Mid-Scale Instrumentation: Regional Facilities to Address Grand Challenges in Chemistry

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MID-SCALE CHEMICAL INSTRUMENTATION:
REGIONAL FACILITIES TO ADDRESS GRAND CHALLENGES IN CHEMISTRY

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I. Executive Summary

The discipline of chemistry is central to our understanding of the world and the foundation of many existing and emerging areas of technology. Chemistry is frequently described as “the central science” because in addition to the widespread importance of chemistry as a distinct discipline, the tenets of chemistry also underlie and strongly influence many other fields such as biology, atmospheric science, materials science, chemical engineering, electrical engineering and medicine. These connections amplify the impact of discoveries and innovations in the chemical sciences. Consequently, new findings and new developments in chemistry—the reactions of atoms and molecules and the structure of matter—lead to broad impacts, scientifically and for economic development.

In the past, the needs of chemistry researchers have been met through a combination of individual instruments and shared facilities. However, in recent years as chemistry’s role has expanded and as chemists address more complex problems of technological and societal impact, there has arisen increased need for integrated suites of specialized, complementary instruments that can provide unique information that cannot be obtained with individual instruments or conventional “user facilities.” Of particular importance is instrumentation referred to here as “mid-scale” instruments, defined as instruments (or co-located suites of instruments) that fall within a certain monetary threshold of $4M - $120M. As recognized in the 2003 National Science Board Report—Science and Engineering Infrastructure for the 21st Century, “the funding for academic research infrastructure has not kept pace with rapidly changing technology, expanding research opportunities, and increasing numbers of users” (1). The insufficient investment in this category inevitably contributed to the slowdown of US’ technological and economic competitiveness at the global level.

To determine what needs and opportunities might exist for mid-scale instrumentation (MSI), two workshops were held in fall of 2016 to explore opportunities within the discipline that could be provided by such investment:

- One workshop was convened to explore the need for co-localization of existing instrumentation at a regional or cyber-enabled facilities (addressed in this report, “Mid-Scale Instrumentation: Regional Facilities to Address Grand Challenges in Chemistry”).
- A separate workshop was convened on opportunities for instrumentation development, led by Paul W. Bohn (University of Notre Dame) and Marcos Dantus (Michigan State University) and addressed in a separate report (“Needs and Opportunities for Mid-Scale Instrumentation in Chemistry”).

In this report, we identify different areas where investment in such MSI facilities would be highly beneficial. These appear as six “grand challenges” that can be summarized here as follows:

1. Structure and dynamics at interfaces
2. Highly parallel chemical synthesis and characterization
3. Transient intermediates
4. New science arising from the characterization of heterogeneous mixtures
5. Multi-scale dynamics of complex systems: integrating transport with reaction
6. Structure-function relationship in disordered and/or heterogeneous systems

In addition to the grand challenges, other aspects of MSI were discussed.

Contemporary problems in chemistry increasingly involve molecules, nanoparticles and molecular assemblies having a high degree of chemical, structural, spatial, and/or temporal complexity. One consequence of this complexity is that individual measurements often do not provide a sufficiently complete picture. Similarly, there remains an unmet need for improved synthesis tools and robust reproducible methods for synthesizing functional chemicals (moieties) “on demand.”

While current approaches to chemistry research frequently employ individual state-of-the-art instruments or common laboratory instruments typically found on university campuses, the complex challenges identified above require large-scale, coordinated efforts of equipment and personnel of complementary capabilities and skills, which can only be made possible with mid-scale investment. Indeed, in many areas, such facilities are essential to science advancement. The National High Field Magnetic Laboratory, funded by the National Science Foundation and state of Florida is one such example.

MSI facilities would also support the close integration of instrumentation, coupled with data collection and analysis, thereby leading to more rapid interpretation. Extracting useful chemical information can capitalize on the speed-up in handling, processing and integration of these data streams and co-located instrumentation.

Like the national (defense) laboratories where a “mission-oriented” objective brings together teams to solve science and engineering challenges, MSI facilities would pool expertise across a range of instrument types and would utilize teams of scientists to address the unique needs of the chemical systems under study. In such a scenario, aspects of the chemistry, sample handling, and analysis can readily be shared and controlled—a capability absent when addressed in individual labs. Facilities where entire suites of studies are conducted on individual samples would provide fundamentally new chemical insights by linking studies of composition, structure, and dynamics. Similarly, distributed facilities linked by cyber-enabled instrumentation would also greatly expand capabilities and provide new science insights into global chemistry processes by linking the reaction dynamics from geographically diverse locations.

Regional and cyber enabled facilities, by their very nature, permit a broader participation of researchers in the science being conducted. This not only provides more opportunity and access for geographically isolated areas, but also opens the way for broadened participation based on institution type and the demographics of individuals. Regionally based and cyber supported facilities enable access by students and researchers who are otherwise underrepresented in research endeavors. Their inclusion brings new insights and strengthens the U.S. workforce.
MSI facilities would also address the fact that the chemical sciences have a unique challenge of integrating together many different types of disparate data, often obtained on instruments from different manufacturers and using different, often proprietary file formats.

Advances in acquisition of chemical data can be amplified by taking advantage of the revolution in data science, which is on the cusp of providing the ability to link together many disparate types of chemical and structural data into synergistic, autonomous networks, as well as the ability to integrate automated decision-making into chemical measurements. Ultimately, the integration of data science with chemistry research holds the promise of dramatically increasing the translation of data into true information.

Major conclusions from this workshop include:

- Research conducted at mid-scale regional and/or cyber-enabled instrumentation facilities could have a transformative impact in many existing and emerging areas of chemistry. Many of these areas have been identified by NSF, the Department of Energy (DOE), and other federal agencies as high-priority areas for future investment (2,3).

- Access to specialized mid-scale chemical instrumentation would provide substantial benefit to the broadly defined chemistry community by providing access to suites of chemistry-specific instruments not currently available to most. Such co-located instrumentation offers unique opportunities for control and handling of samples that are sensitive to their environment (i.e., humidity, temperature). Not only will new research be enabled, but researcher education and training will be substantially enhanced by gaining experience with diverse suites of instruments for chemical analysis.

- Due to the diverse range of needs and opportunities within the chemistry community, several high-priority research areas were identified as examples for potential investment, but these were not prioritized with respect to one another.

- Investment in mid-scale regional instrumentation facilities for chemistry was viewed very positively, but federal investment in regional instrumentation facilities should not replace single-investigator grants.

- Staff support was viewed as particularly important to successful operation of mid-scale instrumentation facilities, especially by non-local users. Investment in mid-scale regional instrumentation facilities should include mechanisms to ensure adequate staffing levels and instrument upkeep for the usable lifetime of the equipment.
II. Introduction and Background

As the “central science,” chemistry plays a key role in maintaining our nation’s status as the world’s leader in science and technology. Over the past decade there has been incredible growth in the chemical sciences, both in the core of the discipline and also in areas that interface with the other disciplines often characterized by single words such as energy, materials, medicine, and the environment. Each of these areas addresses an array of challenging, complex problems. The ability of chemists of to contribute to solving these problems often hinges on the ability to characterize the structure, composition and other properties of complex chemical systems.

The vast array of chemistry problems leads to the continuing need to improve existing instruments, to develop entirely new types of instruments, and to develop new approaches to solve complex problems through the synergistic combination of multiple types of measurement.

Whether it is the structure of defects and interfaces at a molecular level, characterizing dynamic molecular systems as they react in relevant environments, understanding chemical properties in novel materials, probing chemical dynamics in the environment, or understanding the biochemistry of living systems, the limits of knowledge in chemistry are often set by the boundaries of the instrumentation used to probe the composition, structure and dynamics of complex systems.

Development of new instrumentation as well as applications of unique combinations of instruments (e.g., co-located in instrumentation facilities) affords opportunities for making new discoveries, accelerating research progress, and surpassing the limits of sensitivity, spatial resolution or speed set by current instrumentation. Cyber-enabled and data-related tools can both further augment instrumentation by enhancing capabilities for acquiring and analyzing data, and by improving accessibility and sharing. However, the development and/or implementation of suites of instruments and cyber-enabled tools often lie beyond the limits of current funding mechanisms.

A workshop was convened at the National Science Foundation (NSF) in September 2016 to address the needs and opportunities for mid-scale instrumentation investments in the chemical sciences. We have defined “mid-scale instrumentation” to be facilities consisting of integrated suites of co-located instruments with an aggregate cost between $4 million and $120 million per facility. These limits are chosen because this range encompasses the range of anticipated instrumentation costs and because instrumentation in this cost range exceeds the capacity of the existing Major Research Instrumentation (MRI) (4) program and is less than the minimum funding criteria for the Major Research Equipment and Facilities Construction (MREFC) (5) program.

In order to assess the potential needs and opportunities for regional shared facilities consisting of co-located mid-scale instrumentation, the workshop co-organizers conducted an initial assessment through an online survey instrument. This survey was disseminated to the chemistry
community in order to solicit input into perceived needs and opportunities, as well as suggestions of individuals who would be good representatives of the chemistry community’s needs in this area. The organizing committee also conducted several conference calls to solicit input from an additional dozen participants, primarily those from predominantly undergraduate institutions. The survey results and other inputs were used to identify a set of 37 workshop attendees (Appendix A), who met on September 29 and September 30, 2016, in Arlington, VA. On-site workshop participants were selected in an attempt to encompass the full scientific breadth of the chemical sciences, the diversity within the chemistry community, and the range of different types of educational institutions that could benefit from mid-scale instrumentation. This workshop report describes the discussions that took place on those two days and is also informed by additional input received through the pre-meeting survey instrument.

Workshop participants provided input to this report in several forms, including: PowerPoint presentations and short descriptive narratives provided by each participant prior to the workshop (and disseminated to all workshop participants); discussions during breakout sessions; written reports from each breakout session; and group discussions. Appendix B summarizes the workshop schedule. After the workshop, the workshop co-organizers and several attendees prepared an initial summary and draft of this report, which was subsequently refined and edited by the workshop co-organizers. All attendees were provided a draft of the report and provided the opportunity to suggest modifications prior to submission of the final report in January 2017.

The needs for federal investment in advanced instrumentation have been noted in recent reports from the National Science Board and from the National Academy of Sciences (6-7), and the workshop has identified opportunities that could be realized with existing instrumentation (or combinations of existing instrumentation) and new cyber-enabled tools.

Integration of Workshop Topics with Programs and Initiatives at NSF
The workshop aligns well with the goals outlined in the 2012 National Science Board Report to Congress on Mid-Scale Instrumentation (6). To quote the report: “In accordance with NSF’s mission to promote the progress of science and its strategic goal to transform the frontiers, the Board underscores the critical importance of investment in research infrastructure in balance with support for research and human development to advance and maintain the Nation’s leadership in science and engineering. Indeed, from the beginning of the NSF’s existence, the Foundation has funded a great variety of research infrastructure across many scales from small to very large in support of the evolving
needs of, and to create opportunities for research by the U.S. scientific community.”

There are emerging opportunities as well in data-driven science, which may make use of co-localized instruments to develop new insights into chemical science. Such opportunities were recently highlighted in a Dear Colleague Letter from NSF’s Chemistry (CHE) division (8).

Among the CHEMISTRY grand challenges identified in this workshop report, there is significant overlap with a number of the categories in the Big Ideas report, including: Understanding the Rules of Life: Predicting Phenotype; The Quantum Leap: Leading the Next Quantum Revolution; Harnessing Data for 21st Century Science and Engineering; and especially Growing Convergent Research at NSF.

The expected science drivers that frame needs for mid-scale instrumentation from the perspective of chemists and chemistry were articulated and developed at the workshop. Conversations will be continued and will engage the entire chemical sciences community as opportunities arise. Symposia at various national meetings, (e.g., Pittcon 2017) are one such mechanism.

One report available on this site is “10 Big Ideas for Future NSF Investments,” (10) which specifically highlights “Mid-Scale Research Infrastructure.”

NSF has also developed a “Toolkit,” which is a set of resources provided for Congress and the public to learn more about the agency’s mission (9).

Understanding the Rules of Life. Credit: NSF.
We finally reflect that this workshop report provides a framework for developing new ideas, especially for those who are just starting their careers. This workshop report is written to build awareness of the significant needs for mid-scale instrumentation and for chemical applications that are enabled by the combination of such instrumentation in shared facilities, potentially with cyberinfrastructure resources.
III. Key Issues and Limitations That Drive the Need for Co-located Mid-Scale Instruments

Solving the grand challenges of the 21st century will require highly interdisciplinary and integrated scientific platforms that measure, understand, model, and innovate the chemistry of diverse and complex systems. Mid-scale instrumentation facilities will provide expertise, instrumentation, and data in a distributed platform, enabling molecular and elemental studies on multiple length and time scales at interfaces, surfaces, in situ, in the atmosphere, and in operando environments. Work conducted at/by such facilities will address critical issues of importance to conserving the environment and its resources, enhancing global health and security, and driving discovery.

These areas of diverse complex chemical systems are highly interdisciplinary, in that they often overlap significantly with a variety of other disciplines, including molecular biology and environmental geochemistry. The fundamental challenges in many of these systems are chemical in nature. Yet, because of their intrinsic complexity the information needed to make transformative advances cannot be obtained with any single instrument, but instead requires the synergistic application of multiple, complementary instruments, each of which provides unique information and insights.

Current approaches to chemistry research frequently employ individual state-of-the-art instruments, but it is typically not possible to apply multiple state-of-the-art techniques to an individual sample.

Furthermore, the close integration of instrumentation, coupled with data collection and analysis, will enable more rapid interpretation. Extracting useful chemical information can benefit from the speed-up in handling, processing and integration of these data streams and co-located instrumentation.

Existing university-based instrumentation facilities typically fall into two models:

- **The centralized instrumentation facility.** These are usually collections of individual, stand-alone instruments that are selected and organized to serve the maximum number of users and are co-located primarily for logistical reasons associated with upkeep and training. Such facilities are well suited for routine measurements, but are usually not able to provide inter-operability and/or to be effectively integrated together into a synergistic instrument suite.

- **The specialized facility.** These focus on one class of measurement techniques, such as the National High Magnetic Field Lab. Such facilities provide outstanding capability for specific types of measurement but do not provide the breadth of measurement types needed.
In contrast, mid-scale instrumentation facilities would consist of integrated suites of complementary instruments, specially designed and located to solve specific types of problems in the chemical sciences. The cost of individual state-of-the-art instruments such as transmission electron microscopes, NMR spectrometers and ultrafast laser spectroscopy systems can easily range from $1 million to $5 million each; consequently, an integrated suite of instruments would likely require funding of $4 million or more.

Regional facilities where multiple state-of-the-art instruments are co-localized would offer a range of specific benefits, including:

- The pooling of expertise across a range of instrument types, where aspects of the chemistry and analysis can readily be shared
- Transport of a sample from one measurement modality to another with environmental control is critical for several of the “grand challenge” areas (e.g., studies of the solid-liquid interface). Facilities where entire suites of studies are conducted on individual samples would provide fundamentally new chemical insights by linking studies of composition, structure, and dynamics.
- Regional facilities enable the development of geographically localized clusters of expertise including academic and non-academic users, facilitating innovation and technology transfer and ultimately enhancing regional economic growth.

Mid-scale instrumentation facilities would have several impacts, not just within the chemistry community, but also within economic and social spheres as well. A recent study (11) found that a large fraction of funding for basic research went to purchasing goods and services, among which over 30% to businesses in the facility’s home state.

Also, according to a recent article called “Why Federal Investment in Science Matters” on the website of The Science Coalition (http://www.sciencecoalition.org/federal_investment), investment in basic research, such as that which could be performed at a mid-scale instrument facility, leads to:

- Creation of jobs for researchers and for the ancillary businesses that support the facility (including local area industries and everyday support services)
- Discoveries that directly affect: the quality of life in the U.S. and worldwide; the health of U.S. industries that depend on basic science; and national security
- Workforce education, training and implementation through affiliation with the facility
- Benefits to our economy and global competitiveness, with chemistry-driven discoveries and innovation being a hallmark of product developments in pharmaceuticals, commodity chemicals, polymers, and numerous commercial sector uses
IV. Unmet Instrumentation Needs in the Chemical Sciences

Contemporary problems in chemistry increasingly involve molecules, nanoparticles and molecular assemblies having a high degree of chemical, structural, spatial, and/or temporal complexity. One consequence of this complexity is that individual measurements often do not provide a sufficiently complete picture. Chemical systems often undergo transformations on time scales of picoseconds to nanoseconds, demanding chemical identification with high specificity on short time scales. Species of interest are often located at solid-liquid interfaces that are inaccessible to the common laboratory instruments typically found on university campuses.

Similarly, there remains an unmet need for improved synthesis tools. For example, chemically functionalized nanoparticles are now routinely used in a wide range of environmental, nanoscience, and biomedical applications, but robust reproducible methods for synthesizing functional nanoparticles “on demand” with specific sizes, shapes, and compositions do not exist.

While in the biological sciences rapid, computerized data acquisition and real-time analysis are integral to modern research, chemical science data has a unique challenge of integrating together many different types of disparate data, often obtained on instruments from different manufacturers and using different, often proprietary file formats. This limits the ability to link together data sets from multiple measurements.

In the U.S. there are extant user facilities for the execution of scientific research. Many user facilities are what we sometimes define as major single capability resources (i.e., neutrons, X-rays, NMR) that cover a range of needs but are built around one type of measurement modality. For example, within DOE these are documented in a specific document devoted to just this subject. (https://science.energy.gov/user-facilities/user-facilities-at-a-glance/)

Nevertheless, even with such user facilities, there are objectives that can be identified.

For example, the (DOE) Environmental Molecular Sciences Laboratory and Basic Energy Sciences nanocenters have a range of capabilities that may be favorably compared with the mid-scale regional centers discussed here. Although there are advantages to the DOE user facilities there
are some good reasons for augmenting U.S. MSI capabilities that include:

- A limited number of facilities, (for example, at EMSL), allow or even have a focus on some in situ real-time measurements that are important to advancing science, and these capabilities have limited capacity (high demand), limited flexibility (optimized for one or a few science challenges) and often do not have the flexibility or resources to adjust or focus on the range of important scientific challenges. In part this is because they are required to respond to either a very specific or more general user set. Uniquely configured and designed midscale instruments addressing a particular type of science question may not be available from an existing user facility.

- User access and flexibility – many user facilities have a very formal proposal approval process for access. This is a fair and open process, but the limited periods of access do not fit all types of science needs. In particular, persistent ongoing access is not easily available. Not all projects can benefit by access just a couple of times per year. Some types of research need time and space proximity of synthesis, processing and characterization that may not fit a user facility mode of research.

- Although students and postdocs do important work at DOE facilities, DOE does not have a primary responsibility for teaching, and universities or collections of universities might benefit from a midscale resource on which students can learn teamwork, cooperation and other skills needed for modern science.

With respect to the National High Magnetic Field Laboratory (NHMFL) funded in part through NSF, there is a distinct area of unmet need—both in terms of new technology development and how that impacts U.S. leadership and competitiveness in this field. In particular, the U.S. is falling behind the rest of the world in high-field magnet technologies, because currently there is no funding mechanism in the U.S. to stay up-to-date. Some representative examples:

- In the UK there is an announcement that research funds have been made available to place an order for two 1.2 GHz class instruments.

- The Magnet Lab in Hefei, China is beginning to produce world-class magnets, and this year successfully brought to field a 40T hybrid magnet.

- The Japanese continue to develop high temperature superconducting coils for NMR magnets. They have published excellent NMR spectra at 1.02 GHz using an HTS NMR coil demonstrating the high field stable NMR spectroscopy with this technology.

- In South Korea there are very significant investments in a novel NMR technology called “no-insulation REBCO.” A demonstration of this technology has recently been achieved at the NHMFL with a field 42.5T in a resistive background field of 30T.

- Finally, even in terms of commercial equipment, as of early 2017 there are 9 orders for 1.2 GHz class instruments in Europe. There is also a 1.0 GHz instrument ordered for Toronto, Canada, and there are no orders for 1.0 or 1.2 GHz instruments for the U.S.
Existing Department of Energy, Department of Defense, National Institutes of Health, and other national laboratories, such as the National High Field Magnetic Laboratory are often “mission-oriented.” Gaps exist to support fundamental chemistry research and to serve a broader user base. Bringing together teams to solve fundamental science challenges, MSI facilities would pool expertise across a range of instrument types and would utilize teams of scientists to address the unique needs of the chemical systems under study.
Recent developments in chemistry and related fields have led to dramatic improvements in the acquisition and analysis of data produced by chemical measurements. For example, development of sub-diffraction-limited imaging techniques now provide the opportunity to image fluorescent molecules species with ~ 10 nm spatial resolution. Ultrafast lasers in the femtosecond regime provide the ability to achieve very high instantaneous electric fields, thereby enabling second-harmonic and high-order nonlinear processes to be accessed at low average powers and also minimizing sample damage. Multidimensional optical techniques have been developed that allow decomposition of the spectra of heterogeneous, complex mixtures. The advent of tabletop synchrotrons, laser-initiated x-ray sources, and time-resolved electron microscopes provide unique opportunities for characterizing chemical systems with high spatial resolution.

These advances in acquisition of chemical data can be amplified by taking advantage of the revolution in data science, which is on the cusp of providing the ability to link together many disparate types of chemical and structural data into synergistic, autonomous networks, as well as the ability to integrate automated decision-making into chemical measurements. Ultimately, the integration of data science with chemistry research holds the promise of dramatically increasing the translation of data into true information.
VI. Overview of Grand Challenges

[Note: The following are examples come from workshop attendees, and not intended to represent the entire field of chemistry.]

1. Structure and dynamics at interfaces

Examples:
- Coupled electron- and ion-transfer processes at interfaces
- Photo-driven charge transfer across complex interfaces
- Interaction of biomolecules with solid interfaces
- Charge-transfer processes, such as photovoltaics and batteries

Key challenges:
- Behavior confined to thin (approximately nanometer-scale) thickness interfaces between two phases, which are often disordered
- Characterizing charge transfer at buried solid-liquid interfaces
- Often only ~ 10 to 100 picomoles/cm$^2$ of material available for study, and critical phenomena may be associated with only a small fraction of surface sites

2. Highly parallel chemical synthesis

Examples:
- Design of new and improved catalysts
- New chemistries for solar cells
- New pathways for combinatorial synthesis

Key challenges:
- Chemical synthesis is typically serial in execution
- Little existing infrastructure for this approach
- Not part of the conventional chemistry curriculum
- Limits on starting materials and reaction conditions
- Development of appropriate reactivity tests
- Separation challenges arising from product thermodynamic and kinetic similarities
3. Transient intermediates

Examples:
- Biomolecular functions and biological systems
- Photo-activated transition state complex
- Surface-molecule complexes
- Excited state dynamics of plasmonic hybrid materials
- Coupling of structure with dynamics for full characterization

Key challenges:
- Determining the chemical attributes of molecules that are intermediates, which:
  - Have short lifetimes
  - Are found at low concentrations
  - Are often present in complex mixtures

4. New science arising from the characterization of heterogeneous mixtures

Examples:
- Intrinsically heterogeneous systems:
  - Metabolites
  - Natural organic material
  - Crude oil
  - Radioisotope tracers

Key challenges:
- Advanced separations of chemically similar species
- Comprehensive characterization and quantification of species present, resolved in space and time

5. Multi-scale dynamics of complex systems: integrating transport with reaction

Examples:
- Biogeochemical cycling
- Fate and transport in the environment
- Chemical conversion/alternative energy
- Atmospheric chemistry

Key challenges:
- Identifying chemical species and speciation in complex mixtures that vary in space and time
- Identifying reactive species and determining reaction rates in coupled abiotic-biotic systems
- Scaling of molecular and nanoscale processes and mechanisms to macroscopic systems
6. Structure-function relationship in disordered and/or heterogeneous systems

Examples:
- Chemically disordered systems – lacking long-range order
- The chemistry of amorphous structures such as polymers, glasses, ceramics
- Structures of membrane-bound proteins

Key challenges:
- Lack of long-range order limits the ability of such systems to be structurally characterized
- Few total characterization tools
- Existing tools are optimized for specific components of the chemical system
- Establishing structure-function relationships for tailored synthesis and design
VII. Grand Challenges

GRAND CHALLENGE 1: Structure and dynamics at interfaces

VII.1A. Description of the Grand Challenge
When solids interact with liquid phases, ions and molecules within the liquid phase can adsorb to the surface and strongly influence the chemical and electrochemical properties of the interface and the nature of the interface can alter the nature of the solvent and molecules near the interface. The additions of energy from photons or electric fields further modify the processes that may take place. In many cases the interfacial layers are amorphous, very thin (~1 nm) and fluctuate dynamically. Interaction of biomolecules with surfaces can involve changes in secondary and tertiary structures. Transfer of electrons and ions across interfaces are critical. Solvation and desolvation processes at solid electrode surfaces dominate the energetics and rates of electrochemical processes.

VII.1B. Important Scientific Areas Impacted

Example 1. Coupled electron- and ion-transfer processes at interfaces
The intercalation of ions across interfaces is the key process that underlies lithium-ion batteries as well as many more advanced energy storage approaches under investigation. Yet, in most cases many of the critical performance characteristics are controlled by chemical reactions that occur at the solid-liquid interface (12). So-called “solid-electrolyte interphase” or “SEI” layers on anodes and cathodes play key roles in stabilizing batteries (13). Yet, these SEI layers remain poorly characterized after more than 20 years of effort, due in large part to the fact that they are compositionally inhomogeneous, chemically complex, and are rapidly altered by exposure to air, water, or other solvents (14).

Credit: Flickr, James Almond.

Example 2. Photo-driven charge transfer across complex interfaces
Photovoltaic energy devices typically involve multiple interfaces of distinct chemical composition. Recent developments in solar cells based on organic-inorganic perovskite materials such as CH3NH3PbX3 have the potential to greatly impact energy storage and conversion (15). However, understanding and controlling chemical interactions at interfaces is important, as processes including ion migration and water adsorption can greatly impact other properties of interest (16-18).
Example 3. Interaction of biomolecules with interfaces
The interaction of biomolecules with solid surfaces plays an important role in many areas of science (19). Adsorption of biomolecules to surfaces is a first step in generating an inflammatory response (20), and understanding the fundamental chemistry associated with biomolecule binding to surfaces would have significant implications for biomedical research. The behavior of nanomaterials in the environment is also controlled by the adsorption of proteins and other biomolecules, forming “coronas” that significantly alter the behavior of the materials (21). Many of these molecular interactions with surfaces can be weak, resulting in significant dynamical exchange between the surface and the adjacent medium. Proteins may also have specific domains that may provide greater or less binding to surfaces. Much remains to be learned about the fundamental interactions that control the interaction of biomolecules with surfaces and especially their interactions with nanomaterials.

VII.1C. Unique Aspect of Instrumentation Needed to Address This Challenge
Characterizing interfaces typically requires probing with some form of externally applied particle or electromagnetic field. Interfaces are sometimes abrupt, but in many cases an “interface” can extend as far as 1 micrometer away from an abrupt physical interface. A typical atomic number density at an interface is \(~6\times10^{14}\) atoms/cm\(^2\), or approximately 1 nanomole per cm\(^2\). In many cases the specific surface sites of interest many constitute less than 0.1% of the available surface area, making picomole/cm\(^2\) sensitivity necessary.

Because of the small amount of material constituting the interface region and the presence of large amounts of solid and/or liquid, techniques suitable for characterizing interfaces must be both highly sensitive and highly selective for the interface region. Interfacial structures are often disordered and dynamically fluctuating on time scales ranging from femtoseconds to seconds.

In order to reduce the influence of non-interfacial atoms, techniques that are inherently sensitive to interfaces are strongly advantageous. For example, non-linear optical methods are often symmetry-forbidden in bulk centrosymmetric media, while the symmetry-breaking at the interface can provide selectivity (22). Similarly, some types of scattering processes involving x-rays (23-24), neutrons (25-26), or other particles can probe interfaces; the discontinuity in the complex dielectric properties at interfaces can often be exploited to provide selectivity to the interfacial region.

VII.1D. Combining Existing Instrumentation for Delivering Novel, High-impact Science
Example 1. Coupled electron- and ion-transfer processes at electrochemical interfaces
A key aspect of electrochemistry is correlating changes in physical and chemical structure with changes in electrochemical properties.
Key questions include:

- Do specific solvent molecules from within a complex solvent mixture preferentially adsorb at electrode interfaces?
- How do liquid-phase molecules orient near an interface?
- What are the detailed mechanisms involved in solvation and desolvation of Li+ and other ions?
- What are the chemical compositions and structures of the “solid-electrolyte interphase” layers that form, and what are the underlying chemical mechanisms (27)?

Because the relevant interfaces are often highly sensitive to air, water, and even N₂, an instrument suite would likely need to couple a suitable electrochemical cell directly to other instruments and allow transport of samples in vacuum or argon environments while maintaining proper electrochemical control. Ideally these properties should be measured while in direct contact with relevant liquid electrolytes; in some cases, it might be suitable to remove them from the liquid environment, but in all cases exposure to air would be eliminated. The need to characterize through a liquid layer and to also maintain electrochemical control makes the design of a suitable sample holder a particularly challenging aspect of research in this area.

Prior studies have shown that nonlinear optical methods can provide key insights into factors such as local orientation of solvent molecules at electrochemical interfaces (28-30), while the use of x-ray techniques such as EXAFS can provide direct measurement of processes occurring at electrode interfaces (31). Confocal Raman (32-34) and infrared spectroscopy using total internal-reflection techniques have also been applied advantageously (35). NMR using magic angle spinning methods could also provide unique insights (36). The coupling of electrochemical measurements with in situ analysis of the chemical changes occurring within a few nanometers of the interface, both in the liquid and in the solid, would provide very important information about the fundamental chemical changes that occur at interfaces.

Instrumentation suites that allowed simultaneous measurement of the chemical processes occurring within the electrolyte, in the formation of solid-electrolyte interphase layers, and within the electrodes would provide important mechanistic insights that currently do not exist.

Example 2. Photo-driven charge transfer across interfaces
Interfaces relevant to photocatalysis and to solar-energy conversion share many of the same challenges described above. In this case, however, the relevant chemical reactions are stimulated photochemically and/or photoelectrochemically.
Understanding the dynamics of how electrons and holes are transferred across interfaces requires the availability of tunable femtosecond light sources at wavelengths suitable to specific excitation processes, and may require non-linear methods with multiple coherent beams intersecting at a sample in a complex matrix environment. Coupling optical excitation with near-field methods can be used to achieve sub-diffraction imaging. Scanning tunneling microscope tips can also be used as an optical antenna to concentrate the electric field into a nanometer-sizes region, providing the potential to achieve measurements at the space-time limit.

**Example 3. Interaction of biomolecules with nanomaterials and extended surfaces**

Binding of biomolecules to surfaces is especially challenging because of the dynamical nature of the interactions. In addition to the adsorption-desorption processes, the intrinsic motion of the molecules likely plays a role in controlling their binding as well as the effect of the interactions on the structure and function of the molecule. Thus, one key challenge is to characterize the molecule connectivity over dimensions of at least several nanometers, while also gleaning information about the intrinsic heterogeneity and dynamical nature of the interactions.

State-of-the-art NMR such as high-resolution magic-angle spinning in a high-resolution solution NMR provides the opportunity to glean new insights into protein-nanoparticle interactions. The ability to characterize both chemical state and the dynamics of spin-lattice and spin-spin interactions can provide insights into molecular connectivity at solid substrates (37-38). Advances in mass spectrometry techniques have the potential to characterize these interactions at the level of single nanoparticles and/or single molecules. Sub-diffraction imaging techniques also could play an important role in providing selectivity and dynamic motion with <10 nm spatial resolution.

![Figure 1. Schematic illustration of the protein ubiquitin interacting with a 4 nm diameter gold nanoparticle. Credit: Robert Hamers.](image-url)
GRAND CHALLENGE 2: Highly parallel chemical synthesis and characterization

VII.2A. Description of the Grand Challenge

Development of tailor-made molecules and materials for demanding applications (e.g., robust catalysts for water splitting or efficient chemical species for solar energy capture) is hindered by the incremental approach adopted by most practitioners. A key challenge is to find methods and instrumentation that facilitate highly parallel synthesis of new substances on demand and allow for high-throughput, multifaceted testing that will generate the data required to understand key features that contribute to desirable and undesirable properties.

High throughput chemistry requires surmounting a number of challenges, including:

- Chemical synthesis is typically serial in execution
- Little existing infrastructure for this approach
- Not part of the conventional chemistry curriculum
- Limits on starting materials and reaction conditions
- Development of appropriate reactivity tests
- Separation challenges arising from product thermodynamic and kinetic similarities

VII.2B. Important Scientific Areas Impacted

Automated, high-throughput methods for chemical synthesis have been used for several years in academia and industry to optimize reactions and generate new targets for drug development (39-42). In some cases, phenomenal successes have been realized, particularly when the reactions are relatively simple to perform and analyze (43-45). However, application of high-throughput methods for the development of catalysts and materials for many demanding applications has been hindered by an inability to combine high-throughput synthesis with multifaceted characterization and appropriate data analysis to understand what features lead to desired properties.

Example 1. Design of new and improved catalysts

Development of robust, highly active, and selective electrocatalysts that will reduce carbon dioxide to liquid fuels under mild conditions represents an important barrier to
the goal of harnessing energy from sunlight in easily storable and transportable forms. High-throughput synthesis and testing could make significant contributions in the area of catalyst development, particularly since it can allow discovery of catalysts that operate through different mechanisms that are typically not found to have both good reduction potentials and turnover frequency (46). However, in addition to the fact that instrumentation for high-throughput synthesis is currently inaccessible to most practitioners, characterization of the catalysts prepared in such a high-throughput way is problematic since it requires a variety of techniques including gas-uptake, electrochemical, and GC-MS or NMR measurements. Combination of versatile high-throughput synthesis equipment with tools for rapid analysis of catalysts under realistic conditions including gas-uptake, electrochemical, and product analysis may allow development of new suites of efficient, robust catalysts that operate at modest overpotentials.

Example 2. Discovery of Novel Constituents for Solar Cells

Solar cells based on small-molecule and polymeric organic compounds have seen huge increases in efficiency, recently reaching over 13% (47). Continued development will require the preparation of a variety of new materials and testing for numerous optical, electrochemical, and physical properties, distinct from the Materials Genome Initiative (MGI) (48) and Designing Materials to Revolutionize our Future (DMREF) (49) programs, with a focus on basic chemical science. As in Example 1, the challenge here lies in developing methods for rapid synthesis of libraries of compounds combined with characterization by a variety of methods under appropriate conditions. An additional issue in this case comes from the probable requirement of specialized processing of the materials after synthesis to facilitate testing. Combination of high-throughput, automated synthesis equipment with the tools to allow multifaceted testing may lead to dramatic improvements in the properties of these materials, partly by generating significant amounts of data that can be mined to allow understanding of what features are most important.

VII.2C. Unique Aspects of Instrumentation Needed to Address This Challenge

To address the challenge of highly parallel synthesis of new molecules and materials with tailored properties, a highly integrated set of instruments is needed to facilitate rapid synthesis and high-throughput characterization by a variety of methods under realistic conditions. Measurement of
multiple different properties will generate much richer datasets for analysis to determine the most important features of generated substances for desired applications.

VII.2D. Combining Existing Instrumentation for Delivering Novel, High-impact Science

Numerous tools for high-throughput synthesis are available and readily configurable, though prohibitively expensive to many practitioners. A key aspect of the proposed suite would be the integrated nature of highly parallel synthesis and characterization, where preparation of a suite of compounds could be quickly followed by testing based on a variety of desired properties. The types of characterization will be determined by the particular applications—for example, a suite of instruments to facilitate catalyst development and characterization. Such a facility would require parallel pressure reactors, electrochemistry equipment, GC-MS, GPC, and calorimetry tools (e.g., infrared thermography). Development of software to analyze data generated by such multifaceted characterization would also be required to make best use of the instruments.
GRAND CHALLENGE 3: Transient Intermediates

VII.3A. Description of the Grand Challenge

A key challenge in chemistry research is characterizing the molecular nature of transient intermediates. Although crucial in defining the nature of chemical reactions, intermediates (i.e., transient intermediates) are short lifetime species. They are usually present at low concentrations and in a complex mixture of reactants and products. Chemistry and biochemistry depend on reactions, a form of dynamics that may be both in and out of equilibrium. Out-of-equilibrium dynamics lead to products that differ from the original reactants, and whose formation will usually involve fleeting transition states of crucial importance in the outcome of the process. Equilibrated systems, though seemingly static, often involve complex equilibria among species at different concentrations, whose importance is not necessarily correlated with their abundance. Life itself is the prime example of these in- and out-of-equilibria chemical systems; but so are a wide range of chemically relevant systems ranging from industrial catalysis to smart self-molding materials. Capturing the structural and chemical nature of these transient intermediates is an open grand challenge for science in general and Chemistry in particular.

VII.3B. Important Scientific Areas Impacted

Example 1. Transient biological systems
Without capturing the nature—and foremost the dynamics—of these intermediates, it is not feasible to understand how enzymes perform their catalysis, how antibodies perform their defense activities, and how protein aggregation is prevented.

Example 2. Photo-activated transition-state complex
Optically initiated processes that are often accompanied by charge and energy transfer events are crucial for endowing photoactive surfaces with their catalytic abilities.

Example 3. Surface-molecule complexes
Many important reactions (e.g., reactions in catalytic converter or ammonia synthesis) take place on solid surfaces (i.e., heterogeneous catalysis). The surface-molecule interaction can determine the catalytic action of the material. Reactions can be initiated through vibrational excitation that may, for example, lead to dissociation on the ground electronic potential energy surface. These reactions can also be initiated by electronic excitation in which case understanding the potential energy landscape of the ground and excited adsorbate species is critical for elucidating charge carrier (i.e., electrons and holes) dynamics. Probing transient intermediates on solid surfaces is a grand chemistry challenge that can lead to an area of enormous implication for surface sciences, impacting a range of chemical technologies spanning catalysis, energy and medicine.

Example 4. Excited-state dynamics of plasmonic-hybrid materials
Concentrated and enhanced local electromagnetic fields of optically excited plasmonic nanocrystals can drive photochemical reactions at low input power. Alternatively, the local field can be utilized for enhancing photocatalysis by coupling
plasmonic and catalytic nanoparticles. In both cases probing transient intermediates created by charge excitation and injection of electrons and holes is imperative for understanding the mechanism of plasmon-driven photochemical reactions and plasmon-enhanced photocatalysis.

VII.3C. Unique Aspect of Instrumentation Needed to Address This Challenge

It is clear that catching fleeting intermediate states—and being able to characterize their chemical attributes—is beyond the ability of any single technique. Different scenarios will arise depending on whether the experimenter is dealing with a one-way, multi-step or equilibrium reaction. Additionally, interfaces, solids and liquids may require different approaches, and concentrations and time scales will differ depending on the problem being tackled. But what seems certain is that in every instance, spectroscopic methods will be essential for interrogating these states. These methods may be tailored to elicit faster speeds, higher spatial resolutions or more exquisite molecular signatures, depending on the problem at hand. But prominent among the main techniques that the workshop identified, are:

- Nuclear Magnetic Resonance—NMR in its spectroscopic and imaging modalities is uniquely poised to provide an integrated view of how structure defines dynamics, e.g., the molecular mechanisms of kinetic processes at an atomic-level resolution.
Mid-Scale Instrumentation: Regional Facilities for Chemistry

(50-51). The system under study can be in vitro or in vivo, solid or liquid. Furthermore, NMR imaging methods are uniquely positioned to provide a link with spatial distribution, with NMR and MRI working in synergy (52-53). For this purpose, the highest resolution and highest sensitivity are required, necessitating the installation of emerging ultrahigh-field technologies, cryogenically cooled NMR probes, and dynamic nuclear polarization (54-55).

- Near-field scanning optical microscopy (56-58) can be used to map dielectric properties (59-61), infrared absorption (62-64) and plasmon modes (65-69) on materials surfaces. Tip-based near-field microscopy may be used as the basis to achieve simultaneous spectral, temporal and spatial resolution of surface chemical properties. In-depth understanding of surface morphology and surface chemical processes may be obtained by complementing the optical measurement with other measurement capabilities such as x-ray photoelectron spectroscopy, high-resolution scanning electron microscopy and mass spectrometry.
- Surface-enhanced Raman spectroscopy (SERS). For surface photochemical processes on plasmonic surfaces, SERS is a highly sensitive, non-destructive vibrational spectroscopy that can be used to monitor chemical changes in situ.
- Computational tools—including chemistry-oriented superclusters—are also essential, but are to some extent available in a multi-user format.

Co-location of such instrumentation creates natural partnerships between specialists in multiple disciplines. For example, there are advantages to co-localization of NMR with cryo-electron microscopes (cryoEM) and diffraction instrumentation for studies of biomolecules, or near-field microscopy and SERS, for the studies of surfaces. Often a single modality will not suffice, and a complementary tool is required. Hence, scientifically there are benefits to doing so, as well as issues related to management and governance, and efficient use of funds.

700 MHz 52 mm solution state NMR system. Credit: National High Magnetic Field Laboratory.
VII.3D. Combining Existing Instrumentation for Delivering Novel, High-impact Science

State-of-the-art, user-oriented, ultrahigh-field NMR facilities could help tackle a number of problems mentioned above, which so far have challenged existing spectroscopic methods. Such facilities could include instrumentation for:

- The characterization of biomacromolecular dynamics through more sensitive high-dimensional correlation methods (70)
- The understanding of how transient misfolded intermediates lead to non-crystalline aggregates (71-72)
- The characterization of reactive sites and the species that bind to them in inorganic catalytic surfaces
- The understanding of spatio-chemical processes occurring in energy-storing materials (73)
- The understanding of the nature of biomineralization and other environmentally related processes (74)

Heterogeneous catalysis involves reactions on metallic (Pt, Pd, Cu, Au, etc.) surfaces that preclude the use of fluorescence microscopy and spectroscopy for probing surface chemical processes. This necessitates the need for developing microscopy based on detection of vibrational signals. Near-field scanning optical microscopy is suitable for this purpose but requires significant advances.
GRAND CHALLENGE 4: New science arising from the characterization of heterogeneous mixtures

VII.4A. Description of the Grand Challenge

The inability to thoroughly characterize the chemical compositions of very complex mixtures of organic compounds hinders advancement in many important areas in our society. The challenge is to couple advanced separations with qualitative and quantitative analysis of the mixture components by techniques such as high-resolution tandem mass spectrometry. The broader impacts outside chemistry include more efficient use and hence increased value for crude oil, economically feasible renewable resources for energy and chemicals, and lower costs for drug development.

VII.4B. Important Scientific Areas Impacted

Molecular-level characterization of many complex mixtures is a challenge due to their vast molecular complexity and the need for non-targeted analysis, rather than identification of a few specific (targeted) compounds only. Several representative examples are discussed below.

Figure 3. APCI/CS2 mass spectrum of a crude oil sample. Each peak corresponds to several isomeric and isobaric compounds. Credit: Hilkka Kenttamaa.
Figure 4. Two-dimensional GC/GC/TOF chromatogram of Jet-A fuel reveals the presence of at least 3,000 compounds (each dot corresponding to a different compound), most with unknown structures. Credit: Hilkka Kenttamaa.

Example 1. Analyzing complex mixtures
Better utilization of the remaining crude oil reserves requires detailed understanding of the molecular compositions of crude oils with different origins. Crude oils are arguably the most complex mixtures of organic compounds found in nature (Figure 3) and hence are extremely challenging to analyze. The knowledge of their chemical compositions would allow the design of the most cost-effective methods to convert crude oil into fuels and valuable chemicals.

Example 2. Identifying trace materials
Development of better alternative fuels requires fundamental understanding of the chemical compositions of successful fuels. The exact chemical compositions of all petroleum-derived fuels (see Figure 4 for the composition of a jet fuel) and many alternative fuels are currently unknown and vary based several parameters, including feedstock. Fuel certification is currently based on physical properties of the fuel and not chemical composition; there has been little incentive to determine the chemical compositions of fuels. However, rational design of economically feasible renewable fuels requires a better understanding on the chemical compositions of successful fuels. In the years to come, these problems will become more significant as the oil industry has to shift from using light crude oil to heavier crude oils containing more asphaltenes (up to 20%) (75-78). A deeper understanding of the molecular composition of asphaltenes (Figure 5) is needed to begin to address the problems mentioned above.
Example 3. Biomass Conversion
Another roadblock for the development of renewable fuels from plant material has to do with the enormous complexity of biomass and its conversion products (Figure 6). Knowledge of the compositional changes upon conversion of biomass to fuels and chemicals is required to design conversion pathways from different plant feedstocks to most valuable fuels and other products. However, the chemical compositions of such mixtures are still mostly unknown (79).

Example 4. Biological Mixtures
The ability to rapidly characterize mixtures of biological origin would, for example, lower the costs of, and facilitate the development of, new drugs. Traditionally, previously unknown, possibly toxic, drug metabolites and degradation products are isolated from mixtures in relatively large amounts and purified for identification by using NMR. However, this approach is tedious, time-consuming and sometimes not feasible (e.g., when drug metabolite is unstable) (80-81).

VII.4C. Unique Aspects of Instrumentation Needed to Address This Challenge
A large centralized facility that brings together suites of instrumentation is needed to advance this research, distinct from a typical university lab, a pharmaceutical center, or from the National High Magnetic Field Laboratory, including not just the means for characterization, but the basic science behind advanced separations.

These instruments should include different types of separation systems, such as GC/GC, HPLC/HPLC, and/or IMS, creatively coupled with various detectors, such as tandem mass spectrometry systems, including low-resolution MS<sup>n</sup> instruments (e.g., linear quadrupole ion traps) and ultrahigh resolution MS<sup>n</sup> instruments (e.g., FT-ICR mass spectrometers). Different approaches are needed depending on the volatility and complexity of the mixtures of interest and the types of mixture components, as well as the type of information desired. Further, optimal evaporation/ionization methods need to be developed for different types of mixtures, separation systems and tandem mass spectrometers. Specific instrument combinations need to be developed for samples requiring very high sensitivity.

VII.4D. Existing Instrumentation for Delivering Novel, High-impact Science
The instrumentation to be combined for this research includes:

- Various separation methods, including those with very high-resolution (such as GC/GC)
- Different types of tandem mass spectrometers, including very high-resolution instruments (such as high-resolution...
magnetic field FT-ICR mass spectrometers), very fast instruments (such as TOF), and instruments capable of MS^n (n > 2) experiments based on dissociation and/or ion/molecule reactions

- Ability to separate ions based on their m/z values (as above) as well as their shape (IMS)
- Analyte evaporation/ionization sources compatible with different types of samples, separation methods and mass spectrometers

Figure 6. HPLC/MS chromatogram for an organosolv lignin sample (degraded lignin isolated from biomass). Top, Total ion current; Bottom, UV absorbance². Credit: Jarrell et al., Green Chem., 2014, 16, 2713-27.
GRAND CHALLENGE 5: Multi-scale dynamics of complex systems: integrating transport with reaction

VII.5A. Description of the Grand Challenge

Chemistry is uniquely situated between the nanoscopic and large-distance scales, as well as between the ultrafast and geological time scales. Complex chemical reactions occur at both the atomic level for individual systems and at an ecosystem-wide level for highly complex systems. Similarly, chemical kinetics can vary within one system from almost instantaneous to decadal reactions. While our chemical understanding of single systems is well developed in many cases, many systems are chemically complex, including evolving planetary atmospheres, environmental systems that have multiple biogeochemical processes, and the fate and transport of an anthropogenic contaminant through an ecosystem and ultimately into humans. The challenge to understand the chemical dynamics that occur over multiple scales is an opportunity that is only recently capable of being addressed.

VII.5B. Important Scientific Areas Impacted

Understanding the dynamics of these complex systems on multiple distance and time scales is critically important for the future of such diverse areas as food, water, the environment and public health. Several representative examples are discussed below.

Example 1. Biogeochemical cycling
Fundamental understanding of complex chemical and biochemical reactions between the biotic and abiotic compartments of Earth's surface environment underlies the continued sustainability of human, engineered and natural systems in the 21st century. Major gaps exist in both fundamental knowledge of chemical processes associated with complex sustainable systems, and the ability to measure and observe chemical transformations. Recent funding initiatives surrounding the food, energy, and water nexus highlight the critical societal needs in this area (e.g., NSF’s INFEWS program) (82).

Much of the research effort, however, has been aimed at system- or process-level analysis, monitoring, optimization, and technological advancement. Less attention has been given to fundamental molecular-scale chemical and biogeochemical processes that control or regulate critical chemical constituents or biogeochemical system functions.

Credit: Oregon Department of Agriculture.
Many opportunities exist to link fundamental chemical processes with hierarchical system descriptions in order to improve resilience and long-term sustainability. A few examples in the food-water area include: development of new materials for water treatment; discovery and development of environment-friendly pesticides; nanoscale sensing and analytical measurements; and regulation and management of critical nutrients for agriculture.

One specific example involves the different forms, and hence the bioavailability, of phosphorus (P) as a critical nutrient (Figure 7). Phosphorus is an essential plant nutrient, and P bioavailability underpins the food production systems that feed the Earth’s growing population (83-84). While P is a limiting nutrient in many environments, excess dissolved P from over-fertilization or animal waste run-off can lead to damaging algal blooms and eutrophication in aquatic ecosystems (85-86). Global climate models have suggested that net primary productivity (NPP) may increase from higher CO2 levels over the next century, resulting in net C storage in terrestrial ecosystems (87). Recent studies, however, point out that productivity increases are dependent on the availability of the nutrients N and P, and emphasize that nutrient limitation is the most uncertain factor in model prediction of terrestrial C storage (88). Thus, the fundamental chemical processes that transform organic and inorganic forms of P, and the dynamic P flux between terrestrial and aquatic ecosystems, are critical for understanding P biogeochemical cycling, bioavailability and balance in ecosystems and agricultural systems at the macroscopic scale.

Basic chemical understanding is needed to advance quantification of the biogeochemical cycling of P in a changing global climate (89-90), inform technologies for P reclamation and recycling (91), and improve prediction of P retention and bioavailability in agricultural systems and terrestrial environments (84,92). New instrumentation will enable such lab- and field-scale comparisons of these biogeochemical cycling parameters.

Example 2. Fate and transport in the environment

The global fate and transport of pollutants traveling through the environment generally involves complex chemical reactions both on a microscopic scale as well as a global scale as these pollutants interact with soils, biota and aqueous environmental systems. Similarly, the time scales can vary from extremely rapid interactions at an environmental interface, to extremely long interactions involving global sinks and reservoirs.

As chemical instrumentation has become more sensitive, lower limits of detection enable quantification of environmental toxins at unprecedented levels. However, most fate and transport understanding has come from models, because no single facility can make all the measurements required to identify sources of toxins.

A network of cross-calibrated instruments at multiple geographic “facilities” that are cyber-enabled for automatic QA/QC between samples would allow thousands of environmental samples to be analyzed and compiled with metadata into large databases of correlated data from which new science would be accessible on the fate and transport of environmental toxins. What is envisioned here is distinct from the NEON network (93) in that it not only includes field observations but would allow real-time instrument analysis of chemical reactions, which will provide insight into
fundamental fate and transport of chemicals.

One specific example of this, which had garnered significant public interest, is the fate and transport of Per- and Polyfluorinated Alkyl Substances (PFAS) in the environment. These man-made compounds are exceptional surfactants because of their C-F bond chemistry and are used ubiquitously in consumer products and industrial applications such as in aqueous film-forming foams (AFFF) used as flame retardants at military and commercial airports around the world. Unfortunately, since the C-F bond is so strong, these compounds have extremely long environmental lifetimes. Thus, they biomagnify and bioaccumulate in the environment, and recently there have been six diseases associated with just two of the hundreds of PFAS chemicals in our environment C8Panel (94).

While PFAS compounds have been detected in the blood of North Americans at an average of 5 ppb already NHANES study (95), the primary source of these chemicals is still unclear. The source could be occupational exposure from industrial use, consumer product contact with food, papers and textiles, or drinking-water exposure from AFFF-contaminated groundwater. To make the necessary measurement of all the possible sources of PFAS for a group of human subjects would require thousands of analytical measurements at many different geographical locations across the U.S. This

Figure 8. Three relatively new spectroscopic applications in plant science (NanoSIMS, MALDI-MS, and PET imaging) that could be used to measure previously unknown chemical dynamics within the complex biological systems that comprise the human food chain. Credit: Richard Ferrieri.

Type of near-real-time assessment of environmental concentrations would allow models of environmental exposure to predict vital public health risks.

Example 3. Atmospheric chemistry
The study of diverse environmental systems could benefit significantly from recent advances in spectroscopy and computational modeling to both measure and model complex dynamics on a variety of distance and time scales. The creation of large centralized facilities to simulate planetary atmospheric conditions, both on Earth and on other planets, could be used to systematically study chemical interactions that determine such issues as how volatile organic compounds interact with ozone, or the effect of particulate matter on planetary albedo. Chemical concentrations and physical conditions of pressure, temperature, and light could be varied to study the dynamics of atmospheric reactions in large-scale tunable, controllable chambers. Hypothesis testing of pre-biotic atmospheres as well as geological and anthropogenic changes to atmospheric chemistry could be simulated with accelerated aging cycles to probe long-term impacts using suitably instrumented reaction chambers.
Similarly, large-scale environmental chambers could be used to probe agricultural or ocean systems, or even indoor air-quality environments. Each of these systems involves multiple phase interfaces (solid/liquid, liquid/gas, solid/gas) that complicate the chemical dynamics of reactions and in each case there is scientific need to obtain chemical signatures, to do real-time- and time-lapse imaging, and simultaneous spectroscopic measurements of different kinds in order to gain the type of understanding that will allow us to model the systems computationally. Some spectroscopic examples are shown in Figure 8, where advances in chemical measurement techniques can be applied in real time to complex biological systems of agricultural significance.

**VII.5C. Unique Aspect of Instrumentation Needed to Address This Challenge**

In this particular grand challenge there emerge two kinds of instrumental approaches that would significantly improve our understanding of the chemical dynamics of these complex systems on multiple scales.

The first approach includes large centralized facilities that bring together suites of instrumentation that could simultaneously measure multiple spectroscopic signatures in complex systems. These instruments would include: mass spectrometers; various light sources; Raman, microwave and ring-down spectroscopy; as well as various nuclear spectroscopic techniques. There could be significant advantages in a complex system to create single experiments that interrogate all spectroscopic frequencies simultaneously, instead of via multiple passes using spectroscopy. These systems would also have to have instrumentation compatible with "dirty" systems and water.

The second approach includes a distributed multi-scale network of chemical sensors to provide a full 3-dimensional chemical map of aqueous and atmospheric composition that could be used to describe the chemistry of atmospheric “micro-environments” and the transformation and transport of environmental pollutants. By feeding local chemical composition data into a centralized hub using advanced cyber infrastructure, big data storage and analysis, multi-institution standardization, quality control and assessment, and next-generation modeling, this system would provide new insights into environmental chemistry with local micro-environments. Such a system would complement efforts to understand atmospheric chemistry and climate change at a global level. One key innovation in such instrumentation is the new basic chemical understanding that would become available from the “big data” available from it. Chemical interactions that were previously not well understood—and which govern the fate and transport of environmental pollutants on multiple scales—would become accessible for the first time.
VII.5D. Combining Existing Instrumentation for Delivering Novel, High-impact Science

The instrumentation for this particular grand challenge is both diverse and strongly dependent on the experimental approach to study global, complex problems, but could easily include:

- High and ultrahigh resolution mass spectrometry for analysis of a variety of biomolecules, proteins, and natural organic matter; co-location with genomic sequencing and computation facilities
- Microfabricated chemical sensor arrays
- Mass spectrometry with imaging, extraction, and/or desorption features
- Several types of electron microscopes optimized for different materials and capabilities, co-located with fluorescence and confocal microscopes
- Combinations of liquid and solid-state NMR instrumentation co-located with FTIR, Raman, and other vibrational spectroscopies
- Integration or co-location of synchrotron x-ray facilities with other instrumentation centers
GRAND CHALLENGE 6: Structure-function relationship in disordered and/or heterogeneous systems

VII.6A. Description of the Grand Challenge

Developing structure-function relationships for non- or semi-crystalline systems is crucial to the addressing and overcoming several grand challenges in chemistry. While structure determination by diffraction provides detailed structural information on crystalline systems, what is needed are analogous techniques to investigate disordered systems and the roles of surfaces on properties—and how they can be influenced by judicious selection of processing conditions.

This program is distinct from others that support materials-related research, such as the Materials Innovation Platform (MIP) (96), Materials Genome Initiative (MGI) (48) and the Designing Materials to Revolutionize our Future (DMREF) (49) programs because the focus here is on the chemical principles that underlie these amorphous structures—at the level of basic science.

VII.6B. Important Scientific Areas Impacted

Many systems of both scientific and technological importance are non- or semi-crystalline and therefore challenging to characterize and understand. To do so requires multiple analytical methods to be combined and the results correlated, leading to the elucidation of the compositions and structures of such materials over diverse length and time scales. The development of integrated suites of equipment with integrated analyses of data would significantly benefit a large number of diverse areas of chemistry (i.e., polymers, glasses, inorganic heterostructures, biological solids) and impact many existing and expanding industries (i.e., semiconductor manufacturing, display technologies, chemical conversion and manufacturing, solar industry, batteries, polymers, drug discovery and pharmaceuticals).

Example 1. Inorganic Structures

Amorphous materials play an increasingly important part in materials chemistry owing to the opportunities for fine-tuning physicochemical properties by composition and processing. Structure is of increasing importance for developing a fundamental understanding of how chemistry influences such composition-property relationships.

In non-crystalline inorganic systems, such as the heterostructures shown in Figure 9, understanding structure-function relationships requires information about composition and structure on the scale of a monolayer. Characterizing composition and structure in small volumes increasingly is important in surface/interface-chemistry-driven industries (i.e., semiconductors, solar technology, batteries) where active regions can have dimensions of a few nanometers. For example, with regard to heterostructures we seek to answer
Figure 9. Characterization of porous Al₂O₃ film deposited from solution and annealed at 500 °C. (a) The diffraction pattern shows the formation of broad peaks consistent with γ-Al₂O₃. The SiO₂ formed upon annealing and is present in both the TEM and in the diffraction pattern centered at ~22°. The silicon substrate peaks are indicated with a diamond (♦). (b) Cross-sectional TEM micrographs of porous Al₂O₃ film deposited from solution annealed at 500 °C anneal. Pores are light in TEM mode. The micrograph clearly shows porous nature of the film. (Data from C. Perkins, D. Keszler, and co-workers, NSF Phase II Center for Chemical Innovation “Center for Sustainable Materials Chemistry.” See “Low-index, smooth Al₂O₃ films by aqueous solution process,” *Optical Materials Express*, 2017, 7, 273-280, doi.org/10.1364/OME.7.000273.)

questions about how chemical moieties locally distort at interfaces due to incommensurate structures and how these distortions control emergent properties—*i.e.*, those that are not found in either constituent alone. In analyzing a film, one wants to obtain information on local and average composition, thickness, roughness and the structure of both layers and interfaces.

Diffraction techniques provide information about the structure of the ordered parts of the film while total scattering and the resulting pair distribution function provides information about the amorphous areas of the film. X-ray reflectometry (XRR) provides information about the thickness and roughness of the area of the film where the top surface is parallel to the bottom surface. Using all three techniques enables the information from different parts of the film to be analytically separated. Combining diffraction information, atomic-resolution electron microscopy with core level spectroscopy, and other analytical methods to measure all these properties in the same sample region and across all relevant length scales is required to understand the structure-function relationships and guide optimization of properties.
Parkinson’s disease, prions for mad cow disease). Cryo-electron microscopy is an emerging tool to characterize “amorphous” soft structures, but the samples are “flash frozen” and atomic-level details are hard to discern with current instrumentation, although data are now becoming competitive with x-ray diffraction (98). Ultrahigh field NMR has also become a central player in structural and dynamic elucidations of membrane proteins, under physiological conditions that escape many alternative structural methodologies (99-100).

VII.6C. Unique Aspect of Instrumentation Needed to Address This Challenge

Typically, a suite of instruments is needed to address these systems, because of the diverse nature of structural motifs and the need for complementary probes of structures (for verification). As an example, FTIR data can identify moieties, and coupling this with NMR can help verify (and quantify) these species.

Non-integrated measurements and analyses tend to lead to technique-centered and technique-specific structural insights, which depend strongly on the different length- and time-scale sensitivities and resolution of the different methods occasionally providing a specialized lens.

VII.6D. Existing Instrumentation for Delivering Novel, High-impact Science

Data from multiple measurement modalities (i.e., x-ray total scattering, electron microscopy-based techniques, NMR and IR spectroscopies, mass spectrometry) are required to characterize heterogeneous disordered systems, surfaces and interfaces. Most institutions have only incomplete sets of these measurement tools available. Access to instrumentation is
critical for chemistry researchers to obtain the required data. While there is a core of basic equipment that needs to be local (NMRs, IRs, UV-Vis, etc.), more specialized and/or advanced equipment is often not feasible for every research institution to acquire, due both to cost and low utilization rates. Researchers should have relatively easy access to this equipment, which could be facilitated by federal funding agencies.

The software tools for the different techniques are also not integrated, making it time-consuming and awkward to use the analytical model from one technique as a starting point for modeling others. Federal funding agencies could play a leading role in spurring the development of coordinated software suites between different techniques and uniform data formats, which would greatly facilitate both the sharing of data and future data mining.

Regional facilities with a cluster of diverse instrumentation that provide access to equipment, develop integrated public domain software packages, and assist users in both acquiring and analyzing the resulting data would have a broad and positive impact on research and national competitiveness.

There are several different modes that could be used to provide access to equipment and expertise to the broad community. One mode would be to have a single technique co-located and managed by an expert user group. This would work well for techniques such as solid state NMR, x-ray reflectivity or electron microprobe. A second mode would be to create clusters of equipment optimized for specific grand challenges regionally distributed across the country that has staff members responsible for assisting researchers during experiments, advising users, and maximizing the use of the facility. An example might include a suite of surface analytical tools, a group of specialized deposition tools with appropriate characterization tools, or a TEM facility.

Finally, there exists a strong need for common source data simulation, modeling and fitting software that can use data from a suite of complementary techniques.
VIII. Human Resources

One of the broader impacts of a new mid-scale instrumentation program, whichever grand challenges are addressed by it, will be the significant ability to attract young scientists into the STEM workforce.

Significant investments in large scientific endeavors—from examples within the U.S. space program to large user facilities such as particle accelerators and observational astronomy facilities—have always captured the attention of both the public and students exposed to the science and the instrumentation.

Typically, large facilities operate outreach programs within their communities to engage future scientists early in the wonder of large instrumentation dedicated to a scientific purpose. Similarly, the continued operation of future facilities would require skilled workers at multiple educational levels, and would provide more such positions than what is typical for smaller instrumentation grants.

However, the greatest impact would come from increased access to modern chemical instrumentation or real-time data from such instrumentation that would allow undergraduate and graduate students to engage with actual experimental results and research experiences that are not otherwise accessible given the often limited resources at most educational institutions.

Credit: Stock photo.
Through cyber-enabling of modern instrumentation and careful attention to educational initiatives involving faculty and students from Primarily Undergraduate Institutions and Two-Year Colleges, this program—built around modern chemical instrumentation—could potentially influence a much more diverse audience early in the educational system. The program could also influence a much larger number of students than could be impacted by separate smaller instrumentation grants. At the site of large instruments, or suites of instruments, there will exist personnel and collaborators that are interested and able to lead educational initiatives that just are not possible at individual institutions typically.

This type of instrumentation, therefore, has the potential to increase recruitment and retention of a diverse student audience within chemistry and related STEM disciplines.

These educational components would serve to help broaden the user base of these facilities, and it would ensure that people from other institutions benefit from the research instrumentation.
IX. Operational Aspects of Mid-Scale Facilities

Guiding principles
Effective use of mid-scale facilities requires ensuring that facilities are accessible to as many researchers as possible in order to have the maximum impact on the chemistry community at a national level. To be successful, mid-scale instrumentation facilities would need to pay careful attention to a number of aspects associated with the operational logistics. Some of these are discussed briefly below.

Sustainability of operations
Advanced instrumentation is only effective when accompanied by staff who are able to provide scientific guidance to prospective users and to train those who come on site to use the instruments. Institutions hosting mid-range instrumentation facilities benefit by having instrumentation located on-site, but are typically expected to provide support such that external users are able to effectively use the instrumentation during short-term visits. Research grants are commonly awarded for a relatively short duration of 1-3 years. A facility based on co-location of existing commercial instruments could easily take several years to achieve full operational status, with the lifetime of usefulness greatly exceeding the lifetime of the award that provides the instrumentation. Careful attention should be paid to financial models that will be able to provide the level of staffing needed to maintain these facilities as national resources accessible to the entire chemistry community.

An important aspect of mid-scale regional instrumentation facilities is the development of partnerships among various stakeholders, including both academic and non-academic users. These partnerships and the associated development of a large and diverse user base can greatly amplify the impact of mid-scale instrumentation regional facilities by impacting translational research, job creation, and development of a trained workforce from both academia and industry. They can also be key in the development and implementation of a financial model that can ensure maximum long-term effectiveness of investments in capital equipment by covering recurring costs beyond those incurred in the initial purchase of the equipment.

Regional facilities with suites of mid-scale instruments would likely have a useful lifetime of 10 years or longer. Such facilities would permit unique opportunities as well as challenges that are difficult for individual investigators to achieve. These would include:

- Infrastructure to maintain instrumentation in peak operating condition
- Instrumentation that is designed and enabled to be used full time, 24 hours a day, 7 days a week
- Cyberinfrastructure that permits remote users to participate by controlling experiments remotely

With these opportunities, come additional challenges:

- Maintaining peak operating condition requires experienced staff, as does cyber-enabling of such experiments
Funding for instrument maintenance and equipment that has a limited lifetime must be integrated into the strategic plan.

Design of user fees to encourage use, while maintaining a high-quality level of technical support, is critical to the sustainability of such an enterprise.

Accessibility
In order to maximize use by the diverse chemistry community, location and associated transportation and housing costs should be considered. While the duration of a set of experiments is expected to vary widely, it is likely that some experiments could extend for many weeks on a continuous or intermittent basis. Large facilities such as the DOE National Labs are frequently able to provide low-cost on-site housing, significantly reducing the financial burden on the facility users. While such an approach may not be feasible for mid-scale facilities, factors such as the proximity to a convenient airport and also local cost and availability of housing should be considered. The possibility of securing preferred rates at university-managed or privately run hotels should be considered.

Localized vs. distributed facilities
In some cases, it may be advantageous to distribute instrumentation among two or more institutions in order to make optimal use of existing expertise. While this scenario can be very attractive for users within easy commuting distance of the different institutions, it can also significantly dilute the benefits of co-localization of instruments, particularly for non-local users.

One distinct feature of chemistry research compared with other fields (e.g., physics, materials, astronomy) is that chemistry research often involves fabricating and characterizing samples that are highly reactive and often sensitive to even brief exposure to air or other uncontrolled environments. While in some cases it may...
be possible to transfer samples from one location using field-portable controlled atmospheres (e.g., “vacuum suitcases”), the practicality of such scenarios is limited. Consequently, it is likely that single-site facilities will be the most practical implementation.

Cyberinfrastructure
In principle, cyberinfrastructure can enhance opportunities for research at one location to influence the direction of experiments at a second location. Advanced cyberinfrastructure may in the future decrease the functional differences between single-site and multi-site facilities. However, at the present time very few facilities have the capability for automated sample exchange among different instruments, necessitating direct intervention either by the user(s) or by facility staff. Future advances in this field may provide emerging opportunities for expanding the user base to remote users. However, at the present time remote operation of tools remains limited.

One of the biggest barriers to effective use of many different complementary instruments is that different manufacturers often adopt their own proprietary software standards, limiting the ability to synergistically apply multiple experimental methods to individual samples.

In some areas of science, data standards have emerged that enhance interoperability. However, within the chemistry community there has been little driving force for standardized data sets and data formatting. A concerted effort to enhance interoperability among different instruments and between different types of data sets could substantially enhance the impact of existing data. Such an effort might involve, for example, the development of open-source data standards that can be applied across many types of instrumentation and that can also include metadata for automated analysis of data sets. When combined with emerging efforts to enhance accessibility of data across the scientific community, the development of standardized data structures could dramatically enhance the ability to make effective use of instrumentation facilities that are based on highly heterogeneous sets of instruments.
X. Workshop Conclusions and Findings

Some overall conclusions from this workshop include:

- Research conducted at mid-scale regional instrumentation facilities could have a transformative impact in many existing and emerging areas of chemistry. Many of these areas have been identified by NSF, DOE, and other federal agencies as high-priority areas for future investment.

- Access to specialized mid-scale chemical instrumentation would provide substantial benefit to the broadly defined chemistry community by providing access to suites of chemistry-specific instruments not currently available to most. Such co-located instrumentation offers unique opportunities for control and handling of samples that are sensitive to their environment (i.e., humidity, temperature). Not only will new research be enabled, but researcher education and training will be enhanced by gaining experience with diverse suites of instruments for chemical analysis.

- Due to the diverse range of needs and opportunities within the chemistry community, several high-priority research areas were identified as examples for potential investment, but these were not prioritized with respect to one another.

- Investment in mid-scale regional instrumentation facilities for chemistry was viewed very positively, but federal investment in regional instrumentation facilities should not replace single-investigator grants.

- Staff support was viewed as particularly important to successful operation of mid-scale instrumentation facilities, especially by non-local users. Investment in mid-scale regional instrumentation facilities should include mechanisms to ensure adequate staffing levels and instrument upkeep for the usable lifetime of the equipment.
Appendix A – List of workshop participants

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Appendix B – Workshop schedule

Wednesday Evening Sept. 28

Arrival of all workshop participants in Arlington, VA.
Thursday Sept. 29 – All Workshop Participants

Morning Schedule AM

7:45 – 8:30 Continental breakfast (Gallery II), Registration (get badges)
8:30 – 8:45 Welcome workshop participants by NSF personnel
8:45 – 9:15 30-second self-introductions of participants
9:15 – 10:15 Goals of the workshop, expectations of the workshop and the workshop participants by co-chairs; short talks by workshop co-chairs, based on input from workshop participants
10:15 – 10:30 Break
10:30 – 12:00 Breakout session I – Grand Challenges in Chemistry (Break into 3 groups, based on interest area and with a goal of distributing expertise, where possible). Our goal is to coalesce on a small number of ideas to report out to the entire group. Begin to prepare overview presentations from Session I in last 20 min.

Afternoon Schedule PM

12:00 – 1:00 Working Lunch – Breakout session scribes craft overview presentations from Breakout Session I
1:00 – 1:45 Report out from Breakout session I and significant discussion from the rest of the workshop participants
1:45 – 3:15 Breakout session II – Instrumentation needs/opportunities centered around specific chemical problems identified (Break into groups, not necessarily equal in size) again distributing expertise and focusing on areas of chemical interest. Scribes begin to prepare overview presentations from Breakout Session II in last 20 min.

3:15 – 3:30 Break
3:30 – 4:15 Report out from Breakout session II and significant discussion from the rest of the workshop participants
4:15 – 5:15 Breakout session III – Operational aspects of regional instrument facilities. (a) Operational needs from user perspectives, (b) How to effectively integrate cyberinfrastructure and advanced data management. Begin to prepare overview presentations from Breakout Session III in last 20 min.

5:15 – 5:30 Break
5:30 – 6:00 Report out from Breakout session III and significant discussion from the rest of the workshop participants
6:30 – 8:00 Dinner, coordinated for all participants

Late Evening: Co-chairs and organizing committee members continue to refine reports from breakout sessions I, II and III based on discussion. Send slides, other materials to nsfmidscale@chem.wisc.edu.

Friday Sept. 30 – All Workshop Participants

Morning Schedule AM

7:30 – 8:00 Continental Breakfast
8:00 – 8:30 Summary of Day 1

Observations: Is a consensus building about general high-priority areas of science that would benefit from mid-scale instrumentation?
8:30 – 9:30 **Breakout Session IV** – Broader Impact on chemistry and beyond chemistry: (a) How to engage with the broader chemistry community including PUls, 2YCs; (b) How to maximize educational impact of MSI-RIC; (c) Public engagement beyond the classroom

9:30 – 9:45 Break

9:45 – 10:00 Report out from **Breakout session IV** and significant discussion from the rest of the workshop participants

10:00 – 11:45 Discussion of overall workshop recommendations

11:45 – 12:00 Discussion of next steps: from the workshop to the report

12:00 – Workshop adjourned.

**Saturday Oct. 1 – Organizing Committee; Report-writing Committee only**

**Morning Schedule AM**

8:30 – 11:45 Wrap-up writing session. Define task lists and deadline dates

Attendees are free to depart unless you have been specifically asked to stay longer.

**Afternoon Schedule PM – Organizing Committee and Report-writing Committee only**

12:30 – 2:00 Lunch

2:00 – 5:00

- Preparation of Final Reports by Organizing Committee
- Preparation of PowerPoint Slides to Summarize Final Reports

Evening – Dinner for Organizing Committee and Report-writing Committee
Appendix C – References: A list of references and URLs to other reports


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32. Stancovski, V.; Badilescu, S. In Situ Raman Spectroscopic-Electrochemical Studies of Lithium-Ion Battery Materials: A Historical


46. Huo, P.F.; Uyeda, C.; Goodpaster, J.D.; Peters, J.C.; and Miller, T.F. Breaking the Correlation between Energy Costs and Kinetic Barriers in Hydrogen Evolution via a Cobalt


48. Materials Genome Initiative (MGI) [https://www.mgi.gov/](https://www.mgi.gov/)


89. Elser, J.J.; Bracken, M.E.S.; Cleland, E.E.; Gruner, D.S.; Harpole, W.S.; Hillebrand, H.; Ngai, J.T.; Seabloom, E.W.; Shurin, J.B.; and Smith, J.E. Global analysis of nitrogen and phosphorus limitation of primary producers in freshwater,


94. C8 Science Panel http://www.c8sciencepanel.org/


