Nanomaterials and the Environment: The Chemistry and Materials Perspective

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Preface to

Nanomaterials and the Environment:
The Chemistry and Materials Perspective

Since the June 2011 NSF-Sponsored Workshop on Nanomaterials and the Environment: The Chemistry and Materials Perspective was convened in Arlington, Virginia, interest in this topic continues to grow. This report captures some of the issues, questions, and challenges that were discussed during the two-day workshop, along with high-priority research topics identified by workshop participants as essential to advance the field. This report does not cover all research needs in this area but instead focuses on the chemistry and materials perspective. The intent of the report is to lay a foundation and provide a framework for some of the critical research, in particular from fundamental and molecular aspects, for chemists, material scientists and others interested in the environmental health and safety issues associated with nanomaterials to address.

As you read through the contents of this report, it is important to recognize that all participants contributed to the workshop and the workshop report by preparing materials for distribution prior to convening in Arlington, VA. Special recognition goes to the organizing committee – Gordon Brown, Stanford University, Howard Fairbrother, Johns Hopkins University, Murray Johnston, University of Delaware and R. Lee Penn, University of Minnesota – for their expertise, commitment and efforts prior, during and after the workshop. The National Science Foundation, including Program Directors Zeev Rosenzweig (Chemistry Division) and Michael Scott (Materials Research Division), should also be acknowledged for support of the workshop.

It is expected that the contents of this report will be accessible and useful to a wide audience. Particularly helpful to chemists and material scientists just starting their careers as well as students who may thinking about these issues so that they can work toward addressing some of the more critical science needs.

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Appendix A – List of workshop participants: Workshop participants included a diverse interdisciplinary group of scientists with a wide range of expertise and National Science Foundation observers.

Appendix B – Workshop schedule: The workshop used presentations to stimulate breakout discussions.

Appendix C – References and footnotes: A list of references, footnotes and URLs to other reports.

Appendix D – Powerpoint contributions from participants: Participants were asked to provide input through a three-slide presentation focused on areas related to: 1 – Research activities relevant to nano/environment of their own research; 2 – Provide a summary of the most important research challenge(s) at the intersection of nanotechnology and environmental science; 3 – Identify opportunities for chemists to contribute to molecular-level science at the nano/environment interface. What are the high-impact opportunities?
I. Executive Summary

Participants of the National Science Foundation (NSF) sponsored workshop *Nanomaterials and the Environment: Chemistry and Materials Perspectives* met in Arlington, VA on June 28 and June 29, 2011 to discuss challenges, opportunities and research needs for understanding the molecular perspectives of nanomaterials and the environment. This report discusses the outcome of those discussions. The workshop identified a number of grand challenges, knowledge gaps, methodology gaps, and research needs where molecular-based approaches could provide significant insights into the effect of nanomaterials on environmental health and safety. The discussion topics focused on five themes: the fundamental properties of nanomaterials that are relevant to environmental processes, nanomaterial interactions with the environment, nanomaterial interactions with biological molecules and systems, enabling technologies, and human resources (Figure 1).

![Diagram](link)

*Figure 1. Grand challenges, knowledge and methodology gaps, and research opportunities and needs for five areas – Fundamental Properties of Nanomaterials, Nanomaterial Interactions with the Environment, Nanomaterial Interactions with Biological Molecules and Systems, Enabling Technologies, and Human Resources – were the focus of the NSF-sponsored workshop Nanomaterials and the Environment: Chemistry and Materials Perspectives held in Arlington, VA on June 28 and 29, 2011 (Figure credit: Vicki H. Grassian).*

The *Fundamental Properties of Nanomaterials* discussions identified grand challenges and knowledge and methodology gaps for several topics: (i) understanding nanomaterial
surfaces and surface reactivity – separating thermodynamic from kinetic factors, (ii) understanding and predicting nucleation, (iii) measuring in real-time and in-situ structure and reactivity of nanomaterials, (iv) quantitative characterization of surface composition and surface chemistry, (v) surface coatings, (vi) nanoparticle-nanoparticle interactions, aggregation, and agglomeration, and (vii) theoretical understanding of surfaces and reactivity of nanomaterials.

The Nanomaterial Interactions with the Environment discussions identified grand challenges and knowledge and methodology gaps for a list of topics: (i) the scalability and complexity of nanomaterials in environmental systems, (ii) released quantities and forms of engineered nanomaterials, (iii) the persistence of nanomaterials in the environment, (iv) heterogeneous distribution of nanomaterials: dilution, geoconcentration and bioaccumulation, (v) analytical methods for the quantification of nanomaterials in complex environmental matrices and at low nanomaterial concentrations, (vi) size and shape distributions, and (vii) defining key transformation processes of nanomaterials in the environment and their effects on nanomaterial behavior.

The Nanomaterial Interactions with Biological Molecules and Biological Systems discussions identified grand challenges and knowledge and methodology gaps on several topics: (i) nanomaterial uptake into biological systems, (ii) nanomaterial interactions with biological molecules, (iii) the molecular basis of nanomaterial-induced biological response, (iv) identification of biological markers of nanomaterial exposure, (v) the dynamic nature of nanomaterial-biomolecule interactions, (vi) nanomaterial metrics relevant to biological response, and (vii) nanomaterials as delivery agents of potential toxicants.

The discussions of Enabling Technologies - Infrastructure, Instrumentation and Computation identified grand challenges and critical knowledge and methodology gaps: (i) infrastructure for ensuring cross-laboratory validation using reproducible, well characterized nanomaterials, (ii) analytical tools for characterizing nanomaterials in environmentally relevant matrices, (iii) the advancement of quantum-based computational methods, (iv) achieving computational accuracy at environmentally relevant length scales, and (v) addressing the configuration space of nanomaterial interfaces.

This report also highlights a number of Human Resource Needs: (i) educational activities and curricula that engage students in society relevant problems, (ii) interdisciplinary and collaborative approaches to sustainability and environmental science problems, and (iii) participation and leadership from the chemistry community in these issues to positively impact society. Human resources will bring a chemistry and materials science perspective to broad areas of sustainability and environmental science.
II. Introduction and Background

The field of nanotechnology has advanced enormously in the past decade and, as a result, researchers have synthesized a large number of materials with at least one dimension in the nanoscale size regime for a diverse set of applications. Moreover, given societal needs in the 21st century and beyond, nanoscience and nanotechnology can provide many of the science and technology innovations and advances needed for global sustainability (1). Because of the potential for increased and widespread use of nanomaterials in different applications and consumer products, the release of at least small quantities of nanomaterials into the environment during their product life cycle may be inevitable (Figure 2). The potential for environmental release raises concerns since little is known about the fate, transformation, and toxicity to the environment of the engineered materials (2,3). To address the concerns, US National Nanotechnology Initiative (NNI) and several international consortia have increased their attention on the environmental health and safety (EH&S) issues associated with nanomaterials. Several recent reports highlight the broad research needs in this area (4-13), and a journal recently published a themed issue on the topic (15). In addition, the Gordon Research Conference Environmental Nanotechnology was recently established and brought together a wide-range of scientists and engineers to discuss cutting edge research on chemical, biological and environmental effects of engineered nanomaterials (14).

![Diagram of product life cycle stages and risk assessment paradigm](http://www.nano.gov/you/environmental-health-safety)

**Figure 2.** Environmental, health and safety (EH&S) considerations of engineered nanomaterials integrate the risk assessment paradigm (on left) with nanomaterial life cycle stages (across top) (Taken from the National Nanotechnology Initiative website. Figure credit: N.R. Fuller of Sayo-Art at [http://www.nano.gov/you/environmental-health-safety](http://www.nano.gov/you/environmental-health-safety)). Workshop participants discussed opportunities for research using molecular based approaches to significantly enhance our understanding of EH&S of nanomaterials.
Given the growing interest in proactively addressing the potential EH&S effects of nanomaterials, a diverse group of scientists with a wide range of expertise met on June 28th and June 29th, 2011 in Arlington, Virginia to discuss important issues, challenges, and the vital science needed to better understand “Nanomaterials and the Environment” from a chemistry and materials perspective (see Appendix A – Workshop Participants). This workshop report entitled *Nanomaterials and the Environment: The Chemistry and Materials Perspective* describes those two days of discussion and input by workshop participants. Contributions from participants came in several forms including a Powerpoint presentation and two-page write up prepared by each participant in advance of the workshop, discussions during breakout sessions, breakout session reports, and full group discussions of these reports. See Appendices B and C for details of the workshop schedule and format of individual presentations. The ultimate goal of such a workshop is to ensure the development of sustainable nanotechnology.

The workshop focused on some of the uncertainties in understanding nanomaterials, including nanoparticles, in the environment due to gaps in fundamental knowledge as well as methodologies needed to better understand these materials. On the macroscale, materials properties are relatively independent of size and shape, but a unique aspect of nanomaterials is that their properties and behavior are highly dependent on many factors including size, shape, composition, and crystallinity (16-20). These strong dependences lead to major challenges for understanding nanomaterials in the environment. Although recent reviews on the potential fate of engineered nanomaterials address a number of important issues (21,22), major gaps in knowledge remain. Many of the dependencies on size and shape are a result of the large surface to volume ratio and the large contribution of the surface free energy to the overall total free energy of nanomaterials (23,24). For example, classical models do not take into account any details of the surface structure and surface energetics that are needed to fully understand nanomaterial behavior (25).

An additional complexity in understanding the EH&S effects of nanomaterials is that nanomaterials of a single composition can exhibit vastly different behavior depending on whether they are individual (primary) particles, aggregated particles, or particles embedded in a matrix. Furthermore, environmental factors such as pH, ionic strength, and the presence of complexing molecules can alter the surface chemistry of these materials, resulting in deaggregation, aggregation and modifying subsequent interactions with macromolecules such as biopolymers and natural organic material (26,27). All of these factors will affect the distribution, uptake and toxicity of nanomaterials. Some of the grand challenges for understanding these processes include building a greater understanding of the size- and shape-dependent chemistry and properties of nanomaterials that are important in environmental processes (e.g., redox behavior), of the transformations of nanomaterials in the environment from their original form, and of their complex interactions with biological systems. To meet these challenges, researchers must devote theoretical and experimental efforts toward understanding nanomaterials and the properties that are important in their mobility, uptake and toxicity.
The development of instrumentation for field studies and linking advanced computational methods with molecular-level experimental data are just a few ways that researchers might pursue addressing the grand challenges, and funding agencies provide support for efforts in these areas and more. At the National Science Foundation (NSF), several research funding opportunities focus on EH&S issues associated with engineered nanomaterials. Currently the Directorate of Biological Sciences co-funds two research centers with the Environmental Protection Agency (28-30). Within the Directorate of Engineering, a program through the Division of Chemical, Bioengineering, Environmental and Transport Systems entitled “nano-EHS” is another opportunity. Chemistry, a branch of science dealing with the structure, composition, energetics, properties, and reactive characteristics of substances at molecular length scales, is uniquely situated to discover factors that are important to understanding the environmental and health effects of materials synthesized and fabricated on the nanoscale. Within the Chemistry Division of NSF, the Environmental Chemical Sciences Program supports research efforts in these areas as does the Division of Materials Research.

The topic of the workshop, Nanomaterials and the Environment, underscores a society-relevant research area where a chemistry and materials perspective can play an important role. Although society-relevant problems have many economic, political, and human dimensions to them, this workshop report focuses on the basic molecular-level aspects of understanding EH&S effects of nanomaterials and nanotechnology. The workshop and workshop report focus on three science themes – fundamental aspects of nanomaterials; nanomaterials and the environment; and nanomaterials and biological molecules and biological systems – that were discussed separately; however, important connections among them and several common research needs emerged. The next sections of the report highlight the grand challenges, knowledge and methodology gaps, and the opportunities for innovative and transformational science from the chemistry and materials perspective in these areas. Particularly noteworthy is the need for hypothesis driven scientific approaches, infrastructure, instrumentation and computation development, and interdisciplinary teams to tackle some, if not most, of these problems. These efforts can span funding opportunities across different directorates at NSF. Strategic partnerships between NSF Divisions of Chemistry and Materials Research and the National Institute of Standards and Technology (NIST) were also brought up at the workshop.

Finally, the importance of molecular-based approaches and the role of chemistry and material science in the broad areas of environmental science and sustainability (31, 32) such as in the NSF-wide Science, Engineering and Education for Sustainability (SEES) initiative needs to be recognized as discussed in this report. NSF established the SEES investment area in Fiscal Year 2010 to promote the research and education needed to address the challenges of creating a sustainable human future. SEES funds conceptual, theoretical, empirical, and computational research to further develop the basic science,
engineering, education, and policy knowledge base relevant to sustainability. Through SEES, NSF seeks to enable the discoveries that lead to environmental, energy and societal sustainability (33). SEES may serve as a model integrating scientists from multiple disciplines to address highly complex problems that impact the world in which we live.

III. Fundamental Properties of Nanomaterials

Introduction
There is increasing recognition that nanomaterials play major roles in environments such as in natural waters, soils, sediments, industrial and municipal waste-water, mine tailings, and the atmosphere (34,35). The materials include the enormous quantity of natural, incidental nanomaterials that are byproducts of human activities (e.g., coal-combustion) as well as manufactured or engineered nanomaterials. On a per-mass basis, nanomaterials have immense surface areas relative to millimeter-sized and larger particles, and because reactivity typically scales with surface area, chemical reactions at nanomaterial surfaces can play a dominant role in determining environmental processes. Understanding how fundamental surface properties such as adsorption and reactivity vary as a function of size, shape, and chemical composition is an important step toward building the picture of how nanomaterials affect the environment. In the environment, nanomaterials are almost always in contact with atmospheric gases or aqueous solutions that contain natural organic matter, soil components, and/or microbial organisms (Figure 3). The interaction results in complex nanoscale interfacial regions where critical chemical processes occur: water dissociates on surface defect sites, solute ions and molecules adsorb and desorb, ligand exchanges and acid-base reactions take place, material dissolves or precipitates, reactive oxygen species form, and nanomaterials aggregate (36). Classical electrical double layer (EDL) models qualitatively describe the interfacial region between the particle and an aqueous solution (Figure 3), but real environmental interfaces are much more complex than the simple EDL description.

While synchrotron-based x-ray methods and nonlinear optical methods have enabled significant understanding of adsorption reactions on solid particle surfaces in complex matrices, major knowledge gaps remain. For example, little direct knowledge can describe the structure of the EDL at the molecular level, even in simple systems. The mechanisms of adsorption/desorption reactions, including rate-limiting steps, are largely unknown, and in addition, researchers know virtually nothing about the structure of solid surfaces, particularly nanomaterial surfaces, in contact with aqueous solutions or atmospheric gases. The few molecular-level studies on hydrated single crystal surfaces show that their structures are generally not simple terminations of the bulk structure; surfaces relax and reconstruct, resulting in different structures and stoichiometries. Direct molecular-level observations about the structure of water and aqueous solutions at solid-aqueous solution interfaces are rare. Furthermore, nucleation is a phenomenon critical to many processes associated with nanomaterials in the environment yet the
initiation of new structures and phases at all scales is poorly understood. Molecular-level studies of increasing complexity could fill these knowledge gaps and provide a solid fundamental basis for understanding the chemistry that occurs at nanomaterial interfaces (36-38).

**Figure 3.** The schematic of a nanoparticle in aqueous solution illustrates some of the complexity at environmental interfaces where fundamental studies are needed. A close-up view of a highly simplified model of the electrical double layer at the nanoparticle-aqueous solution interface is also shown (Figure credit: Gordon Brown, modified after Ref. 36).

**Grand Challenges and Major Knowledge and Methodology Gaps**

Grand challenges and major knowledge and methodology gaps for understanding fundamental nanomaterials properties that are important to environmental processes are given next.

**Understanding nanomaterial surfaces and surface reactivity; separating thermodynamic from kinetic factors.** A major knowledge gap exists in delineating between surface kinetic factors which are proportional to surface area and thermodynamic factors which are driven by surface free energy contributions both impacting the reactivity of nanomaterials. Thermodynamics can drive large shifts in
oxidation-reduction and other phase equilibria at the nanoscale, especially for very small nanomaterials (39,40). Recent studies show that oxidation-reduction reactions in transition metal oxides at the nanoscale have very different thermodynamic behavior from those in bulk materials (39). In addition, because of the low surface energy of spinel oxides (Co$_3$O$_4$, Mn$_3$O$_4$, Fe$_3$O$_4$), their stability regions are much larger at the nanoscale than in bulk (see Figure 4). Often the underlying reasons for the thermodynamic phenomena are not well understood. New findings to fill this gap could also shed light on the behavior of transition metal oxide catalysts used for carbon dioxide reduction and for solar fuel generation, important issues in sustainability and energy.

**Figure 4.** Comparing phase diagrams of iron and iron oxide reveals the difference in stability between bulk materials (left plot) and 10 nm particles (right plot). The temperature scale is in inverse temperature to make a linear plot, although the labeled are in temperature units (Kelvin). The nanoscale calculation finds no stability for 10 nm wustite Fe$_{0.947}$O. (Figure credit: Alexandra Navrotsky, adapted from Ref. 40).

**Understanding and predicting nucleation.** Molecules connecting to form clusters and clusters joining to build extended structures are all nucleation processes that occur across different length scales. The initiation of new structures and phases is a phenomenon critical to many processes involving nanomaterials in the environment and yet is poorly understood. From the nucleation of particles in different environmental compartments (air and water) to the safe-by-design synthesis and formation of nanomaterials, understanding these processes is a grand challenge. Additionally, nucleation processes play a key role in mitigating climate change with “geoengineering” approaches, such as by the release of stratospheric sulfate aerosols and the mineralization of calcium carbonate during carbon capture and sequestration.

**Measuring in real-time and in-situ the structure and reactivity of nanomaterials.** Currently, spectroscopic and imaging techniques to interrogate the structure and behavior of nanomaterials, even in simple systems, are not readily available. Continued
development of spatially and temporally resolved spectroscopic techniques and isotopic and elemental analytical techniques with nanoscale resolution is essential to measuring nanomaterial structure and dynamics in the future. Increasing the available spectroscopic and imaging techniques that can measure the reactivity of nanomaterials in complex heterogeneous and environmentally relevant media is especially important.

**Quantitative characterization of surface composition and surface chemistry.** Currently, no experimental methods can measure the surface structure of nanomaterials under *in situ* conditions (i.e., in the presence of water or more complex environmental media). Standard surface structural methods such as low energy electron diffraction and helium scattering require ultra-high vacuum are therefore not capable of *in situ* studies. Vacuum-based approaches for nanomaterial characterization have disadvantages: dehydration of samples and other modifications and alterations of the materials from their native state due to vacuum. Surface-sensitive x-ray scattering and spectroscopic methods that can provide detailed structural information on single-crystal surfaces in contact with water – such as crystal truncation rod diffraction, x-ray reflectivity, grazing incidence x-ray absorption fine structure spectroscopy, and x-ray standing wave methods – do not work for nanomaterials. Too few molecular-level techniques can probe nanomaterial surface structures under *in situ* conditions.

**Surface coatings.** In many environments, nanomaterials will interact with complex species such as natural organic matter, soil components, and microbes, resulting in coatings that modify the nanomaterials’ surfaces. Researchers have little detailed molecular level information on the nature of the coatings, how they form, their structure, and how they affect nanomaterial reactivity and fate, including microbial interactions. Techniques such as x-ray photoelectron spectroscopy can measure, to some extent, coatings for flat extended structures, although curved surfaces, which are important for nanomaterials, are more difficult to measure. Building a knowledge base about surface coatings is essential. In addition, developing model systems that can mimic the function of complex and heterogeneous coatings are also critical. For example, what are the correct model compounds to mimic natural organic matter?

**Nanomaterial-nanomaterial interactions, aggregation and agglomeration.** Another fundamental challenge is understanding the factors that control particle-particle interactions. What physico-chemical parameters control the kinetics of aggregation, which is considered irreversible, and agglomeration, which is considered reversible? Controlling aggregation and agglomeration properties of nanomaterials may be possible by manipulating these parameters. Furthermore, different aggregation pathways and the extent of aggregation can affect nanomaterial reactivity, properties, and biological interactions as well as accessible surface area.

**Theoretical understanding of surfaces and reactivity of nanomaterials.** Our ability to model the behavior of nanomaterial surfaces under environmentally realistic conditions is
in its infancy. Successes in surface science and catalysis demonstrate the promise that density functional theory (see Ref. 41) and similar atomistic-based methods hold for predicting reactivity from first principles. Extensions of these approaches to environmental nanomaterials will require an interplay between theory and experiment, including benchmark data on well characterized nanomaterials. Ultimately theoretical studies that can offer predictive insight on cases where experiments cannot be performed are highly desirable.

**Opportunities for Chemists to Make Transformative and Innovative Contributions**

Chemists bring a fundamental molecular-level approach essential for unraveling the innumerable processes that occur in complex environmental systems, particularly those processes involving nanomaterials. Materials scientists bring expertise in synthesis and characterization methods to the problem, and chemists can also bring insight to structure-property relationships. Researchers have many opportunities to make major contributions either alone or as part of interdisciplinary teams on the environmental science of nanomaterials.

**Synthesis of well-defined nanomaterials.** Numerous EH&S studies of nanomaterials have been done on relatively poorly characterized materials. Conflicting results of the seemingly same material make reaching a consensus on the research outcomes difficult, but chemists and material scientists can overcome this barrier through the synthesis, characterization, and modification of well-defined nanomaterials. Materials with systematically varied key physicochemical properties such as size, shape and surface chemistry would be a starting point for comparison across studies. In concert with synthetic efforts, the development of high throughput methods for characterization of nanomaterials to better understand structure-function relationships are also highly desirable.

**Characterization and physicochemical properties of well-defined nanomaterials: ensemble versus single-particle approaches.** Growth mechanisms, morphology, phase stability, reactivity, redox activity and solubility of well-defined nanomaterials as a function of size and shape are just a few properties where careful fundamental studies are needed. What is the paradigm for these types of studies - single-particle analysis or ensemble approaches? Because single particle analysis is difficult, most studies have emphasized ensemble measurements; however, both kinds of studies are essential. In single particle analysis, researchers measure individual particles and use population statistics to determine the material’s affect on the environment. Furthermore, they can determine if the distribution of properties is “statistical” or if the properties derive from distinct sub-populations. Generation of statistical distributions from single-particle measurements is, however, very time-consuming, and in many cases measurements of ensemble properties are important. No matter what the paradigm, determining how to
deal with heterogeneity in the environment is a key opportunity for understanding the effects of nanomaterials in the environment.

**Dynamic changes of nanomaterials and nanomaterial surfaces.** Experimental approaches that yield information on the dynamic changes in nanomaterial-water systems, particularly surface structure and composition, as a function of time are needed. Such information is crucial for understanding the transformations of nanomaterials under different environmental conditions, the kinetics of such transformations, and the impact of these transformations on toxicity. Many of the experimental and theoretical approaches of physical chemistry and analytical chemistry are well suited for deriving this information. For example, recently developed ambient ionization methods in mass spectrometry permit direct analysis of nanomaterials in flowing systems and can extend the sensitivity to contaminant species associated with nanomaterials at very small concentrations. In addition, pump-probe UV-vis spectroscopic studies will be useful in studying reaction kinetics. The application of recently developed synchrotron radiation-based methods (e.g., ambient pressure photoemission spectroscopy) can provide information on the interaction of water and aqueous solutions with nanomaterials and its effect on their reactivity under in situ conditions.

**Physicochemical controls for aggregation, agglomeration and particle-particle interactions (i.e., What makes a particle “sticky”?)**. Examples of the importance of understanding and controlling aggregation of nanomaterials arise in investigations of nanotoxicity, where studies find that aggregation can neutralize the effect of the material’s size on its properties and may also change its biological interactions. Possible mechanisms causing the loss in size dependence include burying reactive sites and defects during aggregation, changes in the material’s plasmonic properties, and a decrease in accessible surface area and diffusion coefficients through membranes as particle size increases. Questions about aggregation also relate to the kinetics and effects of disaggregation. Further questions ask how aggregated structures form and transform in complex environments when the aggregates may be composed of more than a single type of nanomaterial and will also likely include larger sized particles. The presence of different types of species may also change aggregation and agglomeration kinetics of nanomaterials (i.e., heteroaggregation).

**Surface area: Total, accessible, and reactive.** A related concept to aggregation and agglomeration state is surface area, which can be broken down into total, accessible, and reactive surface area. Considering aggregation, the accessible surface area decreases as a function of increasing aggregation. Thus, the accessible surface area of an aggregate is expected to be substantially decreased as compared to the total surface area of its constituent primary particles. In addition, the fraction of accessible surface remaining after aggregation will depend upon the structure of the aggregate. Take, for example, when an aggregate is composed of primary particles with a small number of primary-primary contacts (e.g., two to three contacts). The aggregate will have a more open
structure and more accessible surface area than an aggregate composed of primary particles with more contacts per primary (e.g., five or more). Another way to describe the contacts is with fractal dimension, which describes mass-radius relation in aggregates. Smaller fractal dimensions (one to two) correspond to more open structures and larger fractal dimensions (two to three) to more closed structures. Furthermore, surface area is composed of molecular scale sites of varying reactivity. Thus, description and quantization of surface area (i.e., accessible versus non-accessible, reactive versus non-reactive) and the distribution of surface sites is important. Finally, do aggregation and agglomeration selectively consume specific surface sites, and thus reactive surface area? Could there be other fundamental changes as a consequence of aggregation; for example, do particle-particle interactions result in a change or loss of quantum size effects?

**Interfacial region between nanomaterials.** When considering aggregation and agglomeration, an additional consideration is the structure of material at the interfaces between primary particles. In the case of aggregates (i.e., particles held together irreversibly), interfaces are composed of grain boundaries, which may serve as sites of increased reactivity. In the case of agglomerates (i.e., particles held together reversibly), the interfaces may contain solvent molecules such as water in environmental systems as well as other chemical species such as biomolecules and inorganic polyatomic ions. Thus, chemists might eagerly ask what the atomic- and molecular-scale structure of these interfaces are. The structure of water at the interfaces between primary particles composing an agglomerate could be quite important to understanding the kinetics and reversibility of agglomeration as well as to understanding how particles can transform from weakly bound agglomerates to strongly bound aggregates. Finally, the structure of water and other species in the spaces between primary particles could strongly influence accessible reactivity. If species are able to diffuse into those spaces, then that surface area could be considered accessible and possibly reactive, or those spaces could serve to sequester specific species from the environmental system.

**Application of molecular-based mechanistic studies to understand surface reactions of nanomaterials in complex media.** One way of examining nanomaterials in a larger scale, complex environment while applying fundamental molecular-level chemical studies is to use a reductionist approach. Studies might begin by examining highly simplified model systems (e.g., oriented single crystal metal oxides in the presence of deionized water) as a function of water pressure. Such studies can reveal the p(H₂O) at which surface hydroxylation occurs and also shed light on reaction rates and the extent of monolayer hydroxyl and molecular water coverage as a function of relative humidity. The next step could involve determining the surface structure of hydrated solids, be followed by careful studies of uptake of adsorbates from aqueous solution, and then be followed by spectroscopic characterization of adsorption products. Considering the effects of natural organic matter and, in subsequent experiments, microbial biofilms on the surface reactivity of the solid would add additional complexity to the system. Such an approach builds fundamental studies of surface reactions in a controlled, step-wise
fashion. Close coupling of experimental results and atomistic theory is very useful for interpreting experimental results at a fundamental level. A similar approach is needed for understanding the environmental surface chemistry of nanomaterials, but given the current limitations on molecular-level methods for nanomaterials, further instrument development of analytical tools is necessary first. Issues remain, however, in determining how far a reductionist approach can be useful and how to simplify an experiment so that it is tractable but retain enough complexity that it retains the essence of the real complex environment.

**Development of experimental and theoretical methods for the study and control of nucleation processes.** New particle formation is the process of transformation from the molecular scale of individual molecules in the gas phase to a condensed-phase material. In order for a particle to nucleate, the energy released as the volume of the new particle grows (scaling as diameter cubed) must overcome an activation barrier arising from the energy cost of the new surface of the incipient particle (scaling as diameter squared). A major focus for development is improved (lowered) detection limits on instruments to investigate smaller particle/cluster sizes and lower concentrations to determine what species participate in new particle formation. In this regard, characterization of sub-10 nm particles is particularly important in both aqueous and air systems while computational studies of nucleation processes are needed to interpret and predict experimental measurements. Furthermore, modeling nucleation clusters extends the use of advanced molecular computational techniques in a matter that could act as a bridge to investigating larger particles.

**Examples of What Chemistry Research is Needed**

Chemistry and materials research is needed in many areas in order to better understand the fundamental properties of nanomaterials. Examples are given here.

- Develop new tools for nanomaterial characterization especially under ambient conditions and in complex and heterogeneous media.
- Understand the molecular evolution of dissolved aqueous species to small clusters to nanomaterials to bulk precipitates and then back again.
- Develop computational tools that bridge length and time scale gaps.
- Develop computational tools that can be used to predict the static, dynamic and evolutionary properties of individual nanoscale materials in realistic, complex environments so as to impact the design and safe stewardship of nanomaterials.
- Determine the effect of particle characteristics on surface chemistry and surface properties to better understand nanomaterial reactivity.
- Determine the effect of particle characteristics on reaction rates and pathways (e.g., redox chemistry, dissolution behavior and production of reactive oxygen species).
- Elucidate nucleation pathways and mechanism.
- Develop kinetic models of nucleation and particle formation.
- Develop a set of standard materials and methods for interlaboratory comparisons and benchmark reference points for experimental and theoretical studies.
- Develop and understand structure-function relationships using well-defined and systematically varied nanomaterials.
- Elucidate the link between surface chemistry and the kinetics and reversibility of aggregation.
- Determine the role of surface bound species in heterogeneous and homogeneous aggregation.

IV. Nanomaterial Interactions with the Environment

Introduction

Analyzing nanomaterial-environment interactions depends on building a solid scientific model of nanomaterials alone and on understanding their surface reactions with the complex environment. Nanomaterials themselves can take many forms (Figure 5), and their size, composition, shape, structure, coatings, and surface chemistry will influence their nanomaterial-environment interactions in ways that are not yet well understood. For example, pristine nanomaterials such as the ones shown in Figure 5 may aggregate or change properties over time. Additionally, nanomaterials might sequester ions and transport them long distances (42), and changes in environmental conditions might trigger the release of adsorbed contaminant species. An important example is the case of arsenate ions adsorbed onto iron oxide nanoparticles. The release of arsenate ions in Asia has contributed to serious health effects and has exposed over 100,000,000 people to concentrations of arsenic exceeding the World Health Organization maximum contaminant levels (43). \textit{In situ} molecular-level studies are needed to fill knowledge gaps about chemical processes such as this one and to understand the behavior of nanomaterials in complex environments.

\textbf{Figure 5.} Nanomaterials can be made in a wide range of shapes, sizes and chemical compositions. The large number of combinations for study represents one of the challenges in understanding nanomaterials and their interactions with the environment and biological molecules and systems. (Figure credit: Sherine O. Obare, adapted from Refs. 44-47).
Grand Challenges and Major Knowledge and Methodology Gaps

The grand challenges and knowledge and methodology gaps associated with investigating nanomaterials interacting with the environment span several areas. There is a need to determine how nanomaterials transform in complex matrices such as air, water, soil, and biological environments and how nanomaterials form from available precursors. There is lack of specific information on redox chemistry and light-driven transformations, including the creation of reactive sites by photochemical pathways. Furthermore, there is a need to understand how different chemical processes lead to degradation or transformation and how nanomaterials interact with photoreactive organic species such as natural organic matter.

Importantly, once nanomaterial-environmental interactions are better understood, the knowledge can be used to develop the sustainable production of nanomaterials and to apply them toward solving global environmental problems such as mitigating atmospheric carbon dioxide and providing clean water supplies for an increasing population. Grand challenges and major knowledge and methodology gaps for understanding nanomaterial interactions with the environment, their potential uses in environmental applications, and the development of sustainable nanomaterial syntheses are given next.

**Scalability and complexity of nanomaterials in environmental systems.** Given that simple laboratory model experiments may only poorly approximate environmentally-relevant time and volume scales as well as the chemical complexity of environmental systems, a major challenge is to translate knowledge from model systems to realistic environmental conditions. One challenge when studying nanomaterial behavior is to design models that best represent natural, environmental systems in ways that are both scalable and address important questions. For example, major knowledge gaps exist about the nature of environmental interfaces, particularly those that consist of complex mixtures of nanomaterials, aqueous solutions, natural organic matter, plant material, and microbial organisms, the latter often in the form of biofilms.

**Released quantities and forms of engineered nanomaterials.** One aspect of understanding how the release, fate, and transport of nanomaterials impacts the environment requires developing knowledge about the release mechanisms and release rates of nanomaterials from different sources (e.g., during manufacture or from consumer products). Another critical element is developing methods that quantify the amounts of nanomaterial released during the full life cycle of nanomaterials: production and processing, normal use, wear and tear, and disposal of materials and products. The matrix surrounding the nanomaterial might also release with the nanomaterial, and the whole complex might transform when in environmental or biological systems. Knowledge of the amounts of materials released into the environment in different situations (e.g., in landfills or water treatment plants) is important in making predictions about the effects of
nanomaterials on environmental systems and ecosystems.

**Persistence of nanomaterials in the environment.** When considering the release and transport of nanomaterials into environmental systems and ecosystems, it is important to understand the persistence of the material. What properties make a nanomaterial resistant to environmental processes like dissolution and other transformation processes? Furthermore, what range of species could be concentrated on or within those nanomaterials, thus making the nanomaterial a potential carrier and/or transformer of such species (i.e., facilitated transport)? And finally, could such species change the environmental impact of these nanomaterials? Thus, a major challenge is understanding the factors that influence the persistence of nanomaterials in environmental systems. One challenge is to develop new paradigms for quantitative predictions of the fate and transport of environmental nanomaterials. From an equilibrium perspective, can researchers develop distribution coefficients ($K_d$ values) for nanomaterials similar to octanol-water $K_d$ values so the coefficients can be used in environmental engineering models of nanomaterial transport?

**Heterogeneous distribution of nanomaterials: dilution, geoconcentration and bioaccumulation.** In comparison to natural materials on and near Earth’s surface, engineered and incidental nanomaterials represent an exceedingly small amount of actual material. Detecting dilute concentrations in air and water is consequently a significant challenge. The release, transport, and fate of the materials is furthermore likely to result in a heterogeneous distribution across the environment. For example, if some nanomaterials bioaccumulate, then we could expect ever-increasing concentrations of the nanomaterials higher up the food chain, and if specific types of materials preferentially capture nanomaterials, geoconcentration may occur. Grand challenges for study include issues related to bioaccumulation, predictors of bioaccumulation, and predictors of geoconcentration.

**Analytical methods for the quantification of nanomaterials in complex environmental matrices and at low nanomaterial concentrations.** Chemists must develop methods able to characterize systems of greater structural and chemical complexity while maintaining the ability to acquire detailed molecular level information. Ideally, methods that allow for detailed measurements in complex matrices and at low concentrations of nanomaterials are needed for these types of studies.

**Size and shape distribution.** A nanomaterial’s size and shape strongly influence its mobility and reactivity. The transport of a nanomaterial within environmental systems depends on its size and shape, and the mechanisms by which cells incorporate nanomaterials change as a function of these parameters as well. Aggregation and agglomeration also play important roles in fate and transport of nanomaterials in environmental and biological systems. A challenge remains, however, in defining and characterizing size and shape. The quantitative description of particle size is critical.
When considering aggregation and agglomeration, several sizes are important including the size of the primary objects composing the secondary object as well as the size of the secondary object. How to appropriately normalize and/or represent data originating from systems with heterogeneous size distributions is often unclear. For example, nanomaterial-induced effects may scale with nanomaterial number, surface area, or total mass depending on the physical processes involved.

**Defining key transformation processes of nanomaterials in the environment and their effects on nanomaterial behavior.** Molecular-level information of how nanomaterials transform over time and in different environments is lacking. Figure 6 is a cartoon representation of the release of nanomaterials into air and water along with chemical and physical processes that might occur (48). When manufactured or incidental nanomaterials are released into the environment, they are often exposed to conditions very different from those encountered when they formed. As a result, the nanomaterials undergo transformations in structure and composition. For example, silver (Ag) nanoparticles receive wide attention because of their antibacterial and antifungal properties; however, when exposed to environments containing reduced forms of sulfur, these nanoparticles are transformed to Ag$_2$S. (49). The resulting Ag$_2$S surface coatings are much less soluble than the pristine Ag nanoparticles, which greatly reduces the release of Ag$^+$ ions into solution. The released Ag$^+$ ions are thought to be the major source of Ag nanoparticle toxicity to organisms, but as a result of this Ag$_2$S coating, the environmental impact and bioavailability of nanoparticle silver are greatly reduced. The whole idea of aging and how nanomaterials change in various environments is a concept that is, at best, poorly understood. As soon as a nanomaterial is formed, aging begins. Phase composition, composition, aggregation and agglomeration, size and size distribution, all change substantially as a function of time; thus, we need techniques that detect dynamics of nanomaterial structure, composition, surface chemistry, and aggregation state as a function of time.

![Figure 6](image-url) **Figure 6.** The figure depicts the release, transport and transformations of nanomaterials in the environment. Different processes occur upon release of nanomaterials from a point source. (Figure credit: Linsey Marr and Marina E. Quadros, adapted and reproduced with permission from Ref. 48, *Journal of Environmental Quality* 39: 1883–1895 (2010)).
Opportunities for Chemists to Make Transformative and Innovative Contributions

Chemists and materials scientists have many opportunities to make major contributions either alone or, in many cases, as part of interdisciplinary teams to better understand nanomaterial interactions with the environment.

Chemical approaches to the complexity issue. Researchers might use two distinct approaches to bridge the gap between the lab and the complexity found in the field or the whole organism. The first, a reductionist approach, is to start with very simple experiments such as a suspension composed of just a few components (e.g., synthetic and homogeneous nanomaterials, buffer, purified water, and reactive molecule) and move towards more and more complex studies by systematic changes in experimental variables. An example is research examining the reactivity of goethite ($\alpha$-FeOOH) nanoparticles. Natural samples of goethite typically have substantial cation substitution, and work with synthetic materials demonstrated that the presence of trace concentrations of aluminum increases the rate of reductive dissolution and higher concentrations of aluminum slows the rate (50). Thus, the increasing complexity results in the composition of the synthetic material resembling the natural materials more closely. One goal is to identify the most important control parameters and then draw comparisons between lab and field materials. In contrast, the other approach is to take the complex system and move toward more simple experiments. This is the approach often taken by researchers investigating complex biological systems; as specific variables are controlled, the important control parameters can be elucidated. Both approaches have opportunities for gaining knowledge as well as in bridging the gap between understanding detailed molecular aspects and capturing complexity.

Scale: What is the ideal scale for these experiments? What are ideal scales for experiments focused on the release, transport, and aggregation of nanomaterials? From individual cuvettes in which aggregation and agglomeration state can be monitored using techniques like dynamic light scattering and UV-Vis spectroscopy to real lakes to which doses of particular materials could be delivered, the ideal scale for experiments spans many orders of magnitude. One cannot assume that conclusions derived from the results of milliliters of suspension contained in clean glassware will scale to results from real lakes composed of heterogeneous and reactive container walls (i.e., lake sediment). Mesocosms offer potential experimental solutions for examining complexity; examples include model environments like “forest in a bottle” and “smog chambers.” The experimental models can inform and provide data about how nanomaterials move, aggregate and react into predictive reactive transport models. At the present time, few computational codes are able to combine these. Experiments and models that move toward developing rate constants that describe real reactions that occur in heterogeneous groundwater, surface water, and atmospheric systems are needed.
**Aqueous and atmospheric systems to investigate different nucleation pathways.** In aqueous systems, fundamental studies on the nucleation pathways for the formation of nanomaterials are critical if controlled methods for the synthesis of nanomaterials with particular properties, size, and shape will be possible. In the natural and human impacted environment, nucleation is a poorly understood but critical phenomenon. For example, in atmospheric systems the process of new particle formation ultimately affects a number of important climate and health-related endpoints of human interest: the number concentration in the atmosphere of cloud condensation nuclei (i.e., so-called "indirect effect" of aerosol particles on climate) and the number concentration of sub-100 nm particles in urban environments, which have been directly implicated as a human health hazard.

**Nanomaterial thermal and photo-degradation pathways in the environment.** As described previously in this report, one expects that nanomaterials transform and degrade in the environment; therefore, the chemical and/or physical properties of nanomaterials must be studied in detail as a function of degradation or transformation and in a manner that is predominantly in ambient environment conditions. Researchers need to determine the dominant mechanisms of nanoparticle/nanomaterial degradation and focus on measuring/quantifying the details related to nanomaterial life cycles, such as the release, lifetime, and eventual fate of nanomaterials. Studies on the photodegradation pathways is also an area of need. Specifically, are the nanomaterial cores absorbing the light, the ligands or both? And the importance of photooxidation in these pathways is important to delineate yet poorly understood. Measuring the temporal evolution of nanomaterial transformations over multiple scales is another major research need, including the factors that influence nanomaterials and their transformations. For example, zero-valent iron nanoparticles undergo extensive changes as a function of aging in aqueous solutions, particularly in the presence of natural organic matter. In air, nanomaterials can undergo atmospheric processing which includes heterogeneous chemistry and photochemistry as well as aqueous phase cloud processing that may alter physicochemical properties of the material. For metal-containing nanoparticles, these transformations can result in an increase in dissolved metal ions (see Figure 7). Information on ligand adsorption, nanomaterial/ligand interactions and the fate of ligands as a function of environmental exposure is similarly needed. Understanding the molecular-level mechanisms of these types of transformations and associated kinetics is a major challenge for environmental chemistry.
Figure 7. Nanoparticles emitted into the atmosphere can undergo atmospheric transport and processing. Nanoparticles can undergo heterogeneous chemistry and photochemistry with trace and aqueous phase, cloud processing. For metal and metal oxide nanoparticles, these processes can transform the particle making it more hygroscopic and potentially yield more soluble metal ions. These transformed particles can then undergo deposition into aqueous and terrestrial ecosystems with very different physicochemical properties from the freshly emitted nanoparticle. Understanding these processes and transformations is key to understanding nanomaterials in the environment. (Figure credit: Vicki H. Grassian, adapted from Ref. 51).

**Develop new strategies for applications of nanomaterials.** Carbon dioxide capture, carbon dioxide reduction and conversion, and developing clean water supplies for the global population are all potential applications for nanomaterials. The knowledge base developed through molecular-level and macroscopic studies of aqueous contaminant ion interactions with nanomaterial surfaces could lead to new strategies for waste-water treatment using, for example, reverse osmosis membranes without the normal problems of membrane fouling. The development of environmental applications of nanomaterials remains an important research endeavor for chemists and materials scientists. The development of nanomaterials is surely to play a role in solving many global problems.

**Sustainable synthesis of engineered nanomaterials.** A number of considerations are necessary for the sustainable synthesis of engineered nanomaterials. For example, a fundamental understanding of nucleation could lead to synthetic methods for nanomaterials with specific and controlled properties, to smaller waste streams during production of nanomaterials and other manufacturing processes, and to the preparation of environmentally benign nanomaterials. Developing energy efficient methods to synthesize nanomaterials of specific physical dimensions, surface structure, and composition is directly tied to EH&S and sustainability. Researchers need to consider reducing the use of energy and the environmental implications of the applications of engineered nanomaterials. Furthermore, additional experimental studies of the environmental properties of nanomaterials are needed. Studies of the properties of nanomaterials in the environment will provide insights and potential guidelines for the manufacture of safe-by-design nanomaterials.
Examples of What Chemistry Research is Needed

Chemistry and materials research is needed in many areas to better understand nanomaterial interactions with the environment. Some examples of research needs to better understand the environmental release, transport and aggregation; chemical and photochemical alteration and degradation of nanomaterials in the environment; and nucleation of nanomaterials in the environment are given next.

- Determine the structure (including defect sites and concentration) and composition of nanomaterial surfaces under in situ conditions.
- Identify how physical structure and chemical composition of the surfaces of nanomaterials are transformed and altered in the environment.
- Develop tools that can characterize surface composition of nanomaterials after environmental exposure.
- Better understand how nanomaterials change in natural ecosystems and manmade environments (e.g., water treatment plants) as examples of dynamic and reactive environments.
- Determine how nanomaterials transform over time.
- Determine how transformations impact nanomaterial surface structure, composition and reactivity.
- Determine how surface functionality impacts the stability of nanomaterials and delineate the details of the surface adsorption process including the mode of adsorption, reversibility of adsorption, and the possible displacement reactions that can occur in the environment.
- Identify various reaction mechanisms that nanomaterials can undergo in the environment, in all environmental compartments – air, water and soil – to better understand transformations that are most likely to occur.
- Better understand molecular-level aspects of particle-particle interactions as well as particle interactions with other species in environmental systems.
- Determine the most important factors that control the impact of nanomaterials on the environment.
- Develop low energy pathways for nanomaterial production.
- Develop sustainable synthetic approaches for engineered nanomaterials.
- Develop new paradigms for fate and transport.
- Develop new and robust theories for the formation of nanomaterials from aqueous solutions and ambient air.
- Understand aging processes and phase transformations of freshly nucleated particles in water and air.
- Incorporate “aged” or altered nanomaterials into studies of pristine nanomaterials.
• Measure the kinetics and mechanisms studies of chemical/photochemical transformations that are potentially important in the environment and determine the impact of particle characteristics on these transformations.
• Better characterize interactions between natural organic matter and nanomaterials and how these interactions influence stability and mobility in the environment.
• Determine the structure of precursors of amorphous (intermediate) phase formations.
• Characterize the real-time evolution of nanomaterial distributions and topology at an active interface without dehydration.
• Determine how confined nanopore spaces affect nanomaterial nucleation and growth under diverse environmental conditions.
• Determine how manufactured and incidental nanomaterials are transformed in natural ecosystems and manmade environments (e.g., water treatment plants) and how these transformations affect properties.
• Develop experimental approaches so that data acquired from model systems can be translated to more realistic (complex) environmental conditions.
• Design nanomaterials with predictable properties and environmental fate for environmental remediation and other applications.

V. Nanomaterial Interactions with Biological Molecules and Biological Systems

Introduction
Understanding how nanomaterials affect the health and safety of the environment requires a strong grasp of how nanomaterials interact with individual biological molecules, cells, and whole organisms (Figure 8). The physical, chemical, and temporal complexity of biological systems makes developing a molecular-level understanding an extremely challenging problem. The potential influence of nanomaterials to adversely affect humans and other organisms in the environment revolves around understanding the delivered dose and mechanisms by which nanomaterials induce toxicological response in organisms. Toxicological responses depend on a number of intertwined factors, including transport (how nanomaterials enter an organism), uptake (how nanomaterials are internalized by target cells), distribution (where nanomaterials are transported within an organism), metabolism (in vivo processes that alter nanomaterials), toxicological response (how an organism responds to the presence of nanomaterials), and elimination (how an organism eliminates nanomaterials and alteration products) (52).
The discipline of toxicology associated with nanomaterials (sometimes referred to as nanotoxicology) is complicated by the fact that nanomaterials in the environment undergo a number of chemical and physical changes, such that the species interacting with biological organisms may have little resemblance to the engineered nanomaterials from which they started. Because of these weathering and alteration processes, nanomaterials in the environment must be treated as a *dynamic system* -- at the same time as nanomaterials are influencing their local environment, they are also being acted upon and modified by the environment. As a consequence, in order to understand nanomaterial interactions with biological systems, pushing for the development of methods and tools capable of performing the most complete analyses of nanomaterial properties possible *in vivo* is imperative (53).

![Figure 8](credit: Robert Hurt, Brown University)

**Figure 8.** The nanomaterial-biological interface is the site of physical and chemical interactions between the nanoparticle surface and target biological molecules and cells. Interdisciplinary research involving materials scientists and toxicologists is required to understand the physical and chemical properties of nanomaterials associated with different toxicological responses. (Figure credit: Robert Hurt, Brown University).

While the need for *in situ* measurements in the environment and ideally *in vivo* measurements within living organisms is clear, *in vitro* laboratory-based studies play an important role in addressing the fundamental molecular-level interactions. A key question, however, is identifying which molecular interactions to study. Cells contain
high densities of many different macromolecules. Some will interact strongly and some will interact weakly, but it is not clear that the most strongly-interacting molecules are the most important in understanding nanomaterial-induced biological response. Indeed, heterogeneous catalysts with the highest activities have molecule-surface interactions that are neither too weak nor too strong, leading to a "volcano plot" of reactivity as a function of interaction strength (54). Similarly, nanomaterials might induce the strongest biological response when interacting with macromolecules of intermediate binding strength. Given the huge number of possible peptides, proteins, nucleic acids, lipids, and other macromolecules, a key challenge is to identify a rational basis for deciding which biomolecular interactions should be studied in detail.

One of the greatest challenges associated with studying nanomaterial interactions with biological systems is measuring processes inside highly complex, internally structured matrices. While measuring the surface chemical composition of a nanomaterial in even a simple liquid is already difficult, doing so for nanomaterials residing within cells or tissues of more complex organisms is virtually impossible at the present time. Yet potential solutions are on the horizon as continued development of new x-ray methods and super-resolution optical microscopy may be able to perform analytical measurements at the necessary length scales.

**Grand Challenges and Major Knowledge and Methodology Gaps**

**Nanomaterial uptake into biological system.** Cells have intrinsic mechanisms for recognizing, sequestering, and degrading or expelling foreign objects. Cells, for example, have cell surface receptors that control the interactions between cells and exogenous materials, allowing the cells to take up or reject foreign objects. Nanomaterials, however, can have physical dimensions and surface coatings that allow them to be internalized by cells. Cell membranes, for instance, have hydrophobic interiors that can interact strongly with nanomaterials having hydrophobic coatings, facilitating the entry of nanomaterials into the cell. At present, however, whether uptake is required for adverse cellular effects is unknown.

**Nanomaterial interaction with biological molecules.** Once inside an organism, nanomaterials can interact with a wide range of biological molecules that affect the subsequent distribution of nanomaterials in the organism (e.g., movement within the circulatory system, crossing the blood-brain barrier, sequestration in the liver or kidneys) and their reactivity with target cells and molecules. Of particular importance is the interaction of nanomaterials with biological macromolecules that affect cellular metabolism and proliferation. Some cases show that the interaction of nanomaterials with peptides induces changes in the secondary and/or tertiary structure of the peptides (Figure 9) (55,56). Because misfolded proteins (prions) are associated with a number of diseases (e.g., bovine spongiform encephalopathy or “Mad Cow Disease”, human Creutzfeldt-Jakob disease, type II diabetes, Alzheimer’s disease, and Parkinson’s
disease)(57,58), the scientific community has great interest in understanding at a molecular level how nanomaterials interact with proteins and peptides, in particular.

Understanding these processes will derive from a molecular-level understanding of how nanomaterials interact with biological molecules including proteins and peptides, DNA, lipids, extracellular matrix constituents, and biological barriers that may limit entry into the skin, respiratory tract, and gastrointestinal tract. A nanomaterial might come into contact with a large number and variety of macromolecules, which makes developing this molecular-level knowledge an extremely challenging problem. For example, eukaryotic proteins are comprised from sequences of 21 different amino acids, and a peptide consisting of N amino acids will therefore have $21^N$ different possible sequences. For a short peptide consisting of 10 amino acids, more than $10^{13}$ possible sequences of amino acids are possible. Because of this large number of possible molecular interactions, materials scientists and nanotoxicologists must develop new approaches to identifying which macromolecules are most likely to bind to nanomaterials. A limited knowledge base already exists from studies of biomedical applications attempting to increase the residence time of nanomaterials in the bloodstream to facilitate their use as drug delivery agents. Very little is known, however, about the more general behavior of nanomaterials likely to be encountered in the environment or within other biological matrices. Methods are needed to identify both the persistent molecules that bind to nanomaterials and to the transient molecules that may bind only briefly but may be changed as a result of the interaction. More understanding is similarly needed about what specific materials properties of nanomaterials control the interaction with biological molecules.

**Molecular basis of nanomaterial-induced biological response.** An understanding of how individual biomolecules interact with nanomaterials lies at the core of understanding the EH&S effects of nanomaterials, but it is not sufficient to establish the behavior and effect on the system-based, organismal level. Toxicity measurements reveal the overall effect of nanomaterials on an organism, but they generally do not differentiate whether the effects result from the intact nanomaterial, the nanomaterial surface, or from dissolution/degradation products that form *in situ*. Little is known about how the size, shape, chemical composition, and surface properties (charge state, hydrophobicity, density) of materials influence the interactions. Nanomaterials interacting with a
biological organism can induce a wide range of potential biological responses. Direct toxicity or death, changes in metabolic response, or changes in DNA replication and/or protein expression are a few of the the possibilities that might be induced by many different mechanisms. Since nanoparticles have dimensions comparable to those of many biological macromolecules, nanoparticles likely can induce changes in conformation or alter the folding of proteins and other molecules. Furthermore these changes can be induced by the primary nanomaterial composition (e.g., CdSe “quantum dots”), from degradation products (e.g., Se nanoparticles produced by degradation of the CdSe), from surface ligands, or from other species adsorbed onto the nanomaterial surface. Molecular-level studies will require detailed information about the structure and composition at the nanomaterial-biological interface, but tools that can provide that information do not exist yet.

The interaction of nanomaterials with the surrounding biological matrix can also involve charge exchange by which the nanomaterials serve as electron donors or acceptors and induce oxidative stress through the generation of reactive oxygen species. Understanding how nanomaterials interact with the biological electron-transport chains will be necessary to fully understand the toxicological effects of nanomaterials. In addition, such information will be key to understanding how biological systems modify nanomaterials. For example, oxidation of metal sulfide “quantum dots” will likely oxidize the sulfide and release the metals into the aqueous phase, and semiconductor nanoparticles can generate reactive oxygen species and other radicals that can damage DNA and other biomolecules, leading to genetic damage. Little is known about the redox properties of nanomaterials and how they are different from larger particles.

**Identification of biological markers of nanomaterial exposure.** The interaction of nanomaterials with organisms will produce characteristic changes that can be used to assess exposure without necessarily detecting the nanomaterials directly. For example, exposure to nanoparticles can induce inflammatory response and oxidative stress in cells, which can be detected through specific chemical changes such as increased concentrations of reactive oxygen species and/or specific cell adhesion proteins and inflammatory mediators (59). Such molecular-level biomarkers of nanomaterial exposure can provide a mechanistic basis for nanomaterial induced changes in biological structure and function. At the present time few biomarkers have been identified, however. These and other methods of detecting sub-lethal changes in biological structure and function in response to nanomaterial exposures are in their infancy.

**Dynamic nature of nanomaterial-biomolecule interactions.** While engineered nanomaterials are typically synthesized with well-defined surface coatings (often consisting of organic ligands), the coatings are likely to be unstable in environmental/biological systems. The subsequent alteration or “weathering” of the nanomaterial may alter the surface structure and/or composition, including replacement of external organic coatings with polysaccharides, proteins, or other biological
macromolecules. For example, extracellular matrix proteins can form coatings on nanomaterials or can induce formation of reactive oxygen species that can induce degradation of the nanomaterials. Nanomaterials that are taken up by organisms are rapidly coated with proteins, forming a “protein corona” around the nanomaterials. The proteins that initially bind to the nanomaterials are those with the fastest binding kinetics, while on longer times scales they may be replaced by other proteins and macromolecules with higher thermodynamic bonding strength (60,61). Nanomaterial degradation may increase in biological matrices (Figure 9), leading to uncertainty as to the nature of the nanomaterials at any given point in time. One important consequence of the weathering and alteration phenomena is that the nanomaterials and biological system must be treated as a coupled, time-dependent (dynamic) system.

Figure 10. A nanoparticle degrades from left to right in the graphic. Biological response to nanoparticles may arise from the intact nanoparticles or from degradation products. (Figure credit: Robert Hamers).

Nanomaterial metrics relevant to biological response. One of the major challenges in studying nanomaterials is that nanomaterials with precisely defined composition, sizes and shapes are not commercially available. Most researchers use commercially available nanomaterials, but particles having different sizes are often produced using different methods that may change properties other than size. While researchers recognize that well-characterized particles are necessary, we do not yet know precisely which properties are most important to characterize. Is characterizing the composition, size, and shape sufficient? Or should we routinely characterize other factors such as purity and/or other measurable physicochemical parameters (excited-state lifetimes, point of zero charge, redox potential, etc.)? Few well-defined protocols for characterizing biological response of nanomaterials exist as well. While procedures have been developed for characterizing the toxicity of chemicals, nanomaterials are far more complex in size, shape, composition, and more likely to have substantial time-dependent changes in their properties. How the lack of measurement protocol across laboratories affects the reports of biological response outcomes is unclear, producing uncertainties when researchers compare results results across laboratories. Analytical tools for characterizing the location and/or properties of nanomaterials in biological systems in a quantitative manner
do not exist. Agglomeration is likely to be important in solutions of high ionic strength, but no methods can characterize nanomaterial aggregation in situ. Furthermore, agglomeration/deagglomeration might be dynamic processes following uptake. Efforts must be made to identify what the most important parameters to characterize are and to develop quantitative metrics for them.

Nanomaterials as delivery agents of potential toxicants. The high surface area of nanomaterials facilitates adsorption of other species, including potential toxicants, onto their surfaces (62), suggesting that nanomaterials can deliver toxic payloads into biological organisms. The amount of toxicant delivered may be more pronounced on nanomaterials compared with larger particles or extended surfaces because the small size of nanomaterials exposes high-energy crystal faces that are anticipated to have higher binding strengths for adsorbed species.

Opportunities for Chemists to Make Transformative and Innovative Contributions

Development of reproducible, scalable methods for synthesizing nanomaterials with precisely controlled chemical and physical properties. The synthesis of nanomaterials is often difficult to control, and nanomaterials are often thermodynamically unstable. Synthetic methods commonly produce materials with wide ranges in size and shape, and researchers often lack complete characterization of surface species and/or contaminants that may strongly influence the toxicity of nanomaterials. Without reproducible starting materials, however, systematic and quantitative assessment of structure-activity relationships becomes impossible. The development of improved nanomaterial synthesis methods to produce, for example, nanomaterials with defined sizes would facilitate the ability to cross-check results in different laboratories. Likewise, the availability of sample sets that vary by only single properties (e.g., size, surface groups, shape) would significantly advance our understanding of how these properties affect response outcomes.

Development of high-throughput screening methods for identifying important nanomaterial-molecule interactions. Due to the wide range of biomolecules with which nanomaterials might come into contact, developing methods to identify which molecular interactions have important biological effects is essential. Because of the high degree of complexity of environmental systems, researchers must develop new methods or adapt existing ones that will allow them to identify the important interactions in the presence of complex matrices. The molecular biology community has developed and implemented a wide range of high-throughput screening methods that can be applied to nanotoxicology (63,64). The methods could be used to identify the nanomaterial-biomolecular interactions with the strongest binding affinities; however, as noted previously, the strongest interactions are not necessarily those of greatest importance.
Use metabolomics, proteomics, and transcriptomics to create fingerprints of nanomaterial exposure. Since nanomaterial exposure will likely induce changes in metabolic pathways, a deeper understanding of how nanomaterials affect cellular processes including metabolism, gene transcription, and protein expression may shed light on the underlying molecular-level interactions and enable determination of the pathways for bioavailability and potential toxicity.

Development of analytical tools for characterizing the structure and composition of nanomaterials in vivo. Measuring the dynamic nature of nanomaterial-biomolecular interactions requires improved methods for identifying the composition of nanomaterials and adsorbed surface layers in vivo. Nanoparticles quickly become coated with a protein corona, but the nature of the corona is poorly understood (60,61). The corona is also dynamic; at longer time scales, biopolymers that have more favorable thermodynamic binding energies may quickly replace an initial set of quickly binding proteins. Deeper understanding of the dynamic system can support the design of nanomaterials that interact in a directed way with living systems.

Characterization of thermodynamic and kinetic factors affecting biopolymer interactions with nanomaterials. Because of the dynamic nature of nanomaterials in the environment, improved methods are needed for characterizing both the thermodynamic and kinetic behavior associated with nanomaterial interactions with DNA, proteins, and other macromolecules. Since nanomaterials have dimensions comparable to those of many biological macromolecules, proteins and other target molecules that bind to nanomaterials likely can exhibit changes in their conformation or folding (65,66). Systematic measurements of nanomaterial-biomolecule binding interactions and how these depend on factors such as the properties of the nanomaterial (size, shape composition) and the primary, secondary, and tertiary structure of the biopolymers would serve as a fundamental basis for understanding the detailed molecular mechanisms of interaction that ultimately control biological response and toxicity.

Establishment and validation of methods for simulating biologically-induced alteration processes on nanomaterials. Nanomaterials interacting with biological systems will be altered by processes such as generating reactive oxygen species that are specific to the environment. The development and validation of laboratory methods for simulating these processes would facilitate comparison of the likely toxic properties of different types of nanomaterials and could be used for screening purposes.

Development and validation of multiscale computational methods for characterizing nanomaterial interactions with biological systems. In the last few years advanced computational methods have advanced to allow researchers to treat complex systems containing, for example, nanoparticles, biomolecules, and an aqueous phase (67,68). New computational approaches that can address a wide range of length scales (atomic to tens of nanometers) and incorporate both strong forces (ionic, covalent) and weaker
forces (van der Waals') would greatly enhance a molecular-level understanding of nanomaterial interactions with biological systems. If the computational methods could be extended and validated against a suite of experimental systems, they would transform our ability to address important environmental problems.

**Synthesis and design of safe nanomaterials.** Ultimately, one key desired outcome of nanomaterials research is to understand the physical and chemical properties that induce toxicity, leading to the establishment of a set of “design rules” that minimize the toxic impacts of nanomaterials while preserving their desired function. We cannot develop these rules at the present time due limited understanding of nanomaterial-biomolecule interactions.

**Examples of What Chemistry Research is Needed**

To make progress in this area, a number of areas of chemistry and materials science require substantial additional research. Some key areas include:

- Develop and apply next-generation screening methods to identify which molecules in complex biological systems are interacting with nanomaterials.
- Identify fundamental mechanisms of uptake of nanomaterials into cells and organisms.
- Determine mechanisms by which nanomaterials alter the behavior of individual molecules (e.g., altering protein folding patterns) and ensembles of molecules (e.g., disrupting cell membranes).
- Develop methods that will enable identification of the location and concentration of nanomaterials in vivo and in single- and multicellular organisms.
- Investigate the catalytic generation or scavenging of potential toxicants such as hydroxyl radicals, superoxide ion, and other species by .
- Understand the adsorption of biological macromolecules and humic substances on nanomaterials and the influence of nanomaterial size, shape, and composition on the interaction.
- Develop and validate methods for relating laboratory-based studies with behavior in the natural environment; this could involve development of biomimetic approaches to characterizing weathering/alteration of nanomaterials.
- Develop an understanding of how nanomaterial surface coatings impact subsequent biological interactions.
- Develop and validate multi-scale computational methods against a suite of model systems to establish predictive ability.
- Develop high-throughput screening methodologies of libraries of functionalized nanomaterials that can be used to understand how the particle surface directs interactions with biomolecules.
• Establish standardized procedures, protocols, and best practices that could be shared across laboratories and facilitate comparison of results from different laboratories is needed.
• Characterize and understand the extent of electron transfer between nanomaterials and biological targets.
• Develop improved methods that take into account factors such as aggregation, secondary modification, and the size, shape, and composition of the nanomaterials are required for assessing nanomaterial dose delivered to specific tissues and organs.
• Use metabolomics, proteomics, and transcriptomics to create fingerprints of effects caused by specific specific nanomaterials and bioavailable constituents, enabling determination of pathways for bioavailability and toxicity.
• Develop a nanomaterial database (e.g., via NIST) that can be relatively standardized and distributed to multiple labs for comparative experimentation.
• Develop laboratory protocols that will consistently and reproducibly alter nanomaterials from pristine to more environmentally-relevant conditions.
• Investigate the interaction of nanomaterials with natural organic material along with how these interactions influence the stability and mobility of nanomaterials in the environment.

VI. Infrastructure, Instrumentation and Computation

Introduction

Understanding the effects of nanomaterials on environmental safety and health requires tools that provide a breadth and depth of detailed information on complex systems. Characterizing systems on length scales from nanometers to kilometers and on time scales from femtoseconds to years clearly cannot be achieved with a single instrument; gleaning the necessary fundamental insights will require combining a wide range of chemical and physical measurements.

The ultimate challenge for measurement techniques of nanomaterials in the environment is to characterize, quantify, and track ensembles of individual nanomaterials in situ, in enviro, and in vivo. Ideally one could elucidate the full range of chemical, physical and biological descriptors of a single nanomaterial, an ensemble, and/or nanomaterial aggregates with a high degree of accuracy, precision, reproducibility and repeatability and to follow the location and evolution of the materials through time and space. in situ, in enviro, and in vivo emphasize that measurements are to be performed in the appropriate biological or environmental system or state without perturbing or destroying the nanomaterial or its surroundings.

When developing new measurement strategies and specific methodologies, a key challenge is the ability to perform the necessary measurements in situ, or at a minimum, under environmentally relevant conditions. in situ measurements are a particularly
pressing challenge when characterizing nanomaterial-biological interactions where researchers clearly need instrumentation and methods capable of chemically and physically analyzing individual nanomaterials embedded within living organisms. Such capabilities simply do not exist today. More detailed methods that can provide detailed characterization must complement measurements in environmentally relevant matrices; however, detailed methods currently may require pristine samples under idealized conditions. Even measuring nanomaterial size can be complicated in environmental or biological matrices. The challenge ultimately facing researchers in this field is to understand how to cross-correlate and validate (or invalidate) the information content from these different measurements to achieve a holistic understanding of nanomaterial interactions in the environment. Standardization of methods and implementation of a suite of "best practices" for characterizing nanomaterials could be as important as the development of improved tools.

In addition to physical and chemical measurements, computational methods play a key role in uncovering the effects of nanomaterials in the environment by screening complex systems, providing fundamental insights, and ultimately providing predictive ability. While "bioinformatics" is a well established field at the intersection of computer science and biology, one can envision a similar field of "nanoenviro-informatics" in which informatics approaches aid in investigating environmental systems. For example, by mining complex datasets for hidden correlations, chemists and materials scientists can then use computations to help identify the key variables to address in more detailed hypothesis-driven studies.

Nanomaterials in the environment are highly variable in composition, heterogeneity, and length scale. The range of processes governing the behavior of nanomaterials in the environment extends beyond a single length scale or approach, and the processes are time-varying.

Figure 11. Relationship between different computational approaches, with purely quantum-mechanical computational approaches at the center and semi-empirical methods at the periphery. (Figure credit: William Schneider)
No single computational method is consequently capable of addressing the full range of research questions that chemists have about the interactions between nanomaterials and environmental systems. Recent advances in density functional methods, however, and in the use of multi-scale methods that link atomistic, quantum-based calculations with semi-empirical empirical calculations provide exciting opportunities in the years ahead.

Computational approaches on long length- and timescales must necessarily compromise the high accuracy of rigorous, ab initio methods. The need for atomistic modeling depends on the specific research questions at hand. An essential goal is to meld macroscopic behavior with a microscopic basis, and the means is multiple approaches with the potential to converge. Of particular interest is how to span the boundaries between different modeling approaches. Theoretically rigorous methods towards the center of Figure 11 ideally should be used to parameterize outer (semi)-empirical methods, or hybrid methods embedding different models into simultaneous simulations should be built. Over time, the capability to apply ab initio methods to systems of greater size and complexity will emerge, allowing better parameterization and validation of more approximate methods. (That is, the process of bridging methodology gaps is continuous and should be updated as capability permits.)

Regardless of the details of the underlying theory, a ubiquitous challenge for computational methods applied to nanomaterials in the environment is accounting for the influence of the surroundings on the particle. Modeling not only multi-component but also multi-phase systems, including key reactivities at the interfaces, creates unique modeling challenges and opportunities in the years ahead.

**Grand Challenges and Major Knowledge and Methodology Gaps**

*Infrastructure for ensuring cross-laboratory validation using reproducible, well characterized nanomaterials.* One major impediment toward understanding the environmental impact of nanomaterials is that nanomaterials prepared by different synthetic routes may have vastly different properties. Since most researchers purchase nanomaterials with little or no information about how the nanomaterials were synthesized, attempts to compare experimental results from different laboratories are rarely taken. The important roles that the synthesis method and the presence of defects and impurities can have on nanomaterial properties have been widely recognized for carbon-based materials (69). In general, however, these roles are not clear in other materials such as metal oxides, for example, where the display of exposed crystal faces for a crystal structure (e.g., anatase versus rutile for TiO₂) can depend on the synthesis method (70). Most synthetic methods performed on a laboratory scale are not sufficiently reproducible to lead to well-defined nanomaterials. The absence of "standard" well characterized nanomaterials precludes researchers from sharing information on nanomaterials properties. As nanomaterials with well-defined compositions become available, infrastructure for archiving and retrieving information about nanomaterials...
would facilitate more robust data sharing across scientific disciplines and among different research groups and/or consortia. The standardization challenges further extend to sample collection and preparation; since nanomaterials have dynamic properties, nanomaterials collected in the field may change before analysis. The lack of documented "best practices" for collecting, storing, and preparing samples further reduces the validity of field studies unless measurements are performed \textit{in situ}. Equipment and procedures for making well-defined, pure, and homogenous nanomaterial samples on a scale sufficiently large to be widely used as a basis for developing, evaluating and benchmarking measurement technologies do not exist today.

\textit{Tracking and analysis of anthropogenic and engineered nanomaterials}. A key challenge is developing analytical tools to detect, analyze, and track nanomaterials in the environment and especially within organisms. One problem is that engineered nanomaterials may be present at low concentrations, below the detection limits of existing methods. In addition, however, nanomaterials of natural origin are widely distributed throughout the biosphere. While such natural nanomaterials may have potential health risks, the potential for unintentional effects from "engineered" nanomaterials, in which the composition, size, shape, and other properties have been designed to display specific properties, prompts greater concern. To understand the influence of \textit{engineered} nanomaterials on environmental health and safety, researchers want to know the kinds and quantities of nanomaterials present due to natural phenomena and to discriminate among natural, incidental, and engineered nanomaterials in the presence of much larger concentrations of background species that exist in complex and heterogeneous environmental media. Because water and air might readily transport nanomaterials, any understanding of the exposure and dose of nanomaterials must take into account transport in the environment. At the present time the ability to track nanomaterials in the environment is limited. Ideally the tracking of nanomaterials should be linked to real-time chemical analysis. Such monitoring has been achieved for some types of nanomaterials in air, but not for nanomaterials in water or soils. Tracking of nanomaterials in the environment may require development of nanomaterial "tags" that permit the nanomaterials to be followed with high sensitivity over a range of space and time.

\textit{Analytical tools for characterizing nanomaterials in environmentally relevant matrices}. A major challenge in instrumentation is that while characterizing the properties of nanomaterials is possible in a laboratory, no satisfactory methods are available to characterize nanomaterial size, shape, and chemical composition (core, surface, adsorbate) in condensed media. Nanomaterials change in form (isolated particles versus aggregated), size (coarsening and ripening phenomena) and surface composition (redox reactions, incongruent dissolution, and surface adsorption), and researchers acutely need continuous, real-time chemical characterization methods for nanomaterials in the 1-10 nm size range.
To fully understand the health risks of engineered nanomaterials, chemists need reliable methods to determine the localization of engineered nanomaterials in plant cells and organelles, and they also need to analyze their chemical speciation in edible components of plants after translocation. Therefore, developing complementary analytical tools that can be applied to elucidate the mechanisms of engineered nanomaterials internalization, translocation, and bioaccumulation in food crops is imperative. The continued development and application of super-resolution optical microscopies (71,72) and advanced x-ray methods (73,74) could greatly enhance the analysis of nanomaterial properties.

Size is an important factor controlling the properties of nanomaterials, but a lack of reliable tools for measuring the sizes of individual nanomaterials and measuring distributions of sizes in ensembles of nanomaterials under environmentally relevant conditions limits understanding of materials properties. Transmission electron microscopy (TEM) provides excellent imaging capability but requires that samples be dried, which can completely change the nature of the particle and its aggregation state. Similarly, dynamic light scattering (DLS) measurements typically require high concentrations where aggregation may be important and may be affected by surface ligands and other ions. Indeed, defining at the nanoscale exactly what "size" means becomes important since the hydrodynamic radius of a particle in solution will necessarily be different from the diameter inferred from transmission electron microscopy and that differs from mobility diameter and aerodynamic diameter that are typically measured for atmospheric aerosols. A recent comparison of different approaches to measuring nanomaterial size concluded that all the available methods had significant faults, recommending that the use of multiple techniques to be confident in the results (75).

**Advancing quantum-based computational methods.** Quantum-based computational methods such as density functional theory (DFT) are desirable for their ability to provide molecular-level detail about the structure and reactivity of nanomaterials in the environment. As a result of advances in computer speed and algorithm efficiency, DFT has become a tractable method for modeling systems of (at least) several hundreds of atoms and is often capable of quantitative prediction of system properties. It is capable of detailing the structure, bonding, and energetics of environmental nanomaterials, and it can be the basis of dynamic simulations via Born-Oppenheimer or Car-Parrinello molecular dynamics. A number of advances, such as self-interaction correction, hybrid functionals, DFT+DMFT (dynamical mean field theory) (76), Van der Waals density functionals, along with post-DFT methods (such as DFT+U) and related methods such as the GW approximation, have expanded the capabilities of DFT-based predictions in the past decade (68). However, relatively poor scaling of computational cost with system size, difficulty in achieving accurate descriptions of excited states, the lack of universal functionals for heterogeneous environmental systems, and the bridging of DFT models to other length scales are persistent obstacles. Improving the calculation speed on one
processor or across multiple processors in parallel, particularly for low-symmetry and heterogeneous nanomaterials, presents an ongoing challenge. Computational capabilities are on the cusp of simulating atomic step edges, faceting, and possibly entire tiny nanomaterials, especially when algorithms exploit periodicity in the structure such as in certain surface defect geometries. Presently, advances in modern hardware favor algorithms with a high degree of parallelization, while traditionally DFT parallelization is limited and only over specific calculation parameters, such as k-points or the number of bands.

**Accurate computational predictions at environmentally relevant length scales.** Describing nanomaterial behavior often requires linking molecular-level phenomena with microscopic behavior. For example, the detailed surface chemistry of a nanomaterial can dramatically affect aggregation and therefore the form that the nanomaterial takes in the environment. While computational tools are available to access phenomena in the sub-100 nm length scale, rich environmental processes unfold in the ~100 nm to 1,000 nm range, where materials with a range of sizes, structures, compositions, and other properties reside. Current methods can predict the properties of perfectly ordered systems such as single crystals, but computational methods cannot model defected structures and heterogeneous systems at this length scale, let alone the structure and interactions occurring at boundaries between different grains. The inherent multi-scale and phenomenological range of nanomaterials and their interfaces drives the effort to bridge methodologies, both by defining connections between model outputs at one stage with model inputs at the next and by developing/expanding hybrid methods. Currently no conceptual framework integrates different modeling approaches, nor is a starting point obvious for either a top-down or bottom-up approach to multi-scale modeling. Large-scale dynamic simulations require parameterized potentials to decipher chemical speciation and adsorption phenomena of nanomaterials and their interfaces with environmental media. Challenges lie in how to move beyond highly and specifically parameterized potentials that are not transferable toward more universal forms. The standard approach in force field design relies on pair potentials that do not fully take into account the total environment. The lack of an intrinsically multi-body basis for force field design limits the ease of construction and general applicability. Particular emphasis needs to be placed on developing new theories for describing electrostatics within nanoscale environments that are highly curved, i.e., where the dimension of the nanomaterial is smaller than or comparable to the Debye length.

**Addressing the configuration space of nanomaterial interfaces.** “Gaps” between computational methods and real world measurements can stand in the way of reliable and robust model predictions. Specifically, the “configurational gap” refers to the exponential explosion in the possible arrangement of atoms as a system is extended to include multiple phases and interface effects. Modeling all properties of a system, whether the equilibrium structures, thermodynamic properties, reaction rates, or long-time-scale dynamics, boils down to sampling a vast configurational space that may have
many local energy minima. Radically new approaches to sampling nanoscale configurations are essential to predicting the chemistry of nanomaterials.

**Opportunities for chemists to make transformative and innovative contributions**

*Development of reproducible, scalable instruments and methods for synthesizing nanomaterials on a large scale with precisely controlled chemical and physical properties.* As noted previously, the synthesis of nanomaterials is sometimes difficult to control, and synthetic methods commonly lead to a wide distribution in size and shape and often lack of knowledge of surface species and/or contaminants that may strongly influence the toxicity of nanomaterials. While some researchers will have the capability to synthesize and characterize their own nanomaterials, the general absence of reproducible starting material limits the systematic and quantitative assessment of reactivity trends among the vast majority of researchers. Automated synthesis has produced some nanomaterials on small scales, however (e.g., laboratory-based systems of growth of carbon nanotubes). The development of improved nanomaterial synthesis methods to produce (for example) nanomaterials of specific sizes and shapes would facilitate comparing and benchmarking materials in different laboratories. Ideally these methods would allow researchers to purchase a limited number of well-defined nanomaterials with specified size, shape, purity, and other properties, in a manner similar to most commodity chemicals, to serve as benchmarks. Agencies such as the National Institute for Standards and Technology (NIST) may play a key role in the development of standard nanomaterials and in developing best practices that could be recommended or applied more broadly.

*Development of improved methods for validating and sharing information about nanomaterials and their interactions.* While the absence of standard nanomaterials greatly inhibits the ability of researchers to share and compare results, the development of "best practices" for characterizing nanomaterials would facilitate comparing data across laboratories even when using non-identical nanomaterials. With data mining techniques, researchers could analyze databases of information linking various types of nanomaterial properties to identify property correlations that might not be immediately recognizable from more casual analysis of the data. A central repository of nanomaterial property information could provide a basis for cross-validating different types of information made in different laboratories and provide increased confidence in the conclusions of scientific studies using nanomaterials.

*Development of new tools to characterize the properties of nanomaterials in complex matrices.* While substantial developments in characterization tools, many of them synchrotron-based, have enabled high spatial and chemical resolution studies of materials, similar capabilities do not currently exist for the study of nanomaterials in their native environmental or biological matrices. Adding to the measurement challenge is the substantial need for direct characterization methods if one wishes to learn about the
system under investigation and not about a label or other modifier. While some direct tools exist, they do not address the in-situ and on-line measurement requirements, and while some in-situ tools exist, they not address the direct and on-line requirements. The challenge for researchers in the area of environmental effects of nanomaterials is therefore to develop tools for addressing the science question simultaneously in-situ, on-line, and directly. As a disclaimer, ex-situ, off-line, and indirect studies do produce meaningful data, but work from those methods should include a clear explanation of the opportunity costs. As an example, we mention high-resolution microscopies that provide exquisite views of atomic positions, but the matrices or low-pressure environments needed to make them operational make them only partially adequate to address the driving science questions in this field.

Advanced non-linear optical methods (77) such as second harmonic generation, vibrational sum-frequency generation, and higher-order optical mixing processes have the potential to provide new insights into chemical composition within complex environmental matrices (78). Specifically for the case of nanomaterials having sizes ranging from one to tens of nanometers, coherent optical spectroscopies (79) and imaging (80) methods have the potential to provide molecular level data on systems to which other spectroscopies or microscopies are blind and to track chemical and physical details over various spatial and temporal scales with very high sensitivity, even in inhomogeneous samples (81). Heterodyning (82) (placing the analytical signal at a specific, user-selected frequency away from noise and interferences) is a particularly useful process implicit in coherent methods that can produce large signal amplification for direct and label-free detection of particular species in complex environments. Likewise, nonlinear optical methods give phase information and the tensor properties, providing exquisite structural information enabling a detailed statistical analysis in the form of response distributions as opposed to the average provided by an ensemble measurement.

**Leverage the unique capabilities of national laboratories for state-of-the-art analysis.** National laboratories and university consortia such as the National Nanotechnology Infrastructure Network provide unique resources for research in the areas of nanotechnology and environmental science. For example, synchrotrons and free-electron lasers are able to produce electron and x-ray pulses of femtosecond duration and high intensities, enabling measurements not possible with conventional laboratory-based methods. As an example, researchers use high-intensity pulses from a free-electron laser to measure the diffraction patterns from individual nanoparticles on femtosecond timescales (74,75,83). However, access to national laboratories is limited by geographic constraints and often requires a high level of expertise in the instrumentation, causing barriers to more widespread use. Enhancing the facilities to make them more accessible to a wider range of scientists with a broad range of backgrounds could provide unique insights into the structure of nanomaterials.
Data-mining approaches to nanomaterial-environmental interactions. One problem with existing data on nanomaterial interactions with the environment is that nanomaterial properties vary between experiments in different laboratories, making direct comparison of results difficult. However, if a database could store information on nanomaterial properties and environmental impact (especially using standardized characterization methods), data mining approaches could potentially be used to search through large and disparate data sets to help identify non-obvious correlations. Given the highly complex nature of nanomaterial-environmental studies, the use of such methods might provide new insights, and facilitate creation of new knowledge from limited and imperfect data sets. This approach would complement the more traditional hypothesis-driven research.

Development of more efficient and accurate computational algorithms and codes to extend quantum-based methods to larger systems. The need for molecular-level understanding of nanomaterial structure and properties motivates advances in DFT methods that will enable more accurate and faster calculations and thereby facilitate ab-initio modeling at larger length scales. In a calculation, the choice of exchange-correlation functional largely controls the accuracy of DFT. While in theory a single functional should give accurate results for all systems, in practice some functionals perform better than others and the choice of functional is often a compromise, especially in heterogeneous systems. For example, a given functional may achieve a high degree of accuracy in predicting the properties of a mineral surface but completely neglect dispersive forces. The development of functionals for modeling interfaces between phases, particularly between nanomaterials and ion-containing aqueous phases, without the need to favor one component of the model system would greatly facilitate the use of computational methods to address important problems related to nanomaterials and the environment.

Development of computational search engines for nanomaterial interactions. In theoretical heterogeneous catalysis work, researchers used correlations between dissociative adsorption energies and transition state energies to couple DFT information with a microkinetic model, leading to a “computational search engine” for new catalysts in which theory guides and directs the discovery and design of surfaces with novel and targeted reactivity. Similar approaches could be applied to nanomaterials-environmental interactions. The ability of computers to search a large number of biopolymer-nanomaterial interactions would be particularly useful in learning 'design rules' underlying nanomaterial toxicity and would allow researchers to focus on the most important biopolymer systems for more detailed experimental and computational study. Advanced methods connecting theory to experimentally measured figures of merit for reactivity or other properties of interest would steer development of "materials by design" and could lead to development of nanomaterials with high functionality and reduced adverse impact on the environment.
Validation of multiscale computational methods and parameterized force fields in addressing environmental problems. Underlying many existing computational methods is a validation procedure in which basis sets, hybrid density functionals, exchange-correlation interactions are developed from an optimization process against a suite of model systems. Multi-scale models are being developed that use parameterized results from quantum-based calculations as the basis for addressing computational problems on longer length scales. As one example, ReaxFF force fields are particularly popular for their ability to account for bond formation/breaking as well as non-bonded interactions and have been applied to environmental process models such as water dissociation at mineral surfaces. While still about 10 to 50 times slower than non-reactive force fields, parallelization of ReaxFF methods now enables dynamic simulations on system sizes of greater than 1,000,000 atoms. Gauging how well a force field developed for one system will perform in another remains difficult, however, and force fields can involve a large number of adjustable parameters. Researchers have not investigated in a standardized way the systematic and non-systematic errors necessary to validate their predictive power in addressing more complex problems.

Examples of What Chemistry Research is Needed

To make progress in this area, a number of key areas of chemistry and materials require substantial additional research. Some key areas include:

- Establish infrastructure for large-scale synthesis of well characterized nanomaterials to facilitate replication and validation of experimental results by multiple research groups.
- Use cyber-infrastructure to enable non-expert users remote access to state-of-the-art facilities at national laboratories and at universities participating the National Nanotechnology Infrastructure Network.
- Establish methods to distinguish natural and incidental nanomaterials from engineered nanomaterials.
- Develop methods for tracking nanomaterials at low concentrations in the environment.
- Develop super-resolution optical microscopes to enable imaging and spectroscopic analysis of individual nanomaterials in complex matrices.
- Develop facilities and procedures for comparing and validating different analytical methods for chemical characterization.
- Establish and disseminate standardized protocols and procedures for characterizing nanomaterials, possibly using NIST as a vehicle, as a means to facilitate comparison of results between laboratories.
- Develop methods for continuous, real-time chemical characterization of atmospheric nanomaterials in the 1-10 nm size range at ambient concentrations.
- Develop more reliable, general-purpose electronic structure methods able to address strongly correlated materials, heavy elements, and excited electronic states.
• Develop computational "search engines" able to identify specific types of materials and/or identify interactions relevant to nanomaterials.
• Develop data-mining approaches to identify correlations between nanomaterials properties and subsequent environmental impact.
• Develop computational methods with realistic models of bulk and interfacial water.
• Validate multi-scale computational methods against a suite of environmentally related problems to identify systematic and non-systematic errors.
• Develop user-friendly computational programs that will allow experimentalists and other non-theoreticians to use advanced computational methods with predictable levels of accuracy.
• Develop more reliable, general-purpose electronic structure methods able to address strongly correlated materials, heavy elements, and excited electronic states.
• Develop computational codes that include long-range weak interactions (e.g., dispersion forces) along with shorter-range forces.
• Implement methods able to address problems relevant to excited electronic states.
• Implement methods that allow dynamics of molecular systems to be followed for long periods of time.
• Develop methods that effectively implement atomic coarse-graining to facilitate addressing molecular-level interactions in highly complex systems and optimize use of computational resources.
VII. Human Resources: Education, Collaboration and Interdisciplinary Approaches and Leadership In Environmental and Sustainability Issues (Such as Nanomaterials and the Environment)

Education

The workshop addressed a number of issues in chemical and materials education; in particular, participants discussed education across the continuum as it relates to sustainability and socially relevant problems. Since students are increasingly concerned with the environment and sustainability-relevant issues, nanomaterials and the environment make an excellent topic for discussion.

In educational settings, the concepts presented and experiments performed need to be directed toward real-life problems. Fundamental chemistry concepts applied in laboratories coupled to real-time problems help students appreciate the value of chemistry while retaining the basic concepts they learn in the classroom. Chemists could develop sustainability courses with applied scientists and engineers to incorporate chemistry into sustainability curricula. Chemists need to play a central role and provide leadership in campus-wide sustainability educational initiatives related to the environment.

Graduate programs in chemistry and materials science need to carefully evaluate how they are educating the next generation of scientists and engineers who will address sustainability and environmental science problems. Currently, graduate programs are narrow and discipline specific. While graduate students need a solid disciplinary base, they also need to work on interdisciplinary problems to teach them how to better communicate with other scientists and to solve important societal problems such as developing sustainable energy systems and protecting biodiversity. The gap in interdisciplinary training needs to be addressed both through coursework and research.

Further, by engaging in dialogue with the public and those outside the chemistry discipline, chemists will more clearly understand what misconceptions about the chemical sciences exist in the general public and even in other disciplines. Improving how chemistry is communicated will help the public view chemistry as part of the solution to societal problems rather than the cause.

Collaborative and Interdisciplinary Approaches

Chemists and materials scientists must not only conduct studies alone on some of the issues discussed in Sections III-VI, but they must also conduct collaborative studies with environmental engineers, geochemists, microbiologists, and toxicologists, among others,
to bridge the gaps between controlled laboratory experiments and real environmental systems. Oftentimes a multidisciplinary team is best for defining the appropriate environmental nanomaterial systems for molecular-level studies and for characterizing complex systems. For example, geochemists now have the expertise in aquatic chemistry to tackle complex environmental systems involving nanomaterials and aqueous solutions, including reactive transport processes in aquifers. Mineralogists similarly can provide much of the expertise needed to understand complex natural nanomaterials and their atomic-level characterization using synchrotron radiation-based methods and laboratory methods such as transmission electron microscopy and can work in concert with materials scientists. Moreover, microbiologists and geomicrobiologists can provide the needed expertise in microbial interactions at nanomaterial surfaces, and organic geochemists and soil chemists can provide the expertise to understand the natural organic matter in complex environmental systems. Toxicologists, working closely with the chemists, geochemists, mineralogists and others, are needed to conduct the bioavailability studies on organisms to ensure that the nanomaterials used in toxicological studies are well characterized. Environmental engineers can provide expertise about engineered processes such as wastewater treatment and contaminant remediation. Physical chemists are well positioned to provide the fundamental chemistry approach to molecular-level studies of chemical reactions on nanomaterial surfaces, including their mechanisms and kinetics, and analytical chemists can characterize and quantify extremely small concentrations of aqueous and airborne species. Computational chemists are also essential for providing the theoretical basis for understanding chemical reactions at environmental interfaces. Only with a collaborative approach can real progress be made on complex environmental systems containing natural, incidental, and engineered nanomaterials and a variety of other inorganic, organic, and living components.

When researchers address broad issues related to sustainability and environmental science problems, two approaches are common: (1) research led solely by chemists and materials scientists, or (2) research led by engineers or toxicologists. Regardless of the approach taken, each group is likely to overlook important scientific questions or methodologies that are needed to address the overall challenges. The willingness and ability of chemists to initiate collaborations is bound to lead to meaningful collaborations. While they are often difficult to establish and maintain, collaborations remain critical to advance science needed to solve societal problems. Funding agencies must also encourage such collaborations. Often proposal calls request for entire centers to be established to address such challenges; however, in some cases, important scientific discoveries arise from smaller research teams involving two to four scientists. The availability of funding to support such work will certainly impact the leadership of chemistry in sustainability and environmental science. Nanoscience and nanotechnology as they relate to environmental health and safety are ideally suited for these types of interactions.
Leadership Roles for Chemists in Sustainability and Environmental Science

Chemists and materials scientists need to play important roles in sustainability and environmental science. From the development of new materials to ensure a clean water supply to the development of catalysts for converting carbon dioxide into useful chemicals not harmful to the environment, chemists and materials scientists will be part of the solution to global sustainability issues. The importance of chemistry in environmental science and sustainability is often not recognized. The fundamental and molecular-based research needed to solve environmental problems is essential. Lack of an understanding of chemistry contributes to why the public does not always appreciate how chemistry can be part of the solution to important societal issues.

Chemists at academic institutions as well as in industry are well suited to take on leadership roles to address some of the challenges related to environmental science and sustainability; yet, oftentimes chemists do not lead these efforts. Several barriers and reasons may prevent them:

- Chemists are not trained in a systems-based approach to research that is often used to address sustainability and environmental science.

- At most academic institutions, chemistry departments are located in arts and science colleges. Academic administrators and leaders in these colleges do not encourage interdisciplinary research and centers as they do in engineering colleges.

- When chemists choose to branch out and work in interdisciplinary research involving environmental science, their work may not be as strongly valued as disciplinary research by their peers.

Chemistry is a detail-oriented science, and chemists are often not trained to deal with the kinds of complex systems that are encountered in environmental science. One consequence is that while chemists have made important contributions to important sustainability issues related to environmental science, they typically have not had the breadth of view necessary to lead. Training next-generation chemists to make connections between fundamental science and societal problems such as environmental impact of nanomaterials is increasingly important.

Sustainability initiatives and proposal calls at funding agencies such as the National Science Foundation need to include chemistry research as an important component to solving problems. If proposal calls do not specifically ask for their input, few chemists will apply to these funding opportunities, resulting in little insight from the chemistry community on these important problems. Leaders within the funding agencies who understand the role of fundamental molecular-based science are consequently an important component of sustainability research. Involvement of chemists in major
funding initiatives and in promoting interdisciplinary work between federal funding agencies is essential for advancing leadership on sustainability and environmental research within the academic chemistry community.

Finally, the importance of chemistry and molecular-based approaches and their role in sustainability and environmental science needs to be better communicated to non-chemists. Sometimes chemists submit important work on sustainability and environmental science to chemistry-discipline specific journals that environmental scientists often do not read. How can chemists improve the way they communicate the impact of the work they do? One idea is for more chemists to submit viewpoints to publications designed for a more general audience. This approach would be more successful, however, if editors whose journals target a broader applied scientific and engineering community encouraged chemists to do so. Overall more positive public relations communicating chemistry as part of the solution to societal problems is needed.
Appendix A – List of workshop participants: Workshop participants included a diverse interdisciplinary group of scientists with a wide range of expertise and National Science Foundation observers.

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Appendix B – Workshop schedule: The workshop used presentations to stimulate breakout discussions and collaborations on workshop recommendations.

Monday June 27th

Arrival of all Workshop Participants

7PM Organizing Committee Only Meets with Dr. Zeev Rosenzweig to review and discuss materials collected from workshop participants, presentations for Tuesday AM and strategies to insure workshop goals are met.

Tuesday June 28th

Morning Schedule AM

8:00 – 8:30 Continental Breakfast

8:30 – 8:45 Welcome Workshop Participants by Dr. Zeev Rosenzweig, NSF Program Officer Environmental Chemical Sciences Program and Dr. Matthew Platz, Chemistry Division Director

8:45 – 9:00 Define the Goals of the Workshop in Identifying Science Drivers as well as Expectations of the Workshop and Workshop Participants: Co-Chairs Robert Hamers and Vicki Grassian

9:00 – 10:40 Short Talks by Members of Organizing Committee, Gordon Brown, Howard Fairbrother, Murray Johnston and Lee Penn Based on Input from Workshop Participants

Gordon Brown 9:00-9:20 to discuss
Overview of Participant Input on Fundamental Properties of Nanomaterials: Surface adsorption and reaction processes relevant to environmental science (e.g., ROS generation) and Infrastructure and Human Resource Needs in Nano/Environmental Science: Computational tools

Howard Fairbrother 9:20-9:40 to discuss
Overview of Participant Input on Fundamental Properties of Nanomaterials: Influence of size, surface structure, surface coatings, compositional and structural complexity (nanocomposites) on fundamental properties and Interaction of nanomaterials with biological molecules and biological systems: Biological transformation of nanomaterials

Murray Johnston 9:40-10:00 to discuss
Overview of Participant Input on Nanomaterial interactions with the environment: Nucleation of nanomaterials in the environment and Infrastructure and Human Resource Needs in Nano/Environmental Science: Instrumentation
R. Lee Penn 10:00-10:20 to discuss
Overview of Participant Input on Nanomaterial interactions with the environment: *Environmental release, transport and aggregation*
and
Interaction of nanomaterials with biological molecules and biological systems: *Nanomaterial-induced toxicity, changes in gene expression*

Vicki Grassian 10:20-10:30 to discuss
Overview of Participant Input on Nanomaterial interactions with the environment. *Chemical/Photochemical alteration and degradation of nanomaterials in the environment*

Bob Hamers 10:30-10:40 to discuss
Overview of Participant Input on Interaction of nanomaterials with biological molecules and biological systems: Molecular and chemical basis of bioavailability

10:50 – 12:30 Breakout Session I: Fundamental properties of nanomaterials

Group A. Influence of size, surface structure, surface coatings, compositional and structural complexity (nanocomposites) on fundamental properties
   Aga, Castner, Elder, Fairbrother (lead), Johnston (scribe), Jun, Kane, Marr, Martin, Navrotsky (co-lead), Obare, Orr, Szakal

Group B. Surface adsorption and reaction processes relevant to environmental science (e.g., ROS generation)
   Brown (lead), Baer (scribe), Forbes, Geiger, Gilbert, Haynes, Holden, Ivanisevic, Kim, Lead, Mason, McGuire (co-lead), Penn, Ranville, Sadik, Vecitis, Schneider

Afternoon Schedule PM
12:30-1:15 Working Lunch to Review Information from Breakout Session I for Report Out

1:30 – 2:15 Report Out by Each of the Co-Leads (Navrotsky and McGuire) from Breakout Session I with Discussion and Additional Input From All Participants

2:15 – 3:45 Breakout Session II: Nanomaterial interactions with the environment

Group A. Environmental release, transport and aggregation
   Aga, Elder, Fairbrother, Geiger, Haynes (scribe), Kane, Kim, Lead, McGuire, Orr, Ranville (co-lead), O’Bare, Penn (lead)

Group B. Chemical/Photochemical alteration and degradation of nanomaterials in the environment
   Baer, Brown, Castner (co-lead), Gilbert, Grassian (lead), Holden, Ivanisevic, Mason, Schneider, Szakal (scribe), Vecitis

Group C. Nucleation of nanomaterials in the environment
   Forbes (scribe), Johnston (lead), Jun, Martin (co-lead), Marr, Navrotsky, Sadik

4:00 – 5:00 Report Out by Each of the Co-Leads (Ranville, Castner and Martin) from Breakout Session II with Discussion and Additional Input From All Participants
Dinner on own: Co-chairs and Organizing committee members and leads continue to refine reports from Breakout Sessions I and II based on discussion

**Wednesday June 29th**

**Morning Schedule AM**

8:30 – 9:00 Continental Breakfast

9:00 – 10:30 Breakout Session III: Interaction of nanomaterials with biological molecules and biological systems

Group A. Molecular and chemical basis of bioavailability
   Brown, Gilbert, Hamers (lead), Johnston, Jun, Kim (scribe), Lead (co-lead), Mason, McGuire, Navrotsky, Ranville, Sadik, Schneider

Group B. Nanomaterial-induced toxicity, changes in gene expression
   Aga, Castner, Kane (co-lead), Marr, Martin, Obare, Orr (scribe), Penn (lead), Szakal, Vecitis

Group C. Biological transformation of nanomaterials
   Baer, Elder (scribe), Geiger, Fairbrother (lead), Forbes, Haynes, Holden (co-lead), Ivanisevic

10:45 – 11:45 Report Out by Each of the Co-Leads (Lead, Kane and Holden) from Breakout Session III with Discussion and Additional Input From All Participants

**Afternoon Schedule PM**

11:45 – 1:00 Working Lunch

1:00 – 2:30 Breakout Session IV: Infrastructure and Human Resource Needs in Nano/Environmental Science

Group A. Computational tools
   Brown (lead), Gilbert, Marr, Martin, Mason (scribe), Navrotsky, Schneider (co-lead)

Group B. Instrumentation development
   Aga, Baer, Castner, Fairbrother, Geiger (scribe), Haynes, Ivanisevic, Jun, Johnston (lead), Lead, McGuire, Ranville, Penn, Sadik (co-lead), Szakal

Group C. Chemistry leadership in environmental science
   Elder, Forbes, Grassian (co-lead), Hamers (lead), Holden, Kane, Kim, Obare (scribe), Vecitis

2:45 – 3:45 Report Out by Each of the Co-Leads or Scribes (Schneider, Sadik and Obare) from Breakout Session IV with Discussion and Additional Input From All Participants

3:45 – 4:30 Grand Synthesis and Coherent Summaries for Workshop Report
Discussion amongst all participants of breakout session findings and to determine if there are commonalities/differences/interplay between areas

4:30 – 5:00 Executive Summary of Workshop and Next Steps (Hamers, Grassian and Rosenzweig)
Workshop Participants Done – Thank you!

Thursday June 30th

Morning Schedule AM
8:00 – 8:30 AM Continental Breakfast for Organizing Committee
8:30 AM – 12:30 PM Organizing Committee Continues to Work on a Draft Workshop Report and Workshop Presentation as well as Prepares Executive Summary with Science Drivers and Steps Forward to Share with NSF Personnel.
Appendix C – References and footnotes: A list of references, footnotes and urls to other reports.


25. Mudunkotuwa, I. A. and Grassian, V. H. “The devil is in the details (or the surface): Impact of surface structure and surface energetics on understanding the behavior of nanomaterials in the environment” *Journal of Environmental Monitoring* 2011, 13, 1135.


27. Mudunkotuwa, I. A.; Grassian, V. H., Citric acid adsorption on TiO₂ nanoparticles in aqueous suspensions at acidic and circumneutral pH: Surface coverage, surface


Appendix D – Powerpoint contributions from participants: Participants were asked to provide input through a three-slide presentation focused on areas related to:

Slide 1 – Research activities relevant to nano/environment of their own research;

Slide 2 – Provide a summary of the most important research challenge(s) at the intersection of nanotechnology and environmental science;

Slide 3 – Identify opportunities for chemists to contribute to molecular-level science at the nano/environment interface. What are the high-impact opportunities?

Power-point slides contributed by workshop participants can be downloaded from the Nanomaterials and the Environment Workshop website at http://nsfenv-nano.chem.wisc.edu/