biological catalysts are assembled and function can inform the development of improved homogeneous and heterogeneous catalysts. It is of fundamental interest to understand the disposition of specific redox-active centers with respect to one another and how this influences function – how, for example, the polypeptide environment modulates reduction potentials, provides proton/electron relays, and imparts cooperative behavior that enhances catalytic performance. In addition, the design principles elucidated in biocatalysts can be used to develop improved homogeneous and heterogeneous catalysts, as well as photo- and electrocatalysts.

Potential for Energy-Relevant Technologies

The section "Topic 2: Novel Approaches to Energy Transformations" in the Technical Perspectives Factual Document, which accompanies this report, describes a number of technology areas that would benefit from improved electrocatalysis, including electrification of the transportation sector, grid-scale electrical energy storage as fuels such as hydrogen through water electrolysis, and transformation of CO_2 into chemical feedstocks. Current costs for renewable electricity are competitive with conventional electricity production in favorable locations, enabling new opportunities to employ this variable form of electricity for chemical manufacturing that utilizes abundant feedstocks such as CO_2 and water. One of the broad technical challenges in converting oxidized carbon in CO_2 into fuels or other chemicals is that highly selective and active electrocatalysts are needed. Consequently, the biggest impacts of improving catalyst design are to decrease the number of synthetic and separation steps, to improve reaction yields by minimizing byproduct formation, and to decrease the energy input into reactions.

For grid-scale energy storage, the biggest impact of improving catalyst design is to increase the efficiency of solar- and wind-derived H_2 generated from water. Fuel cells are one of the means to convert H_2 directly to electricity that can be added to the power grid. Alternatively, it opens the door to using water-derived H_2 as a feedstock for carbon fuels which could be added directly to the gas-distribution grid. In the long term, completely new electrocatalyts and electrochemical processes would enable a variety of sustainable and distributed technologies for production of chemicals such as ammonia, hydrogen peroxide, ozone and many others.

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Panel 3 Advanced Chemical Conversion Approaches

Utilizing non-traditional feedstocks for the production of fuels and chemicals will require equally non-traditional approaches to make them cost competitive with today's industrial processes. To advance in this technology space, catalysis researchers will need to consider how feedstocks will be used to build in needed functionality and robustness. Catalysts employed in a process with varying feedstock inputs will need to be able to adjust to rapidly changing process conditions. Catalyst exploration will require detailed knowledge of the needed active sites and how they will respond to different process stimuli. Likewise, to process a more distributed feedstock, it may be necessary to utilize novel manufacturing approaches where multiple process steps are combined, and these approaches will likely require new catalysts capable of operating under very complex process environments. Knowledge and techniques to control matter across multiple length scales will be required to build in the needed chemical specificity, kinetics and reactivity. Studies will be necessary to link active site design with systems design, and advances in characterization and computational techniques are needed to build the knowledge base to construct these robust catalytic systems.

CURRENT STATUS AND RECENT ADVANCES

In the past decade, a number of low-cost feedstocks have emerged that are being used or studied to produce low-carbon fuels and chemicals. A rigorous life cycle assessment shows these feedstocks to have lower CO_2 emissions compared to their counterparts derived from petroleum throughout their entire life cycle.[1] The availability of alternative feedstocks such as biomass, solid waste materials (e.g., food waste, agricultural residuals, municipal solids, and forestry residues), liquid wastes (e.g., cheese whey, waste vegetable oils, manure) and gas wastes (e.g., biogas, waste streams from steel production, CO_2-rich fermentation streams) creates opportunities for diversification of feedstocks, production of low-carbon fuels and chemicals, improved-performance products, and potentially lower-cost technologies.

Owing in part to growing concerns about the effects of greenhouse gas emissions, a number of governments are requiring the use of low-carbon fuels and chemicals.[2] Just as catalysis science drove the twentieth century's industrial success by efficiently converting our non-renewable, fossil-based feedstocks into fuels and chemicals, catalysis science is now called upon to utilize these new feedstocks for the twenty-first century and beyond. These feedstocks present several unique challenges, different from traditional petroleum-derived feedstocks, and as such unique innovations are required in order to utilize them effectively. The biomass-derived feedstocks typically contain large amounts of oxygen (even up to 60 wt%) or are present as dilute streams (as in the case of whey), giving them a low energy density; further, they are often distributed over wider geographical regions than fossil fuels. Their assorted locations may require processing in smaller plants closer to the underutilized resources. To be economically competitive, new reactor designs that can accommodate higher intensity processes compared to conventional petrochemical reactors may be necessary. Process intensification (PI) is a chemical and process design approach that can lead to substantially smaller-scale, cleaner, safer and more energy-efficient process technology. This intensification is achieved by imparting multiple functionalities, such as reactions, separations, and fast heat and mass transfer, into a single system that improves efficiency and lowers costs.

The presence of impurities, the multicomponent nature, and the complex chemical composition of many of these feedstocks render their conversion challenging. Model compounds provide essential information about various aspects of catalyst function by mimicking these systems. However, they are often poor surrogates for actual feedstock streams because of their simplified molecular architectures and because they lack the interactions

among multiple components. Owing to the low volatility of solid materials, conversion often occurs in a solvent. Some solvents can cause catalyst leaching and affect catalyst activity and selectivity in poorly understood ways. Furthermore, organic feedstocks often contain functional groups that can bind to catalytic sites, and often polymerize during processing, making catalyst deactivation a crucial challenge. Robust catalysts that are resistant to these poisons and to leaching are currently lacking. These challenges require a paradigm shift in the development of a new generation of catalysts.

Fundamental research leading to the design of improved catalytic materials for the utilization of these resources offers the potential to expand U.S. manufacturing, improve rural economies (which is where many of the underutilized resources are located), decrease greenhouse gas emissions, and improve national security.

SCIENTIFIC CHALLENGES AND OPPORTUNITIES

A multi-disciplinary approach is needed to address the challenges described above. Researchers will be required to think beyond the catalyst itself and to consider the reactive systems as well as how those systems will be deployed. Increasing control over complex phenomena at multiple length scales—from atom to nano, meso, and system-level—provides a means to access currently uneconomical or even unknown catalytic chemical transformations. The challenges are not just to control the substrate-catalyst interactions, but also to manage reaction selectivity; process heterogeneous feedstocks that may be inconsistent in supply, purity, or other characteristics; and incorporate more efficient chemical and physical management of the reactants, intermediates, and products.

Conversion of complex feedstocks introduces fundamental challenges in how catalysts are designed and evaluated beyond the standard metrics of selectivity and product yield. As an example, catalyst stability must be maintained in the presence of impurities, catalyst poisons, solvents, and complex feedstocks. The design of catalytic materials that lead to lower upstream and downstream separation burdens can have significant economic and energy benefits. Similarly, many of these reactions are run in solvents, and catalyst and separation performance can change drastically with solvent, but in terms of process economics, minimizing the number of solvents is often preferable to selecting a separate solvent for each process. Integrating a catalyst into a separation system presents challenges such as catalyst leaching and regeneration tolerance, and provides an opportunity to improve performance through cooperativity.

REACTION SYSTEMS

Complex Feedstocks – Some alternative feedstocks, such as food waste and lignocellulosic biomass, are complex, solid materials. Conversion technologies for these feedstocks are challenged by a lack of analytical methods for fast and complete compositional characterization of the raw material, which is exacerbated by seasonal and geographic variability of feedstocks, solids handling, complex solvent effects, and the inability of model compounds to adequately capture the 3D architecture of biopolymers. Moreover, it is challenging to delineate the interactions among the feedstock components and the complex interactions of multiple intermediates, reactants, and products with the active site. Systematic techniques for reaction network construction are lacking. Multiple functional groups in the building blocks of the biopolymers require multifunctional catalysts, and the large size of biomass derivatives renders microporous materials such as zeolites inadequate. In addition, there are tremendous selectivity challenges associated with cleaving specific bonds during the deconstruction and subsequent upgrade of derivatives. The selectivity challenge is often overcome by lowering the reaction temperature, leading to uneconomically low reaction rates. Creating the ability to handle complex feedstocks will require major advances in analytical and reaction network methodology, in spectroscopic and modeling tools to deal with complex molecules in complex environments, and in catalyst design to deliver active, selective, robust, multifunctional, hierarchically multi-scale catalysts for these transformations.

Understanding Kinetic Behavior for Complex Mechanisms and Reaction Networks – For the most challenging transformations, completely new mechanisms must be discovered. Specifically, there is a need to identify elementary steps and thoroughly characterize their kinetic behavior to extract appropriate activation and thermodynamic parameters. Additionally, it is important to accurately describe the structures of transition states for each chemical step. In order to achieve these objectives, combined spectroscopic, kinetic, and computational studies are needed for complex reaction networks in complex environments.

Spectroscopic techniques need to be developed under *operando* conditions to identify the kinetically relevant reaction intermediates of complex catalysts including gas-solid and liquid-solid interfaces and for complex feedstocks. These will include (i) multicomponent solids with ill-defined structures such as those found in porous oxides, (ii) minority sites that are highly reactive (e.g., at the metal-oxide interface), and (iii) short-lived, kinetically relevant intermediates present at very low concentrations that are largely undetectable.

The time and spatial resolution of experimental techniques needs to be improved to follow the dynamics of complex reactions in real time and at specific active sites. Spectroscopic detection should be complemented by kinetic measurements, which can be aided by steady-state and transient studies and by isotopic labeling. The kinetic parameters extracted from such measurements may be used to identify rate-limiting steps and map out reaction trajectories for relevant, elementary reactions. Additional mechanistic probes should involve judiciously chosen perturbations to the catalyst structure, to evaluate steric and electronic influences on reactivity and establish structure-function relationships. Finally, calculations should complement the experimental work by confirming spectroscopic assignments, by providing additional information on the energetics and structures of transition states and fleeting intermediates in complex environments, and by elucidating the principles of active-site design in complex environments.

Catalysts for Tandem/Cascade Reactions – Chemical processes that combine two or more consecutive reactions in a single reactor have a number of advantages, including not having to isolate and purify intermediate compounds. This integration of multiple chemistries to intensify the process, overcome equilibrium limitations, or treat complex multifunctional substrates offers tremendous opportunities for advanced conversion technologies. However, tandem/cascade reactions introduce complexity associated with catalyst design, including the appropriate type, density and spatial distribution of catalyst sites within the catalyst and reactor. Design of complex cascade and tandem catalytic systems requires a fundamental description of elementary reactions to allow for the kinetic matching of site densities and temperature to maximize performance.

Distributed and Integrated Processes – Distributed chemical manufacturing is essential to convert feedstocks that are expensive or impossible to transport long distances because of their low energy density, or lack of chemical infrastructure in remote locations, or because they are toxic and hazardous. Designing these smaller units creates unique challenges due to higher manufacturing costs stemming from working against economies of scale, which could be partially mitigated through the intimate integration of multiple functions in a single device. The small scale of distributed manufacturing plants, which implies lack of large-scale heat integration, and the thermal sensitivity of some feedstocks, such as food waste and biomass, may require different separations and heat management strategies, and would require catalysts that operate at lower temperatures and are more selective to minimize the need for subsequent separations.

In intensified processes, catalysts are often integrated with separation, heat transfer, and transport processes in novel reactor architectures. Examples include integration of reaction with distillation, adsorption,[3] extraction[4] and membranes or integration of catalysts in heat exchangers. This integration leads to process intensification with greater energy efficiency and higher productivity. In these systems, catalysts can be exposed to concentration and temperature gradients, and undergo rapid transients associated with periodic operation, start-up and shutdown, or disruption or volatile supply of feedstock.[5,6] Catalysts that are active, robust, and selective while operating under widely varying conditions will be needed.

Combining catalysts with separation processes, such as distillation, adsorption, membranes, absorption, and extraction, can be beneficial because of the potential to reduce capital cost, overcome equilibrium limitations, or minimize side reactions of intermediates. Catalyst development for integrated reaction and separation processes is challenging and requires new designs (Sidebar 1). For example, in reactive distillation, a classic example of process intensification, catalysts must exhibit tolerance to temperature gradients throughout the column and abrasion of multi-phase (liquid-vapor) flow. In reactive extraction, catalysts must have functionalized surfaces for suitable spatial distribution of catalytic components in each phase. In reactive adsorption or absorption, catalysts must handle the transient nature of the separation, including rapid pressure or temperature swings resulting from sorbent loading and unloading. For all reactive separations, catalysts must have reaction kinetics that closely match the rate of separation.

SIDEBAR 1. COMBINED REACTION/SEPARATION TO ENHANCE CATALYTIC EFFICACY

Biomass-derived sugars are water-soluble because of their high oxygen content. These sugars can be catalytically converted into value-added products that are more soluble in an organic solvent. Dumesic and coworkers have demonstrated the selective dehydration of sugars (fructose, glucose, xylose) to furan derivatives such as 5-hydroxymethylfurfural (HMF) and furfural (Sidebar Figure 3.1).[7] The overall efficacy of the process can be enhanced by using a two-phase reactor system wherein the sugar is dehydrated in an aqueous phase, while the furan derivative product is continuously extracted into an organic phase, thus reducing side reactions. This concept can be applied to any process in which the product and reactants have different solubility in the two phases.
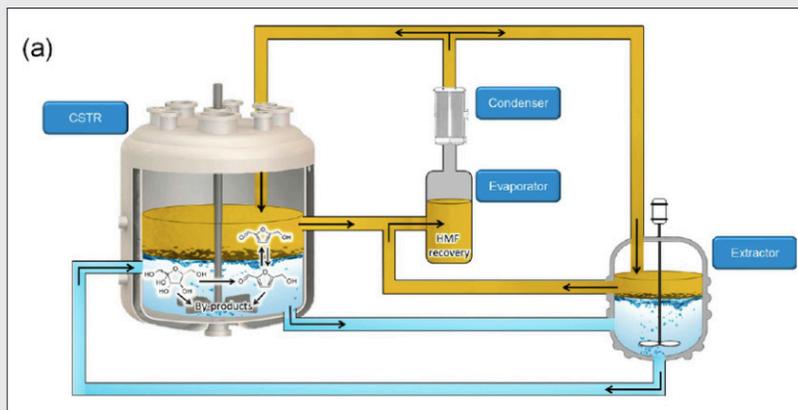
Sidebar Figure 3.1. Reprinted with permission from ACS Catalysis, June 2012, Biobased Chemicals from Conception toward Industrial Reality: Lessons Learned and To Be Learned, P. Y. Dapsens et al. Copyright © 2012, American Chemical Society.[8]

Concept patented under US Patent 20080033188A1, filed Jun. 4, 2007, and issued Feb. 7, 2008.[7]

Catalysts in Structured Microsystems – Porous networks in ceramic foams or complex metal microchannels enable fast heat and mass transfer, and robust structure during transients (e.g., in automotive exhaust). Micron-scale structures including microfilms,[9] have recently been extended, using 3D printing. For such systems to become widespread, new approaches are required to synthesize and deliver catalysts within microscale architectures and ensure long-term stability during exposure to temperature gradients and rapid transients associated with frequent startup and disruption. Also needed are methods for catalyst regeneration, self-healing, and eventually replacement. Fundamental research into materials science to ensure robustness despite differences in thermal expansion coefficients of different materials is also needed.

CATALYST FUNCTIONALITY

Enzymes are complex, hierarchical 3D materials that have properties enabling them to perform a variety of very difficult catalytic reactions under mild conditions. This functionality of performance is largely unmatched by synthetic systems. One of the key features of these systems is how they precisely position functional groups to control various properties, which cooperate to enable a high level of function. This can include proton-coupled electron transfer, spatially and temporally controlled substrate transport, and optimization of the reaction pocket, as well as small-scale and large-scale dynamics which are thought to overcome barriers and enhance reaction rates. A key scientific challenge is to understand the complexity of these interactions in enzymes in order to bring the most critical aspects into the design of synthetic systems with improved performance and scalability.

Cooperativity Between Environment and Active Site – Large-scale dynamics, known as *allosteric regulation,* are used by biological systems for manipulation of enzyme activity with a remote activator, coenzyme and/or deactivator.[10] This type of regulation can influence reactivity, couple proton and electron transfers, or allow for protection of the active site in a stable, unreactive resting state. A structural switch can convert the active site to a more reactive form during catalysis. Similar triggering mechanisms for synthetic catalysts are not well established, and very few chemical triggers that tune the reactivity of such catalysts have been demonstrated (Sidebar 2). Developing this area of catalyst design and synthesis would enable regulation of systems with eventual implications for catalyst control, stability, and tandem catalysis.

SIDEBAR 2. TRIGGERING MECHANISMS FOR SYNTHETIC CATALYSTS

Biological systems dynamically regulate reactivity by controlling the structure, and consequently access to the binding site, along with the electronic configurations and coordination geometry of the active site. Notably, the remote triggering of electronic properties (e.g., electrophilicity) at a metal center, by binding of an activator to a metal complex, is postulated to enhance catalyst performance in the Periana system for the selective oxidation of methane.[11,12] Mirkin and coworkers have developed metal-containing macrocycles that open and close upon coordination/decoordination of simple ligands.[13] Another strategy is highlighted by a system developed by Miller and coworkers, which uses cation binding as a trigger to generate an open coordination site.[14] In addition, Bergman and Tilley have demonstrated possible triggering mechanisms that greatly alter electrophilicity at a metal center, by binding of Lewis acids to remote positions in platinum complexes featuring chelating, nitrogen-containing heterocyclic ligands. This binding can result in rate enhancements for biaryl elimination of more than 100 million.[15-17]
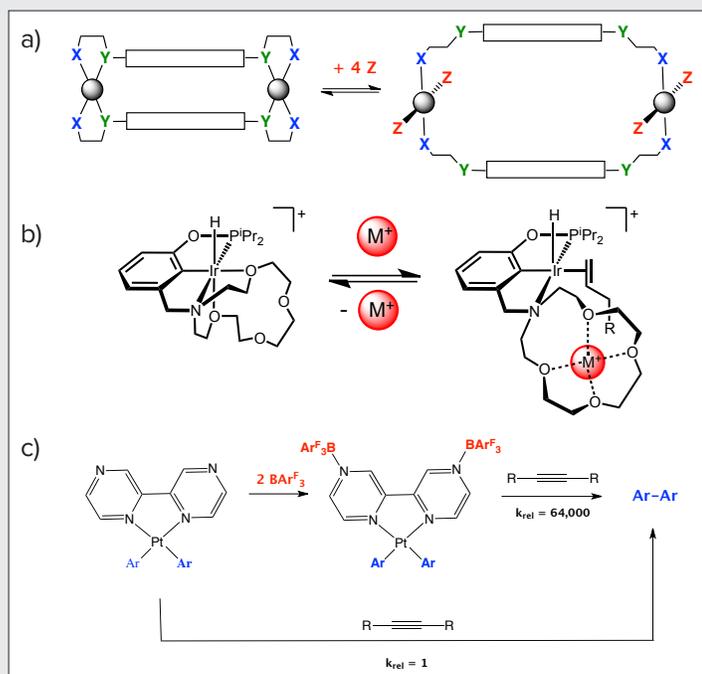
Sidebar Figure 3.2. Triggering mechanisms in molecular catalysts: (a) ligand binding induces macrocycle opening.[13] Reprinted with permission from *Inorganic Chemistry*, May 2013, General Strategy for the Synthesis of Rigid Weak-Link Approach Platinum(II) Complexes: Tweezers, Triple-Layer Complexes, and Macrocycles, R. D. Kennedy et al. Copyright © 2013, American Chemical Society. (b) ion coordination to a crown ether moiety frees a vacant site for substrate docking at the cationic iridium center.[14] Reprinted with permission from The Miller Group, 2018, Pincer-crown Ether Complexes for Cation-Controlled Catalysis, A. J. M. Miller. Copyright © 2018, Miller Group. (c) Lewis acid binding triggers C-C reductive elimination in Pt(II) complexes.[15-17] Reprinted with permission from *Journal of the American Chemical Society*, June 2013, A Remote Lewis Acid Trigger Dramatically Accelerates Biaryl Reductive Elimination from a Platinum Complex, A. L. Liberman-Martin et al. Copyright © 2013, American Chemical Society.

An immediate goal of this area is to develop mechanisms for regulation of catalyst activity with controllable triggering involving external stimuli (small molecules or ions, or via photo- or redox-switching). A more advanced stage of this research should demonstrate a regulated process whereby two or more catalysts cooperate to carry out a multi-step chemical transformation. The ability to regulate catalyst activities in a multicomponent system, with a high level of control, will allow more efficient chemical conversions that bypass isolation and separation steps in a manner reminiscent of that employed by Nature.

In addition to dynamic regulation of catalytic performance, enzymes control reactivity with a finely tuned ensemble of features, beginning with an energetically tuned active site that is thermodynamically matched to the protein scaffold. This matching includes flattened barriers, avoidance of very high or low barriers, and leveling ground state energies so that the overall process requires minimal energy. This is achieved by manipulating the electronics of the metal and the functionality participating in substrate and product transport through placement of functional groups or hydrogen bonds. It necessarily involves structural control, placing reactive groups in precise locations and using non-covalent interactions, such as π–π stacking, to control active-site structure or functional-group positioning. This has been demonstrated in bioinspired complexes, but additional examples are needed to allow a deeper understanding of all of the interactions needed. Furthermore, developments in theory are needed to accurately predict these small interactions (<2 kcal/mol, <1 pKa unit). Finally, synthetic strategies that allow precise atomic placement of functionality are also needed to develop these features in heterogeneous catalysts. An example of where this approach has been utilized is highlighted in Figure 3.1. Early efforts have focused largely on homogeneous self-assembled monolayers or capping ligands used in colloidal synthesis.[18]

Control of functionality in heterogeneous and nanoparticle systems extends beyond organic ligand and surface functionalization. It is particularly important for supported nanoparticle catalysts, which require control over metal nanoparticle size (and potentially morphology), metal-support interactions, and metal-conjugate interactions to create the additional (non-metal) functionality. Metal nanoparticles must be placed in intimate contact with supports and other functional materials. This will likely require some combination of, at a minimum, (1) solution phase nanoparticle synthesis combined with directed deposition methods, (2) the selective functionalization of support materials at the metal-support interface, or (3) the development of metal nanoparticle-ligand conjugates in solution followed by deposition onto a support.
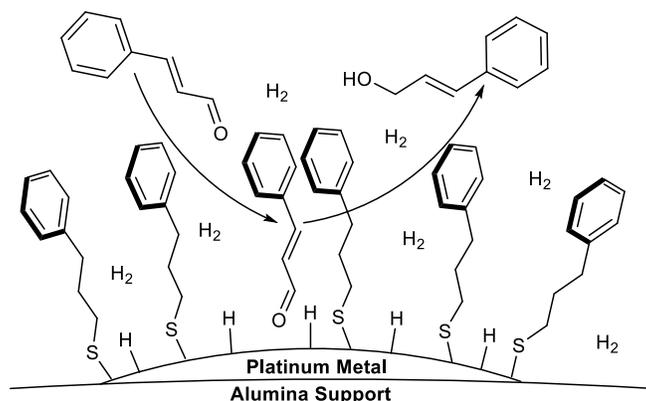
Figure 3.1. Non-covalent interactions in the near-surface environment such as π–π stacking can drive selectivity.[19] **Reprinted with permission from** *Journal of the American Chemical Society*, **Dec. 2014, Control of Metal Catalyst Selectivity through Specific Noncovalent Molecular Interactions, K. R. Kahsar et al. Copyright © 2014, American Chemical Society.**

Interplay Between Active Sites - The last ten years have seen significant strides in the synthesis and characterization of atomically precise active sites. These catalysts have been shown to be active, selective and stable for a number of important reactions. Now the opportunity arises to create and control more than one type of active site. Multiple active-site catalysts are ideal for tandem reactions and complex substrates such as biomass and food waste, which contain multiple functional groups and a complex network of elementary steps. For multicomponent streams, different reactions could occur on the same catalyst and, for example, new cross-coupling chemistry could occur. Furthermore, catalyst performance may be tuned on stream with a pulse of a trace amount of a spectator species that binds to one of the active sites and increases or decreases its reactivity. This opens up avenues for product distributions to be dynamically controlled. While such processes are practiced in industry—for example, the use of chlorine-containing gas-phase promoters in ethylene oxide catalysis[20]—there is much room for improved understanding through theory to survey binary and ternary active-site combinations and map out structure-activity space.

Recent modeling studies have demonstrated that hybrid materials have the potential to provide revolutionary improvements in catalyst performance.[21] These hybrid systems possess multiple functionalities to produce a cooperative catalyst. Use of hybrid materials in catalysis is common; for example, employing metal oxides as carriers for metal nanoparticles. It has long been recognized that the particular combination of metal and metal oxide in such systems can sometimes have a major influence on overall catalyst performance, with sites at the interface between two materials often invoked as being critical for reaction. Characterizing and achieving control over such sites has been challenging; even quantification of the density of active sites on multifunctional catalysts can be problematic and is an issue in understanding trends across different catalysts.

Therefore, methods for developing structure-property relationships for sites at interfaces, sites in close proximity carrying out cooperative catalysis, and sites in isolation carrying out tandem reactions, are necessary to enable major advances and rational design of such catalysts. Recent progress in synthesis and characterization methods provide both well-defined model systems to investigate such interactions and a route to production of new materials with unprecedented catalytic performance (Sidebar 3). It is important that these studies be complemented by computational investigations that have sufficient sophistication and accuracy to capture the relevant interfacial physics. As an example, recently the Dumesic group has developed a controlled surface reaction (CSR) synthesis approach to prepare catalysts that have uniform concentrations of sites.[22]

SIDEBAR 3. INTERFACIAL ACTIVE SITES

Metal oxides are commonly used as carriers for transition metal catalysts. It has long been recognized that such carriers—particularly "reducible" metal oxides like TiO_2 that allow removal of oxygen from the material under reaction conditions—can play a cooperative role with the metal in accelerating the reaction. Recent advances in nanomaterials synthesis and characterization have enabled more elaborate and effective approaches toward the design of highly reactive interfaces. For example, work led by Chen and co-workers has shown that pretreating Rh/TiO_2 catalysts under appropriate conditions (using a mixture of CO_2 and hydrogen) can generate a permeable TiO_2 coating over the Rh particles (see Sidebar Figure 3.3).[27] The TiO_2 coating produced in this manner provided highly reactive sites for reduction of CO_2 to fuels.
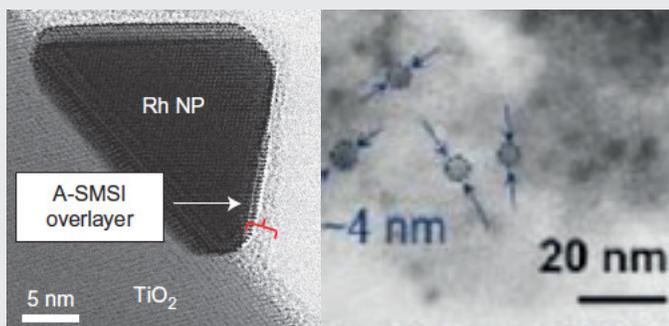
Sidebar Figure 3.3. Electron microscope images of novel interfaces. Left: Rhodium nanoparticles coated with an amorphous layer of titania improve activity for methane production from CO_2.[27] Reprinted with permission from *Nature Chemistry*, 9, 120–127, 2017, Adsorbate-mediated Strong Metal–support Interactions in Oxide-supported Rh Catalysts, J. C. Matsubu et al. Copyright © 2016, Springer Nature. Right: Palladium nanoparticles encapsulated by titania allow optimization of catalyst rates and selectivity based on pore size for deoxygenation of biomass derivatives.[28] From J. Zhang, B. Wang, E. Nikolla, and J. W. Medlin, Directing Reaction Pathways through Controlled Reactant Binding at Pd–TiO_2 Interfaces, *Angewandte Chemie International Edition*, 2017, 56, 6594–6598. Copyright 2017 Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

Related work has demonstrated that TiO_2 films can be formed around well-defined Pd nanoparticles to encapsulate them (see Sidebar Figure 3.3).[28] By changing the synthesis procedure, the size of the pores within the TiO_2 coating could be controlled to regulate the type of access afforded to reactants. Use of the smallest pores enabled much higher activity and near-perfect specificity for conversion of biomass-derived compounds to potential fuels, representing major improvements over simple supported Pd/TiO_2 materials.

This approach was used to measure the concentration of interfacial sites and, as a consequence, the intrinsic activity of the interfacial metal-metal oxide sites on supported heterogeneous catalysts for reverse water-gas shift,[23-25] methanol synthesis,[26] and ethyl acetate synthesis reactions.[26] The intrinsic activity of the interfacial metal-metal oxide site is approximately an order of magnitude higher than the monometallic sites for these catalytic reactions.

Dynamic Function of Catalysts – Catalysts are inherently dynamic materials whose local and extended structures change continuously, beginning when the components are assembled into a catalytically active architecture and continuing as materials interact with reaction mixtures. Some examples include the following:

☐ Redistribution of Cu in Cu^{2+}-exchanged SSZ during selective catalytic reduction of NO_x by NH_3;[29]

☐ Dynamics of catalytic activity as monomers are added to a growing polymer chain as monitored by single-molecule fluorescence;[30]

☐ *In situ* formation of metal-oxygen site pairs on transition metal cluster surfaces during methane oxidation,[31,32] methane reforming,[33] dimethyl ether oxidation,[34] and methanol partial oxidation reaction;[35,36]

☐ Gold atom evolution on ceria or iron oxide supports in the water-gas shift reaction, as followed by *in situ* EXAFS and STEM and E-TEM;[37-39]

☐ Real-time visualization of single polymer chain growth using a pair of magnetic tweezers, optical microscopy, and spectroscopic techniques;[40]

☐ Active transition of Rh-Pd clusters to core-shell structures with different chemical compositions on the surfaces and the cluster bulk in response to changing gas phase environment (NO−CO, NO−CO−O₂);[41] and

☐ Direct synthesis and elaboration of an ethyl-bound intermediate on a silica-supported tetra-iridium cluster.[42]

A recent review article on catalysts under dynamic conditions is pertinent.[43] As a representative example, consider the reduction/ignition of individual Pt and Rh nanoparticles as the partial oxidation of methane takes place and is monitored by using XAS techniques. The instantaneous creation of active sites and the site dynamics during catalysis are kinetically consequential, detectable only when perturbing the catalytic systems while changing the gas-phase environment and thus the chemical potentials.[44]

Challenges in this field include (i) assessing the rates in the kinetically controlled regime, free of concentration and temperature gradients, (ii) connecting intrinsic rate and selectivity data to the catalyst structures obtained with atomically resolved spectroscopies, and (iii) interpreting rate parameters with energetics derived from computational studies. Addressing these challenges will require advancing kinetic and isotopic methods, possibly through transient kinetic experiments that perturb the gas phase concentrations and the relative coverages of the various reactive intermediates together with mathematical models that capture the time-dependent evolution profiles of the various products. It also requires interrogating and monitoring the changes of the catalyst structures and the relative abundances of the surface species with *in situ* spectroscopies, and interpreting the observable molecular events with advanced, multiscale calculations that capture the relevant length and time scales of the catalyst and reactive intermediates simultaneously. Specific foci are the kinetically validated and relevant intermediates that may form at the minority, but highly reactive sites, such as the defects or coordinatively unsaturated sites on metal surfaces, at the interface between metal and the underlying oxides,[45] and when solvated by a solvent.[46]

ADVANCES IN CATALYSIS AND RELATED SCIENCES

Participants in Panel 3 also discussed a variety of catalysis science topics that may become important for the conversion of emerging and non-traditional feedstocks using advanced conversion approaches.

Active Site Design – Homogeneous catalyst design continues to advance at a rapid pace. Newly demonstrated concepts include the controlled synthesis and assembly of multimetallic clusters and heterobimetallic complexes; the use of 'non-innocent', redox-active ligands that can contribute reducing or oxidizing equivalents to the metal sites; the use of steric interactions to block coordination, resulting in 'frustrated' Lewis acid/base pairs; and the emergence of heterolytic and cooperative bond activation mechanisms that intimately involve ligand participation. In heterogeneous catalysis, owing to the advent of nanotechnologies and characterization techniques, especially precise single-site and nanoparticle syntheses, sub-atomic-resolution microscopy, and advanced computational methods, more opportunities are emerging. For instance, colloidal, dendrimer-based, and other materials synthesis methods are available for the preparation of monodispersed metal nanoparticles. The control of particle shape is more difficult but has also been advanced significantly during the last few years,[47] as has the controlled synthesis of nanoscale alloys. The application of controlled reaction chemistry between catalyst precursors using aqueous, organometallic, and gas-phase approaches has rapidly advanced to assemble single sites, synthesize nanoparticles with controlled sizes, and produce modified catalyst support functionalities, including protective "overcoats". Catalyst synthesis is described in greater detail in Panel Report 4.

Theory and Modeling – First-principles calculations have advanced to the level that they can effectively screen potential candidates for more active and selective catalysts, predict and assign spectroscopic features, and help elucidate mechanisms. Modern electronic structure theory screening for the best candidates can save the catalysis community a great deal of time in development of more efficient catalysts. For example, Mavrikakis and coworkers have searched for bimetallic core-shell nanoparticles where the core is made of one metal and the shell of another, so that they can maximize activity and selectivity for preferential oxidation of CO in the presence of H₂ (PROX). Through density functional theory studies, a Ru-core/Pt-shell nanostructure, with only 1-2 atomically thin monolayers of Pt deposited on the Ru cores, was identified as a candidate material to work at much lower temperatures compared to pure Pt. This new catalyst is much more selective than the original pure Pt-based catalysts owing to its intrinsic structure and to the lower operational temperature for the PROX reaction.[48]

In another example, descriptor-based microkinetic models have been used to predict the optimal binding energies of nitrogen and hydrogen atoms that maximize the activity in ammonia cracking to produce H_2 (Figure 3.2). These binding energies were subsequently matched using cheminformatics with electronic structure calculation data for various core/single monolayer shells of bimetallic catalysts to determine that Ni on Pt is the best Pt-based catalyst for this chemistry. Surface science experiments revealed that Ni/Pt is indeed active and desorbs N_2 at lower temperatures than Ru, the best single-metal catalyst.[49] Given that Ni and Pt are very low-activity catalysts but Ni/Pt core/shell is very active, these systems exhibit synergistic behavior that can be exploited by tuning the molecular architecture of the catalyst. Advances in theory and computational modeling for catalyst science are described further in Panel Report 4.
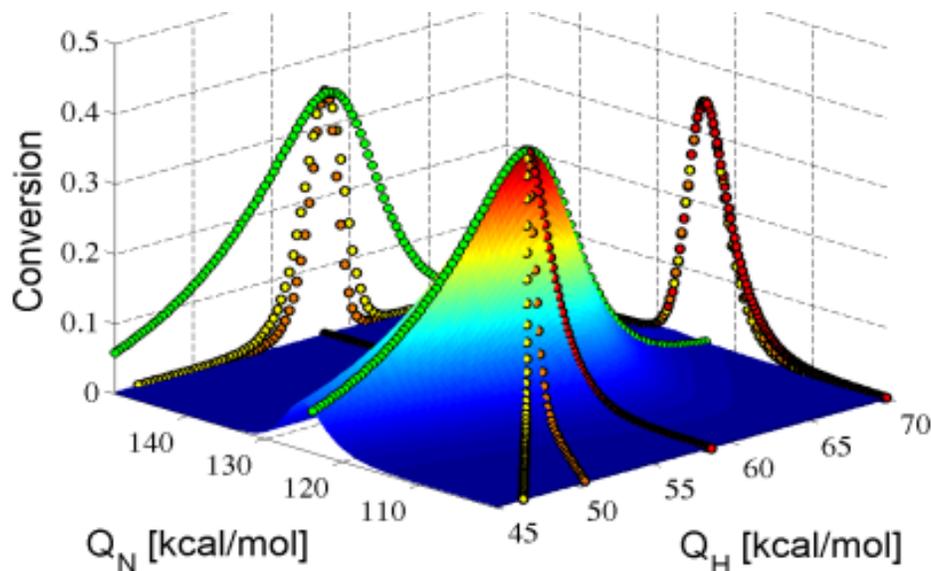
Figure 3.2. Optimal binding energies of nitrogen and hydrogen atoms for the ammonia decomposition reaction predicted from descriptor-based microkinetic modeling at 350 ˚C and 1 atm.[49] Image courtesy of Dion Vlachos (University of Delaware).

Single Metal Atom Catalysts – Designing supported metal catalysts at the single-atom limit has been another area of active research during the past decade.[50,51] These catalyst designs offer 100% atom efficiency, and more importantly, they may have distinct product selectivity, different from that of extended metal surfaces. The strongest demonstrations of atomic dispersion of metals on supports are images showing that all the metal atoms are separated from each other. Such demonstrations are recent, made possible by modern microscopy methods, especially aberration-corrected-HAADF/STEM. Many atomically dispersed supported metals on oxides have been synthesized by either chemisorption of organometallic precursors reacting with the support OH groups or adsorption of metal salt precursors on support surfaces and treatment to give anchored single-site species. On non-reactive supports, such as silica or zeolites, single gold atoms (cations) were recently prepared by a gold precursor and NaOH, making oxo-clusters of mononuclear gold coordinated with up to ten sodium ions through $-O$ linkages, with structure $Au(III)-O_x-Na_y(OH)_z$.[52]

Single metal atoms on supports other than oxides have also been reported. For example, mesoporous polymeric graphitic carbon nitride was used to support single Pd atoms in near-surface cavities coordinated with nitrogen atoms. The selective hydrogenation of 1-hexyne to 1-hexene takes place on these catalysts under ambient conditions.[53] And a new atomically dispersed platinum catalyst supported on α-MoC particles was reported to be active for methanol conversion with water under mild conditions.[54] In another example, chlorine-coordinated isolated single-gold-atom $[Au-Cl_x]-$ species on carbon have been identified as the active centers in acetylene hydrochlorination to vinyl chloride monomer.[55] This area of research has been expanded recently by the design of single atom alloys (SAAs), whereby single atoms of a metal, typically a precious metal, are alloyed in the surface of an inert but selective host metal, like Cu, creating an active and selective catalyst with good stability in hydrogenation reactions.[56] Over the past five years, SAAs have been demonstrated for many reactions including selective hydrogenations of alkynes and alkadienes, formic acid and alcohol dehydrogenation, and coke-resistant low-temperature activation of C$-$H bonds.

Construction of Hybrid Organic-Inorganic Structures – Synthesis of well-defined organic environments around metal/metal-oxide cluster sites offers opportunities for achieving step change increases in catalytic activity and selectivity. As an example, Zr_6-oxide clusters of metal organic framework (MOF) NU-1000 show the highest catalytic activity for the hydrolytic deactivation of a GD (Soman) chemical warfare agent and simulant analogues, whereas nearly no catalytic activity is observed for soluble Zr_6-oxide clusters or inorganic $Zr(OH)_4$ in solution. This function relies on an inorganic construct in which two zirconium cations are bridged by a hydroxyl ligand, similar to that found in bacterial phosphotriesterase enzymes.[57] Decreasing connectivity of organic functionalities to the node results in increasing activity (Figure 3.3), possibly owing to greater cluster accessibility.[58] As another example, the dehydration of fructose to 5-hydroxymethylfurfural (HMF), an attractive platform biomass-derived chemical, over the pristine (unmodified) Zr_6-oxide cluster node of NU-1000 MOF leads to low selectivity, whereas surface modification with phosphate leads to decreased Lewis acidity and increased HMF selectivity. Similar modification of bulk zirconia led to no catalytic activity, thereby illustrating the crucial nature of the active site, as well as its isolation as enforced by the MOF structure.[59]
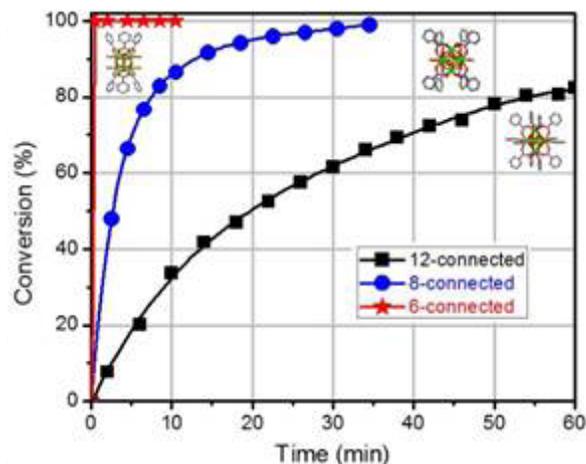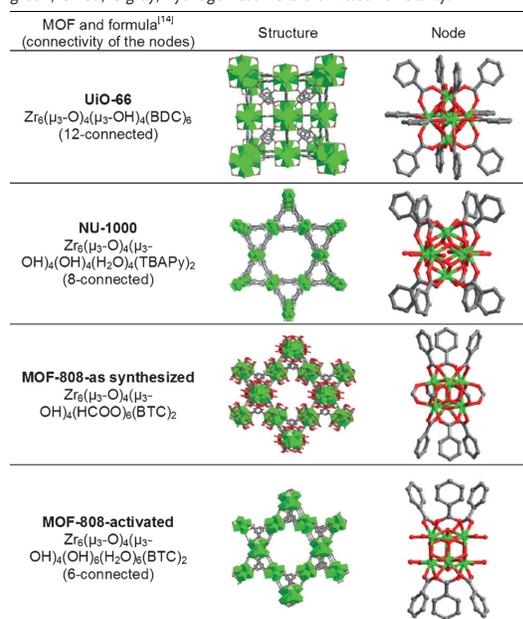
Figure 3.3. (Left) Structure of NU-1000 and related MOFs. **(Right)** Data showing the effect of Zr-node organic connectivity to hydroloysis activity of a phosphate nerve-agent simulant. From S.-Y. Moon, Y. Liu, J. T. Hupp, and O. K. Farha, Instantaneous Hydrolysis of Nerve-Agent Simulants with a Six-Connected Zirconium-Based Metal–Organic Framework, *Angewandte Chemie International Edition*, 2015, 54, 6795-6799. Copyright © 2015 Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

Advances in Silicates and Aluminosilicates – The oxides of silicon, aluminum, and silicon-aluminum mixtures are inexpensive, reliable, and widely used supports for many industrial catalysts, and the aluminosilicates (zeolites) find use as both supports and catalysts. Delaminated zeolites, which present well-defined crystalline 2D surfaces accessible to molecules that are typically too large to be transported into the 3D microporosity of conventional zeolites,[60] may prove useful for a wide variety of processes where the catalytic applications are on large, complex molecules or the catalysis would be limited by mass transfer into and out of a crystalline framework with larger dimensions. Likewise, advances in synthesis, atomic-scale characterization, and computing power continue to point to new opportunities for research in these materials.[61,62] In particular, understanding how to manipulate crystalline and amorphous materials from the atomic to nano and mesoscales has proven particularly fruitful.

Amorphous silica, alumina, and related materials are particularly challenging to characterize, but recent work has also shed light on the atomic-scale structures and distributions of sites, as well as the dynamics of the amorphous material rearrangements/evolutions for these classes of materials.[63-65] The effect of various

distributions of support structures on the performance of single-site catalysts and nanoparticles can now be addressed computationally,[66-68] though better models and more computational resources are needed.

Additional synthetic control over the support structures and construction of catalytic sites is needed, especially with respect to incorporating multiple catalytic functions for tandem, bioinspired, or other complex reactions. Molecular-level understanding of the surface structures and the opportunity to extend our understanding of the dynamics of surfaces continue to be of interest. Advanced characterization, such as enhanced NMR techniques,[69] *operando* synchrotron X-ray radiation and vibrational techniques will also provide invaluable information about catalyst function and support structure.

Overcoming Linear Correlations in Adsorption Energies and Activation Energies – Linear scaling relationships (LSRs), which correlate adsorption energies of species to each other, have proved invaluable in understanding trends among metal catalysts. In parallel, the Brønsted–Evans–Polanyi (BEP) relationship, which relates the reaction activation energy to its reaction energy for a homologous series, has enabled understanding of activity in terms of fundamental surface adsorption properties.[70-72] Combined, the BEP and LSRs form the basis of the Sabatier principle realized over 100 years ago, yielding "volcano"-shaped plots; metals which have low enough activation barriers to dissociate reactants, but weak binding energies to allow products to desorb, are the best catalysts. While these correlations are useful in understanding catalyst activity, extension to selectivity requires full microkinetic modeling. Furthermore, the ability to achieve higher rates and selectivities depends on identifying systems where these correlations are bypassed. Near-surface alloys, in which a metal surface is modified by a layer of a different element below, have been shown theoretically to yield both weak binding and a low activation barrier for CO_2 reduction (see Figure 3.4); however, owing to mixing, only a few examples of this synergy have been shown to be possible experimentally.[73-77] Similarly, core-shell structures, defect sites in bimetallics, and interfacial sites in metal/oxide systems often show unprecedented performance, likely due to creating multiple active sites that carry out different parts of the catalytic cycle.
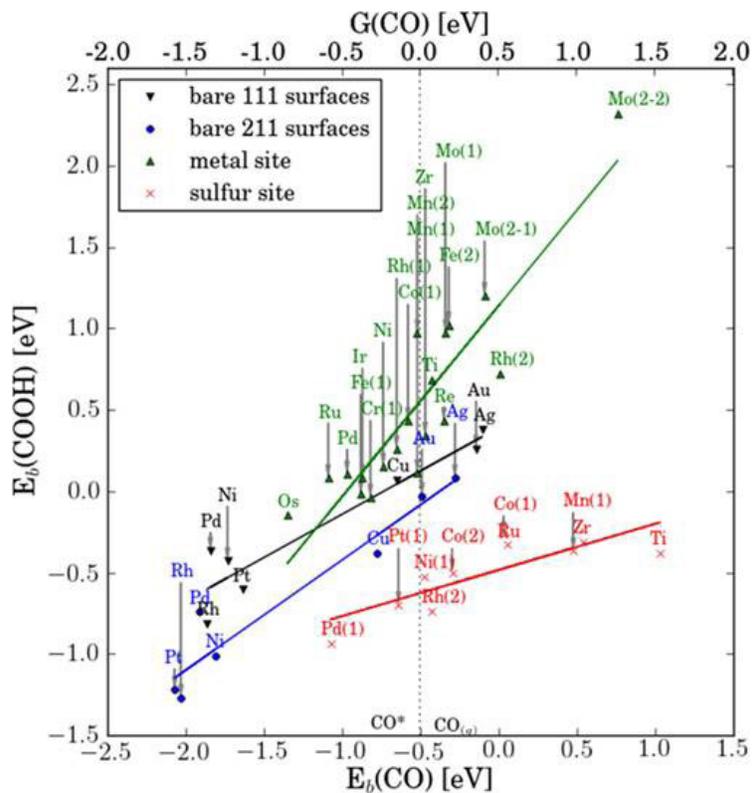

Figure 3.4. Binding energies E_b(CHO) vs. E_b(CO) for the metal and sulfur site of doped sulfur edge of MoS_2, demonstrating the breaking of transition metal scaling relations for electrochemical CO_2 reduction. The transition metal (111) and (211) scaling relations are depicted for reference. Reprinted with permission from ACS Catalysis, May 2016, How Doped MoS_2 Breaks Transition-Metal Scaling Relations for CO_2 Electrochemical Reduction, X. Hong et al. Copyright © 2016, American Chemical Society.

Moving forward, catalytic surfaces with a richer degree of spatial heterogeneity may offer a means to escape linear scaling. For example, if reactants dissociate at element A and intermediates bind at element B, then the BEP relationship breaks down.[56,78] In another example, if atom A is more catalytically active than B, then both low activation energies and weak binding of intermediates are possible. Therefore, multifunctional systems that present two or more active sites at the surface under reaction conditions may be better catalysts by virtue of cooperative interactions, allowing escape from linear scaling.

POTENTIAL FOR ENERGY-RELEVANT TECHNOLOGIES

The current fossil-based petrochemical industrial complex is built on more than a century of technology development. While there are still opportunities for improvements in current catalytic approaches, this industry is quite mature and optimized. Because of process integration, attempts to move to new feedstocks will generate changes in downstream chemistries and introduction of anything but a simple drop-in new feedstock will be a significant challenge, even if the new feedstock opportunity is less expensive than current ones. This is demonstrated by the shortage in aromatics and propylene that has resulted from the increased cracking of lighter feeds due to shale gas development. However, as this example illustrates, even a feedstock shift within a well-established technology space can offer opportunities for new chemistries and catalysts in response to the need to augment aromatics and propylene supplies. Thus, maintaining a highly effective catalytic research pipeline will be an ongoing necessity for industry for the foreseeable future.

Through catalysis, the petrochemical industry supplies the building blocks and fuels needed for modern life. Developing the processes to enable moving that industrial base to new feedstocks offers challenges which will be every bit as impactful as the catalytic cracking and alkylation technologies that revolutionized fuel production. The field will need to balance fundamental catalytic science with practical industrial needs in order to realize these future opportunities.

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Panel 4   Crosscutting Capabilities and Challenges: Synthesis, Theory and Characterization

The development of systematic feedback between *in situ* and *operando* characterization, theory and computational modeling, and experimental kinetics methods could accelerate the synthesis of catalytic materials by rational design and enable catalyst discovery extending beyond traditional empirical approaches. Nanoscale-level feedback on performance, stability, and mechanisms could expedite development of catalytic systems with improved efficacy that can perform multistep processes in complex and demanding catalytic processes.

CROSSCUTTING CHALLENGES AND OPPORTUNITIES

Multidisciplinary strategies are required to advance our current understanding of the interaction between metal centers and their surrounding environments (see Figure 4.1), ranging from redox non-innocent organic ligands in homogeneous catalysts to semiconductor or metallic surfaces with local/interfacial conditions. It is essential to correlate structure to function, including mechanistic understanding of catalyst activation by changes in the surrounding environment and passivation under reaction conditions. *Operando* measurements could enable direct correlation between activity and formation of key reaction intermediates, serving as feedback for theory refinement and prediction.

Capturing metastable states and intermediates
Operando measurements and dynamic kinetic modeling correlate structure-activity

Spanning length scales
Observation of atom scale processes at the binding site to mesoscale phenomena (confinement and cooperativity effects)

Incisive Characterization

Resolving kinetic and mechanistic pathways

Directing active site structure and stability
Site cooperativity, self-healing, and sinter resistance

Bridging multiple time scales
Permits study of pre-catalyst activation, turnover at the binding site, and catalyst evolution

Predictive Theory & Computation

Precision Synthesis

Controlling interfacial interactions

Figure 4.1. Transformative capabilities of an integrated approach with feedback between theory, synthesis, and characterization. Figure courtesy of Basic Research Needs for Catalysis Science 2017 Workshop Committee.

Synergy and combination of novel approaches in synthesis, characterization, and theory (including computational modeling) could be instrumental when addressing fundamental questions for practical applications, including:

☐ How do we organize heterogeneous, homogeneous, and biological catalysts, as well as adsorbates and non-bound species, in specific spatial arrangements?

☐ How do we design complex catalytic architectures, and characterize them during operation?

☐ How do we achieve stability of catalytic surfaces, interfaces, molecules, and nanostructures under operating conditions?

☐ How do we create self-healing catalysts to regenerate active sites?

▢ How do we construct multilayer supports with independent tuning of surface area, surface reactivity, electronic properties, and supported catalyst domain size?

▢ How do we increase the intrinsic activity of catalysts containing little or no precious metal?

The combination of precise synthesis, predictive theory and computation, and incisive characterization could provide significant advances in the field of catalysis, allowing utilization of the greater diversity of feedstocks that will become increasingly available to the chemical and fuel industries, including biomass and upgraded feedstocks from the shale gas and remote oil fields. The complexity, diversity, and purity of these feedstocks require development of novel approaches to concentrate and purify them to acceptable levels, with obvious consequences for energy efficiency. Therefore, advances in the development of complex catalysts, including nano-structured materials and mesoscopic phases, could open a wide range of possibilities to achieve multi-step separation and reaction processes, to convert raw materials selectively, and to prevent nonproductive reaction of other components and impurities.

Within the last few years, BES has held workshops and published reports in the following areas that directly relate to the crosscutting topics explored by Panel 4:

▢ Basic Energy Sciences Exascale Requirements Review (2015)

▢ Basic Research Needs for Synthesis Science for Energy Relevant Technology (2016)

▢ Basic Research Needs for Innovation and Discovery of Transformative Experimental Tools (2016)

To avoid duplication of those reports, the sections below focus on the aspects of synthesis, theory and computation, and characterization that are most relevant to catalysis science.

SYNTHESIS

Catalyst synthesis is foundational to the discovery, development, and optimization of all catalytic processes. Advances in theory have opened the door to predictions of candidates for new catalytic materials, but synthesizing the targeted structures is required for experimental validation. As an example, once a heterogeneous catalyst is identified, synthetic capabilities are instrumental in improving and optimizing its catalytic performance by exposing larger numbers of active sites or enhancing intrinsic activity. Interfacing catalysts with support materials, as well as molecules and enzymes, can offer further functionality, but requires additional synthetic processes capable of creating interfaces between solids and molecules. Synthetic requirements in catalysis science therefore require control over multiple length scales, spanning atom arrangements, nanoscopic clusters and particles, and larger microscale and macroscale architectures.

The fundamental challenge is to understand how to design and synthesize catalyst structures to control catalytic activity and selectivity. Indeed, many of the current challenges in catalyst synthesis come down to our lack of understanding of how to precisely control the placement of atoms, molecules, clusters, and nanoparticles—key pieces of catalytic active sites—to achieve highly efficient catalysts while maintaining long-term stability under often harsh reaction conditions. Once all components of a catalytic system are identified or hypothesized, it is necessary to be able to place them at precise locations and know that they remain in those locations, as well as understand how they evolve during catalysis and how their structure correlates with catalytic activity. To do so requires significant advances in precision synthesis across multiple length scales. It is imperative to control nanostructure, which includes size, shape, uniformity, composition, and architecture (alloy, core/shell, hybrid, and/or porous structure). This is especially important for catalyst systems having low platinum group metal (PGM) content, no PGM components, and metal-free systems, where the principles governing their formation and nanostructure control are not well understood. Incorporating all activity-defining components may also require identifying and controlling the arrangements of adsorbates and non-bound species, as well as tethered molecular and/or biological entities. The effort that goes into active site design and synthesis must lead to sustained catalytic activity, and therefore achieving stability of the constituent materials and molecules under operating conditions is important. Strategies include self-healing, regeneration, and antifouling; creating and sustaining metastable surface structures; and hydrothermal stability and resistance to sintering. Underpinning

the challenges in catalyst design and synthesis is basic knowledge of a targeted structure, from either theoretical predictions or other inputs, including data analysis, machine learning, and/or chemical intuition. Synthesis can also enable new discoveries in systems not yet anticipated, predicted, or known. Methods to synthesize and screen a diverse scope of materials, made under a wide range of conditions and spanning a massive phase space, provide a complementary framework to introduce new catalytic targets.

RECENT ADVANCES, SCIENTIFIC CHALLENGES, AND RESEARCH OPPORTUNITIES
Synthesis of Supported Catalyst Materials

A large class of heterogeneous catalysts consists of ions (oxides, sulfides, phosphides, nitrides, or carbides) or zero-valent metal clusters or nanoparticles anchored onto a support that is conventionally an oxide or carbon material. The support is chosen for properties that include surface area, stability, thermal/electrical/ light conductivity/transparency, or beneficial interactions with the active component. Supported metal catalysts are synthesized either from (1) pre-synthesis of a metal nanoparticle or metal cluster, followed by deposition of the metal on the support,[1,2] or (2) deposition of a precursor complex, followed by controlled decomposition to the metal. The former approach can leverage advances in nanoparticle or cluster synthesis, and is well suited for model studies. Additional understanding should be sought with respect to the resulting robustness of the connection between the support and the particle, and the complete removal of any protecting ligands.

In contrast, the latter route encompasses established techniques such as incipient wetness impregnation (IWI), ligand exchange/grafting of organometallics, or strong electrostatic adsorption (SEA).[3] In all these routes, careful control of loading, precursor structure, and the subsequent oxidative and reductive activations are critical. Careful catalyst preparation by 'conventional means' can dramatically improve catalyst uniformity and performance, and will require understanding at the molecular level.[4] Processes such as electroless deposition (ED) and photodeposition (PD), or charge-enhanced processes like SEA, can combine simultaneous deposition and reduction to the metal, and can lead to biased deposition of one species on another to create alloys and to add promoters.[5,6] While the above techniques emphasize supported metal nanoparticle catalysis, similar issues of atom-precise synthesis must be addressed in supported cationic catalysis (e.g. oxides, carbides, phosphides, nitrides or chalcogenides). Studies continue to elucidate the importance of precursor type, surface density, and support[7] and to quantify numbers of active sites in structurally complex supported oxides.[8] Advanced precursor design, including pre-formed clusters and precision surface organometallic chemistry will lead to new, more precise forms of supported oxide catalysts.[9-11]

Atomic layer deposition (ALD), a technique for the deposition of metal, oxide, and sulfide catalysts,[12,13] exploits self-limiting half reactions that sequentially graft a metal precursor, then remove the ligands by oxidizing or reducing treatments or hydrolysis. Repeated cycles of metal precursor and treatment, in a rapid and automated fashion, build up the target material, which may be either the active phase, additional support material, or a modifier. There is significant potential for ALD, due to the ability to access targeted, metastable structures (e.g. near-surface alloys or heterobimetallic oxide clusters), the development of combinatorial libraries of catalysts and promoters, and the ability to carry out simultaneous synthesis, characterization and catalytic investigations.[14] However, continued precursor and method development, as well as additional understanding of the process, is needed. Of particular interest is understanding, designing, and subsequently exploiting preferential reactivity of certain precursors on existing surfaces (e.g., metal vs oxide), which can give rise to nanostructured alloys or mixed oxides.[15] Templated oxide layers can give rise to size-selective screening analogous to zeolite behavior.[16] Future opportunities involving ALD include positional control of metal nanoparticles or clusters over macroscopic length scales, within the interior or exterior of porous materials,[17] or on patterned surfaces to enable directional, tandem catalysis or to operate on complex feeds.

A critical issue in supported catalysis is stabilization of reactive surfaces against sintering, changes in morphology, adsorption of poisons, or other forms of deactivation. This problem is particularly acute when using small metal domains, metals nanoparticles with specific facets or shapes, or aggressive reaction conditions. Advances have been made here by over coating of supported metal nanoparticles with oxides by ALD, which serves to protect the supported metal against thermal sintering and leaching in aggressive liquid environments.[18,19] Alternate strategies for stabilization of supported metal clusters include modification with thin carbon layers,[20] or deposition of 'anchor' domains of other oxides, for example, to form isolated domains of TiO_2 active for photodeposition.[21] Emerging areas for supported metal stabilization include strategies to maintain

metal nanoparticle shape, while simultaneously leaving accessible the desired active sites. Forms of selective poisoning using inorganic or organic surface ligands that occupy part, but not all, of a catalytically active surface are another potential route to protecting metals and controlling their selectivity.[22-26]

Support development is an active area of research, due to the importance of the interface between the active phase and the support in catalyzing certain reactions or inducing significant alterations to the structure and function of the active phase. Nanocrystalline oxides as supports can be used to understand these effects, as can the development of oxide supports other than alumina and silica.[27,28] The latter may engender enhanced reactivity, or be used to elucidate structure-activity trends. Synthesis of other diverse classes of supports – or catalysts in their own right – include polymer resins and emerging materials such as MOFs, zeolitic imidazolate frameworks (ZIFs), COFs, porous aromatic frameworks (PAFs), and porous organic polymers (POPs). Syntheses to exploit carbides as supports have also been reported.[29]

In practice, catalyst formulations are also optimized by the addition of promoters in small amounts, and conversely, may be strongly impacted by the presence of poisons in the reactant feeds. Increasing knowledge of promoters and poisons has seen comparatively less emphasis within the academic literature, but such understanding could be improved substantially by expanding the scope of catalyst synthesis to include studies where promoters and poisons are introduced in controlled ways. A simple example is the importance of alkali metal cations in controlling supported oxide structure and reactivity.[30,31] Alkali ion contamination is ubiquitous and often uncontrolled on many supports, yet is seldom formally addressed.

While supported oxide catalysts have long considered the importance of catalyst domains, it is also becoming possible to access single atom catalysts limit through surface stabilization. For example, single gold atom Au-$O(OH)_x$ species stabilized with alkali ions on zeolites and mesoporous oxides exhibit unusual low-temperature (<200 °C) catalytic activity for the water gas shift reaction.[32] The mechanisms of reactions catalyzed by many such materials remain a matter of active debate, although there is recognition that the active metal is not likely to be zero-valent. On many supports, single atoms are not necessarily stable even at vanishingly low loadings, although single atoms may be present even if most of the atoms exist as nanoparticles or clusters. Advances in characterization enable visualization and quantification of these species in ways that were not previously possible. Approaches to these types of materials include conventional synthesis followed by extraction to leave behind single atoms or by deliberate deposition of isolated sites that are 'protected' from aggregation by anchoring at a strong acid site, an alkali anchor, or certain supports.[33-36] Additionally, there have been attempts to stabilize single-atom catalysts by oxide overcoating or nanocavity structures (Figure 4.2).[37] These approaches are contrasted by single cations exchanged or embedded into organic or inorganic matrices.[38] Directed synthesis of hypothesized structures by combinations of metal and oxide ALD is expected to be a successful route to controlled production of such materials.[39]
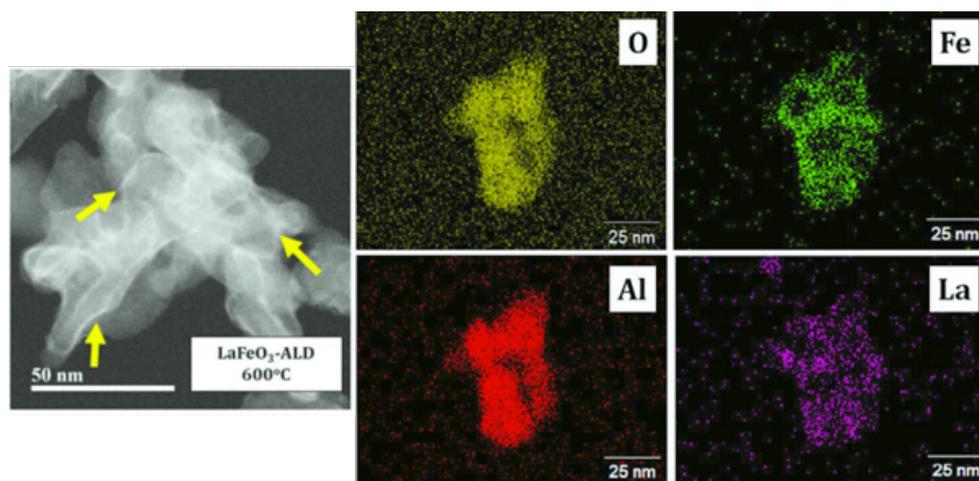

Figure 4.2. STEM and EDS results for a MgAl$_2$O$_4$ sample with a 1.3-nm coating of LaFeO$_3$.[40] Reprinted with permission from the *Journal of the American Chemical Society*, January 2018, Smart Pd Catalyst with Improved Thermal Stability Supported on High-Surface-Area LaFeO Prepared by Atomic Layer Deposition, Onn et al. Copyright 2018, American Chemical Society.

Synthesis of Nanostructured Catalytic Materials

The supported nanoparticle synthesis methods described above produce high surface area supported catalysts that offer desirable features, but lack rigorous control over other key factors that influence catalysis, including size, morphology, and compositional uniformity. Synthetic methods that enable more precise control over such features have advanced significantly in the last decade. To achieve rigorous control over particle size and shape simultaneously, solution synthesis methods are frequently used. Here, metal reagents dissolved in an appropriate solvent chemically react to form insoluble precipitates. Surface stabilizing ligands present in solution arrest growth and can preferentially stabilize various surface facets. A delicate balance among all of the many reaction variables can facilitate the formation of nanoparticles having uniform sizes and morphologies. In practice, these conditions can be difficult to achieve, and much still remains unknown about how all of the variables influence this process, including for well-established colloidal nanoparticle systems such as Au.[41] Advances in electron microscopy, including *in situ* techniques, are beginning to provide powerful atomic-level insights into how nanocrystals nucleate and grow. [42,43] Molecular-level understanding of nanoparticle formation remains largely elusive, yet such knowledge is important for predictive and precision synthesis of targeted nanoparticle catalyst systems.

Colloidal syntheses that yield high quality nanocrystals with uniform sizes and shapes are most mature and best understood, for PGM metals, such as Pt, Au, Ag, and Rh, and for particle diameters near or above five nanometers. While particle size and shape can be rigorously controlled for a growing number of nanoparticle systems, we lack the understanding to predictably achieve rigorous control over particle size and shape for many materials that are most desirable as low-PGM content and no-PGM catalysts, including base metal systems and multi-element alloys and compounds. Moving to smaller particle sizes is of great interest to catalysis. For example, molecularly precise metal clusters such as $Au_{99}(SPh)_{42}$ are being explored as catalysts that bridge heterogeneous and homogeneous systems. [44]

One strategy for expanding catalytic capabilities, as well as reducing the PGM content of expensive precious metal systems, is to employ more sophisticated nanostructuring techniques that produce a variety of alloy, core-shell, and hybrid structures. For example, alloying Pt nanoparticles with base metals, such as Fe, Co, and Ni, has produced high-quality alloy nanoparticles exhibiting enhanced catalytic activity for reactions such as alcohol oxidations.[45] Traditionally, immiscible metal alloys, such as Rh-Ag and Rh-Au, can be prepared as nanoparticles and exhibit high activity for hydrogenation catalysis.[46] $PtNi_3$ alloy nanopolyhedra transform in solution to Pt_3Ni nanoframes with thin Pt skins and exhibit a 22-fold increase in specific activity for the oxygen reduction reaction.[47] Thin shells can be grown on nanoparticle seeds to form core/shell structures, and in some cases the core enhances the intrinsic catalytic activity of the shell material. For example, a few atomic layers of Pt can be deposited onto Pd nanoparticles to produce nanostructures with enhanced catalytic activity for the oxygen reduction reaction.[48] Similar capabilities are now beginning to enable partial shells to be grown at precise locations on nanoparticles of various shapes (Figure 4.3).
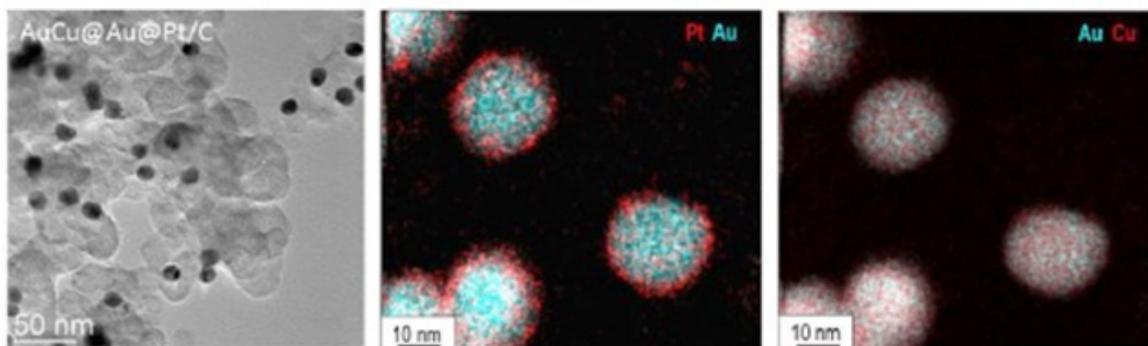
Figure 4.3. Multilayered core-shell Pt alloy electrocatalysts allow improvement of oxygen reduction reaction (ORR) activity by systematically tuning the Au-Pt ligand and strain effect by engineering the core of the nanoparticles with atomically precise composition. The figure shows the EDS elemental maps distribution of Pt, Au, and Cu throughout the nanoparticle.[49] Reprinted with permission from *ACS Catalysis*, November 2016, Nanoscale Engineering of Efficient Oxygen Reduction Electrocatalysts by Tailoring the Local Chemical Environment of Pt Surface Sites, Van Cleve et al. Copyright © 2016, American Chemical Society.

Nanostructuring processes that involve overgrowth of one material on another can be modified to produce hybrid nanostructures. For example, a variety of metal oxides and sulfides can be grown from noble metal nanoparticle seeds to form asymmetric hybrid "Janus" particles, such as Pt-Fe_3O_4 assemblies, for which independent tuning of the sizes of the Pt and Fe_3O_4 domains allows optimization of ORR catalytic activity.[50] Borrowing ideas from concepts used by organic chemists to construct large molecules, higher-order three- and four-component hybrid nanoparticles can be formed in high yield.[51] Knowledge gained about hybrid nanoparticle growth processes is beginning to enable configurational control, which is important to precisely define the types of interfaces that form between components of multifunctional catalytic nanoparticle constructs. For example, nanoparticle analogs of molecular protection/deprotection and addition/insertion reactions can produce A-B-C vs. C-A-B isomers in a growing number of three-component hybrid nanoparticle systems.[52]

Integration of Multiple Catalytic Functions

Coupling multiple materials so they can function cooperatively provides additional opportunities for designing highly sophisticated catalytic systems. For example, assembly of Pt and CeO_2 nanocrystals in a bilayer on a SiO_2 substrate produces proximate CeO_2-Pt and Pt-SiO_2 interfaces, which function in tandem to decompose methanol into CO and H_2 (over CeO_2-Pt), which is then used for ethylene hydroformylation (over Pt-SiO_2).[53] Superlattices of uniform Au and FeO_x nanocrystals provide a model platform for correlating the CO oxidation activity to the number of Au-FeO_x contacts, thereby providing insights into potential catalytic active sites.[54] Further interfacing nanoparticles and hybrid nanoparticles with molecules and biomolecules can add new functions to catalytic systems. For example, biohybrids of CdS nanocrystals and the nitrogenase molybdenum-iron (MoFe) protein enable light-driven enzymatic reduction of N_2 into NH_3.[55]

Higher surface area materials will require new scaffolds for the precise spatial arrangement of multiple catalytic functionalities. These arrangements might be deliberate pairs of active sites placed at specific distances or contain different active sites in the core versus the shell of a catalytically active particle. Supports that intrinsically have multiple different chemical functionalities will be critical to achieve these advances. [56-58]

While tandem catalysis involving multiple types of molecular or heterogeneous catalysts has been explored to some extent, [59] tandem *orthogonal* catalysis presents new opportunities and challenges.[60] In this area, multiple catalyst modalities are combined, for example, photo and thermal, or biological and non-biological, to provide unprecedented control. To move beyond catalysts that fortuitously work well together, new catalysts will need to be synthesized to make them compatible with diverse reaction environments. Modifications could include anti-fouling surfaces to make heterogeneous catalysts compatible with biological media containing salts and proteins, or redesigning a molecular catalyst to minimize its UV absorption cross-section to make it compatible with a tandem photocatalyst. [61,62]

Development of Non-PGM Catalysts

There is a growing need to discover and develop new catalysts having no PGM metals and catalysts where the PGM content is low. Many of the synthetic methods mentioned above are useful for maximizing the catalytic activity of low-PGM catalysts through nanostructuring to expose more active sites, increasing the intrinsic activity, and/or diluting the PGM metals with non-PGM metals. Complementary synthetic methods have also advanced the development of low-PGM content catalysts. For example, strontium leaching of $SrTiO_3$ while catalyzing the oxygen evolution reaction results in the formation of highly active IrO_x surface layers, which outperform benchmark IrO_x and RuO_x systems.[63] As a non-PGM catalyst for the hydrogen evolution reaction, MoS_2 has been extensively studied in the last decade, and its catalytic activity has been significantly improved by synthetic advances that include crystal structure tuning,[64] engineering mesoporosity,[65] and growing MoS_2 directly from an electrode surface with the catalytically active edge sites exposed,[66] to produce a higher density of active sites, and straining to activate the otherwise inert basal planes.[67] The synthetic processes required to achieve similar nanostructuring for other catalysts will depend sensitively on the unique chemistry of each system, and therefore developing general guidelines and also better understanding of nanostructuring in non-PGM systems will be important. Synthetic innovation has also led to discoveries of completely new classes of non-PGM catalysts. For example, nanoparticles of transition metal phosphides that include Ni_2P, CoP, FeP, MoP, and WP were synthesized and found to be highly active HER catalysts.[68]

Perovskite oxides, an important class of mixed oxide, have been attracting increasing attention as potential non-PGM electrocatalysts for OER and ORR.[69-71] Benefiting from the tunability of their compositions and structures,

they can be rationally tailored for targeted catalytic properties. Stevenson and Johnston have recently demonstrated that chemical substitution by controlled nanoparticle synthesis of perovskites can yield phase pure, moderate surface area (~10 m^2 g^{-1}) catalysts that exhibit three to seven fold more current than the industry standard IrO$_2$ on a per-surface area and per-mass basis.[72,73]

Over the past decade, metal-free materials have also emerged as a promising new class of cost-effective non-PGM catalysts for the ORR, OER, and HER reactions. For example, nitrogen-doped carbon nanotubes catalyze an ORR process free from CO poisoning, and include threefold higher electrocatalytic activity, much smaller crossover effect, and better long-term operational stability than do commercially available platinum/C electrodes.[74] The improved catalytic performance was attributed to the doping-induced charge transfer from adjacent carbon atoms to the nitrogen atoms to change the chemisorption mode of O$_2$ and to readily attract electrons from the anode for facilitating the ORR. Various other heteroatom-doped or co-/tri-doped carbon materials, including B-doped carbon nanotubes, vertically-aligned BCN (VA-BCN) nanotubes containing both nitrogen and boron heteroatoms, N-doped graphene (N-graphene) films, nitrogen-doped ordered mesoporous graphitic arrays (NOMGAs), phosphorus-doped graphite layers, and graphitic carbon nitride from CVD or ionic liquid self-assembling, have also been demonstrated to exhibit high ORR activities. Recent studies have shown that certain pure carbon nanocages without any apparent dopants could also exhibit good ORR performance due to defect-induced catalytic activities.[75]

Not all materials predicted by theory are readily accessible synthetically, and synthesis in many cases becomes a bottleneck to catalyst discovery. Advances in nanoparticle synthesis beyond the currently accessible systems will help to bridge the gap between the broad scope of predicted catalytic targets and those that can be experimentally realized as high surface area materials. To facilitate and accelerate the discovery of other new catalysts to meet the demands outlined elsewhere in this report, various screening methods that rely on innovative and strategically chosen synthetic tools can be used to complement theoretical predictions. High throughput methods for catalyst discovery have benefited from recent developments in electrochemistry[76-78] and product detection techniques for both thermal[79,80] and electro-catalysis,[81] which enable the critical evaluation of catalyst selectivity along with activity. As catalyst designs become increasingly hierarchical and multi-functional, the catalyst materials space becomes increasingly amenable to the application of high throughput methods for identifying synthesis routes that yield the desired catalytic environment, and the rapid rise in computationally designed catalysts must be met with a commensurate increase in validation experiments. Capabilities in high-temperature solid-state synthesis provide a diverse scope of polycrystalline and single-crystal materials made under highly reactive conditions and/or at high temperatures (>1000 ºC), providing a broader scope of targets and aligning with the diversity of theoretically-predicted heterogeneous catalysts.

Porous Solids

Introduction of porosity can increase the number of catalytic active sites, and therefore understanding how to introduce nanostructural features into bulk materials can profoundly improve catalytic activity. In the past decade, capabilities in the synthesis and catalytic applications of metal organic frameworks (MOFs) and COFs have advanced significantly. The precise placement of catalytic centers at specific locations within porous materials is an important goal. For crystalline zeolites, which offer molecular selectivity because of their pore sizes as well as interior catalytic capabilities, there has been an increasing appreciation that the localized oxide environment plays a role beyond the molecular sieve aspects in transition state selectivity, as well as achieving site-specific catalysts.[82,83] Applying nanostructure design to zeolite systems, thin sheets of zeolites have been achieved through direct synthesis routes. [84-86] Hierarchical structuring of zeolites may continue to be a route for simultaneous control of the local and longer length-scale properties.[87] The development of new 3D zeolitic structures, including the long-sought chiral zeolites,[88] must be matched with continued investigations into the molecular scale processes of zeolite synthesis. Important avenues of research will be adapting *in situ* characterization tools to handle the often harsh synthetic conditions[89] and developing computational approaches for this explicitly multi-scale problem. Finally, although zeolites and other regular porous materials (mesostructured oxides, MOFs, etc.) have long-range order, control over the structural heterogeneity within a single unit cell remains important. Studies should continue to address the control and understanding of defects and siting of acid sites, exchanged cations, and framework substitutions within these materials.[90]

Advances in Ligand Design and Molecular Catalyst Synthesis

Several new or expanded concepts in ligand design continue to advance the synthesis of molecular catalysts. While N-heterocyclic carbenes are now well-established supports, cyclic (alkyl)(amino)carbenes (CAACs) have been developed as new ligand frameworks.[91] Based on their unique donor properties of being highly σ donating while also strongly π accepting, CAACs are robust supports for a range of transition metals and main group elements. Redox active ligands continue to demonstrate value in catalysis,[92,93] permitting metals to retain their oxidation state throughout a catalytic cycle based on metal-ligand cooperativity. This synergy has been particularly valuable in transitioning catalysis typically observed with PGMs to first row transition metals. Ligands incorporating functionality positioned beyond the binding site, termed secondary coordination sphere effects, also continue to receive extensive interest within the community, allowing secondary interactions to occur between ligand and substrate, contributing to the activation and functionalization of a range of small molecules.[94,95] Related strategies of installing directing groups within the ligand framework have allowed for the development of highly regio- and enatioselective transformations, including challenging sp^2 and sp^3 C–H bond functionalizations.[96] As interest continues in study of multimetallic assemblies for potential use in multielectron mediated catalysis, ligand design has permitted exquisite control over the types of metals that can now be incorporated and their positioning in the complexes/clusters,[97-100] paving the way for well-defined studies of the impact of metal-metal interactions on bond making and breaking processes.

Molecular catalyst development has also seen recent advancements in several areas. In particular, Frustrated-Lewis Pairs (FLPs) have emerged as a complementary strategy to transition metal mediated processes for small molecule activation,[101] such as hydrogenation and hydroboration. While the use of organocatalysts is an established area,[102] development of enantioselective variants, organocatalysts that provide unique polymer architectures,[103] and catalysts that mediate new transformations remain active areas of interest. Switchable catalysis, particularly involving redox and photo-controlled polymerizations,[104,105] has shown advances in the past decade, largely based on the ligand and complex manifolds now accessible. Bio-inspired systems are also receiving increasing interest, based on directed evolution techniques which now allow for creation of libraries of metalloenzymes with subtle alterations to the active and binding site environments.[106] As a result of these techniques, artificial metalloenzymes have been discovered that rival activity of native enzymes while also mediating reactions inaccessible in natural systems (as in olefin metatheses and carbon-silicon bond formation).[107,108] Lastly, strides continue in development of molecular complexes which serve as pre-cursors to extended network materials, providing a bridge between homogeneous complexes and heterogeneous materials. Recent examples include multifunctional, sterically encumbering isocyanide complexes, which permit synthesis of robust networks containing low valent metal centers,[109] and cobalt thiolate coordination networks, for use in electrocatalysis.[110]

A specific challenge which remains within the area of ligand and molecular catalyst design involves development of supports and complexes which can tolerate demanding conditions (elevated temperatures and electric potentials). Particularly in the area of hydrocarbon functionalization, temperatures above 150 °C are necessary to observe viable catalysis. Under such conditions, most molecular complexes readily degrade. While pincer ligands[111,112] and amidates[113] have provided thermally robust frameworks to support high temperature reactivity with a range of transition metals, much work remains in this area. Furthermore, advances in ligands and molecular catalysts are necessary in non-thermal reactions, as even ubiquitous and robust ligand supports have recently been shown to be inadequate in stabilizing molecular catalysts and electrocatalysts,[114] resulting instead in rapid generation of nanoparticles during catalytic reactions.

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THEORY AND COMPUTATION

A fundamental goal in catalyst development is to create specific arrangements of atoms to enable facile and selective chemical transformation. Theory and computation can play a key role for this endeavor. However, the dynamics of catalysis are often complex. The catalyst enables reaction upon binding of substrates that can alter the nature of the local environment, as well as products that can modify the catalyst, affect the reaction conditions, or interfere with substrate binding, creating an interlinked dynamically evolving system. Therefore, computational catalysis must handle large systems on multiple time scales. It must use a wide range of methods, from atomic scale calculations to mesoscale statistical methods for kinetic treatments with realistic models and dynamic treatment and coupling, to macroscale computational fluid dynamic (CFD) treatments of reactor processes.

CURRENT STATUS AND RECENT ADVANCES

Recent investments by BES in computational materials sciences have established centers of excellence to provide cutting edge high performance software for modeling complex materials, validated by integration with experiment.[1] These, and several other software development consortia, have provided a large suite of capabilities that are transforming how the field approaches computational catalysis, enhancing our ability to model reactivity in complex media. High level correlated electronic structure methods (e.g., GW, Quantum Monte Carlo) can now, on large computer architectures, access systems on the order of up to 10^2 atoms. Density functional based massively parallel and/or linear scaling codes, such as Qbox, CP2K, CPMD, and ONETEP, to name a few, allow the catalysis community to perform static structural calculations on systems of on the order of 10^3 atoms at the gradient corrected or hybrid functional density functional theory level of theory.

In conditions relevant to catalysis, such as elevated temperatures, high reagent coverage, solvation, and presence of electrochemical potential, catalysts may undergo major restructuring, and accessing many states simultaneously present in the ensemble, reach some metastable configurations that are particularly relevant for catalysis. Entropic effects are often significant. Theory needs to access the ensemble state, and ensemble-averaged properties of the catalyst, which would be directly comparable to the experiment. The second open question is the fluxionality and dynamics of the catalyst itself, particularly during the catalyzed reaction.

Within the last two decades, there has been a growing interest in the catalysis community to account for reactivity at finite temperature and pressure by reactive molecular dynamics (MD) and/or *ab initio* MD methods.[2,3] Depending on the level of electronic structure methods employed, it is now routinely possible to run dynamics for systems of on the order of 10^2–10^4 atoms with time scales of 10^1–10^3 ps (10^4–10^6 configurations). These simulations allow one to gain valuable information on catalyst structure and reactivity under operating conditions and simulation of spectroscopic observables (IR, X-ray spectra, etc.) including ensemble averaging and anharmonicity. When combined with enhanced sampling techniques, these studies allow for the computation of reaction free energies and kinetic barriers.[4-10]

All atomistic studies require a reliable approach for computing free energies. Invariably the accuracy is inversely correlated to the size/number of atoms one can model within the system of interest and hence the fidelity to which one can represent the chemistry of the system. From the condensed matter physics community, high level correlated electronic structure methods (e.g., Quantum Monte Carlo)[11] now permit modeling systems on the order of up to 10^2 atoms. Likewise, high level correlations can be captured by quantum chemistry wave function-based approaches such as CCSD[T] or multi-reference determinant-based correlation methods. This allows one to account for both ground and excited states, thereby providing both state of the art benchmarks for lower level methods. Although much current effort is being placed on developing variants of these methods with more favorable scaling, these methods typically scale with higher orders N^5–N^7 with system size. Hence, gradient and hybrid exchange DFT methods have traditionally been the tools of choice for computational catalysis as they offer a compromise between accuracy and ability to represent large systems. Nonetheless, the increasing need to include statistical mechanics has led to considerable interest in reactive force field approaches such as NDO, tight binding DFT,[12] and ReaxFF,[13] which, when suitably parameterized, can provide insights on reactive chemical systems with $\sim10^5$ atoms for 10^6–10^7 configurations.

THEORY SIDEBAR 1. INVERSE DESIGN METHODS

Systematic inverse design methods can be used to assist the synthesis and optimization of molecular materials with desired functional properties. Crucial descriptors of reactivity,[18] detailed structure activity relationships,[19] and design of novel catalytic materials through a combination of high throughput screening and theory[20,21] have been reported. The inverse design approach is illustrated in the figure, for molecular frameworks with specific optoelectronic properties. [22]

Inverse design methods start from a lead structure and systematically modify it through continuous "alchemical" transformation to optimize desired properties and functionalities. An advantage of inverse design methods is scalability since they bypass the exponential scaling problem of high-throughput screening techniques. Inverse design has been applied to the development and optimization of linker chromophores for TiO_2 functionalization. [23] A novel anchor (3-acac-pyran-2-one) was found to be a local optimum with improved sensitization properties. Its molecular structure is related to known coumarin dyes that could be used as chromophore anchors for applications in dye-sensitized solar cells. These techniques are ready to be generalized and adapted for development of catalysts and conditions for optimum activity.
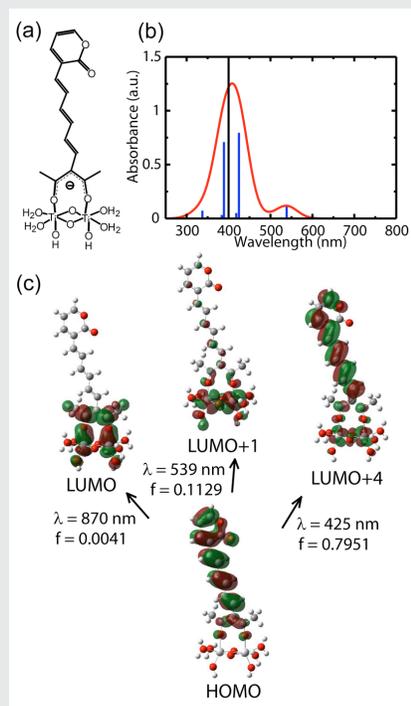
Sidebar Figure 4.1. TiO₂ model surface functionalized with a substituted 3-acac-pyran-2-one found by inverse design to have visible absorption and ultrafast IET.[22]

Reprinted with permission from *Journal of the American Chemical Society*, 133: 9014-9022, 2011, Inverse Design and Synthesis of acac-Coumarin Anchors for Robust TiO₂ Sensitization, D. Xiao et al. Copyright © 2011, American Chemical Society.

Computational approaches have allowed the community to systemize and understand the relationships between reaction energies (see Theory Sidebar 1). Concepts such as Taft inductive parameters allow us to understand and predict linear free energy relationships.[14,15] Combined with the current ability to compute (at the Generalized Gradient Approximation [GGA]-DFT level), this knowledge allows formulation of powerful concepts, such as scaling changes to relationships,[16,17] and in turn reducing the complexity of a reacting system to a few critical variables (descriptors), avoiding brute force calculations in many cases. Instead, this allows one to cast the problem of catalyst discovery in simple terms and thereby allows for computational screening of large families of catalysts.[18]

Only recently has it become clear that simple representations of a potential energy surface do not necessarily suffice for modeling complex systems. Anharmonic effects arise in many areas of catalysis, particularly in liquid phase and confined media or with fluxional particles at high temperature. Within the last two decades there has been a growing interest in the catalysis community to account for reactivity at finite temperature and pressure by reactive MD and/or *ab initio* MD methods. Nonetheless, the relatively small amount of statistics currently available to *ab initio*-based statistical mechanics methods makes enhanced sampling techniques for computing reactivity of paramount importance. Fortunately, there has been a recent explosion of advanced capabilities in this area based on techniques such as blue moon ensemble[24] or umbrella sampling metadynamics[24-26] in a well-tempered ensemble[27] employing either multiple walkers[8] or replica exchange[28] techniques, among others. Finally, modern informatics techniques coupled with enhanced sampling are allowing for on the fly adjustment of collective variables needed to better sample high dimensional spaces. These approaches will be increasingly accessible to *ab initio*-based methods within the next decade, which will allow for an unprecedented ability to sample free energy surfaces including barriers.

The rising interest of considering low temperature thermal and electrochemical conversions has sparked a lively debate about how to model conversions in liquid phase, particularly beyond homogeneous molecular catalysis but including molecular level details of the double layer at solid liquid interfaces. Polarizable continuum models have been the tool of choice in molecular catalysis having experienced great success for modeling organometallic catalysts in liquids.[29] On the other hand, there has been surprisingly less progress for solid-liquid interfaces which are complicated by speciation within the double layer and lack of detailed spectroscopic/ thermodynamic data by which to parameterize models.[30] Recent advances in MD based models have made explicit solvent studies more tractable for catalysis but the brute force computation of solvent relaxation makes the computation of reliable reaction energetics and kinetic barriers a challenge.[31,32]

Micro-kinetic modeling is fundamental in catalysis. Barriers from first principle calculations are routinely used. The active site is generic in these approaches, and hence the description of several surface sites, or the inclusion of interactions with surrounding adsorbates is not so easy. The inclusion of specific local configurational effects is currently enabled by kinetic Monte Carlo schemes.[33,34] These have brought key insights into activity and selectivity, but the present approaches are so far limited to simple model structures of catalysts as single crystal surfaces, even if some specific recent examples tackle more complex cases, such as modeling bi-functional catalysts.

SCIENTIFIC CHALLENGES AND OPPORTUNITIES

Accurate Total Energy Calculations – The energies obtained with currently available DFT functionals are usually quite useful but of limited accuracy (~0.2 eV in average) as well as limited capabilities to model systems that might require multi-reference configuration methods. The limitations of DFT have an impact on quantitative predictions of rates and branching ratios determining reaction selectivities. An outstanding challenge, hence, is to achieve higher accuracy of calculated energies and forces for increasingly complex models of catalysts and their surrounding environments.

Today, one can start to address, with DFT methods, models that include the catalyst nanoparticles, their supports, and the products and reactants. Ongoing developments promise that within the next decade the same systems will be amenable to higher levels of theory, beyond traditional DFT. Alternately, DFT methods will be able to push further into the space of complexity to consider more intricate catalytic geometries, solid surfaces in contact with complex molecular mixtures, and liquid phases.

Many catalytic systems of interest involve strong electronic correlation, making DFT not readily applicable to address their electronic structure. Relevant examples include ground states of magnetically coupled systems, such as nanostructured transition metal oxides; transition states of catalyzed reactions that develop low-spin radical character; and states involved in excited state dynamics in photocatalysis. Furthermore, there is a need for wave function-based methods that accurately treat static and dynamic electron correlation, affordable for large and heterogeneous systems. There is a need for the development of scalable *ab initio* methods, such as MPn, Coupled Cluster, Green's function methods, and multireference family methods for heterogeneous systems with large number of electrons. Strategies for finding local Hamiltonians, and the relevant sub-spaces of electronic excitations, allowing for very large active spaces to be treated, including in conjunction with gradient calculations, are required. Another frontier is the quantum mechanics/quantum mechanics (QM/QM) or embedding techniques, such as wave function embedding, or density embedding.

For example, DFT-QM/molecular mechanics (MM) methods[35,36] can provide *ab initio* quality configurations and self-consistent descriptions of electrostatic environmental effects at catalytic binding sites and outer coordination/solvation spheres, when implemented according to an iterative moving-domain (MoD-QM/MM) decomposition protocol.[37,38] The MoD-QM/MM method partitions the system into molecular domains and obtains relaxed geometries and electrostatic potential (ESP) atomic charges of the constituent molecular domains, sequentially computed by electronic embedding DFT-QM/MM methods, after updating the configuration and distribution of atomic charges in the previously optimized molecular domains. The whole cycle is iterated until a self-consistent electrostatic potential is obtained, accounting for long-range mutual polarization effects. These kinds of methods can bypass the enormous demands of memory and computational resources that would be required by a 'brute-force' quantum chemistry calculation of the complete system.

Photocatalysis and electrocatalysis introduce additional complexity for theory. In photocatalysis, light absorption promotes the system to an excited state where specific approaches are necessary to provide proper descriptions of electronic structures. In electrocatalysis, an electrochemical potential is applied, therefore, the effect of the electric field must be properly included in the description of the electrode and its surrounding Helmholtz interface that influence reactivity.

THEORY SIDEBAR 2. STATISTICAL MECHANICAL TREATMENT OF FLUXIONAL HETEROGENEOUS CATALYTIC INTERFACES

Recent developments for large-scale DFT calculations on metallic systems, such as in the CP2K[39] and ONETEP[40] linear-scaling DFT program, are paving the way for large-scale DFT calculations on metallic nanoparticles at the sizes relevant to practical applications.[41] A recent report by DOE BES[42] forecasts that this trend in growth is on track to continue such that on the system size/complexity accessible by different levels of theory will grow by one to two orders of magnitude over the next decade.

Such calculations have the potential to include the environment surrounding the catalyst (e.g., catalyst support[43,44] and solvent for liquid phase reactions,[45,46] and finite temperature[47,48]) via statistical mechanics techniques. In this context, modern DFT based simulations are now becoming capable of addressing the structure, dynamics and state of a catalyst under working conditions. A variety of catalytic interfaces, particularly those of nanoparticles or modified surfaces, can undergo major rearrangements as the catalytic reaction progresses, and remain in a dynamic state best described as a statistical ensemble of many structures. The structure(s) responsible for the majority of the catalytic activity may be either transient, rare or metastable.[47,48] The discovery of relevant structures of fluxional catalysts, and accounting for their simultaneous presence during catalysis, is essential for a realistic theoretical description of catalytic processes.
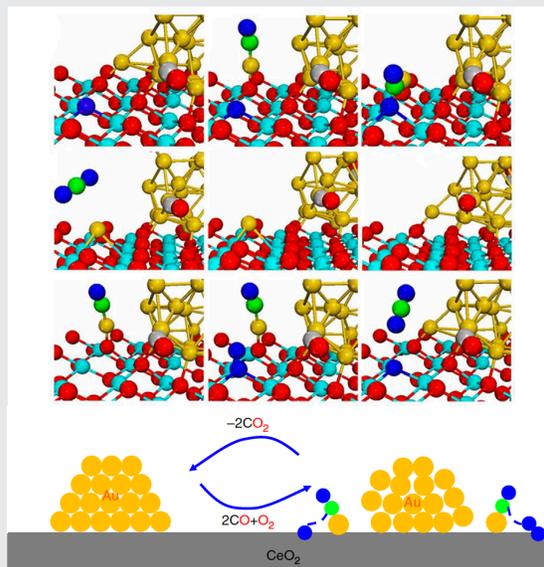
Sidebar Figure 4.2. Proposed reaction mechanism for CO oxidation at a single Au site. Top: configurations of reactants, intermediates and products. Bottom: schematic representation of the dynamic behavior at the interface. Reprinted with permission from *Nature Communications* 6511, 2015, Dynamic formation of single-atom catalytic active sites on ceria-supported gold nanoparticles, Y.-G. Wang et al. Copyright © 2015, Springer Nature.

Affordable Methods — Reasonable treatment of even larger systems (>10,000) can be addressed by using classical force-fields, or reactive force fields. They also can be reached by multiscale methods and QM/MM. Additionally, as the systems of interest get large (e.g., larger vicinities of the active site, solvation shells, or large reagents with significant configurational entropies), accuracy of the electronic energies becomes less important than the accuracy associated with ensemble representation, attained through sufficient statistical mechanical sampling and free energy calculations. Hence, for complexes and large systems, statistical mechanical approaches are emphasized in the present state-of-the-art (see Theory Sidebar 2). Descriptor-based correlation approaches and scaling relations should be extended to complex catalytic structures and interfaces. Machine learning could provide an avenue toward treating complexity through automated descriptor determination, generalization through reuse of data bases, and longer time sampling.

Modeling Experimental Spectroscopies — The tight coupling between experimental spectroscopies and theoretical modeling has two virtues. Theoretical calculations bring insight on the correct interpretation of spectra and images. In return, calculating spectra validates the model and the level of calculation used in the first-principles investigations. Bulk phase characterizations, such as nuclear magnetic resonance (NMR), "linear" vibrational spectroscopies, X-ray scattering and absorption, and neutron scattering, rely for their interpretation on models of well-defined thermodynamic states. Moving beyond the ideal paradigm (and associated simplifications) so often presented in aqueous chemistry is a key area for development. Techniques for interface

studies (sum-frequency-generation vibrational spectroscopy, X-ray or neutron reflectivity, X-ray photoemission, electron-yield X-ray absorption, or transmission electron microscopy and near-field scanning probe) are in even greater need of interpretation based on first-principles calculations. The challenges lie in two key areas: accuracy of simulated measurements and sufficient sampling of the accessible configurational space. Time-dependent DFT is an efficient approach to model optical excited states and can be implemented according to several different schemes. Its main limitations are related to approximations to the exchange correlation kernel. Recent advances employing memory functionals should continue to grow this area. Many-body perturbation theory using the GW approximation (for single-particle excitations) or the Bethe-Salpeter equation (for electron-hole excitations) enables detailed estimates of excited states of condensed phases and molecules, but faster algorithms need to be created. Algorithmic advances in existing methods to reduce time to solution without significant loss in accuracy will enable more realistic modeling of experimental scenarios on complex models.

In the domain of vibrational spectroscopies, Resonance Raman calculations and, for chiral systems, vibrational CD and Raman optical activity, in particular with metal containing systems, remain very challenging. For NMR spectroscopy, the challenges reside in the calculation of quadrupolar parameters for transition metal centers and generally speaking in the treatment of open shell systems. Well-performing methods that do not use simplistic approximations embedded with DFT are needed to treat such systems. Catalytic systems with heavy transition metals often require a treatment of spin-orbit coupling, along with other relativistic effects that currently limit the range of available simulation methods of spectroscopic techniques.

Sampling a Large Number of Configurations – Catalytic systems are typically computationally demanding and exhibit a large number of configurations during catalytic turnover (or electrocatalysis) in liquids. Even in the gas phase, solid surfaces restructure and nanostructures undergo significant changes generating a large number of configurations.

Brute force sampling is often computationally intractable, considering the typical size of catalytic surfaces and clusters, so efficient sampling techniques must be developed. Simple representations of potential energy surfaces are usually insufficient for modeling complex systems. Anharmonic effects arise in many areas of catalysis particularly in the liquid phase and confined media or with catalytic particles at high temperature.

To achieve an accurate theoretical description of the state of a catalyst under operating conditions, methods that would reveal the relevant distribution of states of the catalyst are required. Efficient sampling strategies adapted for catalytic applications could provide a realistic description of the catalyst environment, and the effect of the environment on the structural rearrangements of the catalyst.

Machine learning techniques and reliable activity descriptors for quick characterization of the broad set of sites of interfacial structures may enable faster discovery of catalytically active sites that could be explored by theoretical efforts.

Recent studies have shown that accounting for structural heterogeneity and the dynamical nature of catalytic interfaces under realistic operating conditions provides descriptions that are far from the ground state minimum energy structures. Changes to the catalyst state may include surface restructuring (Figure 4.4),[1] change of stoichiometry, as well as changes in composition or sizes of catalytic nanostructures. [24,49]

Effective methods need to be developed to address the dynamics of catalyst rearrangements, their underlying time-scales and their involvement with the reaction coordinate (i.e., rearrangements that become components of the reaction coordinate). Entropic effects need to be explicitly considered to account for
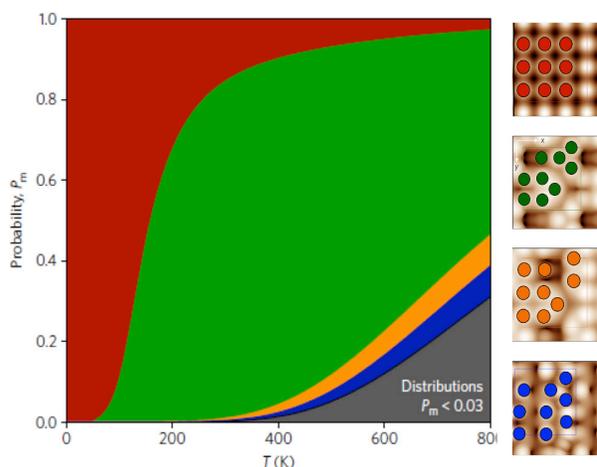
Figure 4.4. Phase diagram of the CeO$_2$ (110) surface: probability of occurrence (Pm) as a function of the temperature for the four main configurations of reconstructed CeO$_2$ (110) (depicted in the right panel by positions of Ce atoms), accounting for both enthalpy, and configurational and vibrational entropies. T-affected nature of the surface reflects in solvation effect and catalysis.[1] Reprinted with permission from *Nature Materials* 16, 328-334, 2017. Entropic contributions enhance polarity compensation for CeO$_2$(100) surfaces, M. Capdevila-Cortada et al. Copyright © 2017, Springer Nature.

distributions of active configurations and complete statistical ensembles. For example, entropic factors at high temperatures were found to be critical for the relative probability of accessible configurations.[25]

In addition to effective sampling of configurations of the catalyst, sampling configurations of the solvent as coupled to the functionality of the catalyst remains challenging. While significant efforts have been invested in the development of solvation models for homogeneous catalysis, the corresponding developments for modeling of solvation effects at solid/electrolyte interfaces remain an outstanding challenge. Such an effort is particularly important for electrocatalysis where solvation depends strongly on the nature of the electrolyte, the capacitance of the double layer interface and polarization effects under applied bias potentials. Furthermore, extensive sampling is required at liquid-solid interfaces as dissolution and decomposition of the catalyst or support are often part of the reaction coordinate during catalytic turnover.

Non-adiabatic Dynamics at Catalytic Interfaces – Dynamics on excited electronic states, including photo-induced processes, or upon adsorption or scattering from surfaces often involves non-adiabatic events. Under those conditions, a single potential energy surface does not properly account for the underlying reaction dynamics, as the system crosses multiple electronic states driven by nuclear motion. An exciting frontier is the development of methods for descriptions of catalytic systems near conical intersections and seams, particularly in the context of a continuum of states of metallic surfaces.[50] Reliable electronic structure methods are urgently needed for calculations of non-adiabatic couplings in periodic systems. Efficient approaches to model the continuum of electronic states, including discretization techniques, could provide valuable new capabilities. Dynamics simulations addressing some of the challenges mentioned have been reported; [26,27] growth in this area could provide significant impact. Tools of this sort are available for molecular and biological systems, but their adaptation for catalytic interfaces and photoinduced reaction dynamics at surfaces needs further development. The relatively small amount of statistics currently available to *ab initio* based statistical mechanics methods makes enhanced sampling techniques of paramount importance for modeling reactivity.

These new tools pave the way to realize computation for both reaction free energy barriers and fully anharmonic rate constants for realistic complex systems. Finally, modern informatics techniques coupled with enhanced sampling are allowing for on the fly adjustment of collective variables needed to better sample high dimensional spaces. These approaches will be increasingly accessible to *ab initio*-based methods within the next decade which will allow for an unprecedented ability to sample free energy surfaces, including barriers for catalytic processes. Enabling and adapting these techniques to heterogeneous systems will be needed.

Elementary Step Reactivity – The exploration of reaction pathways on static model surfaces has come a long way. The main issue is to map various sites on a complex catalyst surface (for example a supported nanoparticle), including metastable sites (precursor state) for the adsorbate or for the catalyst that would allow reaching a lower transition state. Again here, sampling is required, and fast alternatives to brute force energy calculation on large catalyst/adsorbate/environment systems are needed. Similarly, elementary step reactivity with complex reactant molecules that present chemical and conformational complexity is awkward even at the solid/gas interface and novel methods are called upon.

First-principles Kinetic Modeling – More generally applicable kinetic Monte Carlo schemes are needed. They should be able to describe complex catalyst structure, as supported clusters or nanoparticles, and one key challenge is to integrate the dynamics of rearrangement of the catalyst, on top of that of the catalytically active species. The target is to address the evolution dynamics of catalyst under operating conditions, with formation of new surface species (surface carbide, surface oxide) or restructuring of the catalysts. These processes are activated and can be rather slow (time scale of minutes or hours), and their description together with very fast events as adsorbate surface diffusion is very challenging.

Modeling Complex Reaction Networks – Reaction networks pose strong challenges for modeling, because, for rather small molecules (like syngas transformation), a complex network of surface reactions is generated already. If one considers a molecule relevant for biomass transformation, like glucose, the network becomes virtually impossible to sample using first-principle methods. Simplified but efficient methods for prescreening need to be developed. Today's approach would rely on linear scaling and group additivity methods; improved accuracy and error management are required, and the description of multifunctional and complex catalysts will require new

approaches for initial fast exploration of complex reaction networks. Accounting for complex environments, such as solvent effects, is also needed.

Multimethod-Multiscale Modeling – To describe the increasingly complex catalysts, and the long time scales needed, multi-scale multi-physics methods are essential. Although some of these methods exist now, a new generation is required. Different quantum chemical methods should be hybridized with force-field and coarse graining approaches, statistical methods, and continuum fluid mechanics. The target schemes should be able to handle atomistic interactions of the binding site, to its supramolecular environment and connection with the more remote parts of the catalyst and support on the one hand, and with the reacting fluid on the other hand. The complexity and the need for accuracy are such that several methods will necessarily be combined. Time scale is another pressing issue, with a span of femtoseconds for electronic and excited state processes to hours for the evolution of catalysts toward steady-state, or even to months if understanding of deactivation is targeted. Multiple methods need to be combined, based on trajectory or statistical mechanics based, from quantum dynamics to *ab initio* molecular dynamics (AIMD), microkinetics, kinetic Monte Carlo and other schemes.

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CHARACTERIZATION

Significant advances in catalyst characterization have been made since the previous Catalysis Science BRN workshop. These state-of-the-art improvements in both methodology and instrumentation have spanned *in situ* and *ex situ* methods, covering improvements in spatial resolution, time resolution and sensitivity, among others. These methods encompass those developed at the DOE National Laboratory user facilities (synchrotron, neutron and nanoscience centers, including electron miscroscopy) together with those in university laboratories.

SCIENTIFIC CHALLENGES AND OPPORTUNITIES

Catalysts used in real-world applications are generally multicomponent mixtures of metals and metal oxides with multiple phases, defect structures, amorphous overlayers and emergent properties that cannot be emulated with static model systems. In many cases, the active phases of catalysts are formed kinetically and these active/selective phases arise from the history and path taken through the formation and reaction processes. These processes are poorly understood and small changes in a preparation procedure or reaction conditions can significantly alter the kinetic properties of a catalyst. The challenge in catalyst development arises from the intersection of a complex material with a complex reaction mechanism. Catalysis, by its very nature, is a kinetic phenomenon that relies on maintaining a non-equilibrium state. Hence, harnessing dynamical behavior in complex materials and chemical systems is central to efficient catalytic function.

The rapid advancement in the synthesis of new and complex materials in catalysis has created novel challenges for advanced characterization. During the synthesis of catalysts, understanding and controlling elementary reactions and the evolution of materials formed are critical to discovering new phases and to optimizing the preparation and properties of novel materials, for example, with respect to composition, nanostructure and morphology (Figure 4.5).[1]
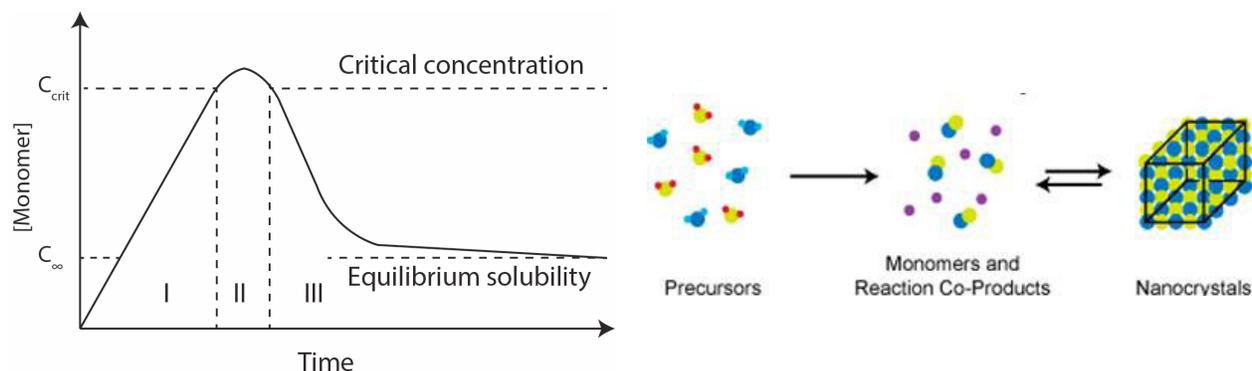
Figure 4.5. (Left) Evolution of "monomer" concentration vs. time during crystal nucleation and growth according to the La Mer model. **(Right)** Scheme showing the transformation of precursors to "monomers" and onto nanocrystals.[1] **Reprinted with permission from** *Chemistry of Materials*, **25:1233-1249, 2013, Conversion Reactions of Cadmium Chalcogenide Nanocrystal Precursors, R. Garcia-Rodriguez et al. Copyright © 2013, American Chemical Society.**

These complex structures are often not uniform and can change in structure and composition under reaction conditions. Indeed, these dynamical changes often lead to activation of the material for specific catalytic reactions.[2] The challenge that will be addressed in this section is how to interrogate and ultimately predict the function and production of these dynamical active states.

Many of the scientific challenges and opportunities associated with characterization of catalyst materials are described in detail in the BES report on Basic Research Needs for Innovation and Discovery of Transformative Experimental Tools (2016). Specifically, Section III contains panel reports on Chemical Reactions and Transformations in Functional Environments, Chemical Imaging of Materials Far Away from Equilibrium, Challenges of Heterogeneity Across Multiple Length Scales and Time Scales, and Transformational Experimental Tools Through Integration of Instrumentation with Theory and Computation. Many of the topics discussed in these panel reports directly address catalysis science.

CURRENT STATUS AND RECENT ADVANCES

Rate Constants – Identifying elementary steps and measuring their rates from model systems to functional catalysts are both important for understanding complexity. Kinetic and transient measurements when coupled with advanced spectroscopy and imaging tools provide the critical link between dynamic structure and catalytic activity and selectivity. Under *operando* conditions, a catalytic cycle is established, but the detection of minority species critical to determine reaction mechanisms is in many cases beyond experimental detection limits. One approach is to use transient methods or reactant concentration modulation. The impulses can be in the form of a transient change in the gas or solution phase composition, heat, electrical potential, or exposure to photons.

High Flux Molecular Beams – High flux molecular beams (MBs) allow the study of transient kinetics in surface science. Some catalytic reactions, including most hydrocarbon hydrogenations, lead to the deposition of carbonaceous deposits on the surface of the catalyst, and are therefore difficult to sustain under ultra-high vacuum (UHV) conditions. There are fundamental differences in the kinetics and mechanistic details between these two regimes, and a qualitative transition takes place in the intermediate pressure range between 10^{-3} and 1 mbar.[3] This regime, seldom explored, has recently been reached using high-flux MBs. Low temperature scanning tunneling microscopy (LT-STM) allows imaging single molecules. The recent coupling of a MB to LT-STM[4] allows *in situ* MB scattering studies directly under the STM tip. This technique opens an opportunity to follow chemical reactions at the local level and potentially derive reaction kinetics directly linked to a single active ensemble.

Temporal Analysis Reactor – A similar approach can be used to study transient kinetics on powder catalysts by using a temporal analysis product (TAP) reactor.[5] In this case, a controlled pulse of reactants is introduced. Transient spectroscopy and kinetic tools taken together with informatics based decision making, can provide new understanding of how catalyst composition influences the directions and weight of multistep reaction mechanisms.

Catalyst Imaging –The growth of imaging capabilities has impacted analysis of catalysts while in reactive environments, as discussed below.

☐ **Single Molecule Spectroscopy** – The ability to detect single molecule catalytic turnovers has been applied to catalysts. The localization of fluorescence emitters leads to a spatiotemporal resolution of approximately 10 nm and 10 ms.[6] For example, recent work by Ristanović et al.[7] used single molecule imaging to study the Brønsted acid-catalyzed oligomerization of styrene derivatives by individual zeolite H-ZSM-5 crystals.

☐ **Spectroscopy with Subnanometer Resolution** – Atomically resolved scanning probe microscopies (SPMs) have flourished in the last two decades. SPMs have also continued to make inroads on the imaging of catalysts in reacting environments going from mbars to atmospheric pressures.

Identifying the chemical nature of surfaces and adsorbates at room temperature and above with a spatial resolution in the nanometer range remains a challenge in the field. One approach that has made recent advances in this direction is the use of tip enhanced spectroscopies. For example, aromatic single molecules can be studied by tip-enhanced Raman spectroscopy (TERS) at 300 K.[9] Recent advances in vibrational nano-spectroscopy based on IR scanning near-field optical spectroscopy (IR-SNOM) make use of atomic force microscopy (AFM) and have improved the spatial resolution down to ~20 nm. The catalytic oxidation of N-heterocyclic carbene molecules adsorbed on Pt nanoparticles of 100 nm diameter deposited on a Si substrate could be followed at the single nanoparticle level before and after reaction using this technique (Figure 4.6).[10]
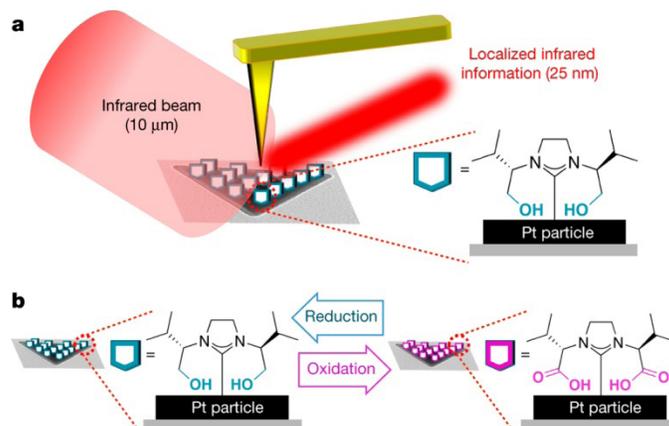
Figure 4.6. High-spatial-resolution IR mapping of catalytic reactions on single particles, combining AFM and synchrotron light.[10] Reprinted with permission from *Nature*, 541, 2017, 511-515 High-spatial-resolution mapping of catalytic reactions on single particles, Wu et al. Copyright © 2017, Springer Nature.

Future advances in the development of tip-enhanced spectroscopies would make spatial resolutions of ~1 nm possible. Incorporating nano-spectroscopies into reactor cells in order to control the reaction environment would allow direct imaging, with chemical sensitivity, the dynamic formation of catalytically active ensembles.

☐ **Electron Microscopy** – Aberration correctors for both Transmission Electron Microscopes (TEM)[11] and Scanning Transmission Electron Microscopes (STEM)[12], has allowed for imaging of catalysts with improved spatial resolution and sensitivity.[13-15] Heterogeneous catalysts can be routinely imaged on the atomic scale with the ability to identify individual atoms embedded within a porous structure and on the surface of supports.[14-15] *Operando* electron microscopy can be split into two distinct areas. Figure 4.7 shows an example of environmental TEM[16-20] in which catalytic oxidation of CO results in a faceting/de-faceting oscillation of a Pt nanocrystal.[16] The alternative approach for *operando* analysis is to use windowed cells to study samples either in higher pressure gases[21] (up to 1 bar or higher) and liquids.[22-30] Windowed cells offer the potential to study solid-liquid interfaces at/near to atomic resolution. The development of direct detection cameras for TEM permits high speed images to be obtained from a wide range of materials.[31] The primary benefit of these detectors for beam sensitive materials is that they can be used to obtain very low-dose images of biological materials, organics and porous systems.[32-33]
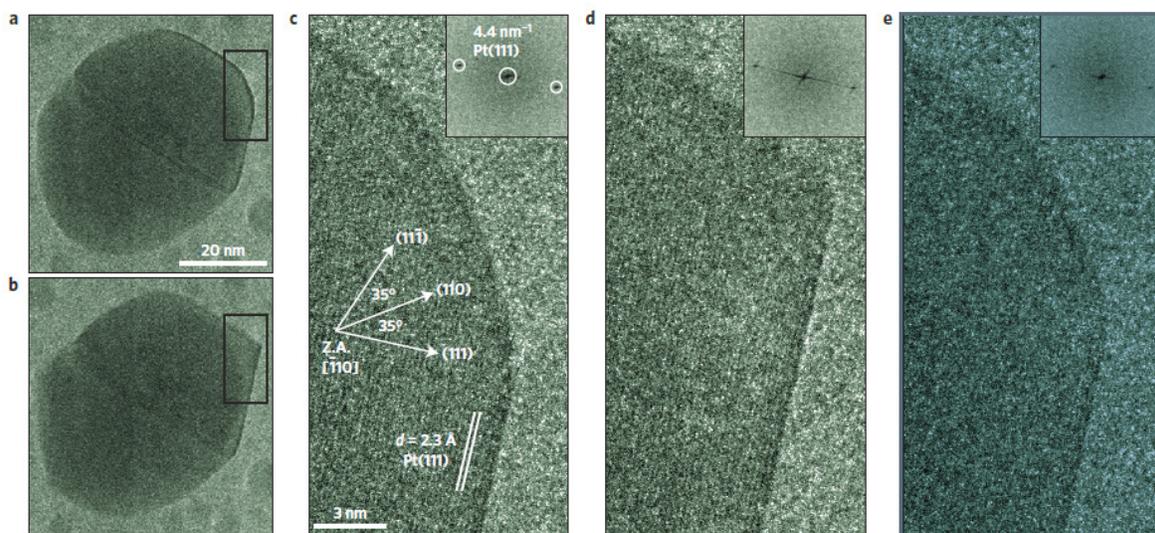
Figure 4.7. Atomic-scale visualization of the dynamic re-faceting of a Pt nanoparticle during oscillatory CO oxidation. The TEM images show the more spherical shape (a,c,e) and the more facetted shape (b,d), during the oscillatory reaction[16] Reprinted with permission from *Nature Materials* 13:884-890, 2014, Visualization of oscillatory behaviour of Pt nanoparticles catalysing CO oxidation, Vendelbo et al. Copyright © 2014, Springer Nature.

Low dose quantitative imaging in STEM mode has focused on the Z-contrast methods used primarily for the identification of small metal clusters on supports.[34] Z-contrast imaging allows metal atoms/clusters to be identified uniquely with single atom sensitivity and precision. Electron energy loss spectroscopy (EELS) can be coupled with high resolution STEM approach to Z-contrast imaging to map atomic scale composition and electronic states.[35] The application of these methods to catalysts has so far been limited by the beam sensitivity under the higher doses needed for spectroscopy. One of the biggest challenges for *operando* (S)TEM is imaging without damage. Using the recent development of compressive sensing/in-painting,[36-38] it is now possible to sub-sample images during acquisition, greatly reducing the dose, increasing the speed of acquisition and reducing the data size.

The framework for atomic scale *operando* imaging and spectroscopy that has been established over the last 10 years has the potential to address a number of the priority research directions in this report. Future work will aim to integrate the methods together with on the fly image processing and analytics, metadata and data sharing, and optimized sampling.

☐ **3D Imaging** – Non-traditional characterization tools or techniques developed by other research areas often can provide unique information when applied to the study of catalysts. Atom probe tomography (APT) is currently the only method capable of spatially resolving 3D elemental distributions at the sub-nm scale. For example, Schmidt et al.[39] used APT to probe the formation of carbon deposits in zeolites and showed that the deposition of coke resulted in agglomerates ranging in size from tens of nm to atomic-scale carbon-containing clusters (Figure 4.8).

Synchrotron Methods – At the synchrotron radiation light sources, advancements have been made from a combination of improvements in the sources, beamlines, optics, detectors, software, and *in situ* cells. Increases in brightness will enable *in situ* atomic resolution structural studies of material nucleation at short times (microsecond to millisecond), and time resolved structural studies of catalysts relevant to solar fuels production that can characterize individual intermediates in a catalytic cycle.

One of the drawbacks of X-ray absorption spectroscopy is that it is a bulk characterization method. If the active phase of the catalyst is well-dispersed, as in nanoparticles <1 nm in size, then the majority of the atoms are surface atoms and the measured signal is representative of the active material. Modulation spectroscopy is one method that has been applied to differentiate the signal from those atoms that respond to a periodic change to those that do not. For example, the synchronous combination of time resolved (energy dispersive) extended X-ray absorption fine structure (EXAFS), diffuse reflectance infrared fourier transform spectroscopy (DRIFTS), and mass spectrometry (MS), was demonstrated for *in situ* and time-resolved study of the behavior of Rh/Al_2O_3 and Pd/Al_2O_3 catalysts during CO/NO redox cycling at 573 K.[40]
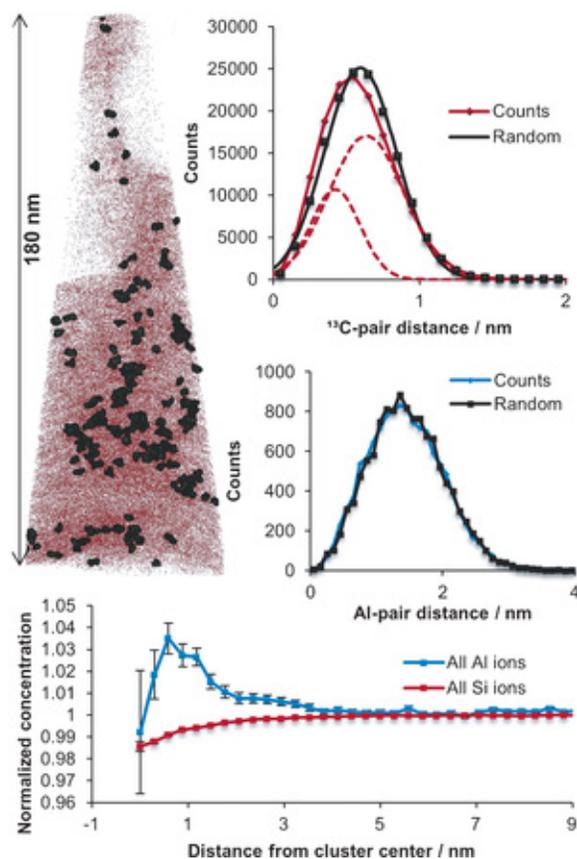
Figure 4.8. 3D Imaging of Coke Formation in a Zeolite Crystal During the Methanol-to-Hydrocarbons Reaction as Studied with Atom Probe Tomography.[39] From J. E. Schmidt, J. D. Poplawsky, B. Mazumder, Ö. Attila, D. Fu, D. A. M. de Winter, F. Meirer, S. R. Bare, and B. M. Weckhuysen. Coke Formation in a Zeolite Crystal During the Methanol-to-Hydrocarbons Reaction as Studied with Atom Probe Tomography, *Angewandte Chemie International Edition***, 2016, 55, 11173-11177. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.**

The use of photon-in/photon-out spectroscopies continues to evolve. One of these innovations applied a crystal spectrometer to energy select a particular fluorescence line. This technique is known as high-energy resolution fluorescence detection (HERFD) XAS. This method has been demonstrated to give greatly enhanced chemical

information, is applicable to *in situ* catalysis studies, and has been applied by a growing community of catalysis researchers. For example, Friebel et al.[41] used *operando* HERFD to study the origin of the 500-fold oxygen evolution reaction (OER) activity enhancement that can be achieved with mixed (Ni, Fe) oxyhydroxides ($Ni_{1-x}Fe_xOOH$) over their pure Ni and Fe parent compounds.

Spectro-Microscopy – The length scales relevant to catalysis span many orders of magnitude,[42] and as such it is only through a combination of imaging and spectroscopic techniques that needed information regarding catalyst structure can be obtained. While mapping the location of an element in a catalyst at ever-increasing spatial resolution provides new information, it does not provide information on the function of that element. An example of the application of multi-scale microscopy revealing the active phase distribution under working conditions is that of Cats et al.[43] They used a combination of transmission X-ray microscopy (TXM), scanning transmission X-ray microscopy (STXM), and STEM-EELS to visualize the changes in the structure, aggregate size, and distribution of supported Co nanoparticles that occur during Fischer-Tropsch synthesis.

The development of soft X-ray ptychography, (a high spatial resolution coherent diffraction imaging technique), has demonstrated a spatial resolution of sub-5 nm.[44] This is exemplified in the work of Wise et al.[45] who mapped the location and chemical state of iron in a spent FCC catalyst and were able to conclude that the iron resulted from both tramp iron and from iron present in the metalloporphyrinic molecules in the feed, providing evidence for two distinct iron-based deactivation mechanisms. Recent advances have opened up the potential of hard X-ray nanoprobe and nano-spectrocopy under *in situ* conditions. Perhaps more importantly, the working distance will be approximately 50 mm, an order of magnitude larger than soft X-ray imaging beamlines, allowing for the incorporation of *in situ/operando* cells; a key requirement for application to the most demanding applications in catalysis.

Multi-modal Characterization – A multi-modal approach is nicely illustrated in the work of Liu et al,[46] who combined X-ray imaging techniques at different length scales, to develop a correlative approach to the metal poisoning of a commercial FCC catalyst (Figure 4.9). A key finding in this work is that deposition of metals affects the resistance to mass transfer, and thus access to the active sites. In another example, Ristanović et al. used a combination of synchrotron XRD and X-ray excited optical luminescence (XEOL) to probe the crystallographic structure and reactivity of a single zeolite crystal.[47]
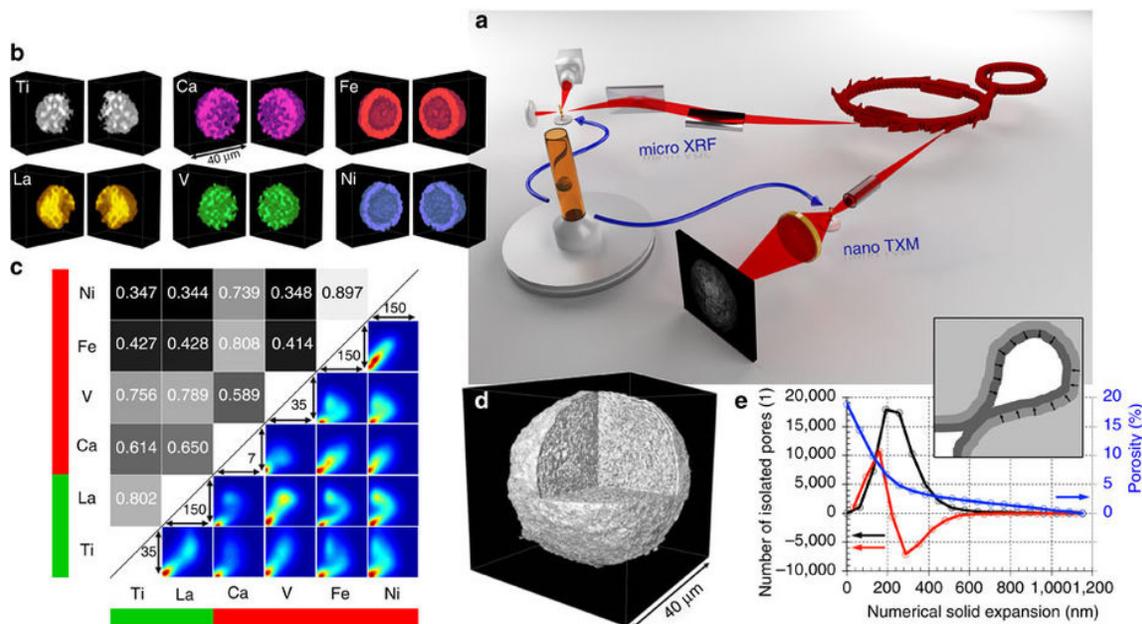
Figure 4.9. Correlative 3-D X-ray microspectroscopy. a) Diagram of μ-XRF and nano-TXM performed on an FCC catalyst particle; b) 3D elemental distributions in the particle; c) spatial correlation plot using Pearson's correlation coefficient (PCC); d) high resolution TXM revealing internal and external structure of a catalyst particle; and e) pore throat analysis developed from the TXM data. Reprinted with permission from *Nature Communications* 7, article no. 12634, 2016, Relating structure and composition with accessibility of a single catalyst particle using correlative 3-dimensional micro-spectroscopy, Liu et al. Copyright © 2016, Springer Nature. DOI: 10.1038/ncomms12634.

Ambient Pressure X-ray Photoelectron Spectroscopy (AP-XPS) – This technique has become widely used for the study of both single crystal and powder catalysts.[48] Pressures in the millibar range can be obtained regularly with most gases, while pressures up to 1 bar have been demonstrated using a graphene window in a cell when filled with an inert gas. Strategies to make possible the use of atmospheric pressures to study catalytic reactions without limitations in the gases used would further enhance the utilization of AP-XPS.[49]

Nano-scale Catalytic Activity – Nanoparticle (NP) materials are ubiquitous in heterogeneous catalytic processes ranging from chemical synthesis to petroleum refining, and there is broad interest in their physical and chemical properties. Due to their complex structure, a combination of theoretical modeling[50] and X-ray experiment is essential to understand the heterogeneity of these systems[51] and their variation under realistic conditions. Global experimental probes such as EXAFS, X-ray absorption near edge structure (XANES), and XPS, only measure ensemble characteristics, obscuring details of local properties.[52] Fortunately, large scale finite temperature DFT/MD simulations are now possible with high performance computational methods, and yield a rich, detailed understanding of their structure and its influence on catalytic activity. These simulations reveal that the local structure and charge distribution are inhomogeneous and dynamically fluctuating over several time scales, ranging from fast (200–400 fs) bond vibrations to slow fluxional bond breaking (>10 ps). The fluctuating interaction with the support is also important since it affects local charge states. For example, Pt atoms in contact with O atoms in the support become oxidized, leading to layering of the internal charge distribution, which in turn affects the interaction with adsorbates.[53] These results highlight the importance of advanced theory as a complement to X-ray spectroscopy experiments.

Inelastic Neutron Scattering (INS) – A less familiar local structural probe than other spectroscopies, the interaction of neutrons with matter is particularly sensitive to hydrogen. Inelastic neutron scattering spectroscopy is a technique that can readily distinguish between molecular and atomic hydrogen. Sample background subtraction in INS is straightforward and reliable, as it is possible to measure very low signals on top of very large backgrounds. Recently, the first direct spectroscopic evidence for the presence of both surface and bulk $Ce-H$ upon H_2 dissociation over ceria was obtained via *in situ* INS. The result has two significant implications for ceria catalysis. First, the dissociation mechanism of H_2 on CeO_2 is clearly a heterolytic pathway, yet the $Ce-H$ is only stable on reduced CeO_2 surfaces and transfers readily to oxygen when the O-vacancy is filled, directly confirming the hypothesis raised in the recent DFT calculation that the homolytic product is more energetically stable than the heterolytic one.[54]

Solid State Nuclear Magnetic Resonance (SSNMR) Spectroscopy – During the last decades, SSNMR spectroscopy has evolved to become one of the premier analytical methods for atomic-scale characterization of heterogeneous catalytic systems. The technique is capable of providing chemical and physical knowledge about catalyst supports, active sites, defects, feedstocks, reacting molecules and reaction mechanisms. However, the fundamental lack of sensitivity of conventional SSNMR limits its applications to bulk phases, large surface area materials, and compounds containing sufficient concentrations of receptive nuclei. Despite the progress, however, there is a critical need in the catalysis community for more advanced NMR tools, offering much higher sensitivity, under both *ex situ* and *operando* conditions. Significant advances were recently made in both these areas.

Since its introduction to surface science in 2010,[55] dynamic nuclear polarization (DNP) has revolutionized SSNMR spectroscopy by allowing the detection of insensitive nuclei (e.g., ^{13}C, ^{15}N, ^{17}O, ^{35}Cl, ^{43}Ca, ^{89}Y, ^{119}Sn, ^{195}Pt) in minute concentrations and on much smaller surfaces (down to several cm^2) than previously possible.[56-57] The technique relies upon the saturation of the electron paramagnetic resonance (EPR) line of unpaired electrons by microwave irradiation and subsequent transfer of polarization to ^1H or other nuclei, which yields enhancements of SSNMR signals under magic angle spinning (MAS) by 2–3 orders of magnitude.[58] The development of micro-autoclave probes capable of performing MAS of sealed samples, which can currently operate at temperature up to 250 °C and pressure up to 100 bar is notable.[59-60] In spite of these remarkable achievements, DNP is still an emerging spectroscopy. Expanding the direct polarization protocols, which will allow observation of non-protonated low-g nuclei, is needed. Especially important for catalysis will be the development of solvent-free sample formulations to eliminate the interactions exerted by the solvent ('ice') that can affect the structure and conformation of studied species.

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Appendix A: Figure Sources

INTRODUCTION

PRIORITY RESEARCH DIRECTION REPORTS

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PRD 2

Sidebar Figure 2.2	25	Rivalta, I., Sultan, M. M., Lee, N. S., Manley, G., Loria, J. P., and Batista, V. S., Allosteric Pathways in the Imidazole Glycerol Phosphate Synthase, Proceedings of the National Academy of Sciences of the United States of America 109 (2012) E1428-1436. DOI: 10.1073/pnas.1120536109.
Figure 2.5	25	Vlatković, M., Collins, B. S. L., and Feringa, B. L., Dynamic Responsive Systems for Catalytic Function, Chemistry – A European Journal 22 (2016) 17080-17111. DOI: 10.1002/chem.201602453.
Figure 2.6	26	Oh, T. S., Rahani, E. K., Neagu, D., Irvine, J. T. S., Shenoy, V. B., Gorte, R. J., and Vohs, J. M., Evidence and Model for Strain-Driven Release of Metal Nanocatalysts from Perovskites during Exsolution, The Journal of Physical Chemistry Letters 6 (2015) 5106-5110. DOI: 10.1021/acs.jpclett.5b02292.
Sidebar Figure 2.3	26	Easter, Q. T., and Blum, S. A., Single Turnover at Molecular Polymerization Catalysts Reveals Spatiotemporally Resolved Reactions, Angewandte Chemie, International Edition 56 (2017) 13772-13775. DOI: 10.1002/anie.201708284
Figure 2.7	27	Lunkenbein, T., Girgsdies, F., Kandemir, T., Thomas, N., Behrens, M., Schlögl, R., and Frei, E., Bridging the Time Gap: A Copper/Zinc Oxide/Aluminum Oxide Catalyst for Methanol Synthesis Studied under Industrially Relevant Conditions and Time Scales, Angewandte Chemie, International Edition 55 (2016) 12708-12712. DOI: 10.1002/anie.201603368.

PRD 3

Figure 3.1	32	Mika, L. T., Cséfalvay, E., and Németh, A., Catalytic Conversion of Carbohydrates to Initial Platform Chemicals: Chemistry and Sustainability, Chemical Reviews 118 (2) (2018) 505-613. DOI: 10.1021/acs.chemrev.7b00395.
Figure 3.2	34	Lu, J., Dimroth, J., and Weck, M., Compartmentalization of Incompatible Catalytic Transformations for Tandem Catalysis, Journal of the American Chemical Society 137 (2015) 12984-12989. DOI: 10.1021/jacs.5b07257.
Figure 3.3	35	Denard, C. A., Huang, H., Bartlett, M. J., Lu, L., Tan, Y. C., Zhao, H. M., and Hartwig, J. F., Cooperative Tandem Catalysis by an Organometallic Complex and a Metalloenzyme, Angewandte Chemie, International Edition 53 (2014) 465-469. DOI: 10.1002/anie.201305778.
Sidebar Figure 3.1	35	Karp, E. M., Eaton, T. R., Nogué, V. S. I., Vorotnikov, V., Biddy, M. J., Tan, E. C. D., Brandner, D. G., Cywar, R. M., Liu, R. M., Manker, L. P., Michener, W. E., Gilhespy, M., Skoufa, Z., Watson, M. J., Fruchey, O. S., Vardon, D. R., Gill, R. T., Bratis, A. D., and Beckham, G. T., Renewable Acrylonitrile Production, Science 358(6368) (2017) 1307-1310. DOI: 10.1126/science.aan1059.
Figure 3.4	36	Maduskar, S., Facas, G. G., Papageorgiou, C., Williams, C. L., and Dauenhauer, P. J., Five Rules for Measuring Biomass Pyrolysis Rates: Pulse-Heated Analysis of Solid Reaction Kinetics of Lignocellulosic Biomass, ACS Sustainable Chemistry & Engineering 6 (2018) 1387-1399. DOI: 10.1021/acssuschemeng.7b03785.
Sidebar Figure 3.2	37	Ulissi, Z. W., Medford, A. J., Bligaard, T., and Nørskov, J. K., To Address Surface Reaction Network Complexity using Scaling Relations Machine Learning and DFT Calculations, Nature Communications 8 (2017) 14621 DOI: 10.1038/ncomms14621.
Figure 3.5	38	Alonso, D. M., Wettstein, S.G., Mellmer, M.A., Gurbuz, E. I., and Dumesic, J. A., Integrated Conversion of Hemicellulose and Cellulose from Lignocellulosic Biomass, Energy and Environmental Science 6 (2013): 76-80. 10.1039/C2EE23617F.

Sidebar Figure 1.1	69	Alonso, D. M., Hakim, S. H., Zhou, S., Won, W., Hosseinaei, O., Tao, J., Garcia-Negron, V., Motagamwala, A.H., Mellmer, M.A., Huang, K., Houtman, C.J., Labbé, N., Harper, D.P., Maravelias, C., Runge, T., and Dumesic, J.A., Increasing the revenue from lignocellulosic biomass: Maximizing feedstock utilization, Science Advances 3 (2017) e1603301. DOI: 10.1126/sciadv.1603301.
Figure 1.3	71	Ingram, A. J., Walker, K. L., Zare, R. N., and Waymouth, R. M., Catalytic Role of Multinuclear Palladium-Oxygen Intermediates in Aerobic Oxidation Followed by Hydrogen Peroxide Disproportionation, Journal of the American Chemical Society 137 (2015) 13632-13646. DOI: 10.1021/jacs.5b08719.
Figure 1.4	72	Sirajuddin, S. and Rosenzweig, A. C., Enzymatic Oxidation of Methane, Biochemistry 54 (2015) 2283-2294. DOI: 10.1021/acs.biochem.5b00198

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Figure 2.1	82	Seh, Z.-W., Kibsgaard, J., Dickens, C.F., Chorkendorff, I., Nørskov, J. K., and Jaramillo, T.F., Combining theory and experiment in electrocatalysis: Insights into materials design, Science 355 (6321) eaad4998. DOI: 10.1126/science.aad4998.
Sidebar Figure 2.1	83	Tanja Cuk (University of Colorado – Boulder)
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Figure 2.4	89	Oh, S., Gallagher, J. R., Miller, J. T., and Surendranath, Y., Graphite-Conjugated Rhenium Catalysts for Carbon Dioxide Reduction, Journal of the American Chemical Society 138 (2016) 1820-1823. DOI: 10.1021/jacs.5b13080.
Sidebar Figure 2.3	90	Brown, K. A., Harris, D. F., Wilker, M. B., Rasmussen, A., Khadka, N., Hamby, H., Keable, S., Dukovic, G., Peters, J. W., Seefeldt, L. C., and King, P. W., Light-driven dinitrogen reduction catalyzed by a CdS:nitrogenase MoFe protein biohybrid, Science 352(6284) (2016) 448-450. DOI: 10.1126/science.aaf2091.

Panel 3

Sidebar Figure 3.1	98	Dapsens, P. Y., Mondelli, C., and Pérez-Ramírez, J., Biobased chemicals from conception toward industrial reality: lessons learned and to be learned, ACS Catalysis 2 (2012) 1487-14992. DOI: 10.1021/cs300124m.
Sidebar Figure 3.2	99	(a) Kennedy, R. D., Machan, C. W., McGuirk, C. M., Rosen, M. S., Stern, C. L., Sarjeant, A. A., and Mirkin, C. A., General Strategy for the Synthesis of Rigid Weak-Link Approach Platinum(II) Complexes: Tweezers, Triple-Layer Complexes, and Macrocycles, Inorganic Chemistry 52 (10) (2013) 5876-5888. DOI: 10.1021/ic302855f.
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Figure 3.1	100	Kahsar, K. R., Schwartz, D. K., and Medlin, J. W., Control of metal catalyst selectivity through specific noncovalent molecular interactions, Journal of the American Chemical Society 136 (2014) 520-526. DOI: 10.1021/ja411973p.
Sidebar Figure 3.3	101	(left) Matsubu, J. C., Zhang, S., DeRita, L., Marinkovic, N. S., Chen, J. G., Graham, G. W., Pan, X., and Christopher, P., Adsorbate-mediated strong metal–support interactions in oxide-supported Rh catalysts, Nature Chemistry 9 (2017) 120-127. DOI: 10.1038/nchem.2607.
		(right) Zhang, J., Wang, B., Nikolla, E., and Medlin, J. W., Directing reaction pathways through controlled reactant binding at Pd–TiO_2 interfaces, Angewandte Chemie, International Edition, 56 (2017) 6594-6598. DOI: 10.1002/anie.201703669.
Figure 3.2	103	Dion Vlachos (University of Delaware)
Figure 3.3	104	Moon, S.-Y, Liu, Y., Hupp, J. T., and Farha, O. K., Instantaneous hydrolysis of nerve-agent simulants with a six-connected zirconium-based metalorganic framework, Angewandte Chemie, International Edition, 54 (2015) 6795-6799. DOI: 10.1002/anie.201502155.
Figure 3.4	105	Hong, X., Chan, K., Tsai, C., and Nørskov, J. K., How doped MoS_2 breaks transition –metal scaling relations for CO_2 electrochemical reduction, ACS Catalysis 6 (2016) 4428–4437. DOI: 10.1021/acscatal.6b00619

Panel 4

Figure 4.1	109	Basic Research Needs for Catalysis Science 2017 Workshop Committee
Figure 4.2	112	Onn, T. M., Monai, M., Dai, S., Fonda, E., Montini, T., Pan, X., Graham, G. W., Fornasiero, P., and Gorte, R. J., Smart Pd Catalyst with Improved Thermal Stability Supported on High Surface Area $LaFeO_3$ Prepared by Atomic Layer Deposition, Journal of the American Chemical Society 140 (2018) 4841-4848. DOI: 10.1021/jacs.7b12900.
Figure 4.3	113	Cleve, V., Moniri, S., Belok, G., More, K. L., and Linic, S., Nanoscale Engineering of Efficient Oxygen Reduction Electrocatalysts by Tailoring the Local Chemical Environment of Pt Surface Sites, ACS Catalysis 7 (2017) 17-24. DOI: 10.1021/acscatal.6b01565.
Sidebar Figure 4.1	122	Xiao, D., Martini, L. A., Snoeberger, R. C., Crabtree, R. H., and Batista, V. S., Inverse Design and Synthesis of Acac-Coumarin Anchors for Robust TiO_2 Sensitization, Journal of the American Chemical Society 133 (2011) 9014-9022. DOI: 10.1021/ja2020313.
Sidebar Figure 4.2	124	Wang, Y.-G., Mei, D., Glezakou, V.-A., Li, J., and Rousseau, R., Dynamic formation of single-atom catalytic active sites on ceria-supported gold nanoparticles, Nature Communications 6 (2015) 6511. DOI: 10.1038/ncomms7511.
Figure 4.4	125	Capdevila-Cortada, M., and López, N., Entropic contributions enhance polarity compensation for CeO_2 (100) surfaces, Nature Materials 16 (2017) 328-334. DOI: 10.1038/nmat4804.
Figure 4.5	129	García-Rodríguez, R., Hendricks, M. P., Cossairt, B. M., Liu, H., and Owen, J. S., Conversion Reactions of Cadmium Chalcogenide Nanocrystal Precursors, Chemistry of Materials 25 (2013) 1233-1249. DOI: 10.1021/cm3035642.
Figure 4.6	131	Wu, C.-Y., Wolf, W. J., Levartovsky, Y., Bechtel, H. A., Martin, M. C., Toste, F. D., and Gross, E., High-spatial-resolution mapping of catalytic reactions on single particles, Nature 541 (2017) 511-515. DOI: 10.1038/nature20795.

Figure 4.7	131	Vendelbo, S. B., Elkjær, C. F., Falsig, H., Puspitasari, I., Dona, P., Mele, L., Morana, B., Nelissen, B. J., van Rijn, R., Creemer, J. F., Kooyman, P. J., and Helveg, S., Visualization of oscillatory behaviour of Pt nanoparticles catalysing CO oxidation, Nature Materials 13 (2014) 884-890. DOI: 10.1038/nmat4033.
Figure 4.8	132	Schmidt, J. E., Poplawsky, J. D., Mazumder, B., Attila, Ö., Fu, D., de Winter, D. A. M., Meirer, F., Bare, S. R., and Weckhuysen, B. M., Coke Formation in a Zeolite Crystal During the Methanol-to-Hydrocarbons Reaction as Studied with Atom Probe Tomography, Angewandte Chemie, International Edition 55 (2016) 11173-11177. DOI: 10.1002/anie.201606099.
Figure 4.9	133	Liu, Y., Meirer, F., Krest, C. M., Webb, S., and Weckhuysen, B. M., Relating structure and composition with accessibility of a single catalyst particle using correlative 3-dimensional micro-spectroscopy, Nature Communications 7 (2016) 12634. DOI: 10.1038/ncomms12634.

Appendix B: Workshop Agenda

Basic Research Needs Workshop for
Catalysis Science to Transform Energy Technologies
Gaithersburg, Maryland, May 8–10, 2017

MONDAY, MAY 8, 2017

7:00 a.m. – 8:00 a.m.   Registration/Breakfast

Opening Plenary Session

8:00 a.m. – 8:15 a.m.   Welcome and Workshop Charge
*Bruce Garrett, Division Director, Chemical Sciences,
Geosciences and Biosciences, BES*

8:15 a.m. – 8:30 a.m.   Chair Welcome and Workshop Structure
Carl Koval, University of Colorado – Boulder, Workshop Chair

8:30 a.m. – 8:45 a.m.   Introductions to Plenary Presentations
*Johannes Lercher Pacific Northwest National Laboratory and
Technical University of Munich, Workshop Associate Chair*

8:45 a.m. – 9:15 a.m.   Catalyst Design for Sustainable Production of Fuels and Chemicals
Jens Nørskov, Stanford University and SLAC National Accelerator Laboratory

9:15 a.m. – 9:45 a.m.   The Nexus of Reaction Mechanism and Dynamic Materials
Properties in Designing Catalytic Processes
Cynthia Friend, Harvard University

9:45 a.m. – 10:15 a.m.   Break

10:15 a.m. – 10:45 a.m.   Opportunities for Catalysis in Utilization of Biomass Resources
James Dumesic, University of Wisconsin

10:45 a.m. – 11:15 a.m.   Creating New Economic Advantages from U.S. Oil and Gas
Jim Rekoske, Honeywell UOP

11:15 a.m. – 11:30 a.m.   Panel Introductions
Susannah Scott, University of California – Santa Barbara

Panel Breakout Sessions
Panel 1: Diversified Energy Feedstocks and Carriers
Geoffrey Coates, Cornell University
Enrique Iglesia, University of California-Berkeley and Lawrence Berkeley National Laboratory

Panel 2: Novel Approaches to Energy Transformations
Morris Bullock, Pacific Northwest National Laboratory
Thomas Jaramillo, Stanford University and SLAC National Accelerator Laboratory

Panel 3: Advanced Chemical Conversion Approaches
Maria Flytzani-Stephanopoulos, Tufts University
Cathy Tway, Dow Chemical

Panel 4: Crosscutting Capabilities and Challenges: Synthesis, Theory, and Characterization
Victor Batista, Yale University
Karena Chapman, Argonne National Laboratory
Sheng Dai, Oak Ridge National Laboratory

11:30 a.m. – 12:00 p.m.	Parallel panel sessions
12:00 p.m. – 1:00 p.m.	Working lunch in panel breakout rooms
1:00 p.m. – 1:30 p.m.	Break
1:30 p.m. – 5:30 p.m.	Parallel panel sessions continue
3:00 p.m. – 4:00 p.m.	Refreshments available
5:30 p.m. – 7:00 p.m.	Break for dinner
7:00 p.m. – 10:00 p.m.	Parallel panel discussions continue

TUESDAY, MAY 9, 2017

7:00 a.m. – 8:00 a.m.	Breakfast plenary session
8:00 a.m. – 8:15 a.m.	Introductions to Plenary Presentations *Susannah Scott, University of California – Santa Barbara,* *Workshop Associate Chair*
8:15 a.m. – 8:45 a.m.	Lessons From the Quest for Cellulosic Biofuels *Kim Johnson, Shell International Exploration and Production*
8:45 a.m. – 9:15 a.m.	Impact of Catalytic Technology on Use of Renewable Energy Resources *Reuben Sarkar, Department of Energy, Office of Energy Efficiency* *and Renewable Energy*
9:15 a.m. – 9:45 a.m.	Frontiers, Challenges and Opportunities in Biological and Bio-Inspired Catalysis *Russ Hille, University of California – Riverside*
9:45 a.m. – 10:00 a.m.	Break

Panel Reports
Carl Koval, Moderator

10:00 a.m. – 10:15 a.m.	Report from Panel 1
10:15 a.m. – 10:30 a.m.	Report from Panel 2
10:30 a.m. – 10:45 a.m.	Report from Panel 3
10:45 a.m. – 11:00 a.m.	Report from Panel 4
11:00 a.m. – 11:30 a.m.	Discussion

Panel Breakout Sessions

11:30 a.m. – 12:00 p.m.	Panel discussions continue
12:00 p.m. – 1:00 p.m.	Working lunch in panel rooms
1:30 p.m. – 5:30 p.m.	Panel discussions continue
3:00 p.m. – 4:00 p.m.	Refreshments available
5:30 p.m. – 7:00 p.m.	Break for dinner (on own)
7:00 p.m. – 10:00 p.m.	Panel discussions continue and preparation for final panel reports

WEDNESDAY, MAY 10, 2017

7:00 a.m. – 8:00 a.m.   Breakfast

Plenary Session

Panel Reports
Carl Koval, Moderator

8:00 a.m. – 8:30 a.m.   Report from Panel 1

8:30 a.m. – 9:00 a.m.   Report from Panel 2

9:00 a.m. – 9:30 a.m.   Report from Panel 3

9:30 a.m. – 9:45 a.m.   Break

9:45 a.m. – 10:15 a.m.   Report from Panel 4

10:15 a.m. – 11:30 a.m.   Discussion

11:30 a.m. – 12:00 p.m.   Closing remarks
Carl Koval, University of Colorado – Boulder

12:00 p.m.   Workshop adjourned

12:00 p.m. – 5:00 p.m.   Working lunch/writing (chairs, panel leads, and designated writers only)

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Appendix C: Abstracts for Plenary Talks

CATALYST DESIGN FOR SUSTAINABLE PRODUCTION OF FUELS AND CHEMICALS

Jens Nørskov

Stanford University and SLAC National Accelerator Laboratory

The lecture will discuss some of the drivers for a new energy and chemical production industry. In particular, the rapidly decreasing cost of solar and wind electrical energy provides arguments for a shift towards using electrons to drive chemical transformations. In most cases, we do not have suitable catalysts for electrocatalytic reactions of interest in the production of fuels and chemicals, and some of the main scientific challenges to catalyst design will be discussed.

THE NEXUS OF REACTION MECHANISM AND DYNAMIC MATERIALS PROPERTIES IN DESIGNING CATALYTIC PROCESSES

Cynthia Friend

Harvard University

Catalytic processes generally and reaction selectivity specifically are by their nature kinetically controlled. To fully understand the kinetics of catalytic processes, understanding the elementary reactive steps and the state of the catalytic material under reaction conditions is essential. The reactive elementary steps provide a means of modeling and predicting kinetics and reaction selectivity. At the same time, the state of material, including the composition, geometric, and electronic structure of reactive sties must be defined under operating conditions because these are all factors in determining catalytic function of a material. Selected examples will be used to illustrate the combined use of fundamental studies to determine reaction mechanism and kinetics with *in situ* studies using ambient pressure X-ray photoelectron spectroscopy (XPS) and environmental transmission electron microscopy (TEM) to follow the evolution of catalytic material under reaction conditions. Gaps and remaining challenges in both experimental and theoretical approaches to catalyst design will be outlined.

OPPORTUNITIES FOR CATALYSIS IN UTILIZATION OF BIOMASS RESOURCES

James Dumesic

University of Wisconsin

Considerable research has been carried out with the aim of developing new catalytic processes for the effective utilization of renewable biomass resources, relying extensively on knowledge gained from studies of catalytic processes in the petroleum and chemical industries. To advance further the potential of developing a bio-based economy for the production of fuels and chemicals from renewable biomass resources, it is necessary to address key fundamental challenges that are especially important for biomass conversion processes. Biomass feedstocks are heterogeneous in nature, requiring pretreatment processes to remove impurities and/or to produce distinct feed streams, such as carbohydrates vs. lignin. Biomass-derived feed streams are highly functional with low volatility, requiring catalysts that are highly selective and operate in the liquid phase. The functionality and impurities of biomass can also cause catalyst stability issues, requiring new paradigms in design of more robust catalysts. We will discuss the key fundamental scientific bases for addressing the aforementioned challenges, with examples that illustrate (i) opportunities for catalysis using biologically-derived feeds, (ii) the promotion of supported metal catalysts to improve activity, selectivity, and stability, (iii) the use of liquid solvent systems to enhance catalyst performance, (iv) synergistic coupling between catalytic and separation processes in the liquid phase, (v) modification of surface properties to enhance catalyst stability, and (vi) linkages between heterogeneous and homogeneous catalysis.

CREATING NEW ECONOMIC ADVANTAGES FROM U.S. OIL AND GAS

Jim Rekoske

Honeywell UOP

Catalysis has been a critical contributor to the enormous success of the U.S. economy since the 1930s. Catalysis made possible high-octane aviation gasoline in World War II, enabled the removal of harmful lead from gasoline, and sparked the current shale-driven refining boom that will make the United States a net energy exporter within the next decade. The hydrocarbon resource pool continues to be plentiful and even grow, creating tremendous opportunities for generating value from U.S. oil, natural gas, and other hydrocarbons. There continue to be many challenges slowing efficient utilization of these assets—particularly in refining and petrochemical production. This presentation will focus on three of those challenges: (a) correcting carbon inefficiencies in the refining complex; (b) more efficient use of methane and natural gas liquids (NGLs); and, (c) the economic benefits of higher octane fuels. We will conclude the talk with a brief narrative of future energy use in the United States, and the role catalysis will play in this scenario.

LESSONS FROM THE QUEST FOR CELLULOSIC BIOFUELS

Kim Johnson

Shell International Exploration and Production

So much work has been done in the effort to develop fuels from cellulosic biomass. Yet, the promise of replacing a noticeable portion of our fuel supply with cellulosic-derived fuels has been slow to materialize. As we look forward to a broader menu of renewable/alternative energy scenarios, new catalysts will be developed, new processes will be proposed. What can we do differently to improve the result? A brief look back at the biofuels journey will be used as a springboard for discussion of how a collaborative, systems approach to catalysis research could yield advances that truly change the game.

IMPACT OF CATALYTIC TECHNOLOGY ON USE OF RENEWABLE ENERGY RESOURCES

Reuben Sarkar

U.S. Department of Energy, Office of Energy Efficiency and Renewable Energy

Achieving market-driven renewable fuels and energy efficient technologies will require dramatic advancements in catalyst performance, cost, and selectivity as well as high-throughput approaches to compress overall R&D lead-times. Renewable fuels such as biofuels and hydrogen require novel catalysts to lower production costs. Advanced combustion strategies for internal combustion engines require catalysts that can operate at lower exhaust temperatures to meet both increasingly stringent fuel economy and criteria emission standards. Fuel cell systems require elimination of platinum catalysts to be competitive with engines. Lowering the overall energy and capital intensity of manufacturing through process intensification requires catalysts with a wide range of performance characteristics. Office of Energy Efficiency and Renewable Energy has a number of initiatives centered on development of new novel catalysts.

FRONTIERS, CHALLENGES AND OPPORTUNITIES IN BIOLOGICAL AND BIO-INSPIRED CATALYSIS

Russ Hille

University of California – Riverside

The lecture focuses on the role of biological and bio-inspired catalysts in energy technologies, and on the challenges, frontiers, and opportunities for their energy-relevant applications. The presentation will include a discussion of the scientific challenges that must be surmounted and the opportunities presented for biological and bio-inspired catalysis, and the outlook for new and emerging scientific approaches to accelerate the advancement of catalysis science for energy applications. An emphasis will be placed on creating the science to enable the use of emerging energy resources, and an effort will be made to identify knowledge gaps and opportunities to effect major transformations and breakthroughs in energy-relevant areas.

Appendix D: Workshop Participants

Basic Research Needs Workshop for
Catalysis Science to Transform Energy Technologies

Chair
Carl A. Koval, *University of Colorado – Boulder*

Associate Chairs
Johannes Lercher, *Pacific Northwest National Laboratory and Technical University of Munich*
Susannah L. Scott, *University of California – Santa Barbara*

Plenary Speakers
James Dumesic, *University of Wisconsin*
Cynthia Friend, *Harvard University*
Russ Hille, *University of California – Riverside*
Kim Johnson, Process Development Chemist, *Shell International Exploration and Production*
Jens Nørskov, *Stanford University and SLAC National Accelerator Laboratory*
Jim Rekoske, Vice President and Chief Technology Officer, *Honeywell UOP*
Reuben Sarkar, *U.S. Department of Energy, Office of Energy Efficiency and Renewable Energy, Deputy Assistant Secretary for Transportation*

Basic Energy Sciences Attendees
Chris Bradley, Jim Davenport, Chris Fecko, Greg Fiechtner, Bruce Garrett, Bonnie Gersten, Matthias Graf, Robin Hayes, Craig Henderson, Linda Horton, Jeff Krause, Peter Lee, Mike Markowitz, Gail McLean, Talia Melcer, Raul Miranda, Chuck Peden, Mark Pederson, Tom Russell, Viviane Schwartz, Andy Schwartz, and Robert Stack

Invited Participants
Anastassia Alexandrova, *University of California – Los Angeles*

Aaron Appel, *Pacific Northwest National Laboratory*

Kathy Ayers, *Proton Onsite*

Simon Bare, *SLAC National Accelerator Laboratory*

Bart Bartlett, *University of Michigan*

Victor Batista, *Yale University*

Gregg Beckham, *National Renewable Energy Laboratory*

Alex Bell, *Lawrence Berkeley National Laboratory and University of California – Berkeley*

Thomas Bliggard, *SLAC National Accelerator Laboratory*

Nigel Browning, *Pacific Northwest National Laboratory*

Morris Bullock, *Pacific Northwest National Laboratory*

Bert Chandler, *Trinity University*

Karena Chapman, *Argonne National Laboratory*

Jingguang Chen, *Columbia University*

Cathy Chin, *University of Toronto, Canada*

Paul Chirik, *Princeton University*

Geoff Coates, *Cornell University*

Michael Crowley, *National Renewable Energy Laboratory*

Tanja Cuk, *University of California – Berkeley and Lawrence Berkeley National Laboratory*

Sheng Dai, *Oak Ridge National Laboratory*

Liming Dai, *Case Western Reserve University*

Paul Dauenhauer, *University of Minnesota*

Robert Davis, *University of Virginia*

James Dumesic, *University of Wisconsin – Madison*

Maria Flytzani-Stephanopoulos, *Tufts University*

Cynthia Friend, *Harvard University*

Anne Gaffney, *Idaho National Laboratory*

Karen Goldberg, *University of Washington*

Rajamani Gounder, *Purdue University*

John Gregoire, *Caltech*

Thomas (Brent) Gunnoe, *University of Virginia*

John Hartwig, *University of California – Berkeley and Lawrence Berkeley National Laboratory*

Charles (Russ) Hille, *University of California – Riverside*

Adam Hock, *Illinois Institute of Technology and Argonne National Laboratory*

George Huber, *University of Wisconsin*

Enrique Iglesia, *University of California – Berkeley*

Tom Jaramillo, *SLAC National Accelerator Laboratory and Stanford University*

Cynthia Jenks, *Ames Laboratory*

Kim Johnson, *Shell International Exploration and Production*

Christopher Jones, *Georgia Institute of Technology*

Anne Jones, *Arizona State University*

Mark Jones, *Dow Chemical*

Matthew Kanan, *Stanford University*

Alex Katz, *University of California – Berkeley*

Beata Kilos, *Dow Chemical*

Paul King, *National Renewable Energy Laboratory*

Carl Koval, *University of Colorado – Boulder*

Harold Kung, *Northwestern University*

Johannes Lercher, *Pacific Northwest National Laboratory and Technical University of Munich*

Chris Marshall, *Argonne National Laboratory*

Manos Mavrikakis, *University of Wisconsin*

Will Medlin, *University of Colorado – Boulder*

Jeff Neaton, *Lawrence Berkeley National Laboratory and University of California – Berkeley*

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Justin Notestein, *Northwestern University*

Umit Ozkan, *Ohio State University*

John Peters, *Washington State University*

Marek Pruski, *Ames Laboratory*

Aniball Ramirez-Cuesta, *Oak Ridge National Laboratory*

Jim Rekoske, *Honeywell UOP*

Daniel Resasco, *University of Oklahoma*

Fabio Ribeiro, *Purdue University*

Amy Rosenzweig, *Northwestern University*

Roger Rousseau, *Pacific Northwest National Laboratory*

Aaron Sadow, *Iowa State University and Ames Laboratory*

Reuben Sarkar, *Office of Energy Efficiency and Renewable Energy*

Philippe Sautet, *University of California – Los Angeles*

Raymond Schaak, *Pennsylvania State University*

Tim Schaffer, *ExxonMobil*

Susannah Scott, *University of California – Santa Barbara*

John Shabaker, *BP*

Wendy Shaw, *Pacific Northwest National Laboratory*

Dario Stacchiola, *Brookhaven National Laboratory*

Shannon Stahl, *University of Wisconsin – Madison*

Yogesh Surendranath, *Massachusetts Institute of Technology*

Charlie Sykes, *Tufts University*

David Tiede, *Argonne National Laboratory*

Don Tilley, *University of California – Berkeley and Lawrence Berkeley National Laboratory*

Cathy Tway, *Dow Chemical*

Dion Vlachos, *University of Delaware*

Aleksandra Vojvodic, *University of Pennsylvania*

Yong Wang, *Washington State University*

Hui Xu, *Giner*

Jenny Yang, *University of California – Irvine*

Francisco Zaera, *University of California – Riverside*

Stacey Zones, *Chevron*

Invited Observers

Sam Baldwin, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Juergen Biener, *Lawrence Livermore National Laboratory*

Jim Boncella, *Los Alamos National Laboratory*

Phil Britt, *Oak Ridge National Laboratory*

David Chandler, *Sandia National Laboratories*

Stanley Chou, *Sandia National Laboratories*

Kevin Craig, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Larry Curtiss, *Argonne National Laboratory*

Max Delferro, *Argonne National Laboratory*

Bob Dixon, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Melis Duyar, *SLAC National Accelerator Laboratory*

Jim Evans, *Ames Laboratory*

Nichole Fitzgerald, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Rebecca Fushimi, *Idaho National Laboratory*

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Vanda Glezakou, *Pacific Northwest National Laboratory*

Frances Houle, *Lawrence Berkeley National Laboratory*

Ken Howden, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Doug Kauffman, *National Energy Technology Laboratory*

Valri Lightner, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Ping Liu, *Brookhaven National Laboratory*

Yijin Liu, *SLAC National Accelerator Laboratory*

Christopher Matranga, *National Energy Technology Laboratory*

Dan Matuszak, *Department of Energy, Office of Fossil Energy*

Eric Miller, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Bryan Morreale, *National Energy Technology Laboratory*

Karl Mueller, *Pacific Northwest National Laboratory*

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Magdalena Ramirez-Corredores, *Idaho National Laboratory*

Sunita Satyapal, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Joshua Schaidle, *National Renewable Energy Laboratory*

Avi Shultz, *Department of Energy, Office of Energy Efficiency and Renewable Energy*

Gurpreet Singh, *Department of Energy, Office of Energy Efficiency and Renewable Energy, Vehicle Technologies Office*

Igor Slowing, *Ames Laboratory*

Bill Tumas, *National Renewable Energy Laboratory*

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