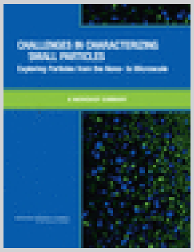

Challenges in Characterizing Small Particles: Exploring Particles from the Nano- to Microscales

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Tina Masciangioli and Joe Alper, Rapporteurs; Chemical Sciences Roundtable; National Research Council

CHALLENGES IN CHARACTERIZING SMALL PARTICLES

Exploring Particles from the Nano- to Microscale

A WORKSHOP SUMMARY

Tina Masciangioli and Joe Alper, *Rapporteurs*

Chemical Sciences Roundtable

Board on Chemical Sciences and Technology

Division on Earth and Life Studies

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Cover art: Ionic map of atmospheric particles enriched in sulfate (green) and methane (blue) typical for a marine environment. Courtesy of Pacific Northwest National Laboratory.

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* These members of the Chemical Sciences Roundtable served on the Challenges in Characterizing Small Particles: Exploring Particles from the Nano- to Microscales workshop organizing committee, but they were not involved in the writing of this workshop summary. In addition to the asterisked members above, Barbara Finlayson-Pitts of the University of California, Irvine and Douglas Ray of the Pacific Northwest National Laboratory also oversaw the planning of the workshop.

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Preface

The Chemical Sciences Roundtable (CSR) was established in 1997 by the National Research Council. It provides a science-oriented apolitical forum for leaders in the chemical sciences to discuss chemistry-related issues affecting government, industry, and universities. Organized by the National Research Council's (NRC's) Board on Chemical Sciences and Technology, the CSR aims to strengthen the chemical sciences by fostering communication among the people and organizations—spanning industry, government, universities, and professional associations—involved with the chemical enterprise. One way it does this is by organizing workshops that address issues in chemical science and technology that require national or more widespread attention.

On October 25-26, 2010, the CSR held a 1.5-day workshop that explored new opportunities, challenges, and approaches to characterizing small particles and understanding their impacts. Small particles—about one nanometer to tens of microns—are ubiquitous in the natural and man-made worlds. In many scientific and engineering domains, uncertainty about the properties and chemical composition of small particles limits our ability to understand, predict, and control their applications and impacts.

The workshop included several overview presentations highlighting the critical importance of small particles in environmental science, materials and chemical sciences, biological science, and engineering. In addition, several presentations highlighted new advances in characterizing small particles, including static, dynamic, experimental, computational, and theoretical approaches.

This document summarizes the presentations and discussions that took place at the workshop. In accordance with the NRC's policies, the workshop did not attempt to establish any conclusions or recommendations about needs and future directions, focusing instead on issues identified by the speakers and workshop participants. In addition, the organizing committee's role was limited to planning the workshop. This workshop summary has been prepared by the rapporteurs Joe Alper and Tina Masciangioli as a factual summary of what occurred at the workshop.

Acknowledgment of Reviewers

This workshop summary has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published summary as sound as possible and to ensure that the summary meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this workshop summary:

Patricia Thiel, Iowa State University and Ames Laboratory, Iowa
Darlene Solomon, Agilent Technologies, Inc., Santa Clara, California
Renyi Zhang, Texas A&M University, College Station, Texas
Kai Loon Chen, Johns Hopkins University, Baltimore, Maryland

Although the reviewers listed above have provided many constructive comments and suggestions, they did not see the final draft of the workshop summary before its release. The review of this summary was overseen by **Richard Flagan**, California Institute of Technology. Appointed by the National Research Council, he was responsible for making certain that an independent examination of this summary was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this summary rests entirely with the authors and the institution.

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APPENDIXES

Acronyms

AMPI	atomistic model for particle interception
API	active pharmaceutical ingredient
CAPs	concentrated ambient PM2.5
CFC	chlorofluorocarbon
CSN	Chemical Speciation Network
CSR	Chemical Sciences Roundtable
CT	computed tomography
EDS	energy dispersive x-ray spectroscopy
EELS	electron energy loss spectroscopy
EPA	Environmental Protection Agency
IPCC	Intergovernmental Panel on Climate Change
NAAQS	National Ambient Air Quality Standards
NCAR	National Center for Atmospheric Research
NIBIB	National Institute for Biomedical Imaging and Bioengineering
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
NOM	natural organic matter
NPACT	National Particle Component Toxicity Initiative
NRC	National Research Council
NRL	Naval Research Laboratory
NSF	National Science Foundation
ORNL	Oak Ridge National Laboratory
PM	particulate matter
SAX	small-angle x-ray scattering
SBIR	Small Business Innovation Research
SEM	scanning electron microscopy
SOPS	Engineering Research Center for Structured Organic Particulate Systems
STEM	scanning transmission electron microscopy
STM	scanning tunneling microscopy
TD-CIMS	thermal desorption chemical ionization mass spectrometer
TEM	transmission electron microscopy

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Overview

Small particles—about one nanometer to tens of microns—are ubiquitous in the natural and engineered worlds. They are in the air, soil, and water on Earth, as well as at the farthest reaches of the universe. One of the major buzz words over the past 10 years, nanotechnology, involves the creation of nanoscale materials with the promise of new and revolutionary properties. Given the size and abundance of small particles, however, there is relatively little understanding about their properties and chemical composition, which limits our ability to understand, predict, and control their applications and impacts in both natural and engineered systems. At the same time, information may be available that just needs to be shared across disciplinary boundaries to increase understanding of small particles.

ABOUT THIS DOCUMENT

The National Academies' Chemical Sciences Roundtable (CSR) held a workshop on October 25-26, 2010, to explore new opportunities, challenges, and approaches to characterizing small particles and understanding their impacts. In many scientific and engineering domains, a lack of understanding about the properties and chemical composition of small particles limits our ability to understand, predict, and control their applications and impacts.

The workshop, "Challenges in Characterizing Small Particles: Exploring Particles from the Nano- to Microscales," explored the critical importance of small particles in environmental science, materials and chemical sciences, biological science, and engineering, and the many challenges involved in characterizing materials at the nano- and microscales. The discussions on characterization included static, dynamic, experimental, computational, and theoretical characterization. The workshop also included several "research tool" presentations that highlighted new advances in characterizing small particles.

This document summarizes the presentations and discussions that took place during the workshop.[1] Where possible, background references have been provided to support statements made or data described. The reader is urged to follow up with individual guest speakers and their institutions for further clarification of statements made during the workshop or to obtain additional reference materials.

WORKSHOP OVERVIEW

Why Small Particles Matter

The workshop began with an introduction by co-chair **Barbara Finlayson-Pitts**, University of California, Irvine, who noted the importance of and challenges associated with characterizing small particles in the atmosphere. **Steve Schwartz**, Brookhaven National Laboratory, continued this theme with a more thorough discussion of the many roles that atmospheric aerosols play in determining climate. Aerosol particles act as the seeds for cloud formation, reflect sunlight away from Earth's surface, and serve as catalytic sites for atmospheric chemical processes. He also described efforts to characterize atmospheric aerosols and model how they influence, or force, climate.

Mort Lippmann, New York University, discussed some of the health impacts caused by airborne particles, which are also known as particulate matter. In particular, he described how the size of these particles, along with the chemicals they pick up on their surfaces, relates to the negative impacts on

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[1] About Open Discussions: All but one chapter (Chapter 4) in this document ends with a summary of discussion topics introduced by speakers and participants in the immediate session, as well as all preceding sessions.

human health that accompany prolonged exposure to particulate matter smaller than 10 microns in diameter. **Michael Hochella**, Virginia Polytechnic and State University, then noted that nanoparticles are everywhere in the environment and that the mass of nanoparticles that nature puts into the environment will always dwarf the mass that humans will ever produce. He discussed some of the ways in which nanoparticles enter the environment, including volcanic eruptions and salt spray, and the effects of human activities on levels of potential toxic nanoparticles found in soil and water.

With his presentation on the ways in which small particles interact with cells, **Gary McDermott**, University of California, San Francisco, brought this session to a close. He described methods for imaging small particles inside cells and showed how they could be used to help with the design of new therapeutic drugs to treat human disease.

Challenges in Chemical Analysis and Imaging of Small Particles

Over the course of two sessions, speakers described the challenges of characterizing small particles and some of the real-world needs for developing new analytical technologies applicable to small particles. **Alla Zelenyuk**, Pacific Northwest National Laboratory, discussed her team's use of single particle laser ablation time-of-flight mass spectrometry to characterize atmospheric aerosols and to study how other atmospheric components influence the morphology and particle chemistry of atmospheric aerosols. **James Smith**, National Center for Atmospheric Research, addressed the phenomenon of new particle formation in the atmosphere and the recent progress that his group has made in quantifying the composition of these spontaneously generated atmospheric nanoparticles.

In his presentation, **Ralph Nuzzo**, University of Illinois, Urbana-Champaign, discussed the rich toolbox that is available for characterizing heterogeneous catalysts at the atomic level. This information is leading to a better understanding of how these particles assemble and how particle structure impacts particle properties. Continuing on the catalysis theme, **Abhaya Datye**, University of New Mexico, stressed the importance of nanoscale characterization for understanding how the interactions between catalytic nanoparticles and bulk-scale supports affect catalytic activity, information that could lead to the development of improved industrial heterogeneous catalysts.

Lee Silverman, DuPont Central Research and Development Laboratory, continued this industrial theme by discussing the tools needed to characterize composite polymeric materials containing nanoscale particle additives. Silverman noted that the information generated using these tools can play a role in the development of new materials that will not endanger the environment or human health. **Yi Qiao**, 3M Corporate Research Process Laboratory, discussed some of the challenges facing those who need to characterize nanoparticle dispersions used in industrial applications. He noted that to meet the needs of a manufacturing environment, a measurement technique must be fast enough to provide feedback on a meaningful timeframe, have few restrictions concerning sample preparation in terms of nanoparticle concentration and purity, and be able to distinguish "good" from "bad" so that a line operator can make necessary adjustments to the manufacturing process in real time. He then described two techniques that meet these requirements.

Rhonda Stroud, Naval Research Laboratory, concluded this session by describing how the techniques used to characterize terrestrial particles can be applied to the characterization of the 40,000 tons of extraterrestrial dust that enter the planet's upper atmosphere annually.

Challenges in Analyzing Nanoparticles in Complex, Real-World Mixtures

In this session, three speakers addressed some of the challenges in measuring and predicting the properties and behavior of complex nanoparticle formulations and discussed the often surprising findings that come from studying nanomaterials as they occur in the real world. **James Lister**, Purdue University, talked about particles in the micron and submicron size ranges that are used in industrial applications, with a specific focus on the delivery forms for these particles. In particular, he addressed some of the methods for characterizing the processes used to create delivery forms such as catalyst pellets and drug tablets. He also described how these characterization tools can provide insights into how manufacturing processes impact the final properties of these delivery forms, such as dissolubility and chemical stability.

Pedro Alvarez, Rice University, then discussed his work on characterizing how nanoparticles interact with microorganisms in the environment. He explained that bacteria, the foundation of all ecosystems, provide a convenient model for studying the potential toxicity of engineered nanoparticles. **Vicki Grassian** concluded the session by describing methods used to understand the transformations and surface chemistry of mineral dust, a major component of atmospheric aerosols. Using these methods, she and her colleagues have been able to show how mineral dust can catalyze a wide range of chemical reactions occurring in the atmosphere.

Modeling and Simulation of Small Particles

In the workshop's final scientific session, **Angela Violi**, University of Michigan, and **Douglas Tobias**, University of California, Irvine, described the use of several computational approaches to modeling nanoparticles to provide insights into how structure and function are related. Violi spoke about a hybrid modeling technique that works at an atomistic level to follow the growth of particles produced during the incomplete combustion of different hydrocarbon-based fuels. She also described a computational model of the cell membrane that can follow how carbonaceous particles, such as those produced during combustion, impact the natural flow of lipids in the cell membrane.

Tobias then spoke about an atomistic computational model that is providing insights into the interactions between a particle's reactive surface and compounds impinging on that surface. He also described a coarse-grained model for studying the atmospheric chemistry of sea salt particles that improves the prediction of the geographical distribution of ozone production in a polluted urban environment.

ORGANIZATION OF THIS WORKSHOP SUMMARY

This document was prepared by rapporteurs Tina Masciangioli and Joe Alper for the Chemical Sciences Roundtable as a factual summary of what occurred during the workshop. In accordance with the CSR's policies, the summary does not attempt to establish any conclusions or recommendations about needs and future directions, focusing instead on issues identified by the speakers and workshop participants.

This summary is organized according to the four main sessions. Overview presentations highlighted the critical importance of small particles in environmental science, materials and chemical sciences, biological science, and engineering. Technical sessions focused more on the research tools used to characterize small particles, such as sampling, nucleation and growth, and chemical imaging. Poster abstracts are provided in Appendix B.

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What Are Small Particles and Why Are They Important?

Small particles—ranging in size from about one nanometer to tens of microns—are ubiquitous in the natural and engineered worlds. In the atmosphere, small particles impact both warming and cooling of the climate. In Earth's subsurface, small particles impact soil and water quality. In living systems, small particles impact organism health and viability. In catalysis and reaction engineering, small particles enhance reaction specificity and rates. In materials design and synthesis, small particles provide new and enhanced properties. However, in all of these scientific and engineering domains, a lack of understanding about the properties and chemical composition of small particles limits our ability to understand, predict, and control their applications and impacts. Speakers in this session discussed the crucial types of information that need to be determined about small particles in different media.

INTRODUCTION

The workshop began with an introduction by co-chair Barbara Finlayson-Pitts, Professor of Chemical Sciences at the University of California, Irvine. She illustrated the importance of small particles by looking at the example of a nanoparticle in the atmosphere, as shown in Figure 2-1.

Research has determined that gaseous precursors form low-volatility products that nucleate to form new particles, but little is known about how this occurs, even after decades of research. Furthermore, little is known about how the particles then grow into nanoparticles. Because of their size, nanoparticles have a high surface-to-volume ratio, which means that the properties of the particles, in terms of their chemistry and photochemistry, will not necessarily be the same as those of the bulk material (because size is one of the unique and desirable characteristics of nanoparticles). Little is known about that chemistry as well.

Finlayson-Pitts explained that a major research objective is to determine the three-dimensional structure of particles in the atmosphere. Based on a large body of chemical data accumulated over many years, it is known that atmospheric nanoparticles contain a large number of polar groups, including carboxylic acids, amines, and alcohols. However, little is known about how the particles assemble. Other unanswered questions include the following: Do particles self-assemble in air? Do the polar groups end up inside a hydrophobic shell, or do they end up on the outside?

Many factors contribute to understanding climate, according to Finlayson-Pitts. For example, understanding the three-dimensional arrangement of the particles is extremely important. If polar groups are on the outside of the particles, then they will be expected to take up water and act as cloud condensation nuclei more efficiently than if they are buried inside the particles. Some of the studies performed in Finlayson-Pitts's laboratory revealed that it is not unusual to find polar groups on the inside at the nanoscale. From a bulk chemical composition point of view, significant water uptake might be expected; however, that does not happen because the hydrophobic shell forms at the nanoscale.

ATMOSPHERIC AEROSOLS AND CLIMATE

Steven Schwartz of Brookhaven National Laboratory discussed the influences of aerosols on climate and climate change, and the challenges associated with representing those influences using models. Understanding how atmospheric aerosols affect Earth's energy balance and sensitivity to climate change is a critical piece to understanding how the greenhouse effect might limit the future development of society's energy economy.

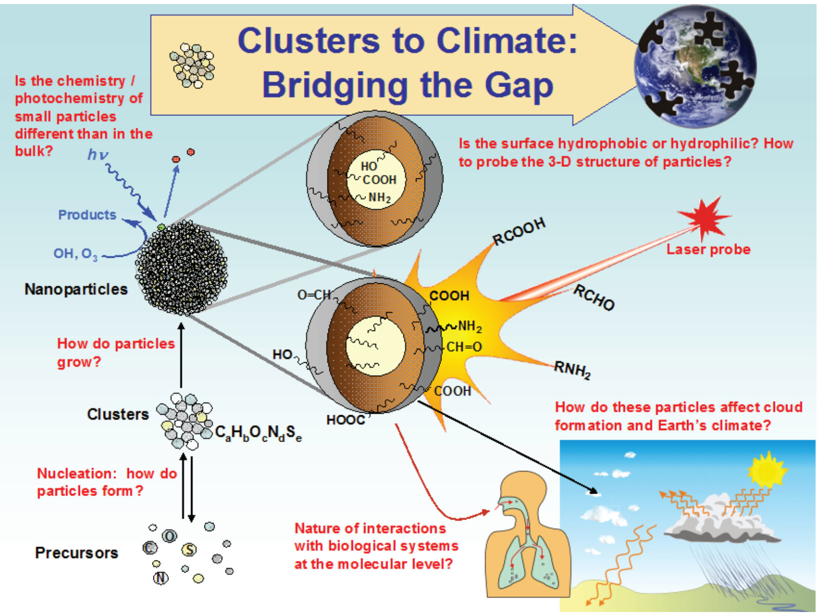


FIGURE 2-1 An airborne nanoparticle can have many fates.
SOURCE: Armandroff, 2011.

Aerosol Influences on Climate and Climate Change

Schwartz explained that aerosols are particles suspended in air and generated from a variety of sources including organic vapors from vegetation, dust, industrial sulfur dioxide emissions, biomass burning, ocean sea salt, and others, as shown in Figure 2-2. All of these materials can undergo chemical reactions in the atmosphere to produce particles. Aerosols are characterized by how they scatter light, producing effects such as urban haze and photochemical smog. For example, the haze that hangs over beaches results from aerosolized sea salt reflecting light. Atmospheric aerosols affect Earth's climate in two ways:

- They reflect sunlight upward, decreasing the amount of sunlight that reaches Earth's surface, which subsequently cools the planet. This is known as the aerosol direct effect.
- They serve as seed particles for the formation of cloud droplets.

Without aerosols, there would be no clouds, and Earth's climate would be very different.

As the atmospheric aerosol concentration, measured in particles per cubic meter (particle/m^3), increases, and if all other parameters are equal, more cloud droplets form. Droplet formation increases the scattering in clouds and therefore the likelihood that sunlight will be reflected from the top of the cloud, which has a cooling influence on the climate. A warming influence can be observed when aerosols absorb rather than reflect sunlight. Schwartz stated that the widely varying impacts of aerosols on climate change "must be understood and characterized, and ultimately represented in climate models."

Earth's Energy Balance and Perturbations

Figure 2-3 shows the relationship of aerosols in the global energy balance. Of the 343 Watts per square meter (W/m^2) of solar power provided from the sun, approximately 70 percent is absorbed (237 W/m^2). The balance of that amount of solar energy with the amount of thermal infrared emitted from the planet (also 237 W/m^2) is essential for maintaining a constant temperature.

The 390 W/m^2 coming from Earth's surface represents the greenhouse effect, which results from the infrared-absorbing gases in the atmosphere, as well as clouds, that radiate energy back toward Earth. Increases in greenhouse gases such as carbon dioxide (CO_2), methane (CH_4), nitrous oxide (N_2O), and the chlorofluorocarbons (CFCs) contribute to the greenhouse effect. These gases together account for about 2.6 W/m^2 of the energy radiating back to Earth's surface, or less than 1 percent of the atmosphere's greenhouse effect. Schwartz said that a major challenge for the climate research community is in representing climate change resulting from those gases in climate models and in confidently predicting what the consequence of perturbation would be as the concentrations of those gases change.

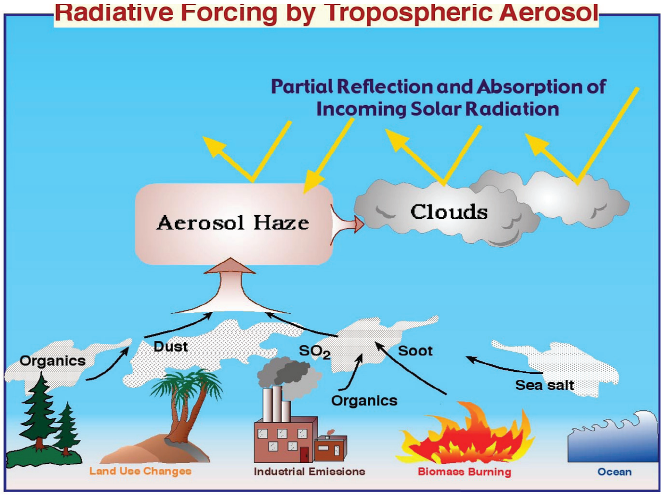


FIGURE 2-2 The role and sources of atmospheric aerosols in the environment.
SOURCE: Schwartz, 2010.

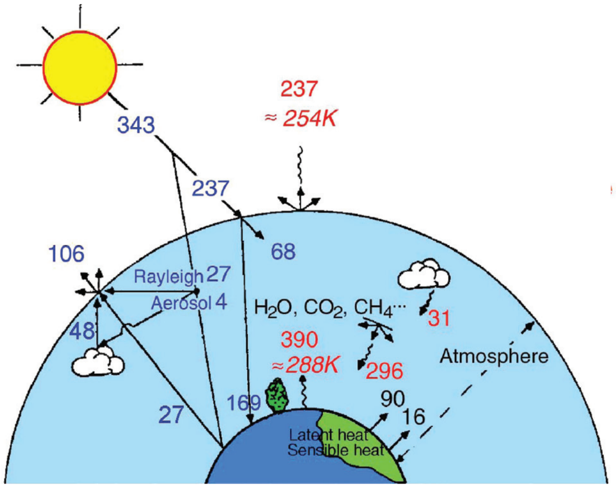


FIGURE 2-3 Schematic of major global, annual average radiant energy fluxes of the Earth-atmosphere system, given in Watts per square meter (W/m^2). Blue numbers represent the short-wavelength radiant energy of the solar spectrum entering the planet, and red numbers represent the long-wavelength infrared radiation being emitted by the planet.
SOURCE: Schwartz, 2010 (modified from Schwartz, 1996 and Ramanathan, 1987).

Climate Sensitivity-Definition, Importance, Past and Current Estimates

Climate sensitivity is a measure of how responsive the temperature of the climate system is to a change in the radiative forcing; it is expressed in degrees Kelvin per Watt per meter squared ($K/(Wm^{-2})$) (Schwartz, 2007). There have been many estimates of climate sensitivity dating back to the late 1970s (NRC, 1979). Schwartz described the attempts that have been made to calculate climate sensitivity from various climate models (Figure 2-4). Large-scale computer models have been used to represent all of the processes that take place in the atmosphere that govern our climate and climate change. In terms of the greenhouse effect, one way is to look at sensitivity and to ask: How much would the global temperature increase if the CO_2 concentration were doubled?

The range of sensitivities in the current models roughly coincides with the Intergovernmental Panel on Climate Change (IPCC) "likely" temperature change uncertainty range of 1.5-4.0°C (for 2090-2099 relative to 1980-1999; IPCC, 2007a).

Given the increases in atmospheric CO_2, CH_4, N_2O, and CFC concentrations over the industrial period, and using the IPCC's 2007 best estimate for climate sensitivity of 3 K, the expected rise in Earth's temperature due to the increase of greenhouse gases, CO_2, CH_4, N_2O, and CFCs over the industrial period (1780 to present) is calculated to be 2.1 K. However, the observed increase since 1860 is only 0.8 K. Schwartz explained (based on a published report, Schwartz et al., 2010) that Earth has not warmed as much as expected from forcing by long-living greenhouse gases for several reasons.

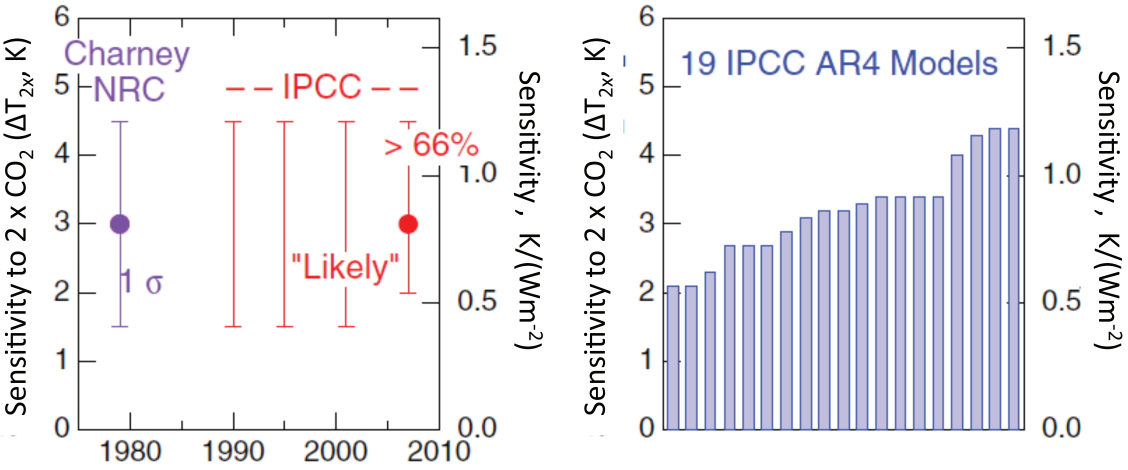


FIGURE 2-4 A summary of major national and international assessments and current climate models of climate sensitivity. (left) Value of climate sensitivity for past assessments by year assessment was conducted, (right) current (2010) values of 19 different IPCC AR4 models. SOURCE: Schwartz, 2010.

A couple of these possible reasons will be discussed in greater detail below.

Schwartz elaborated on climate forcing by aerosols and how estimates of aerosol direct forcing are made by linear modeling and radiation transfer modeling. These calculations use aerosol depth data collected daily over north central Oklahoma by the U.S. Department of Energy (Michalsky et al., 2010), and cloud albedo and radiative forcing data from daily measurements of effective radius and liquid water path (Kim et al., 2003). He reviewed an illustration of climate forcing over the industrial period (Figure 2-5) from the IPCC's 2007 report (IPCC, 2007), which shows that negative aerosol forcing substantially offsets greenhouse gas forcing and that the uncertainty in aerosol forcing dominates the uncertainty in total forcing.

Although Schwartz would have preferred to identify one reason for the difference between the predicted and observed temperature changes, the current state of research leads to two possible explanations: that aerosol forcing counteracts greenhouse gas forcing, or that climate sensitivity is lower than the consensus value. Estimates of climate sensitivity might be wrong because they largely ignore aerosol forcing. Aerosol forcing has been overlooked because individual aerosol particles are short-lived, as was demonstrated when the Chernobyl reactors released a pulse of cesium-137 aerosol particles that resided in the atmosphere for only approximately 1 week. In contrast, greenhouse gases reside in the atmosphere for decades to centuries. However, what this scenario overlooks is that atmospheric aerosols are continually replenished, producing a steady-state level that can influence radiative forcing.

In summary, Schwartz said that climate sensitivity and aerosol forcing are intrinsically coupled, both in climate models and in empirical determination of sensitivity. As a result, if the climate community is going to make the necessary advances in understanding climate sensitivity, then it must determine the parameters that drive aerosol forcing with much greater accuracy than at present. Required going forward, said Schwartz, are multiple approaches that include laboratory studies of aerosol processes, field and satellite measurements of aerosol properties and processes, and consideration of aerosol processes in atmospheric chemistry transport models. The community must evaluate the various models by comparing model results with observations and then using the best models to calculate the forcings for inclusion in global climate change models. In addition, the community must better understand many of the aerosol processes in order to represent them in models (Figure 2-6). Schwartz stressed the need for multiple types of measurements at the same place and time and for laboratory experiments that provide details that cannot be extracted from field measurements.

Schwartz stated that radiative forcing by incremental greenhouse gases already in the atmosphere could potentially lead to dangerous interference with the climate system. Given the present uncertainty of climate sensitivity, the point in time at which greenhouse gas emissions reach an allowable level, range from about –30 years to +30 years. Furthermore, climate sensitivity must be known with much greater accuracy for effective development of energy strategies, and atmospheric aerosols offset an unknown fraction of the warming forcing of incremental greenhouse gases. The present uncertainty in aerosol forcing greatly limits accuracy in determining climate sensitivity, making the need for fundamental aerosol research both essential and urgent.

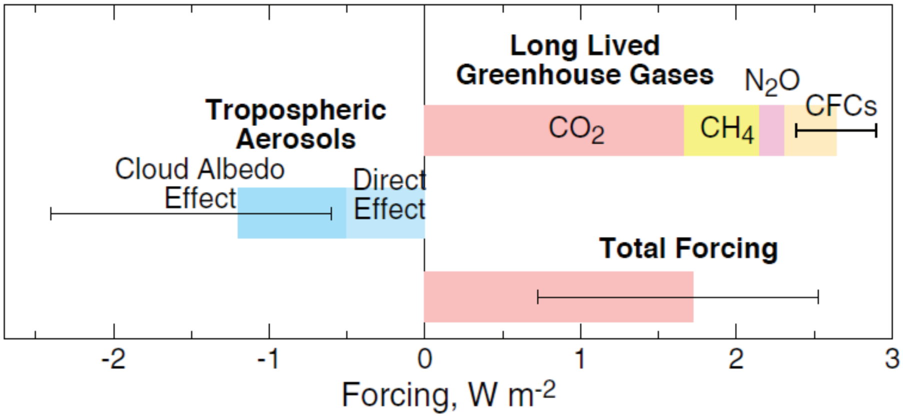


FIGURE 2-5 Atmospheric contributors to positive and negative climate forcing over the industrial period (1780 to present).
SOURCE: Adapted from IPCC, 2007b.

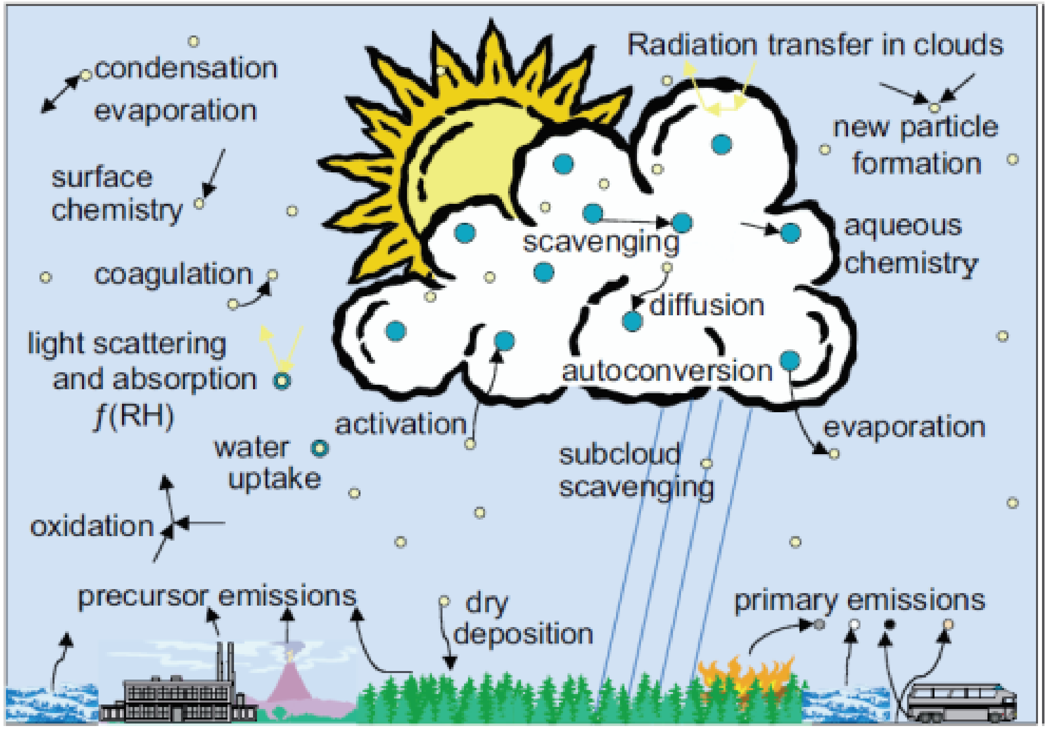


FIGURE 2-6 Aerosol processes that must be understood and represented in models.
SOURCE: Ghan and Schwartz, 2007. © American Meteorological Society. Reprinted with permission.

HEALTH IMPACTS OF AMBIENT AIR PARTICLES

Mort Lippmann of New York University (NYU) discussed the state of science of particles and health research, characterizing our understanding of the correlation between particle chemistry and health as primitive. Airborne particles, also known as particulate matter (PM), are regulated by the weight per unit volume of total PM without regard for chemistry. He likened that situation to regulating all airborne gaseous pollutants in sum. He noted, however, that over time, reductions in the total mass of PM correlate with improvements in human health. Figure 2-7 depicts particle volume distributions by particle size for various PM sources.

Initial PM regulations addressed particles between 2.5 and 10 microns. They were modified, however, when research showed that fine particles, defined as those smaller than

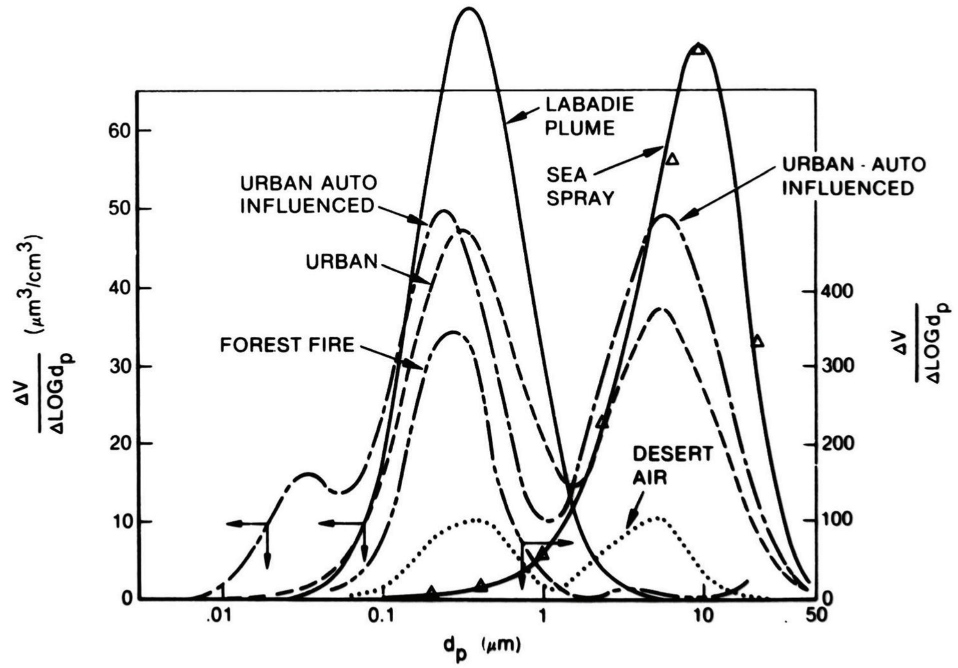


FIGURE 2-7 Particle volume distributions by particle size for various PM sources.
SOURCE: Lippmann, 2010.

2.5 microns (PM2.5) in aerodynamic diameter, are capable of reaching deep into the lungs and are associated with the public health statistics for mortality and morbidity, due to causes such as cardiovascular diseases, liver disease, and to a small extent, lung cancer (Pope et al., 2004). PM10 refers to particle diameter size less than 10 microns (and includes PM2.5). Data reveal a relationship between particle composition and adverse health effects (Figure 2-8), but the relationship is not well understood.

Air pollution enters the body through the nose and mouth. The size of a particle determines where it ultimately ends up in the lungs. Fine particles penetrate and are deposited deep into the lungs. The soluble components, said Lippmann, are extracted and enter the blood stream, traveling throughout the body, which explains the occurrence of adverse effects in the liver, brain, heart, and other tissues. Research is starting to find health effects associated with particles in the 2.5-10 micron range, particularly the exacerbation of asthma.

In summarizing the current knowledge about PM, Lippmann said that measuring PM2.5 mass has been a useful surrogate index of adverse health risks. It correlates better with cardiovascular effects than other monitored air pollutants. However, its risk coefficient varies, presumably resulting from differences in PM composition, and he called for studies aimed at better understanding the relationship between PM composition and adverse health effects. "The epidemiology indicates we reduced the public health impact just by going after the messenger, but you can only go so far following the messenger," said Lippmann. "You have to start getting at the active components."

However, PM10 mass, which is often dominated by contributions from PM2.5, is a poor indicator of the respiratory system risks associated with the fraction of particles that deposits within the tracheobronchial airways. In addition, the effect of PM10 or PM2.5 composition on human health is unknown. Neither PM2.5 nor PM10 mass is useful as an index of risk associated with ultrafine PM (particle diameter less than 0.1 micron). Lippmann noted that, at the time of the workshop, the Environmental Protection Agency (EPA) was planning to lower the standard for fine-particulate mass. The real focus, in his opinion, should be on characterizing the chemical components of fine particulate matter, understanding their impact on human health, and then developing regulations that reduce levels of the most toxic components.

Research in Identifying Health Impacts of PM Exposure

Research to study PM chemistry is under way. At NYU, Lippmann leads the National Particle Component Toxicity Initiative that aims to compile data on elemental tracers from different sources to enable source apportion analysis that can be used to determine what sources generate PM mass. Particles in New York City, for example, are dominated by oil combustion. As a result, there are more than an order of magnitude higher levels of nickel and vanadium in New York City air than in the rest of the United States. In comparison,

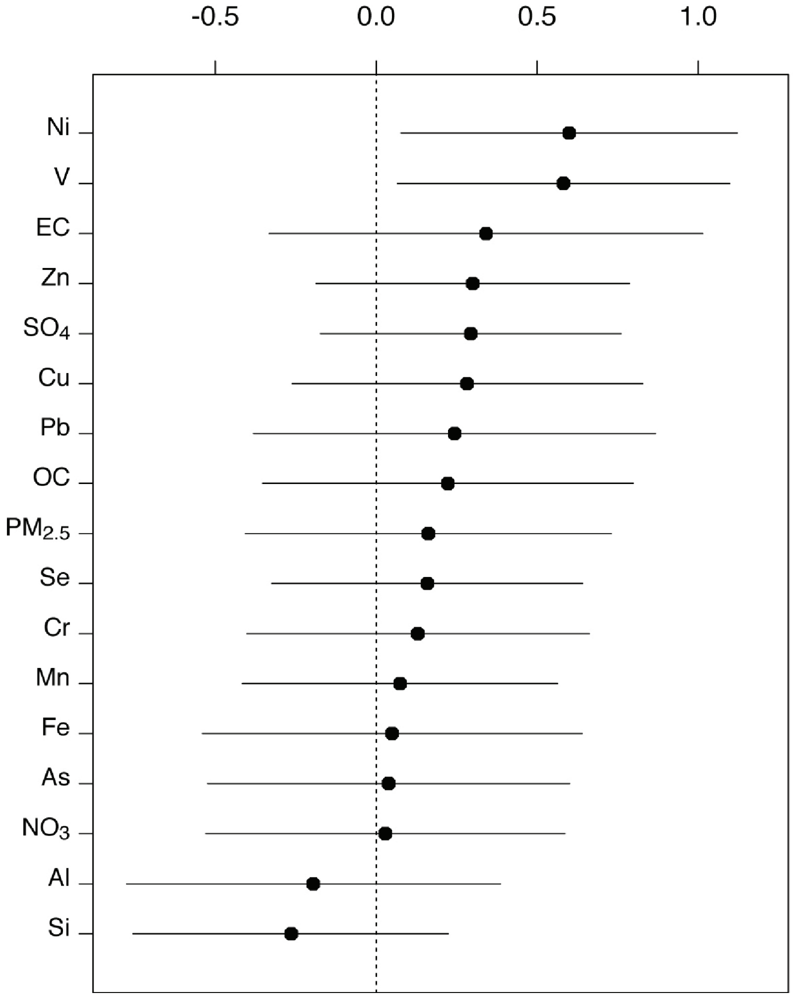


FIGURE 2-8 Chemical composition and relative mortality risk coefficients averaged across 60 metropolitan areas for which fine particulate matter (PM2.5; particles smaller than 2.5 microns) speciation data are available.
SOURCE: Reproduced with permission from *Environmental Health Perspectives*. Lippmann et al., 2006.

tracers associated with steel industry furnaces dominate as the primary PM source in Birmingham, coal sources dominate in western Pennsylvania, and wood burning dominates in Seattle.

Lippmann's group has looked at the distribution of fine particle components within different parts of New York City and found interesting results. Daily samples collected over the course of the year showed that the relative amounts of nickel and vanadium varied between winter and summer months and between the northern and southern parts of the city. This finding led the researchers to identify residual oil burned as the source of these metals. The differences were explained by the fact that there are two primary sources of residual oil pollution—ocean-going ships coming into the Port of New York and New Jersey and boilers used to provide heat and hot water to New York City buildings. These findings are important because Lippmann and others have determined that nickel and vanadium vary "much more significantly with mortality than any other measured elemental component" (Lipfert et al., 2006, Lippmann et al., 2006).

Lippmann said that, in a sense, people are simply aging faster from the chronic exposure. Large cohort studies are now finding significant health effects from exposure to fine PM. For example, the Women's Health Initiative Study, conducted by the University of Washington, has shown that previously healthy women exposed to fine PM develop elevated cardiac disease over time (Zhang et al., 2009). Another study focusing on exposure to particles smaller than 2.5 microns in nine heavily polluted California counties found that overall mortality rose with increasing exposure to fine particles, as did mortality from respiratory disease, cardiovascular disease, and diabetes (Ostro et al., 2006).

Lippmann's group also has been conducting animal studies focused on the effects of chronic PM exposure. In one study, he and his collaborators exposed a strain of mice bred to be susceptible to exposure-induced cardiovascular disease to concentrated Sterling Forest State Park ambient aerosol (which is an index of the regional eastern U.S. aerosol, much of which is secondary from the Midwest and Southwest). Exposure lasted 6 hours, 5 days a week, for 6 months. The bottom line from these experiments is that the mice experienced a wide range of health effects including cardiac dysfunction, atherosclerosis, obesity, and metabolic syndrome (Sun et al., 2009, Ying et al., 2009).

Recently, Lippmann's group has been collecting and analyzing daily fine PM filter measurements made by state agencies. Because funds for this work are limited, his group has restricted its study to data from Detroit and Seattle. Detroit was chosen as typical of the eastern United States where states are struggling to meet PM2.5 of 15 micrograms/m^3, and Seattle as representative of a city that easily meets this standard, with an annual average PM2.5 of 9 micrograms/m^3. Seattle's nickel levels are much higher than Detroit's, largely because it is a big seaport handling ships using cheap heavy oil. As expected, fine particle mass levels are much higher in Detroit.

In terms of cardiovascular disease in the two cities, Seattle's rates are higher, most likely because of elevated nickel, vanadium, and sulfur levels associated with heavy oil burning. Lippmann and his colleagues observed similarly elevated levels of cardiovascular disease near the largest Asian nickel refinery located in China, and 1,000 miles downwind from a nickel smelter in Ontario. Nickel smelters, Lippmann noted, do not emit vanadium, although they do emit chromium and iron in addition to nickel.

In another study, Lippmann's group measured a variety of biological markers in two populations of women in China. The two groups were similar except that one group lived near a nickel smelter while the other lived on the other side of a mountain from a smelter. Particulate levels in the two cities were comparable, at about the average of a typical eastern U.S. city, but nickel levels were 76-fold higher in the city near the smelter. Copper, arsenic, and selenium were higher, too, but not by much. Markers of cardiovascular disease were significantly elevated in the women who lived in the smelter city compared to the matched cohort. From the data, Lippmann concluded that nickel is likely to be the agent most responsible for PM2.5-induced cardiovascular effects, and that copper, arsenic, and selenium may play a role. A reduced capacity for endothelial repair, as measured by changes in several biomarkers, may partially explain the critical role of nickel in PM2.5-associated cardiovascular disease.

Lippmann also discussed a study that he and his collaborators are conducting on cardiovascular plaque progression produced by subchronic exposures to concentrated ambient PM2.5 (CAPs), which is prepared by taking fresh samples and concentrating the particles without filtration. Using a mouse model of cardiovascular disease, his team is comparing the effects of breathing CAPs prepared from air collected at Sterling Forest, New York, and the Mount Sinai School of Medicine in Manhattan with those produced by comparable exposures to freshly generated sidestream cigarette smoke, whole diesel engine exhaust, and the gaseous component of whole diesel exhaust.

In this study, CAPs exposure was about 105 micrograms/m^3. Sidestream smoke averaged 480 micrograms/m^3, but it also contained all the other products of tobacco combustion including carbon monoxide, cyanide, and nitrous oxide. Whole diesel exhaust had particulate levels that averaged 436 micrograms/m^3 plus combustion gases. When the researchers examined plaque accumulation, all three particle-exposed groups had significant plaque excesses compared to mice that were exposed only to the gaseous component of diesel exhaust. The biggest increase was seen in the group exposed to CAPs. It is likely, said Lippmann, that the metal content of the particles drives aortic plaque buildup.

In summary, said Lippmann, epidemiological studies using speciation data show stronger associations of cardiopulmonary effects with transition metals than with PM2.5 mass, and toxicological studies in animals provide support for the influence of transition metals. Data from the Chemical Speciation Network (CSN) on PM2.5 components have been essential to the progress to date in demonstrating stronger associations for metals than for PM2.5 mass, but data on PM2.5 components have been too limited in frequency to adequately support definitive time-series studies and too limited in spatial coverage to adequately identify the effects of PM components that are not uniformly distributed. He recommended that an expanded CSN network could support epidemiological research that could provide a sound basis for the development of National Ambient Air Quality Standards for toxic PM components that contribute only small fractions of PM mass, permitting more targeted controls to benefit public health at lower overall cost and societal disruption.

It is important to keep in mind, Lippmann added, that the effects in mortality and hospital admissions do not affect everybody. Sensitive segments of the population are driving these statistics. Therefore, the impact of the particles will be felt mainly by elderly people, not by healthy young people.

PARTICLES IN SOIL AND WATER

Michael Hochella from Virginia Polytechnic and State University started his talk by giving his major take-home message: "Nanoparticles are everywhere. We're breathing them right now. They've been around the planet since its origin." There are vastly more nanoparticles present every day, in biological systems and in the atmosphere, than humans can ever manufacture. "What's going to be most important as we move into the age of nanotechnology is the overprint that humans can already put on what already exists," he explained.

Humanity has previous experience with a hazardous nanomaterial, asbestos. A complex set of minerals, asbestos is a nanomaterial in Hochella's view because, even though it is a long fiber, two of its dimensions are in the nanometer range, and it is these dimensions that enable it to cause pulmonary fibrosis, lung carcinoma, and mesothelioma. Asbestos was first recognized as a human carcinogen in the 1950s. Two decades later the EPA put in place the first workforce regulations. These were followed in 1986 by regulations pursuant to the Asbestos Hazard Emergency Response Act. Hochella characterized both sets of regulations as responsible reactions to a true hazard, but he also opined that the public and politicians have misused these regulations, with the resulting waste of billions of dollars in misguided asbestos abatement efforts. He stated that society can learn from the mistakes it made in dealing with asbestos and avoid a similar waste of resources in dealing with nanomaterials.

The industrial production of nanomaterials has become a huge business, producing several hundreds of billions of dollars worth of products in the biotech, energy, electronics, and aerospace industries. Hochella predicted that, over the next couple of years, the economic value of nanomaterials will exceed $1 trillion. Although industrial output of nanomaterials is significant, it is dwarfed by Earth's generation of nanoparticles, which is in the hundreds of teragrams/year, or about 1 million metric tons (Figure 2-9). Nanoparticles that Earth produces include nanosilver, fullerenes (C_{60}), and carbon nanotubes.

Even more than 10 years ago, Hochella said, it was already possible to look at nanomaterials at atomic levels in incredible detail, including measuring the electronic spectra of individual atoms. He showed a scanning tunneling microscopy image of a pyrite surface with individual iron atoms visible (Rosso et al., 1999). However, now, many groups, including his, are stepping back to look more at changes in particles due to environmental influences, such as lead sulfide and dissolution of the lead content. It is now possible to examine individual sites such as defects on surfaces as they dissolve, an important process to understand because, as these particles dissolve, they release dangerous species into solution that become bioavailable.

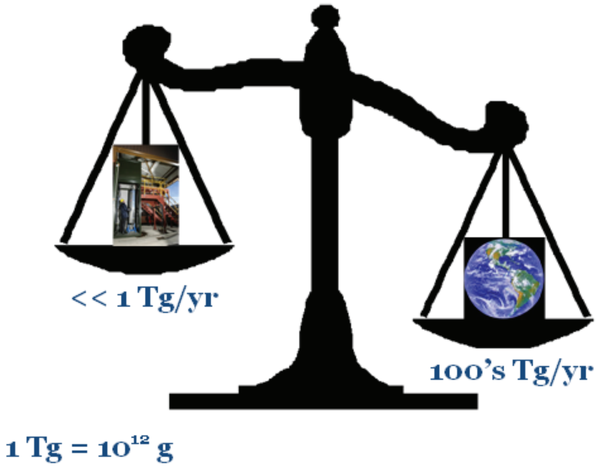


FIGURE 2-9 An inventory of human versus natural production of nanoparticles.
SOURCE: Hochella, 2010.

The whole particles can also be highly bioavailable, particularly as they become smaller and more soluble themselves. However, contrary to thermodynamic prediction, sometimes nanoparticles become less soluble when they become very small, and sometimes their solubility remains unchanged. Hochella noted that these types of studies can provide information on radiative forces that interest atmospheric scientists.

Hochella explained that nanoparticles existed at the beginnings of the universe. Nanodiamonds, about 2 nanometers or 150 atoms in diameter, were recovered from meteors left from the beginning of the solar system. Conditions during Earth's early history were also conducive to the formation of nanoparticles. As a result, biological systems have been exposed to nanoparticles since life first arose on the planet. Hochella and his colleagues are studying how biological systems interact with and even make use of nanoparticles. There are bacteria, for example, that respire using iron nanoparticles as a source of electrons rather than oxygen. These bacteria alter their respiration rate in response to changes in nanoparticle size (Hochella et al., 2008).

Nanoparticles Enter the Environment in Many Ways

"What do nanoparticles in the oceans have to do with climate change?" asked Hochella. A great deal, it turns out, is due to iron oxide nanoparticles being deposited into rivers and from glaciers, which eventually end up into the world's oceans (Raiswell et al., 2006). These nanoparticles provide most of the iron that ocean-dwelling phytoplankton require for photosynthesis, which is the most important biological CO_2 sink in the ocean.

At the largest non-weapons-related Superfund site in the United States, a contaminated mining site in Western Montana the size of Germany, researchers have found previously unknown nanoparticles in the rivers draining into the site from Butte, Montana, including titanium dioxide and lead nanoparticles. These findings prompted Hochella and his group to attempt to better understand how metals as toxic as lead, copper, zinc, arsenic, and cadmium move in the river system. Fifteen years ago, when the group started this effort, nobody understood how these metals were being solubilized, that is, whether they were being carried in river water on organic molecules or bacteria or as nanoparticles.

Using flow field flow fractionation techniques, Hochella's team found that nanoparticles were present in the water.

Upon further analysis using mass spectrometry and transmission electron microscopy, they found that the nanoparticles were covered with metals. Nanoparticles of the iron mineral known as goethite, for example, were carrying arsenic hundreds of kilometers from its source, and in fact, into drinking water. Nanoparticles of ferrihydrite, a different iron oxide mineral, carried arsenic, zinc, and copper into the system, while nanoparticles of the titanium dioxide mineral brookite carried lead into the system. Now that these nanoparticles have been identified, said Hochella, their role in environmental and biological processes can be studied in detail.

As an example, Hochella discussed Schwertmannite, a rare but important iron oxyhydroxide sulfate mineral. Schwertmannite nanoparticles have long, thin whiskers that are visible at 1.8 million-fold magnification and can carry arsenic. Such knowledge enables research focused on understanding how the nanoscale structure of these particles influences their interaction with biological systems.

Ubiquitous Nanoparticles

Recently, Hochella's team obtained EPA samples taken from wastewater treatment plants. They discovered that manufactured silver nanoparticles are common in the sludge from wastewater treatment plants that is applied to farm fields. Atomic-scale electron diffraction Fourier transform microscopy revealed that these are silver sulfide nanoparticles (Kim et al., 2010). These particles are likely entering the ecosystem when they are shed from clothing treated with silver nanoparticles that serve as antibacterial agents.

He presented an inventory of nanoparticle occurrence (Figure 2-10), characterizing them as either manufactured, incidental as a byproduct of diesel emission or industrial activity, or naturally occurring. In discussing this inventory, he said, "We haven't found the way nature makes a quantum dot yet, but we're working on that."

Hochella concluded his talk by noting that there are many sources of natural nanoparticles: dust in the atmosphere, sea spray, and even hydrothermal events in the deep ocean that bleed seawater as a supercritical fluid heated up to 350°C, ripping all kinds of elements out of the ocean crust and thereby creating nanoparticles in the deep ocean. Melting icebergs, rivers, and volcanoes also add nanoparticles to the environment. Figure 2-11 shows a global budget of naturally occurring and organic nanoparticles. Still unknown is what the additional contribution—and impact—of manufactured particles will be given that the nanotechnology revolution is just starting.

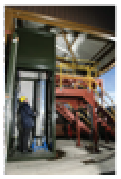
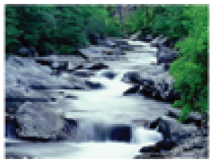
	Manufactured 	Incidental (D) 	Incidental (I) 	Natural 
Au	■			■
Ag	■			■
Fe	■			
FeOx	■	■	■	■
TiO_2	■	■		■
SiO_2	■	■	■	■
CeO_2	■			■
ZnO	■			■
C60	■	■		■
CNT	■			
QD	■			

FIGURE 2-10 An inventory of nanoparticle occurrence. CNT = carbon nanotube; QD = quantum dot.
SOURCE: Hochella, 2010.

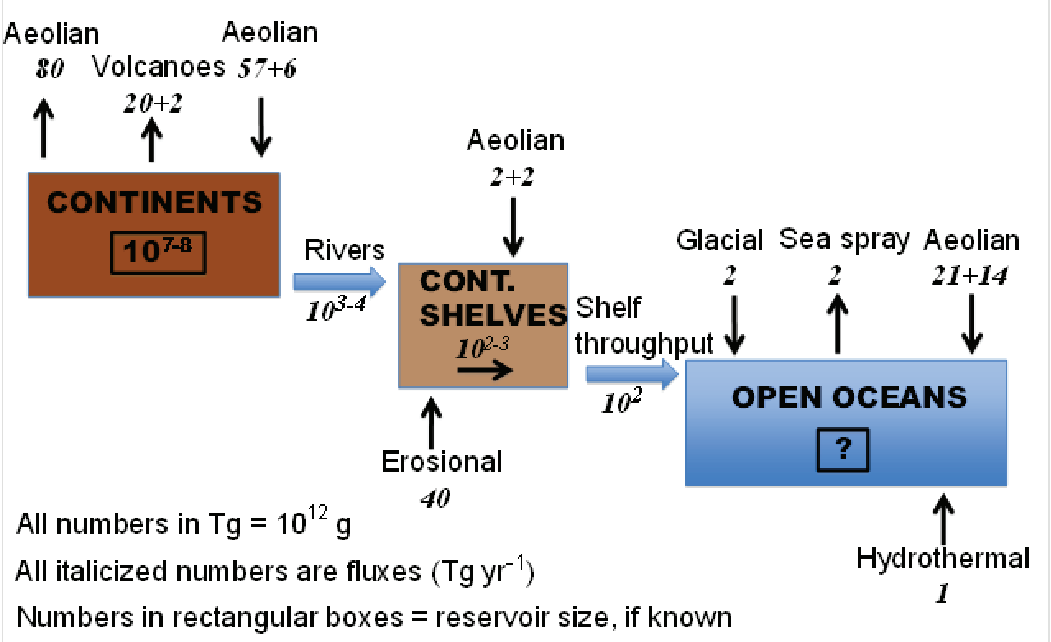


FIGURE 2-11 The global budget for naturally occurring inorganic nanoparticles.
SOURCE: Hochella, 2010.

PARTICLES IN BIOLOGICAL SYSTEMS

Gerry McDermott of the University of California, San Francisco, talked about visualizing where particles end up inside cells and quantifying the number that have entered the cell. Many new imaging tools have been developed over the past few years, including soft x-ray tomography and cryogenic light microscopy (McDermott et al., 2009), that have not yet been used to study nanoparticles in cells but have a huge potential for that purpose.

The rationale for imaging small particles in cells, said McDermott, is to know the location of the small particle, particularly if the goal is to develop a therapeutic delivery system. It is important to know, for example, if a particle delivers a drug to the intended target inside the cell. "Does it go inside the nucleus or does it get stuck in a membrane somewhere?" he asked.

For environmental nanoparticles, intracellular destination is an important aspect of whether the particle can cause a change in cell phenotype. It is also important to understand whether small particles alter the subcellular architecture of the cell or the locations and concentrations of specific molecules or molecular complexes, and whether such alterations cause changes in the fundamental biochemistry that takes place inside the cell.

Two new imaging techniques provide important insight about these issues. Soft x-ray tomography for high-resolution three-dimensional imaging of single cells allows for the direct localization of small, electron-dense nanoparticles (LeGros et al., 2005). Cryogenic light microscopy allows the location of fluorescently tagged small particles or cellular structure inside the cell to be identified (LeGros et al., 2009). Images from the two techniques correlate well, which permits combining data on cellular imaging with molecular localization.

Soft X-ray Tomography

Computed tomography (CT) is an iconic instrument in clinical diagnosis that takes and computationally assembles a series of x-ray snapshots to create a three-dimensional image. Compared to the two-dimensional projection afforded with a conventional x-ray film, CT imaging provides exquisite insight into the internal structure of the human body.

Soft x-ray tomography miniaturizes this concept to provide the same exquisite detail about the internal structure of a cell. With this technique it is feasible to visualize in great detail how a cell responds to environmental factors such as drug molecules or small particles. The structural detail can also yield new insights into fundamental processes of cell biology, such as the cell cycle.

Soft x-ray tomography offers many advantages over conventional imaging such as light microscopy and electron microscopy. Tomography provides spatial resolution as low as 50 nanometers or as high as 10 nanometers, and it does so in three dimensions. It is fast, requiring only 2 to 3 minutes to collect a full tomographic data set, which makes high specimen throughput possible. Cells are imaged whole, hydrated, unfixed, and unstained in a near-native state. The instrument's field of view is large enough to image one eukaryotic cell or about 200 bacterial cells at a time. And, unlike conventional microscopy that uses fluorescent tags to image specific cellular structures, soft x-ray tomography images all of a cell's internal structures at once.

The instrument concept is simple (Figure 2-12), although it only became possible to build the necessary focusing devices in the past 3 years because of the revolution in nanofabrication. Because no material has an appreciable refractive index for x-rays, focusing is done using nanofabricated Fresnel lenses. The outer rings of the zone plate, shown in Figure 2-12, determine the spatial resolution of the microscope.

Although simple in concept, in real life the instrument is large and expensive with many pipes and high vacuum chambers. The x-rays are generated by the Advanced Light Source at Lawrence Berkeley National Laboratory and are delivered to a separate room that houses the microscope. McDermott hopes that, in the future, the microscope will be able to use less expensive plasma x-ray sources. Imaging of whole cells is done in what is known as the water window, a region of the spectrum in which water does not absorb x-rays but biomolecules do.

McDermott showed tomographic reconstructions of a yeast cell (Figure 2-13), and of malaria parasites and gold nanoparticles inside a red blood cell (Figure 2-14). The latter images were used to track how the malaria parasite takes up nutrients once it has invaded a red blood cell (Hanssen et al., 2011).

McDermott also showed images detailing internal structural changes that occur as the pathogenic species of yeast known as *Candida albicans* grows and undergoes a transformation from nonpathogenic to highly pathogenic. These images show that the yeast expands the number of mitochondria-filled tubes during this transformation, suggesting that tube formation could be a fruitful target for drug disruption. Collaborating with a group at Stanford University, McDermott's group developed and tested a series of protease-resistant peptide-like drugs known as peptoids as antifungal agents that would be capable of blocking tube formation (Chongsiriwatana et al., 2008). In tests of two different peptoids, the researchers found that both peptoids were effective at greatly reducing the growth of the mitochondria-filled tubes. However, when fungi treated with the two peptoids were imaged using soft x-ray tomography, they found that one of the two agents produced large changes in the fungal nucleus that could be problematic if that agent ever proceeded to human clinical use (Figure 2-15) (Uchida

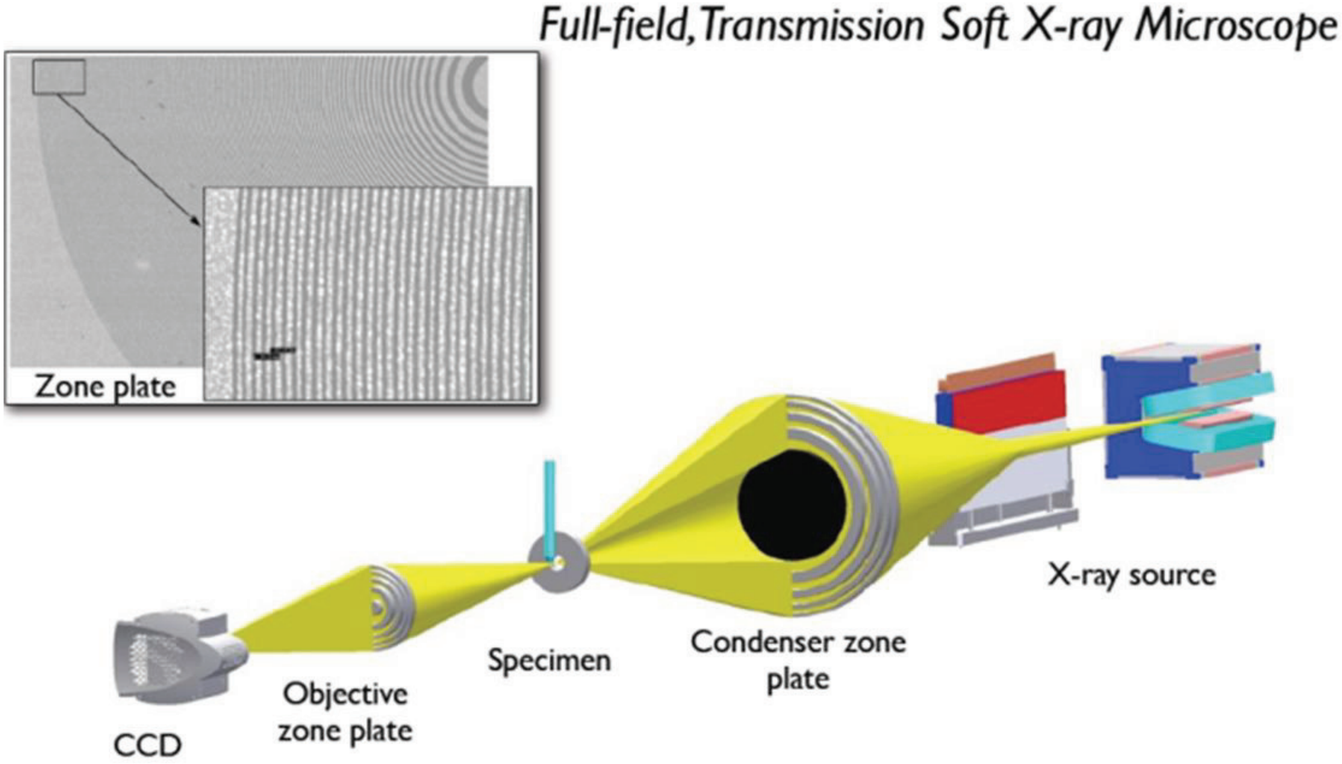


FIGURE 2-12 Full-field transmission soft x-ray microscope.
SOURCE: McDermott et al., 2009.

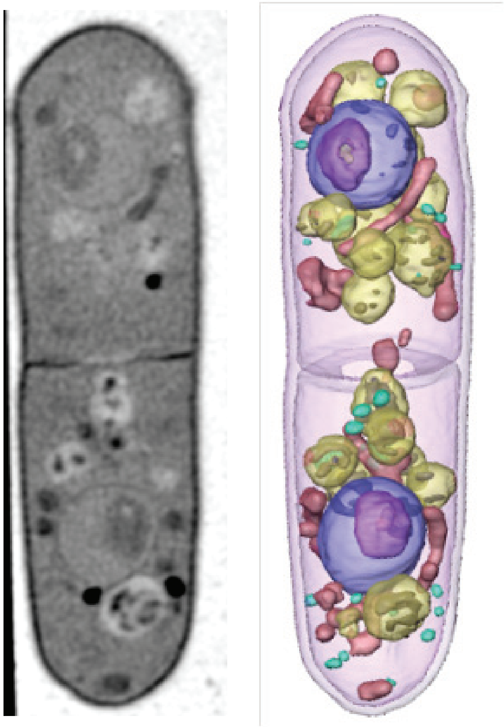


FIGURE 2-13 One slice from a tomographic reconstruction (left) and the three-dimensional reconstruction of a yeast cell clearly shows the individual organelles inside the cell.
SOURCE: McDermott, 2010.

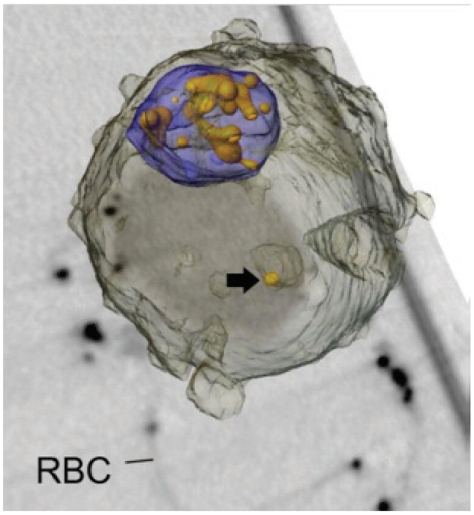


FIGURE 2-14 Tomographic image of red blood cell containing malaria parasites and gold nanoparticles. Parasites were allowed to invade red blood cells containing gold particles. The image is a rendered model overlaid onto a virtual section. The parasite surface is depicted in translucent gray and the digestive vacuole in blue. The model reveals the morphology of the gold particle-containing structure in the parasite cytoplasm. Scale bar, 3.5 μm.
SOURCE: Hanssen et al., 2011.

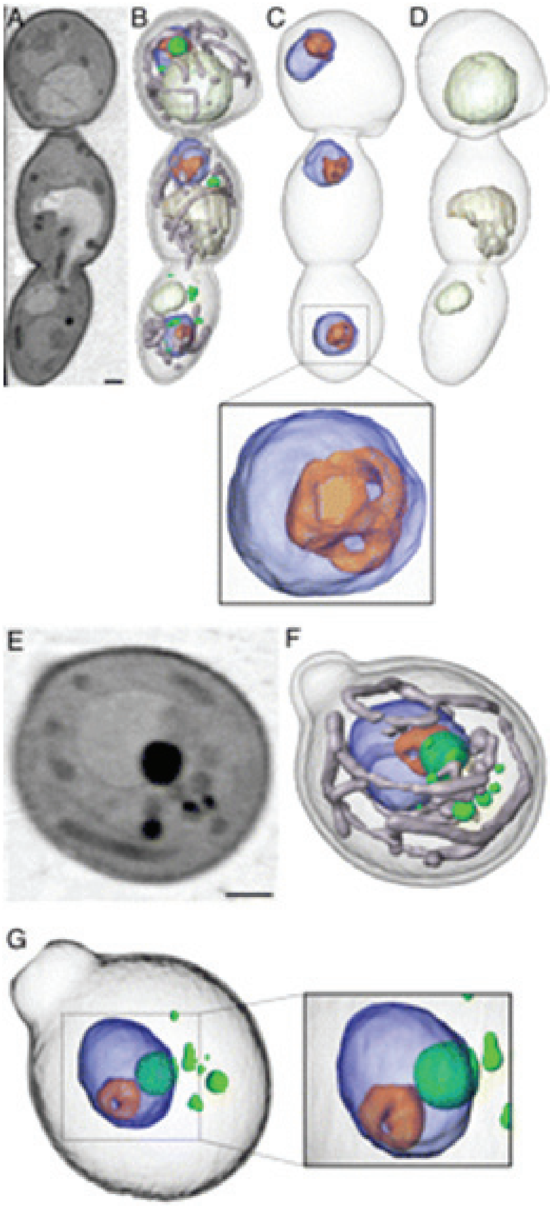


FIGURE 2-15 Soft x-ray tomography of *C. albicans* cells after treatment with two peptoids. The top seven images (A-F) show internal changes seen with the first of two peptoids, while the bottom image (G) shows the larger nuclear changes produced by the second peptoid. These larger changes could prove problematic in human use.
SOURCE: Uchida et al., 2009.

et al., 2009). McDermott also showed images obtained using cryo-fluorescence microscopy in combination with x-ray tomography (Figure 2-16). McDermott concluded by noting that these changes would not have been seen with standard microscopy, which highlights the potential benefits of using these new techniques in cell biology studies.

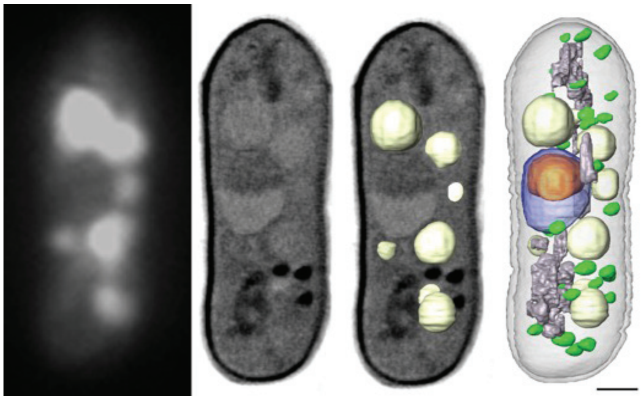


FIGURE 2-16 Correlated cryo-fluorescence and x-ray images of *Schizosaccharomyces pombe*, with the fluorescence image showing labeled vacuoles on the left and x-ray images of unlabeled vacuoles in the middle two images. The tomographic reconstruction on the right shows the unlabeled vacuoles.
SOURCE: McDermott, 2010.

OPEN DISCUSSION

In response to a question from **Pedro Alvarez** of Rice University about the size distribution of natural versus manufactured nanoparticles, Hochella said, “These natural nanomaterials show the same fascinating size-dependent properties as manufactured or synthetic ones do.” He added that nanoparticles with the same chemical composition and molecular structure from the two sources have similar distributions in terms of physical, chemical, electrical, and magnetic properties. However, another participant noted a key difference between natural and synthetic nanoparticles is that synthetic nanoparticles can be much more monodisperse in terms of size and shape and homogeneous in terms of chemical composition compared to naturally occurring colloidal particles.

Barbara Karn of the EPA (now at the National Science Foundation) commented that manufactured nanomaterials often have elements such as indium that are not found in naturally produced nanoparticles. She asked if that was a concern, particularly with regard to water treatment plants and their discharges into waterways. Addressing this comment, Hochella said that for some elements, such as lead or gold, nature has done a good job concentrating them in locations that humans then mine. Those materials are probably found in naturally occurring nanoparticles. For others, however, as Karn noted, humans are now mining materials from much deeper in Earth, elements that would not be exposed on the planet’s surface. These elements are being concentrated and put into products, and the result is that humans are “dramatically changing the distribution of that element on the planet’s surface.” For example, in some cases it can cause a material to become more bioavailable and possibly toxic, which is why there is a need to develop a better understanding of the life-cycle impacts of synthetic nanoparticles on the environment. In fact, elaborated Hochella, that is why Virginia Tech and other institutions around the world are starting sustainable nanotechnology centers. He and his colleagues at Virginia Tech, for example, are studying how cadmium, a critical component of quantum dot nanoparticles, gets into the environment and what its fate will be. By understanding such processes, it may be possible to either move away from using cadmium, or other potentially toxic materials, or design ways to produce these materials in a more environmentally friendly way.

Lippmann followed up by asking Hochella about nanoparticulate silver and whether there is any idea of what the environmental consequences will be. Hochella replied that the answer is no, which is exactly why research is needed now. He noted that nanoparticulate silver is included in a large number of consumer items because of its antimicrobial properties, but there is concern about what will happen to the planet's microbial ecosystems when large quantities of nanoparticle silver enter and become concentrated in the environment.

Lippmann inquired about what asbestos has to do with nanoparticles. Hochella responded that he defines a nanoparticle as one with at least one of its three dimensions in the nanometer range, and asbestos meets that criteria. Clay minerals fit this definition in one dimension, and it is that dimension that in part imparts the special properties of clay and many other minerals as well. He added that catalyst researchers, who worry about stopping agglomeration, can learn from studying the behavior of natural fibers such as asbestos. Lippmann added that even when nanoparticles do agglomerate, they still have nanoscale features on their surfaces that must be considered when designing and studying such materials.

Finlayson-Pitts noted, "Ultimately what we're interested in are the impacts of particles, the good and the bad, and in the case of a bad, how do we mitigate? What should we control?" She remarked that Schwartz, Lippmann, and Hochella addressed different aspects of trace metals and organics carried on the surface of nanoparticles, and she asked if there is an overriding control strategy that will help mitigate the potential impacts on climate and health.

Lippmann responded, "There has been an effective and continuing effort to reduce the emissions of sulfur dioxide into the atmosphere, with the Clean Air Act leading to a 50 percent reduction [in airborne sulfur dioxide levels]." Reducing the sulfur content of diesel fuel has had an additional substantial impact on reducing sulfate aerosols that he predicted "will change the reflectivity of the atmosphere, because sulfate is the best light scatter of all of them."

Schwartz noted that sulfur emissions in general, and particle emission specifically, are increasing in the developing world. He added that a reduction in aerosol emissions may increase the greenhouse effect, which may or not be a good outcome. Hochella suggested that increasing the output of iron-containing nanoparticles, which could boost phytoplankton productivity, could help ameliorate global warming. This possibility, he said, points to the difficulty in developing an overriding control strategy for nanomaterials.

A participant asked the speakers to address any outstanding issues in characterizing small particles. Lippmann replied that he would like to see more work on characterizing the composition of particles in the air and the health implications of the composition given that the tools to do so, such as x-ray fluorescence, are on the threshold of making the needed measurements. He said that such data would enable control efforts to focus on emissions of specific, toxic materials rather than particles in general, which could potentially save a great deal of money.

Schwartz said that he would like to see research develop a better understanding of the processes that are responsible for the formation and growth of atmospheric aerosols. "I think we are really on the cusp of a revolution in terms of characterization of the composition of these newly formed particles," he said. "I think we'll that find many of the aerosol chemistry and growth models that are being used right now to try to estimate aerosol impacts on climate are going to turn out to be all wrong." An audience member added that such studies should also include surface properties because, as the catalyst community knows well, surface properties and composition are both important for determining a particle's behavior.

3

Analysis and Imaging of Small Particles

Although the research community has studied nanoparticles for several decades and has made many advances with imaging and analyzing the chemical composition of individual and mixtures of nanoparticles, it still struggles with understanding how nanoparticles interact and undergo changes in different environments. In particular, investigators are just now developing methods for determining the three-dimensional structure and chemical composition of nanoparticles in the atmosphere and in nanocomposites. They also are designing new techniques for studying and modeling how particles form in the atmosphere and how those processes ultimate determine the nanoparticles' properties and their impact on the environment. Nanoparticle structure and composition also is critically important for the materials and catalyst industries, both for understanding how existing materials and catalysts behave and for improving their design and function. Speakers in this session, as well as the subsequent sessions, discussed the specific challenges of imaging and analyzing nanoparticles and the wide-ranging benefits that will come from solving those challenges.

MULTIDIMENSIONAL CHARACTERIZATION OF INDIVIDUAL AEROSOL PARTICLES

Alla Zelenyuk of the Pacific Northwest National Laboratory (PNNL) reiterated the important point that aerosols are everywhere, with impacts on the climate and health and potential for misuse as agents of terror (Figure 3-1). She also noted that aerosols arise from a variety of sources, each of which produces particles of unique structure and composition. What makes nanoparticle characterization even more challenging is the fact that aerosols are most often mixtures of particles. While it is important to understand the mixture, Zelenyuk and her coworkers are first trying to look at one particle at a time to determine as many relevant properties as possible. Doing so is a daunting task given the size and mass of an individual aerosol particle and their low concentrations in the atmosphere. Particle concentrations range from a few to a few thousand particles/cm^3. However, said Zelenyuk, instruments are now available that are capable of looking at the properties of individual particles, with high sensitivity and resolution, and of determining many properties for the same particle.

One of the main instruments in use is the single particle laser ablation time-of-flight mass spectrometer called SPLAT II. This instrument, shown in Figure 3-2, is used in the laboratory and in the field (Zelenyuk and Imre, 2009, Zelenyuk et al., 2009). SPLAT II was flown for a month in an airplane to determine which particles form in ice clouds and how they affect climate to better understand sources of air pollution over Alaska. Zelenyuk and her collaborators also have developed software capable of examining millions of particles to establish correlations between different properties and different sources.

Zelenyuk and her colleagues are attempting to use SPLAT II and software to quantitatively determine many particle properties, including particle number and concentration, size, composition, and density. They also are examining different aspects of particle shape and dynamic shape factor, that is, whether a particle is spherical or symmetric, and particle morphology in terms of what is on the outside of the particle. Measuring the content of the very thin outer layer of a particle is important because layers of secondary organic aerosols on top of a hydroscopic layer can change water retention and completely stop the water content of these particles from evaporating. After describing how SPLAT II works (Figure 3-2, right panel), Zelenyuk discussed some of the results from the Alaska study. Flying through clouds, for example, the instrument showed that very few particles do not activate and form droplets. By repeatedly sampling

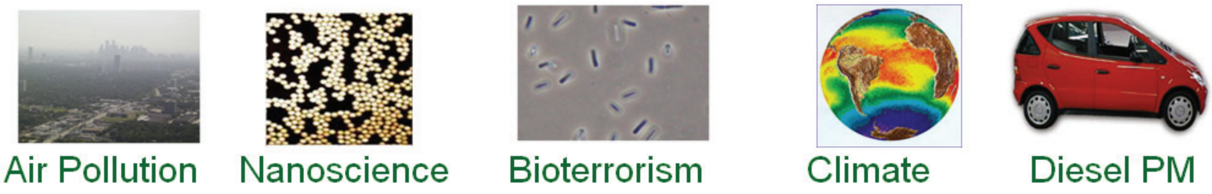


FIGURE 3-1 The importance of aerosols to society are many and varied.
SOURCE: Zelenyuk, 2010.

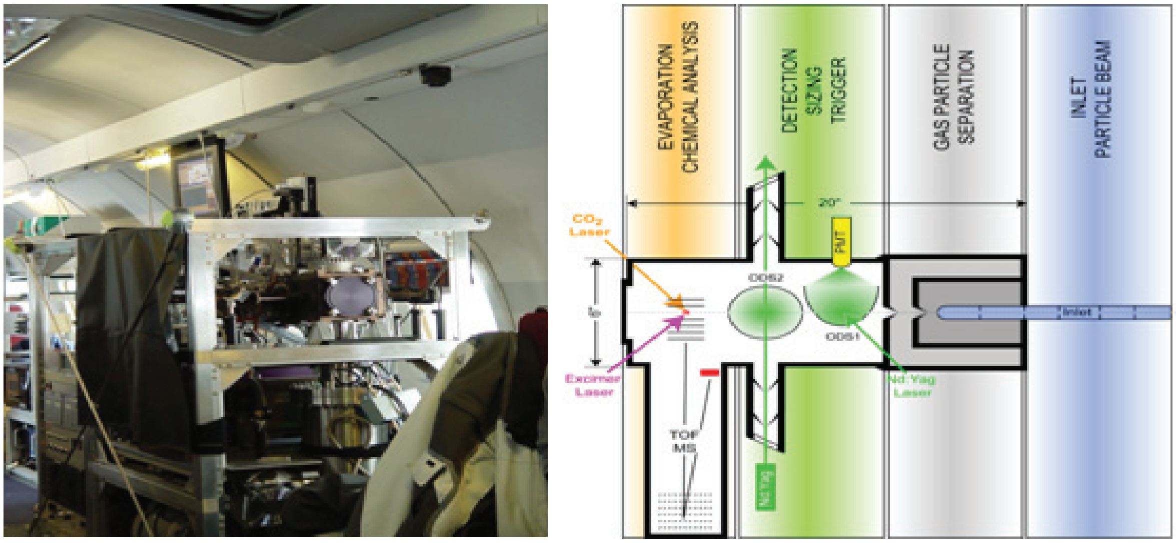


FIGURE 3-2 SPLAT II, an ultrasensitive high-precision instrument for multidimensional single particle characterization.
SOURCE: Zelenyuk, 2010; modified from Zelenyuk et al., 2009.

the free particles, SPLAT II provided information that may reveal what is special about these particular particles in terms of their size, composition, and morphology. Modelers will then be able to use this information to improve their predictions about cloud formation. Zelenyuk noted that any particle more than 100 nanometers in diameter can be detected at levels as low as 1 particle/cm^3 in 1 second of sampling and can be sized with an accuracy of close to 100 percent. Zelenyuk and her colleagues recently demonstrated that they can determine the density of a particle, which is very important for determining the mass of particles, the value of which is regulated by the Environmental Protection Agency.

Characterizing Particle Morphology

When SPLAT II was first developed, Zelenyuk and her colleagues used it to study ultrapure molten salts that form metastable phases in far-from-equilibrium states. These studies enabled them to report the first density measurements for hygroscopic particles found in the atmosphere that exist in highly metastable phases (Zelenyuk et al., 2005). They found, for example, that the shape of sodium chloride particles could vary from spherical to the more typical cubic and rectangular, and that the particles could agglomerate into structures with much larger shape factors. In addition, the researchers demonstrated that they could measure the symmetry of different types of particles and even separate particles in real time based on their shapes. For each shape, they could then measure density, size, and composition (Zelenyuk et al., 2006). Turning to the issue of particle morphology, Zelenyuk showed that it is possible to drill down into a particle to study particle composition as a function of depth (Figure 3-3) (Zelenyuk et al., 2008). In her initial experiments, she worked with the sodium chloride model system and coated the particles with liquid organics and solid organics. The experiments revealed that different organic layers deposited over time on the particles do not mix with one another, contrary to predictions of modeling studies. Instead, the organics develop a layered structure. The researchers were able to create some of these structures and to show that they can be stable for many hours, which Zelenyuk said was surprising.

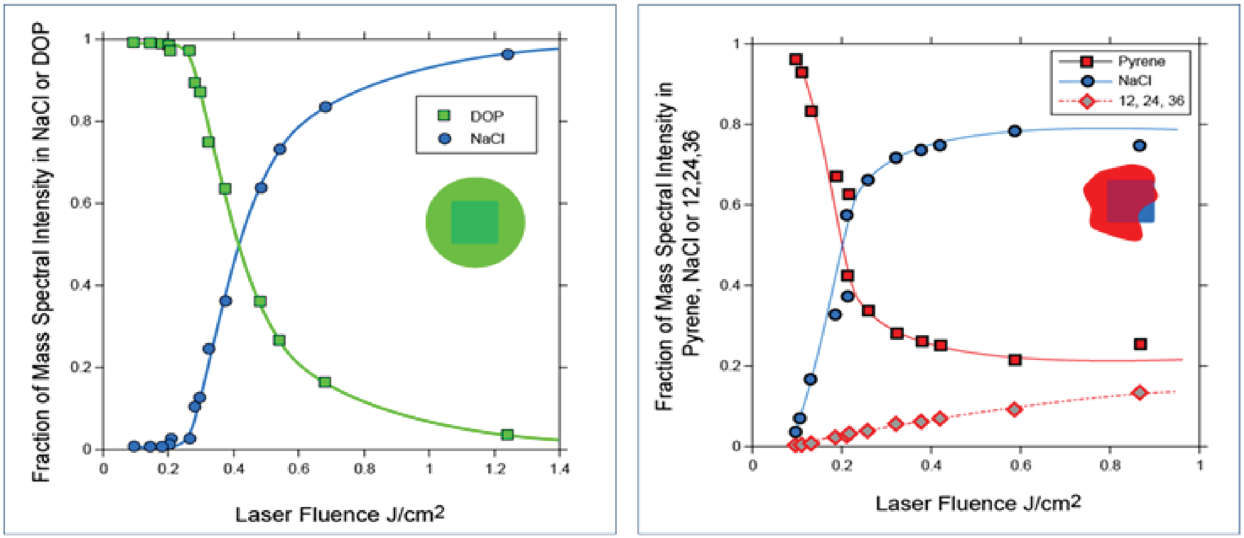


FIGURE 3-3 Characterizing particle composition as a function of depth.
SOURCE: Reprinted (adapted) with permission from Zelenyuk et al., 2008.

Zelenyuk also noted that small amounts of organic vapors, such as those emitted in auto exhaust, can have a profound impact on particle morphology and behavior. One series of measurements, for example, showed that particle chemistry changed as the aircraft travelled through a cloud, implying that the chemistry in a cloud is heterogeneous and changing with location and over time. Another set of experiments found that a thin layer of organics can reduce particle evaporation by 96 percent over 24 hours. Those data are now being used by modelers to attempt to predict the properties and life cycles of different types of particles in the atmosphere. As a final example of the type of studies that SPLAT II can enable, Zelenyuk briefly discussed work being done on engine exhaust. One finding from those studies is that particles emitted by new-generation fuel-neutral[1] spark-ignition direct injection engines are fractal in structure, and that they incorporate polyaromatic hydrocarbons and nitropolyaromatic hydrocarbons at levels as high as 40 percent on their surfaces, which she said was also surprising.

Discussion

Doug Ray of PNNL commented that there is a similarity between the data acquisition presented by Zelenyuk and the work presented in Chapter 2 by Gerry McDermott, in that high-throughput analysis of large numbers of items allows critically new conclusions to be extracted from these data. He said, “That is a theme. If a tool can be built with the capability to perform high-throughput measurements with the proper data analysis tools, it is possible to tease out information that would be otherwise invisible.”

MATERIALS DESIGN AND SYNTHESIS

In his presentation, **Ralph Nuzzo** from the University of Illinois in Urbana-Champaign discussed his work on nanoscale characterization from the perspective of understanding structural dynamics in the context of catalysis. “First and foremost,” he said, “there’s a gigantic toolbox that can be applied to this area.” Among the examples he cited, which were developed through large investments by the Department of Energy, include neutron- and x-ray-based approaches and emerging technologies such as analytic electron microscopy. The development of methods that correct for the complications that come from both chromatic and spherical aberrations were the key factors that enable electron microscopy to reach atomistic resolution.

Using these new techniques, it is possible to obtain atomic resolution images that clearly delineate the atoms in polymer-capped platinum and palladium nanoparticles, for example, as shown in Figure 3-4. A comparison of these two images shows that while the platinum particles have a very well-defined order, the palladium nanoparticles have a significant amount of disorder that is independent of the orientation. It is possible from these images to count atoms and to correlate particle size with atom count in various types of particle morphologies. This study can be extended to more complex structures, including core-shell platinum-palladium and palladium-platinum nanoparticles that are relevant to catalysis (Sanchez et al., 2009a). These types of experiments have yielded important insights into particle

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[1] Not requiring a specific transportation fuel.

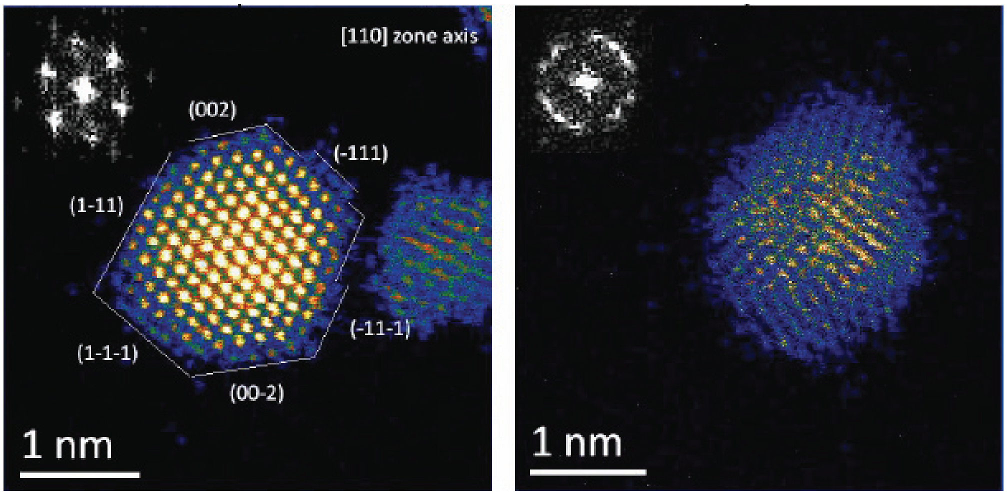

FIGURE 3-4 Atomic resolution electron micrographs of platinum and palladium nanoparticles.
SOURCE: Reprinted (adapted) with permission from Sanchez et al., 2009a.

nucleation and growth and have provided input for modeling studies that have advanced our theoretical understanding of these important processes.

Complementary to these imaging studies are those that involve spectroscopy, which is an averaging technique. Taking a population of clusters, it is possible to use x-ray absorption spectroscopy to measure properties such as the average coordination number for an absorbing atom and average bond distances and bond disorder. Combining microscopy and spectroscopy data can provide information on mesoscopic phenomena such as how bond distances change with temperature. Nuzzo discussed one set of measurements made on platinum γ-alumina, a quintessential heterogeneous catalyst that is used to make gasoline. These experiments showed that bond distances contract as temperature rises when particle diameter reaches sizes as small as 1 nanometer. This phenomenon, known as negative thermal expansion, was correlated with changes in electronic structure (Sanchez et al., 2009b). Molecular dynamics simulations of a 10-atom platinum cluster supported on γ-alumina determined that the bonding between the cluster and the support was dynamic in nature.

Understanding Defects

γ-Alumina is an interesting support at an atomistic level because it has a great many defined defects created by oxygen atom vacancies that cause electronic perturbations in the support. These perturbations occur on a scale that is of the same order as the size of the platinum clusters and therefore perturb the static disorder of the clusters on the support. The level of disorder in these structures is also highly sensitive to nanoparticle size and the presence of reactive gas. In related work, a detailed modeling study, combined with nano-area coherent electron diffraction data of gold nanoparticles, revealed that the vertices of gold clusters are deformed more than expected in an "ideal" structure. This finding makes sense, Nuzzo noted, because atoms at the vertices have the lowest coordination numbers, and, as a result, their structural relaxations are most profound (Huang et al., 2008). This type of structural behavior has been very hard to characterize in the past. Nuzzo also discussed work done on the impregnation and reduction of an iridium and platinum bimetallic catalyst supported on γ-alumina. He showed images detailing the atomic-level structure of this system. The support lattice was observable and identifiable in these images to be near the metal clusters and aligned with the zone axes. These images, he said, illustrate that it is now possible to directly correlate specific lattice planes in face-centered cubic structures, which are essentially single crystals, and to map them onto specific orientations of the γ-alumina structure. Another technique that researchers are putting to use in atomic-level studies is electron energy loss spectroscopy (EELS), which can be used to characterize the electronic structure of a material at the atomic level. EELS can elucidate the patterns of charge transfers using an aberration-corrected microscope and can identify regions in a catalyst support that are not homogenous. Nuzzo showed images of a gold cluster on a titanium dioxide support that clearly identify areas in the lattice that contain a disproportionate number of titanium (III) centers located under the gold clusters (Sivaramakrishnan et al., 2009). He noted that these types of studies are providing information about the nature of catalyst-support interactions and their structural and electronic consequences, which have been the "dark matter of catalysis."

Turning Low-Resolution into High-Resolution Images

As a final example, Nuzzo described the use of coherent diffractive imaging to provide atomic-resolution structural determinations even when an atomic-resolution imaging lens is not available. Using synergistic information from electron diffraction and low-resolution images, Nuzzo's team was able to reconstruct an image showing the chirality and registration of the two concentric walls of a double-walled carbon nanotube (Figure 3-5; Zuo et al., 2003). He also showed a low-resolution image of a cadmium selenide quantum dot and the subsequent, far more detailed, image that had been refined using diffractive imaging (Figure 3-6). In the latter image, the resolution was sufficient to see the separation between cadmium and selenium atoms (Huang et al., 2009).

Nuzzo explained that there are still some important limitations to current analytical techniques that point to future directions for research. Current methods can reveal atomic structure, speciation of elements at the nanoscale, and electronic structure at the atomic scale. However, structural dynamics is still needed, because current methods provide limited or no temporal resolution to monitor ongoing processes. Also needed is the ability to characterize adsorbate-interface bonding at atomic resolution, particularly in terms

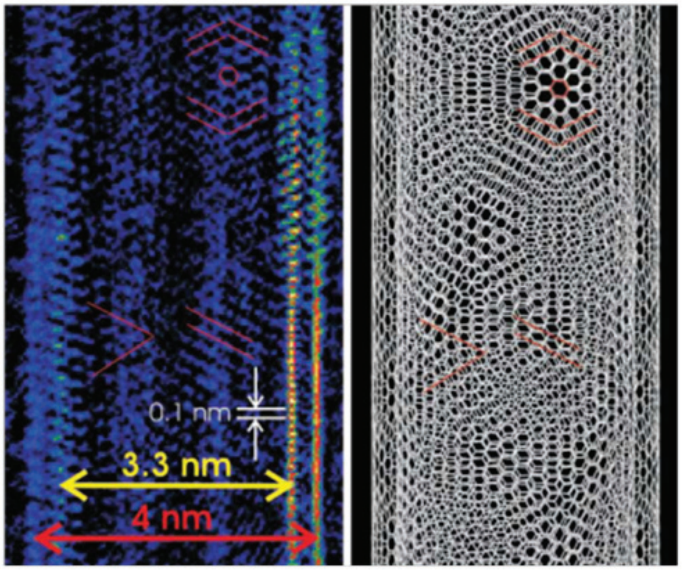

FIGURE 3-5 Coherent diffractive imaging reveals the chirality and registration of the two walls of a double-walled carbon nanotube.
SOURCE: Zuo et al., 2003.

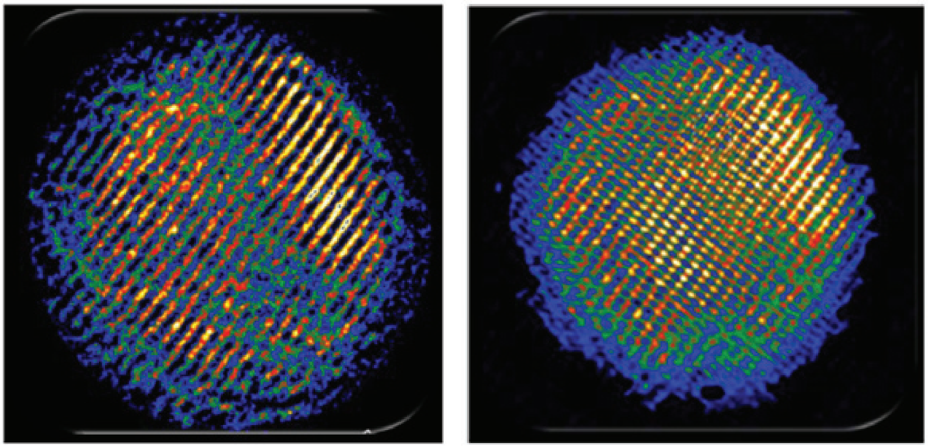

FIGURE 3-6 Coherent diffractive imaging was used to refine a low-resolution image of a cadmium selenide quantum dot (left) and to enable visualization of the separation between atoms in the crystal.
SOURCE: Huang et al., 2009.

of the dynamics of that bonding given that clusters are vibrating and moving, not merely sitting, on the support structure. Finally, there is a need to better merge theory and experimentation to sort out the many atoms and many excited states that actually exist on the catalyst's surface.

PARTICLE CHARACTERIZATION NEEDS FOR NANOCOMPOSITES

Lee Silverman of DuPont's Central Research and Development Laboratory provided an industrial perspective on the kinds of tools needed to analyze nanomaterials. Nanotechnology, he said, is a huge field that includes nanostructured materials, nanotextured surfaces, nanoscale-thick surface films, nanoscale devices, and nanoparticles. "DuPont's interest is in adding nanoparticles to polymers to try to augment the properties of already existing polymer platforms and extend the material applications," said Silverman. "We believe that manipulation of materials on a very fine scale is broadly applicable across all sorts of material platforms, and nanotechnology enables you to combine different property sets into specific materials." As examples, Silverman said that nanoparticles added to a polymer can improve its rheological properties in the molten state and its mechanical properties once the material has cooled. Nanomaterials can add barrier properties to a film while enabling it to remain transparent. For single property materials, turning to nanomaterials is not necessary. Aluminum, for example, makes a great conductive film, and metal films in general make superior barriers. Particle dimensionality plays a large role in defining the bulk physical properties that a nanomaterial can add to the material being designed, and Silverman briefly described the design rules that come from that relationship. "If you want transparency or photonic properties, you use spheres," he explained. "If you want electrical conductivity or thermomechanical behavior, you use rods. If you want barrier properties or flame retardant properties, you turn to plates." Once the nanomaterial is chosen, the polymer chemist selects the polymer that will serve as the matrix based on other physical properties such as temperature capability or tribilogical properties. The real work, said Silverman, comes in developing the nanocomposite so that it has the desired properties and is manufacturable. "Anyone who's done polymer processing understands that it's really easy to take an extruder that's full of polyester, throw clay in it, and make something that comes out with the mechanical properties of chalk and not useful to anybody." In the end, nanocomposite systems require compatible particles, polymers, and processes.

Probing Complex Materials

Although it is interesting scientifically to examine single particles, polymer chemists are more interested in materials with high loadings of the nanoscale filler, and analysis at this level is very difficult (Figure 3-7). It would be useful to know the spacing of the particles in a matrix, and researchers have tried to use small-angle x-ray scattering (SAX) to get

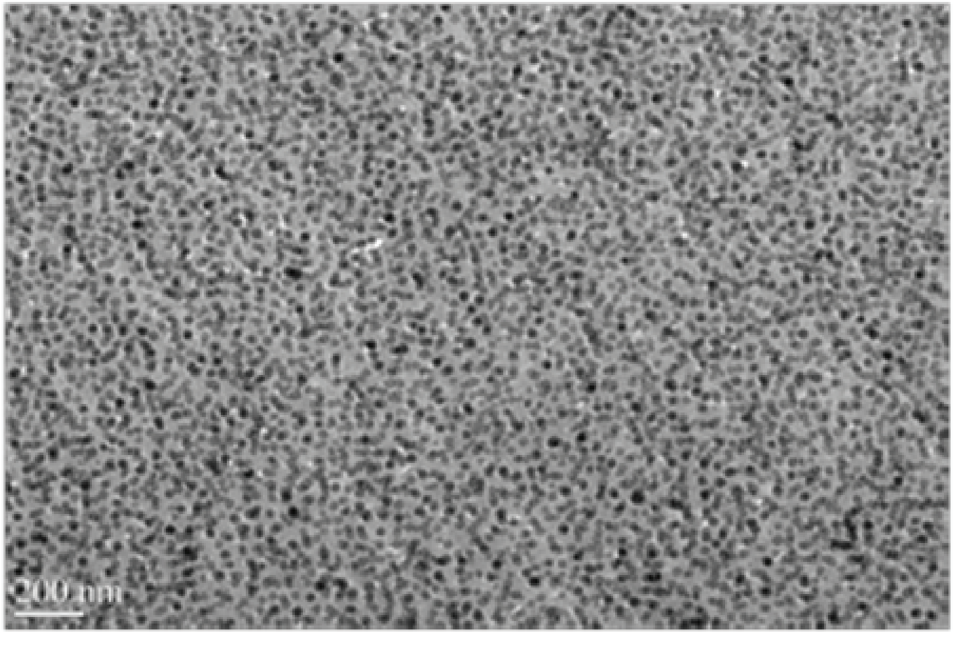

FIGURE 3-7 Silica nanoparticles in polystyrene.
SOURCE: Silverman, 2010.

at the microstructure of a heavily loaded polymer. However, SAX only provides limited detail when an 80-nanometer-thick film is loaded with 20-nanometer-diameter particles and there is little information about how the particles are spatially organized. Silverman also noted that transmission electron tomography is useless in this type of system because the particles are too concentrated.

In his research, Silverman is most interested in plates and rods, because he is concerned with creating nanocomposites with useful mechanical characteristics such as barrier or permeability properties for gases and liquids. Studies on permeability conducted in the late 1960s showed that relative permeability falls substantially as the aspect ratio of the nanorod increases (Nielsen, 1967). Because aspect ratio is the key feature, it would be desirable to have a technique for measuring the aspect ratio in a clay nanocomposite, but such a technique does not exist. Silverman cited another example, this one from the mid-1990s, of a model that relates the percolation threshold of a composite to the ellipsoid aspect ratio of the filler particles as they progress from plates to spheres to rods (Garboczi et al., 1995). The most complete picture of such composites covers spheres, but they are very uninteresting when it comes to them serving as barriers. The problem arises when trying to measure the aspect ratio of plates or rods when they are buried inside a composite. Other properties, such as conductivity, thermal conductivity, and elastic modulus also require particles with larger aspect ratios, not spheres.

Environment, Health, and Safety

The other issue that DuPont worries about, said Silverman, is environmental, health, and safety and product stewardship. “We believe that we are going to need to understand these materials very well before we start putting them in consumer products. We just cannot risk having another ‘asbestos’ or another kind of incident like that,” he explained. For materials that may shed fibers, that understanding must include a complete characterization of fiber dimensions and biopersistence, which are key factors in determining the pathogenicity of a fiber. Silverman believes that no usable techniques exist today that can provide that data for materials that are densely packed with nanomaterials. Many techniques are available for studying dry or dispersed spherical particles, but spheres are not very useful in making high-performance nanocomposites. For rods and plates, scanning electron microscopy (SEM) can provide some information, but only if the particles are in specific orientations and in dilute solution. SEM is not useful for composites. Transmission electron microscopy and SAX are more useful, but the information they generate is only helpful if the plates or rods are aligned in the sample.

Particle size distribution represents just one level of complexity to the analytical challenges found in dealing with composites. The next level adds in multimodal distributions of different types of particles or differently shaped particles. Particles can also be bent and have kinks, which makes them very interesting from the perspective of creating a nanocomposite but introduces still another level of complexity that cannot yet be analyzed at any satisfactory level. Certainly, Silverman noted, this field is hampered by a lack of the kind of physical characterization data that would enable a polymer chemist to predict how any given composite will behave. Silverman summarized the situation by stating that particle shape, size, and size distribution are critical determinants not only for creating useful materials but also for understanding how they will behave from an environment, health, safety, and stewardship perspective. “We know how to characterize monodispersed spherical systems, but characterization of plate and rod-like materials is onerous at best, and is almost impossible in real nanocomposites,” he stated. He added that surface chemistry of nanocomposites is another area that must be better understood, and one that also suffers from a lack of analytical techniques applicable to real-world materials. An audience member from the National Institute of Standards and Technology (NIST) commented that NIST has developed some special techniques for making subsurface measurements in some types of composites using scanning electron microscopy and scanning probe microscopy.

QUANTIFYING THE CHEMICAL COMPOSITION OF ATMOSPHERIC NANOPARTICLES

James Smith, of the U.S. National Center for Atmospheric Research (NCAR) and a visiting professor, addressed the phenomenon of new particle formation in the atmosphere and the recent progress that has been made in quantifying the composition of these spontaneously formed nanoparticles in our atmosphere. Nanoparticles form in the atmosphere by condensation to stable clusters formed by nucleation (Figure 3-8), or they can be emitted directly from sources such as diesel engines.

According to the theory of classical nucleation, particle formation is an endothermic process that creates a stable cluster in the atmosphere. As an endothermic process, molecules that collide and stick to one another tend to fall apart, and so the key is to cause enough collisions to occur that a pair is formed, then a triplex, and so on, until a “critical cluster” is formed. This cluster can contain any number of different compounds. Smith explained that sulfuric acid is a particularly sticky molecule in the atmosphere and that it plays a key role in the formation of critical clusters. Once a critical cluster has formed, any additional collisions involving the cluster will actually cause the particle to grow, which may be a rapid process, although it depends on other factors including constraints in kinetics, concentration and chemical nature of gaseous species, and particle surface properties. A post-doctoral fellow in Smith’s group at NCAR has developed

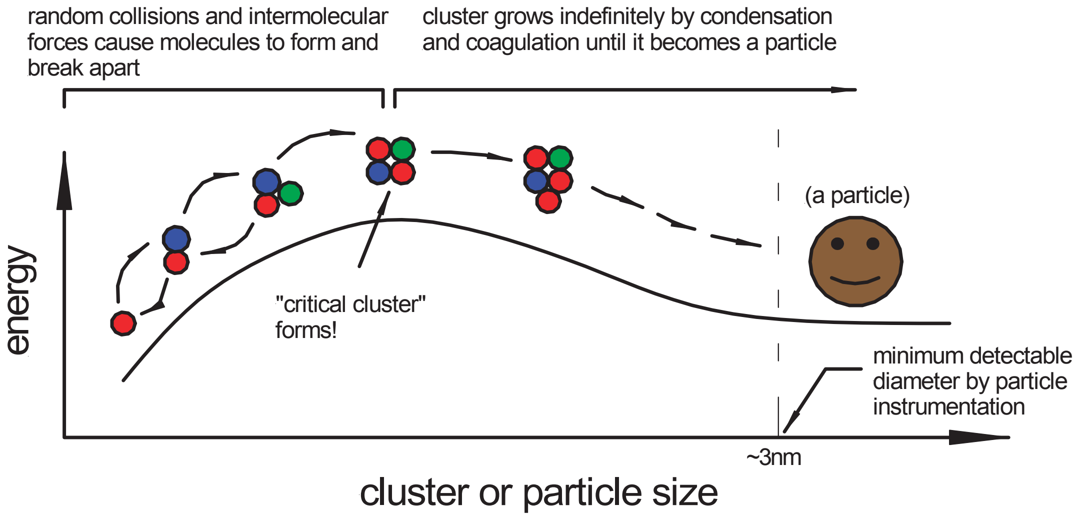

FIGURE 3-8 Formation of atmospheric nanoparticles by classical nucleation.
SOURCE: Smith, 2010.

a unique instrument that for the first time provides direct chemical measurements of neutral clusters in the atmosphere. Smith asked, "Why should we care about new particle formation?" To answer that question, he presented data from the Po Valley in Italy, which is a much polluted region. At one time, researchers thought that particle formation would not occur in such heavily polluted areas, because existing aerosols in the local environment would capture all of the small clusters before they could grow large enough to act as nucleation centers. That idea was proven wrong when it was observed that there can be sudden bursts of particle formation when the atmospheric boundary layer (part of troposphere closest to the Earth's surface) lifts in the afternoon. Particle formation can produce as many as 100,000 particles/cm^3, and growth can be as rapid as 20 nanometers/hour. At 100 nanometers in size these particles can then act as nuclei for cloud droplet formation. Researchers have been modeling this event. They estimate that new particle formation can contribute up to 40 percent of the cloud condensation nuclei in the boundary layer and up to 90 percent in the remote troposphere. Given these numbers, said Smith, "It is imperative to understand this growth event and be able to predict it in models in order to actually get at the role of aerosols in climate." The real mystery is why these nanoparticle growth rates are so high. Smith asked, "What species, other than sulfuric acid, contributes to this remarkable growth?" He presented a collection of observations that detail the growth rates of these particle formation events and make clear that something other than sulfuric acid is involved. These events occurred in a wide range of environments from around the world, from Tecamac, Mexico, near Mexico City, to McCrory Island in the South Pole. "What these data show, universally, is that the growth rates are between a factor of 2 and a factor of 50 higher than is predicted by the only species we really know with 100 percent certainty contributes to growth, and that's sulfuric acid," said Smith. "So the question is, what species are contributing to this?"

Uncovering the Role of Amines

The challenge in searching for these mystery agents is that the quantities of material that need to be analyzed fall in the picogram range. Ideally, Smith will collect about 15 picograms of 5-nanometer particles, but at best, he will collect 800 picograms of a 20-nanometer particle. To analyze these samples, his team has developed an instrument they call the thermal desorption chemical ionization mass spectrometer (TD-CIMS) for characterizing the composition of 8- to 50-nanometer particles. After describing how the instrument works, Smith presented data produced by the instrument from 20-nanometer particles sampled in Atlanta, a strongly sulfur-dominated environment. The instrument revealed large amounts of sulfate compounds, as expected, but also dimethylamine. Smith repeated these measurements on particles collected at Hyytiälä Forestry Field Station in Finland, where they found large amounts of aminium ions. Indeed, measurements from all of the sites his team visited revealed the presence of amines. From these observations, he concluded that aminium salt formation is an important mechanism that accounts for 10 to 50 percent of new nanoparticle growth in the atmosphere (Smith et al., 2010). Smith concluded by stating that acid-based chemistry plays an important role in the formation and growth of these new particles and that amines appear to be important compounds involved in new particle growth. "Time and time again," he said, "We're starting to hear in the atmospheric aerosol field about the growing awareness of the impact of amines on atmospheric aerosol formation." But despite this awareness, very little is known about amines, where they come from, and what their fate is in the atmosphere. Acquiring that information is critical to understanding their impact on the environment and climate, and that, explained Smith, requires more and better atmospheric measurements.

Discussion

Doug Tobias of the University of California, Irvine, asked if the sources of these amines are being worked out. Smith replied that currently there is no real idea of where they originate.[2] However, he said a new instrument can measure amines in the gas phase. The data from this instrument show that the sum of all the amines is about the same as the total concentration of ammonia in the atmosphere. Work from his team suggests that when an ammonium sulfate aerosol is exposed to gaseous amines, the amines can partition into the aerosol and displace the ammonia, producing an aminium sulfate aerosol. Observations by Smith's team and others suggest that agriculture may be a significant source of amines in some parts of the United States and the rest of the world. Amine levels also show diurnal variation, which Smith hypothesized might be related to temperature control.

PARTICLE DESIGN AND SYNTHESIS FOR CATALYSTS

Abhaya Datye of the University of New Mexico reiterated the importance of catalytic technologies to the U.S. economy. Catalysts, he said, are engines that operate at the nanoscale and generate more than $1 trillion in economic activity in the United States each year. Although many people imagine catalytic reactors as being enormous, on the scale of a chemical refinery, they come in all sizes, some as small as the battery that fits in a laptop. In fact, one company has developed a catalytic fuel cell designed to power a typical laptop for about 20 hours. Nonetheless, most catalysts, certainly in terms of volume, are used in large-scale chemical production where it might take 6 months to produce one batch of catalyst needed to turn natural gas into liquid fuels on a scale of metric tons. Given that scale, it is critically important to be able to make catalysts, which are composed of complex nanoparticles, in a highly reproducible manner, which requires the ability to characterize catalysts in great detail.

Probing the Interactions Between Catalyst and Support

Nanoparticles make good catalysts because they provide large surface areas on which both catalysis and contact between the particles and their support material can occur. The latter is critical because many catalysts are bifunctional and require the participation of both nanoparticle and support to drive catalysis. Datye noted that recent work with gold nanoparticles on a titanium dioxide support showed unexpected activity in catalyzing oxidation of carbon monoxide. This activity peaked at a particle size of 3 nanometers, suggesting that some interesting interactions occur between the particles and the support. Because this reaction took place at room temperature and because gold is less expensive than platinum, there is a significant incentive to characterize the nanoparticle-support interactions to better understand how to make use of this discovery. In reviewing the challenges to catalyst characterization, Datye said, "Of course, we want to know the size, shape, bulk and surface structure, composition, oxidation state, and the location of individual atoms." In particular, catalyst researchers would like to pinpoint the location of promoter atoms that are present at parts per million levels and have a significant impact on a catalyst's behavior. Catalyst designers also want a better understanding of the interface between the nanoparticle and its support, as well as the location of nucleation sites and atom trapping sites, all under reaction conditions. This is a difficult challenge, although the development of aberration-corrected transmission electron microscopy (TEM) will help the field tremendously. So, too, will recent advances in performing in situ TEM at pressures up to 1 bar in closed cells, and in energy dispersive x-ray spectroscopy (EDS) and EELS. Datye presented a few examples of how these techniques have been used to study catalytic systems. One example showed how aberration-corrected TEM was used to reveal surface features on a 6-nanometer platinum nanoparticle (Gontard et al., 2007). From such images it is possible to see steps on the particle's surface and therefore to determine how the facets of the nanoparticle interconnect. These interconnects are important features because they are where some of the most active catalytic sites may lie. Annular dark-field electron microscopy is another useful technique that provides atom-by-atom structural and chemical information. Images of the atoms on a single sheet of boron nitrite clearly show the location of boron, nitrogen, carbon, and oxygen atoms (Figure 3-9) (Krivanek et al., 2010). This technique acquires images on a relatively low-power 60 kilovolt microscope. To really understand how a catalyst works, it is necessary to obtain structural information at the single atom level. Aberration-corrected TEM images combined with EELS data can provide such information. Datye described how single lanthanum atoms were imaged inside the bulk structure of a calcium titanium oxide support (Varela et al., 2004). The small size of the EELS probe allowed the material to be scanned column by column to determine the chemical signature of each atom and its state.

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[2] After the workshop was held, new information on atmospheric amines has become available. For example, see Ge, X., A. S. Wexler, and S. L. Clegg, 2011. Atmospheric amines—Part I. A review. *Atmospheric Environment* 45(3):524–546.

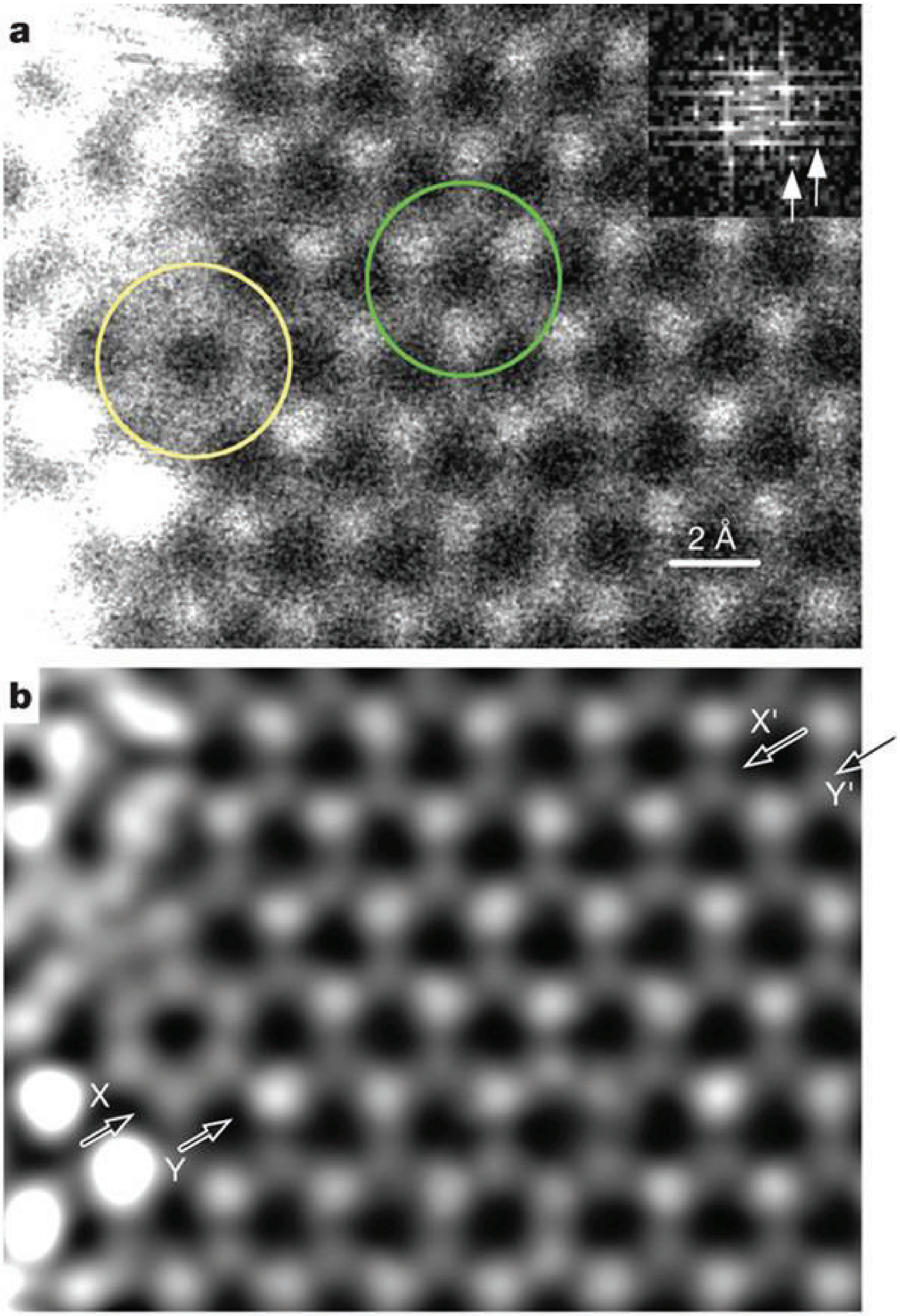

FIGURE 3-9 Annular dark-field scanning-tunneling electron microscope image of monolayer boron nitride (BN). (a) As recorded, and (b) Corrected for distortion, smoothed, and deconvolved. The area circled on the right in (a) indicates a single hexagonal ring of the BN structure, which consists of three brighter nitrogen atoms and three darker boron atoms. The circle on the left indicates a deviation from the pattern. Inset at top right in (a) shows the Fourier transform of an image area away from the thicker regions. Its two arrows point to reflections of the hexagonal BN that correspond to recorded spacings of 1.26 and 1.09 Å. The image was recorded at 60 kV primary voltage, and the probe size was about 1.2 Å.
SOURCE: Reprinted with permission, Krivanek et al., 2010.

Catalysts by Design

Given this level of detailed structural information, the next step, Datye explained, is to use the information to control the features of a catalyst by design. And, in fact, several groups have been able to do just that. For example, Greeley and colleagues were able to design alloys of platinum and early transition metals that were superior oxygen reduction electrocatalysts compared to platinum alone (Greeley et al., 2009). Key to the effort's success was the careful design of the catalyst's surface. Wang and colleagues created a multimetallic gold, iron, and platinum nanoparticle that proved to be a highly durable electrocatalyst (Wang et al., 2011). In this case, the deposition of 1.5-nanometer iron and platinum particles on gold yielded nanoparticles with five-fold symmetry, a structure not seen in bulk platinum materials and one with many exposed facets at which catalysis can occur. This structure was far more stable under catalytic conditions than one constructed from pure platinum particles on a carbon support. The final step in intentional catalyst design is controlling the site of nucleation; that is, controlling the exact placement of catalytic nanoparticles on the support surface. Datye, for example, is working with graphene sheets that have corrugations on the order of an angstrom and is using those corrugations as nucleation sites to anchor ruthenium nanoparticles. He said Farmer and colleagues have capitalized on information about the atomic-level energetics of cerium to stably anchor small gold nanoparticles (Farmer and Campbell, 2010). In real-life application, catalysts undergo changes over their lifetime. For example, by the end of its lifetime, the platinum in an automobile catalytic converter no longer disperses evenly over the support but agglomerates in clumps. It would be useful to understand the mechanism by which the platinum no longer takes the form of a nanoparticle. Using in situ TEM to study this process, Datye has discovered that the clumps appear to form via Ostwald ripening. He explained that it is actually possible to see particles disappearing rapidly and that, by observing this happening many times, he concluded that the particles are not evaporating, which would happen over a much longer time period. Instead, he believes that the particles emit atoms to the surface and then diffuse across the support surface. The particles then form clusters, a few atoms across, at step edges on the support surface in much the same way that blowing leaves collect against a curb. As the particles grow, they become pinned against these edges and eventually become the clumps seen in an aged catalyst. As a final example of the type of structural detail that modern microscopy can provide, Datye described the use of high angular annular dark field scanning transmission electron microscopy to produce tomographic images of nanostructured heterogeneous catalysts. In one study, the investigators compared the dispersion of platinum and rhenium nanoparticles on two different supports. On a typical Vulcan carbon black support used in fuel cells, particles were found in localized areas, but on Norit activated carbon the particles were distributed evenly throughout the support. This suggests that activated carbon provides more nucleation sites to form smaller clusters of metal. To summarize, Datye said that these developments in electron microscopy are providing unprecedented insights into the structure of these catalysts. "As we develop better strategies, we should be able to make these catalysts more stable and more active," he said.

NANOPARTICLE DISPERSIONS

In his presentation, **Yi Qiao** of the 3M Corporate Research Process Laboratory discussed some of the challenges facing those who need to characterize nanoparticle dispersions used in industrial applications. He said there is a disconnect between what academia uses to make such measurements and what industry needs to help its efforts in process control and quality monitoring. To meet the needs of a manufacturing environment, a measurement technique must be fast enough to provide feedback on a meaningful timeframe, have few restrictions for sample preparation in terms of nanoparticle concentration and purity, and be able to distinguish "good" from "bad" so a line operator can make necessary adjustments to the manufacturing process in real time. To address that disconnect, Qiao and his colleagues at 3M have developed two techniques that are now used in manufacturing plants for process monitoring and feedback control. The first technique uses a device called a microfluidic Y-cell (Figure 3-10). This device takes advantage of the fact that fluid flows through a microfluidic device in laminar mode; that is, two fluid streams flowing next to one another will not mix. When a nanoparticle-loaded fluid is introduced next to a buffer solution at one end of a microfluidic channel and the fluids are allowed to flow through the channel, the only nanoparticles that enter the buffer stream will be those that diffuse into it. The diffusion coefficient, which reflects the size of a nanoparticle, can then be measured by passing a laser beam through the microfluidic channel (Figure 3-11).

This very simple technique provides a measure of nanoparticle size in real time. A small amount of a process stream can be diverted into the Y-cell device, providing a line operator with the information needed to make adjustments to a process in real time to ensure particle size falls within the desired parameters. The technique, however, works best with particle sizes less than 15 nanometers in diameter. For larger particles, diffusion occurs too slowly for the device to measure size changes within a useful timeframe. Dielectrophoresis is proving useful for characterizing larger particles, even in the micron range, in manufacturing settings. Qiao and colleagues used microfabrication techniques to create an electrode array that can trap nanoparticles when an alternating electric field is applied to the array. Once the nanoparticles are trapped, the electric field is turned off and the particles are allowed to diffuse, washing out the density

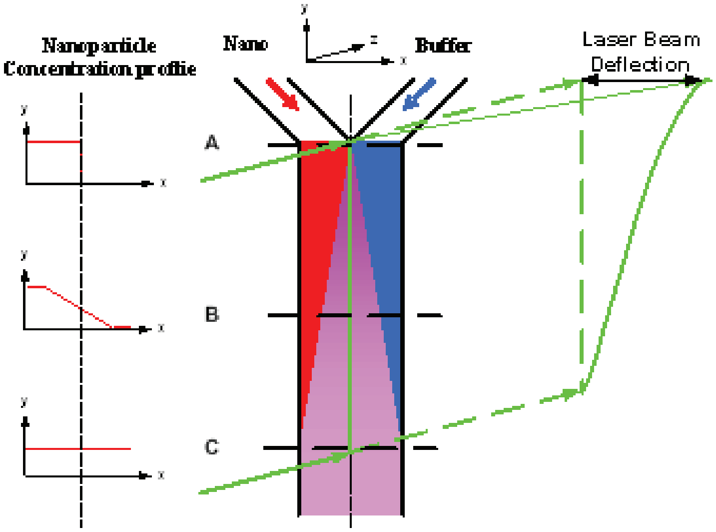

FIGURE 3-10 Microfluidic Y-cell for nanoparticle size measurement.
SOURCE: Qiao, 2010.

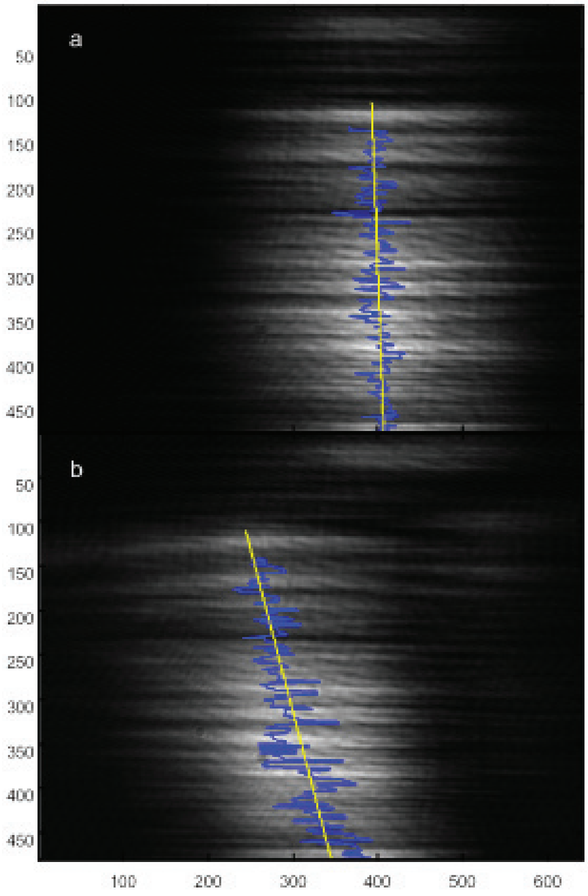

FIGURE 3-11 In a microfluidic Y-cell, a laser beam shows no deflection prior to the admission of nanoparticles into the channel (top). Once nanoparticles are introduced into the channel, the laser beam is deflected with a slope that reflects the size of the nanoparticles.
SOURCE: Qiao, 2010.

gradient that was created by the electric field. A laser beam is then used to measure the speed with which the particles move across the gradient. Key to this device is its ability to make an electrode array capable of generating a large electric field gradient that can overcome Brownian motions. Because the strength of the electric field is controllable, it is possible to measure both nanoparticle aggregates and individual nanoparticles in real time.

DECODING THE UNIVERSE AT THE NANOSCALE

Rhonda Stroud of the Naval Research Laboratory explained that the Navy has long been interested in nanoparticles, primarily for their application as propellants, in photovoltaics, and as fuel cell catalysts. As a result, she has developed a wide range of tools for analyzing the composition of nanoparticles. Some of these methods have proven useful for studying the cosmic origins of the 40,000 tons of extraterrestrial dust that enters Earth's upper atmosphere annually. Although this type of analysis may seem far afield, the challenges to characterizing these types of nanoparticles are the same as those for environmental and engineered nanoparticles. Nanoparticles form in large quantities around dying stars and in interstellar gas clouds. Most of the particles that bombard Earth ablate in the upper atmosphere. In particular, the particles in the 100-micron range, which make up most of the dust's mass, vaporize completely (Figure 3-12). Some of this vapor recondenses to form individual nanoparticles in the upper atmosphere. These nanoparticles are an important source of iron and possibly sodium; therefore, they may play an important role in climate processes.

Stroud and her collaborators at NASA would like to answer three important questions about cosmic dust using state-of-the-art analytical tools:

- Did the dust form in our solar system or around another star?
- How did the dust form?
- Is it pristine or has it been heated, shocked, irradiated, or otherwise altered?

Cosmic nanoparticles have a variety of compositions. Most are silicates, although nanodiamonds may in fact be more abundant. Research has identified dust particles made of silicon carbide, magnesium aluminum oxide in spinel form, graphite, aluminum, calcium-aluminum oxides, and silica nitrite. "The majority of the materials analyzed so far are refractory-type things, essentially interstellar sandpaper materials," said Stroud. "This is part of why they've survived 4.5 billion years."

Snapshots of Single Grains of Dust

One approach to studying cosmic nanoparticles is to map the isotopic signature of individual grains of a meteorite. Stroud and colleagues have developed methods for using a focused ion beam to slice particles as small as 200 nanometers and a combination of Z-contrast imag-

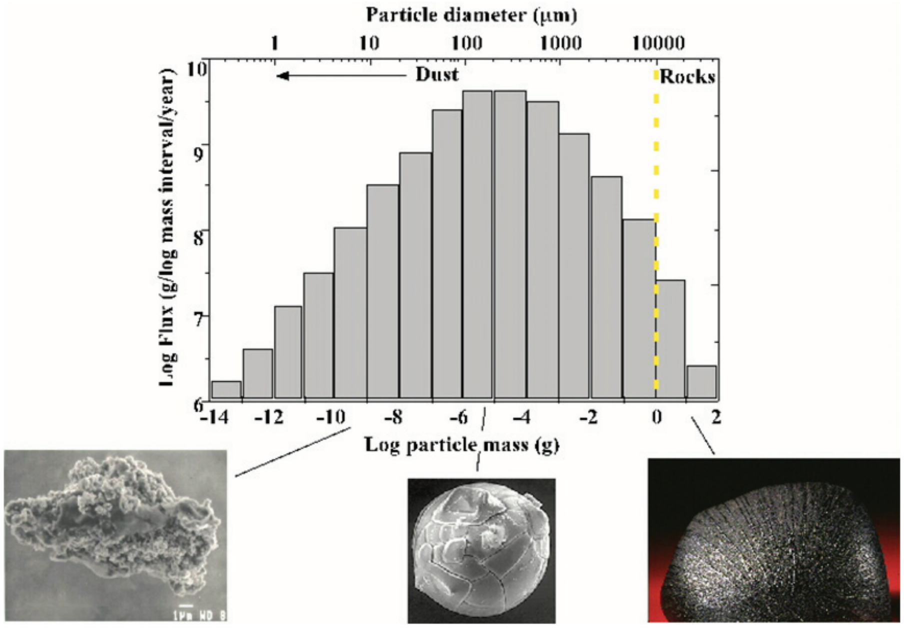

FIGURE 3-12 The flux of extraterrestrial dust.
SOURCE: Stroud, 2010.

ing and EDS to measure the elemental composition of the exposed grains (Stroud et al., 2004). She showed an image of a silicon carbide nanoparticle with an isotopic signature indicating it came from a nova star (Figure 3-13). The image also revealed a number of subgrains that Stroud presumes came from the same star because they were trapped inside this nanoparticle. However, the subgrains are below the size limit at which she can measure individual isotopes to confirm their origin.

Stroud explained that the SEM instruments have a beam spot size of approximately 100 nanometers, and although it is possible to make the spot smaller, it has to be big enough to capture sufficient numbers of atoms to make accurate isotopic measurement. "Mostly we're looking for a few rare isotopes, and there are just not enough atoms present in a 50-nanometer particle in general to get a good isotopic measurement," she explained. Analyzing the origins of individual nanodiamonds, which average about 2 nanometers in diameter, is therefore challenging. In 1987, researchers reported identifying nanodiamonds with an isotopic signature indicating they were formed outside of the solar system (Daulton et al., 1996). However, these measurements were done as bulk average measurements, and they were identified on the basis of signatures in krypton and xenon isotopes. "The problem here is that there is only one xenon atom for 10^5 of these nanodiamonds, so it is not clear which fraction of those nanodiamonds really formed inside our solar system and which came from supernova or somewhere else," explained Stroud. "We would really love to be able to go in and locate the individual xenon atom and say, Aha! That one is probably from a supernova." Identifying nanodiamonds as coming from outside of the solar system is also problematic because spectroscopic studies since 1987 have consistently demonstrated that there is a soot-like component on the nanodiamonds. Stroud recounted a variety of microscopy studies showing that nanodiamond particle aggregates contain multiple phases of poorly ordered carbon sheets, agglomerated nanodiamonds, and what appears to be ordered graphite. To accurately characterize the nanodiamonds, Stroud needed a better microscope. The new aberration-corrected NanoSTEM microscope at Oak Ridge National Laboratory (ORNL) fits the bill. Using this instrument, she and her collaborator at ORNL produced images with subnanometer resolution that clearly identified the various phases of carbon present as well as individual impurity atoms (Figure 3-14). These images showed that the nanodiamonds contain impurities ranging from fluorine and neon to vanadium and chromium, but nothing nearly as heavy as xenon. The presence of individual neon atoms in the secondary phases of carbon, and not in the nanodiamonds, argues for a supernova origin for that material.

Stroud used EELS measurements to further characterize the sheet-like or sub-nanometer-thick layer of carbon associated with the nanodiamonds. She found that the electronic profile of sheet-like carbon was spatially distinct from nanodiamond surfaces in the agglomerate that makes up the dust particle. Inside diamond, however, the electronic signature was distinctively that of diamond. These data suggest that the nanodiamonds did not form in the supernova, but, rather, in the interstellar medium. Flash heating of organic matter would have converted some of that matter to nanodiamond and some to amorphous forms of carbon. In summary, Stroud said that the problem of performing multiple, coordinated,

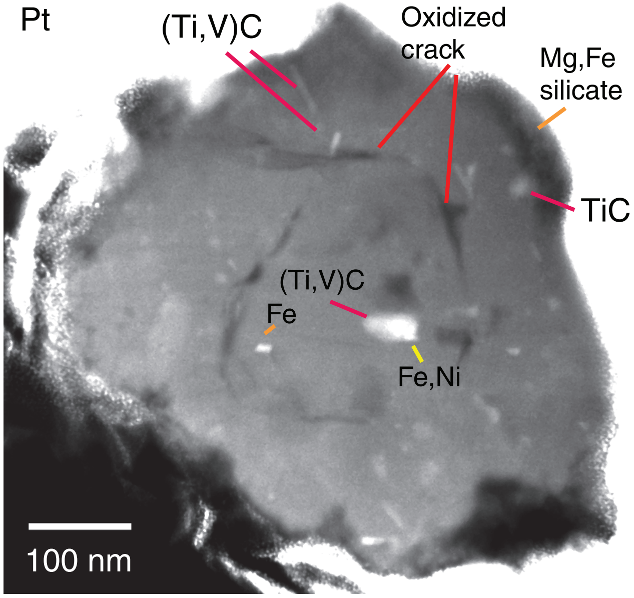

FIGURE 3-13 Z-contrast imaging and energy dispersive spectroscopy reveal subgrain structure and elemental composition of a silicon carbide cosmic nanoparticle.
SOURCE: Stroud, 2010.

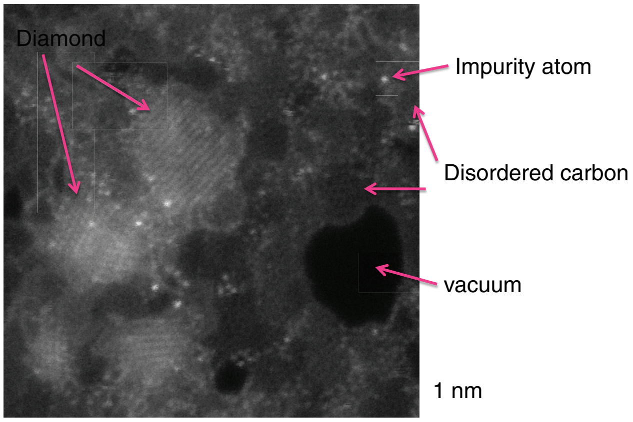

FIGURE 3-14 Dark-field scanning transmission electron micrograph of cosmic particles from the Murchison meteorite.
SOURCE: Stroud, 2010.

nanoscale analyses on particles 200 nanometers and larger has been solved. “We can pick up individual grains, do the isotope measurements, do transmission microscopy, do whatever we like,” she said. “It gets a lot harder to do multiple analyses when you get below 200 nanometers.” Aberration-corrected electron microscopes are effective tools for doing atomic-scale characterizations on periodic or ordered samples with well-constrained impurities. Conducting such analyses on natural samples, where there may be large numbers of different elements present and phase mixtures, some of which are disordered, is more difficult but can be done with the right preparation and patience.

Discussion

When asked by Barbara Finlayson-Pitts about how the noble gas neon manages to remain in a dust fragment for billions of years, Stroud said that the noble gas atoms are only seen when more than one layer of carbon is present. They are likely trapped inside C_{60} cages that formed at the same time as the nanodiamond.

OPEN DISCUSSION

In response to a question from **Jim Litster** of Purdue University about whether he can measure aggregation or the degree of dispersion of nanoparticles in a matrix, Silverman explained that the methods he uses cannot yet make those distinctions. Currently, no tool exists that can provide adequate information at that level of detail. Nuzzo then asked if it was really necessary to make measurements with atomic-level detail for materials such as engineering polymers that are used in bulk-scale applications. Silverman responded that it is not necessary from a process control point of view to know the exact location of every atom in an engineering polymer—a statistical average over a square kilometer or 50 pound sample will do. However, such information is needed to understand how specific properties of a composite material arise, and perhaps more importantly, to understand how the material can fail. Agglomeration of the nanoparticles in a matrix can be meaningless in some materials or applications and catastrophic in others; understanding which will be the case requires the ability to first create a perfect dispersion to show that agglomeration does not adversely affect material performance. **Mark Barteau** from the University of Delaware asked if work to characterize catalyst structure under reducing conditions has been done to the neglect of work to study catalysts under more challenging oxidizing conditions. Nuzzo replied that entire industries have been built on conducting catalysis under reducing conditions, including the petrochemical industry, but he agreed that interesting oxidative reaction conditions require the same amount of attention. Doing so is proving to be a big challenge, however, particularly because most atomic-level characterizations are performed in a vacuum. Datye added that new heating elements that can withstand high-temperature, oxidizing conditions are starting to move that aspect of the field along. **Levi Thompson** of the University of Michigan asked how meaningful these techniques are given the rapid timescale at which catalysis occurs. Nuzzo responded that the rapid timescale of these reactions means that, from a dynamic perspective, the catalysts are in fact sitting still most of the time. However, techniques have been developed to study the conformational dynamics in proteins in real time, which may be useful for studying heterogeneous materials. In response to a question from **Vicki Grassian** of the University of Iowa about small particle monitoring, Lippmann said that there is a clear need for better monitoring of the ultrafine particles to which people are exposed in the environment.

4

Analyzing Nanoparticles in Complex Mixtures

In real-world applications, synthetic nanoparticles are rarely if ever encountered in their native form. Rather, they occur mixed with various inert ingredients to create pills, tablets, and pellets. In the environment, however, nanoparticles interact with other materials, becoming coated with organic matter or clumping together in agglomerates. Research has shown that these and other transformations produce materials with chemical, toxicological, and environmental behavior that differ, sometimes in profound ways, from that of the native nanomaterial. As a result, it can be challenging to predict the consequences of releasing a nanomaterial into the environment. Speakers in this session addressed some of the challenges to measuring and predicting the properties and behavior of complex nanoparticle formulations and discussed the often surprising findings that come from studying nanomaterials as they occur in the real world.

DESIGN AND MANUFACTURE OF DELIVERY FORMS FOR SMALL PARTICLES

James Litster of Purdue University spoke about particles in the micron and submicron size range that are used in industrial applications, with a specific focus on the delivery forms for those particles. For example, catalysts and absorbents are often used in pellet form, detergents in granular form, and drugs in micronized form. Many of the new drug molecules being developed are poorly soluble, so drug formulators are using small particle delivery vehicles to increase the solubility and uptake of these molecules. Dry powder aerosols based on relatively large lactose particles are used to deliver drugs into the lungs, although dispersion of the powder aerosol is often poor. Whatever the route of administration, the goal is to deliver a drug payload in a way that does not change the drug molecule and that does not allow it to aggregate.

Although particulate delivery systems are used widely in many industries to solve specific delivery problems, they are not without their own issues. Dry powders create dust and can be hard to handle. They can flood out of hoppers or not flow at all. If inhaled, they can cause health problems. “We want to take advantage of their properties, but we want to handle them in delivery forms that are suitable for us,” said Litster. To illustrate the versatility of powder processing, he listed many of the reasons for packaging small particles in dry delivery form (Table 4-1).

The processes used to make these delivery forms are many and varied, Litster explained (Figure 4-1). Materials can be compacted by tableting, dry granulation, or compaction. They can be mixed with a liquid binder in a fluidized system to form granules or spray dried from slurries or solutions.

With this variety of methods available for creating small particles, a major area of research involves determining how the choice of method, or a change from one method to another, impacts the structure of the delivery form and its distribution properties. The real goal of research in this field, explained Litster, is to understand both those processes and the properties they impact to facilitate design of a granule that disintegrates and disperses in a particular way, that has a certain resistance to attrition, or that has a certain chemical stability and shelf life. “This is a non-trivial and only partially solved problem,” he said.

Many barriers to progress in this area exist. Researchers lack a quantitative understanding of how microstructure develops during processing of complex, multiphase delivery forms. In addition, predictive and quantitative scaling rules, and process design models that track multidimensional distributions of properties are relatively rare. Finally, robust on-line techniques for measuring the microstructure and distributions of important properties also are rare.

TABLE 4-1 Reasons for Packaging Small Particles in Dry Delivery Form

Reason	Typical Application
To produce useful structural forms	powder metallurgy
To provide a defined quantity for dispensing and metering	agricultural chemical granules, pharmaceutical tablets
To eliminate dust handling hazards or losses	briquetting of waste fines
To improve product appearance	food products
To reduce caking and lump formation	fertilizers
To improve flow properties for further processing	pharmaceuticals, ceramics
To increase bulk density for storage	detergents
To control dispersion and solubility	instant food products
To control porosity and surface-to-volume ratio	catalyst supports
To improve permeability for further processing	ore smelting
To create nonsegregating blends of powder ingredients	ore smelting, agricultural chemicals, pharmaceuticals

SOURCE: Litster, 2010.

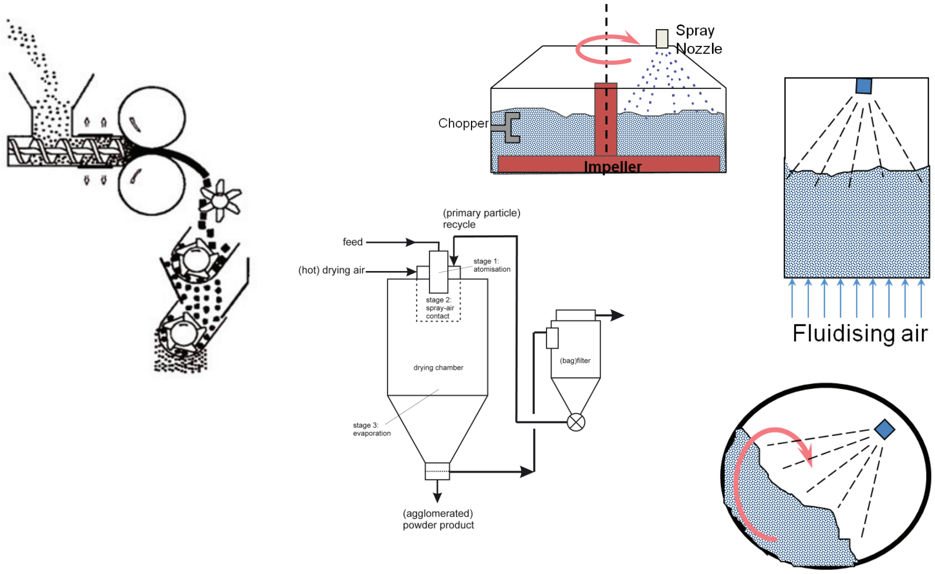

FIGURE 4-1 Approaches to creating delivery forms.
SOURCE: Litster, 2010.

Although these comments apply to powder processing in general, they are especially true when the primary particle size is less than 10 microns. In that size domain, Litster explained, "the surface forces that want the particles to stick together dominate over gravity and inertia of the particle, resulting in particles that are cohesive, flow poorly, and make complex structures with different levels of aggregation at different length scales."

Fine powders behave very differently because they don't fluidize properly. Litster demonstrated this fact with images showing the dramatically different behavior of a drop of liquid on a bed of fine powder versus coarse powder (Figure 4-2). The granule structure of fine powder is round, and the drop burrows into the bed and absorbs loose aggregates of the particles to make relatively round granules. Coarse powder does not have a uniform packing structure, and therefore the mechanism by which the liquid interacts with the powder is completely different. As a result, a disk-shaped rather than a spherical granule forms.

Models for Engineering Design

Creating an engineering design requires understanding at many different levels, including of the physics and accompanying models at different length scales. It is also necessary to understand the physical interactions that occur at the single-granule or single-particle level as well as at the bulk flow level. Also needed are macroscopic models that provide the structure of the delivery form or the distribution of properties and product models and account for how the delivery form

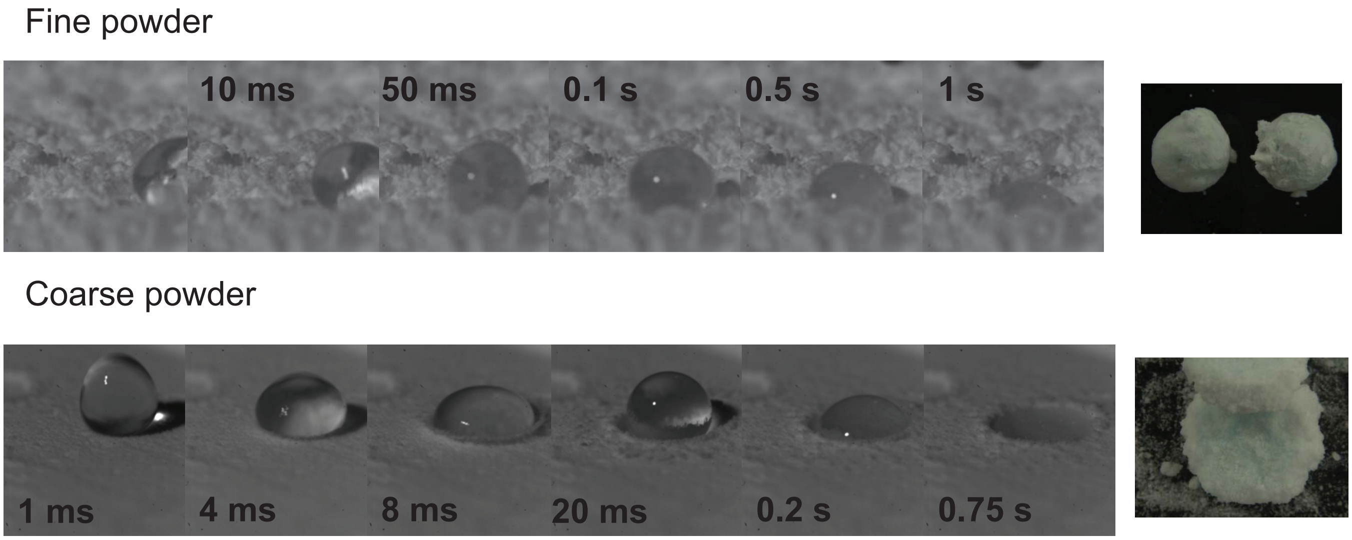

FIGURE 4-2 Differences in behavior for (top) fine powder (5 mm), and (bottom) coarse powder (70 mm).
SOURCE: Litster, 2010.

behaves when used as intended, that is, what happens to a medication tablet when it is swallowed or to a detergent granule when it is added to the washing machine. The properties of the particles of interest and the processing equipment used to make the delivery system serve as the input for the models, which span from the molecular to the bulk scale.

Together with his colleagues at the National Science Foundation-funded Engineering Research Center for Structured Organic Particulate Systems (SOPS), Litster is following a multiscale approach to compaction modeling, with the goal of developing function-structure relationships for the design and optimization of delivery systems. As an example of what this approach entails, he discussed a process wherein particles are used to surface coat a larger micron-sized particle, which then becomes part of a cluster of particles or granules and ultimately a tablet. The functions and properties of each of these particles must be characterized at different length scales. Also needed are modeling approaches that address length scales from the single-particle level through the macroscopic level, ultimately providing the tablet's density and chemical distribution.

Litster discussed two research projects that are being carried out at the Center. The first project involves micron-sized particles of an active pharmaceutical ingredient (API) that are meant to be delivered by an aerosol. The project's goal is to determine if drugs in this size range can be modified by coating them with smaller particles to turn cohesive powders into free-flowing powders that can be more easily metered and dosed in different delivery forms.

In a set of experiments, SOPS researchers used a mechanofusion approach to distribute a silica nanoparticle coating onto API particles and measured the bulk flowability of the powder versus bulk density. The resulting measurements revealed that the coating increased the bulk density of the API particles, which had the beneficial effect of increasing flowability.

Using atomic force microscopy, the SOPS researchers are currently studying a simpler system—one in which aluminum particles replace the API particles—to study how the roughness and morphology of the core particle affect adhesion forces and the properties of the final coated particle. They use a combination of modeling techniques to predict a distribution of adhesive forces across the core particle's surface. The experiments have shown that the adhesion force is substantially reduced when the particles are coated, primarily because the coating creates a larger separation between the API particles, which reduces the overall van der Waal's interaction. The experiments, said Litster, demonstrate that it is now possible to measure single particle properties for real particles that are nonspherical and have rough surfaces. Moreover, the measurements can be used to predict the behavior of the particles and to estimate how much coating is needed to produce the necessary level of disaggregation.

The second project involves making an agglomerate, as opposed to single particles, the delivery form. An intermediate step to making a tablet involves creating and then compacting a ribbon of a formulation, the key properties of which are its bulk density and its distribution. Near-infrared images of the ribbon revealed that variation in the density of the ribbon depends on the formulation used and the conditions under which the ribbon is produced. The ribbon's density affects the granule and ultimately the tablet properties.

The researchers question whether they can predict ribbon density on the basis of particle properties and process conditions. They have created a macroscopic finite element model that predicts the ribbon density distribution using data on the macroscopic bulk properties for the powder going into the ribbon-making machine. Now, the researchers want to be able to predict how the bulk properties of the ribbon would be altered by changes in the properties of the original mixture resulting from, for example, a change in the surface properties of the API.

To explore this idea, the researchers have created a multi-particle finite element model that represents a ribbon under stress. With this model, they can predict the behavior of a particle assembly under shearing or compaction. The surface energy, adhesive properties, roughness, and shape of the constituent particles are model inputs. The model also requires data on the mechanical properties of the particles, such as their elastic moduli and plastic properties.

In conclusion, said Litster, the end performance of small particles depends critically on how they are packaged. However, many problems still must be solved to predict product structure and performance from formulation properties and process variables. However, he added, multiscale approaches to both characterization and modeling hold promise for better engineered products.

Discussion

In response to a question about combination therapy and multiple drug absorption sites, Litster said that research has yet to address the issue of differential drug delivery of this sort, where one drug would be absorbed in the stomach and the other in the intestines. One possibility is to use some of the techniques for dealing with low-solubility drugs. In that case, making the drug particles tiny and delivering them in amorphous form can produce locally high drug concentrations in the stomach, where they will be absorbed faster than expected. It might then be possible to create larger, metastable particles that flow through the stomach and reach the intestines, where they will be absorbed.

Research is being conducted in these areas, and one approach to tackling this problem would be to measure primary properties and rate constants under well-defined conditions. Computer simulations could then predict what combinations of particle size, dissolution rate, and additional nucleation-inhibiting polymer would produce the best system.

In response to a question from Schwartz, Litster stated that the roles that thermodynamics and kinetics play in determining how particle size affects solubility remain controversial. Kinetics likely plays a role, but so, too, will thermodynamics because the concentration of drug in solution is significantly higher than the solubility of the most stable crystalline phase. Litster agreed with Schwartz's comment that a metastable phase will yield a higher solubility, and he added that the pharmaceutical industry is showing a great deal of interest in supplying drugs in a stabilized amorphous state. The downside of such an approach is likely to be reduced stability and shorter shelf life.

PARTICLES IN THE ENVIRONMENT

Pedro Alvarez of Rice University said there is a general consensus in the environmental engineering community that engineered nanoparticles are being used and introduced into commercial products at a rate that is much faster than the rate at which we are acquiring the information needed to ensure that these materials are compatible with the environment, that we can handle them responsibly, and that we can dispose of them properly. It is his belief "we are at that point in history where we can actually steward nanotechnology as a tool for sustainability as opposed to it becoming a future environmental liability, but this requires taking a proactive approach to risk assessment, and I would like to argue that we are not doing enough in that regard."

To make his point, he noted that the number of research publications on nanotechnology are doubling every 3 years, but the number of publications relating to environmental nanotechnology account for only 5 percent of that total. And in fact, the papers that actually make important contributions to understanding the fate, transport, reactivity, and bioavailability of nanoparticles in the environment account for only 0.25 percent of the total nanotechnology literature.

Alvarez's group's contribution to the field is in the area of how nanoparticles interact with microorganisms in the environment. Bacteria are the foundation of all ecosystems, but they also are very convenient models for studying cytotoxicity and therefore can serve as a useful model system for studying possible environmental impacts of nanotechnology. In other words, if a microbe is adversely affected by exposure to a substance, it indicates a need to worry about what the substance may do to higher order organisms.

After 7 years in the field, Alvarez has learned that it is difficult to generalize about the potential impact of nanomaterials because of the many ways in which they can interact with the microbial ecosystem. For example, some engineered nanomaterials, such as the fullerenes or ceria, require direct contact with the cell to exert a toxic effect. For those materials, anything that happens in the environment that hinders their bioavailability—becoming coated with organic matter, for example—could mitigate any potential toxicities. Other materials, such as quantum dots, can release toxic ions that kill microorganisms. Titanium dioxide nanoparticles and aminofullerenes can generate reactive oxygen species that kill microbes.

Understanding how these materials impact the microbial ecosystem is challenging because much of the work conducted today uses pure and very well-characterized nanoparticles, which Alvarez referred to as "virgin nanoparticles." However, nanoparticles can undergo a wide variety of modifications and transformations when they are in the environment (Figure 4-3). "They are going to agglomerate, they are going to be chemically or biologically transformed," he said. "They may aggregate and precipitate, and at the very least, they are going to lose coatings or acquire coatings."

Each of these modifications will affect a nanoparticle's mobility, reactivity, bioavailability, and toxicity. As a result, said Alvarez, the field has a real need for more analytical methods that allow for dynamic characterization of nanoparticles as they interact with bacteria in conditions that resemble their environment. For example, the idea of dose is not well understood because it is unclear how much of a material actually gets into a bacteria and whether it agglomerates or partitions inside a cell.

What is known, Alvarez said, is that nanoparticles tend to aggregate. Salts in the environment promote coagulation and precipitation, which reduce the potential toxicity of a nanomaterial. Aggregation reduces the specific surface area of a particle, which, in turn, decreases toxicity. Changes in surface chemistry and reactivity can also reduce the toxicity of aggregated particles compared to individual particles.

It is also clear that nanomaterials almost certainly end up in wastewater streams and ultimately in sludge. Therefore, it is important to consider the impact that nanoparticles in sludge might have on the terrestrial food chain. Using carbon-14 labeling, Alvarez's group has shown, for example, that fullerenes accumulate in earthworms (Li et al., 2010).

Commonalities

Alvarez made two points about commonalities. First, as the concentration of nanoparticles increases to the point that it exceeds the absorption capacity of the soil, the nanoparticle no longer exists in its original structure. Instead, the nanoparticle forms large aggregates and precipitates that are more difficult to bioaccumulate. To illustrate why this is important, Alvarez compared the bioaccumulation of C_{60} to that of the polynuclear aromatic hydrocarbon phenanthrene. In theory, phenanthrene is less hydrophobic than C_{60} and, therefore, should be less bioavailable. However, bioaccumulation of C_{60} is 100 times lower than that of phenanthrene because its molecular size makes it more difficult to transport across the cell membrane. "The take-home message here is that the traditional risk assessment protocol using thermodynamically based partitioning coefficients to predict fate in the environment does not work," said Alvarez.

The second commonality is found in the interaction of nanoparticles with natural organic matter (NOM). In the case of C_{60}, NOM can serve as a sponge that traps this compound, hindering direct contact and bioavailability, and therefore toxicity. In one set of experiments, Alvarez's team showed that adding just a few of milligrams of C_{60} to a bacterial culture caused the organisms to stop producing carbon dioxide, a sign of metabolic activity. Adding clean sand to the culture along with the C_{60} had no protective effect, but adding even

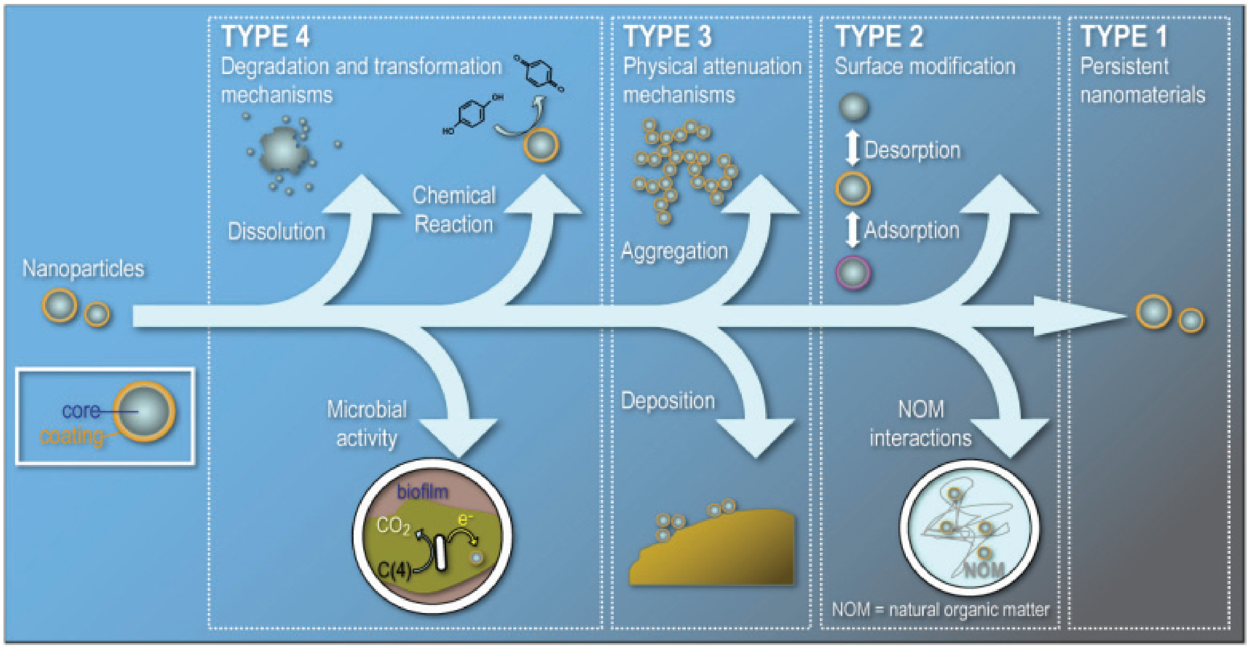

FIGURE 4-3 Processes that can possibly transform manufactured nanoparticles or modify their surfaces and aggregation states in the environment.
SOURCE: Alvarez et al., 2009.

a little bit of soil containing only 0.2 percent organic matter had a marked effect on bioavailability and restored metabolic activity (Li et al., 2008). They found that they could produce this protective effect by adding as little as 0.1 milligrams/liter (mg/L) of humic acid to the culture medium. Because of these results, and the fact that NOM levels in water in the environment are typically on the order of 3-10 mg/L or higher, Alvarez said he is much less worried about the acute ecotoxicity of C_{60}.

Particle coating can also influence nanomaterial toxicity, explained Alvarez. His group has shown, for example, that iron nanoparticles coated with polyaspartate do not stick to bacteria, eliminating toxicity. The caveat to this observation is that coated nanoparticles are also more stable in the environment and more likely to bind to NOM in water, which may increase transport in the environment. Therefore, there may be a tradeoff in terms of reducing the possibility of acute toxicity versus increasing transport and long-term accumulation.

The bottom line, said Alvarez, is that no matter how toxic a material might be, if there is no exposure, then there is no risk. Preventing exposure by intercepting nanomaterials before they enter the environment might be the most effective means of limiting potential environmental damage. If eliminating exposure is not feasible, then another approach is to engineer away the properties that make a nanomaterial hazardous without compromising the properties that make it useful. This approach was taken when hydrofluorocarbons were engineered to replace chlorofluorocarbons when the latter were found to be environmental hazards.

Nanoparticles Are Abundant in Nature

Alvarez reiterated the ideas that the environment is filled with nanoparticles and that, given the large number of naturally occurring nanoparticles compared to the number of engineered nanoparticles, it may be difficult to discern the risk from exposure to the engineered nanoparticles. He believes that the size-dependent properties of engineered nanoparticles are more accentuated than those of many of the naturally occurring nanoparticles that have been in contact with nature for millions of years.

To truly understand exposure and risk, there is a need to obtain more information about the sources of nanoparticles. To do so, three questions need to be answered:

- What are the main entry points of engineered nanoparticles and the scale of discharge into the various environmental compartments?
- What forms of an engineered nanoparticle are being discharged?
- What are the realistic, environmentally relevant exposures to those forms?

He said the matter of inventorying nanoparticle production, use, and release within well-defined spatial domains must be settled. There is still debate as to whether inventorying should be mandatory or voluntary, and whether products should have labels informing consumers about the presence of certain nanomaterials. Some in the scientific community have suggested that nanoparticles be labeled (for example, to be fluorescent, or with a radioisotope) so they can be traced in the environment.

Alvarez noted that in March 2009 Rice University held an international workshop on the eco-responsible design and disposal of engineered nanomaterials at which about 50 environmental engineers and scientists were asked to address the question, "What critical knowledge gaps and opportunities exist to inform and advance the design of environmentally benign engineered nanomaterials and the management of wastes containing them?" Figure 4-4 summarizes their consensus (Alvarez et al., 2009).

Alvarez concluded by saying that there is much to learn about nanomaterial bioavailability, potential toxicity, and mechanisms of action by looking at how these materials interact with bacteria and other microorganisms, with the implication that materials that impact microbial processes can seriously damage an ecosystem's health. The good news, he added, is that many things in the natural environment interact with nanomaterials in a way that reduces their bioavailability and therefore their potential to cause harm. Although nanotechnology-triggered microbial toxicity represents a worry, nanotechnology also offers many new approaches to addressing environmental problems in a more benign way. For example, nanomaterials may enable new approaches to disinfecting water that does not require the use of chlorine.

Discussion

Barbara Finlayson-Pitts commented that one message she got from Alvarez's presentation was that equilibrium modeling is not going to work, just as it is not working with atmospheric nanoparticles. Alvarez agreed with this assessment, noting that nanoparticles constantly change in the environment as they acquire and lose surface features and undergo reactions with materials in the environment. Therefore, modeling their fate in the environment is very challenging; models for predicting the behavior of nanomaterials are not going to be as accurate as are models for dealing with pure chemicals.

Finlayson-Pitts also asked Alvarez to discuss how the shape and dimension of a nanoparticle affects its health impacts. Alvarez replied that it is important to consider that there are two categories of properties that matter for determining health impacts. The first is how the particle moves to a receptor, and the second is the properties of the original particle (such as shape or dimension). In terms of impact

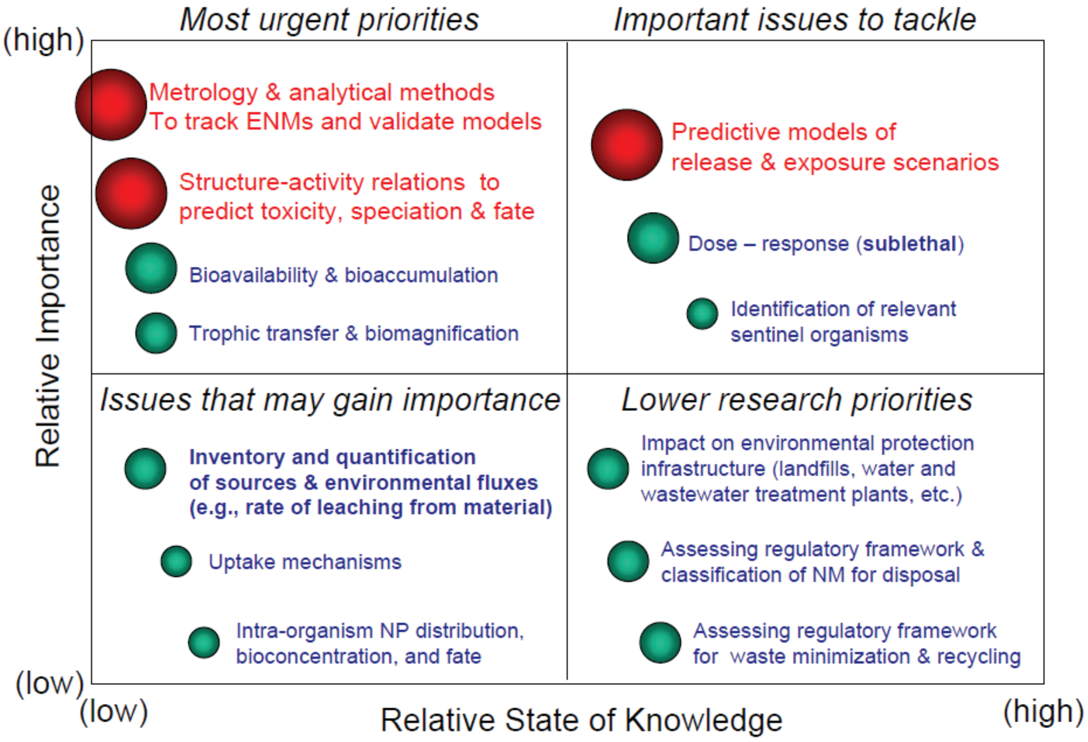

FIGURE 4-4 Toward eco-responsible nanotechnology.
SOURCE: Alvarez et al., 2009.

or reactivity, it may be that the properties of the original nanoparticle will end up being the most important, but that is still unknown.

Andrea Violi of the University of Michigan asked if there is more exposure to engineered C_{60} or to C_{60} particles emitted during combustion or volcanic eruption. Alvarez did not know the answer but noted that C_{60} reportedly can be produced by volcanic eruptions and that it might exist at trace levels in nature. He added, however, that when it comes to human health, the leading source of risk is likely to be associated with respiratory uptake of particles in the work environment.

SURFACE CHEMISTRY, TRANSFORMATIONS, AND GLOBAL IMPACTS

Vicki Grassian of the University of Iowa focused her remarks on transformations and surface chemistry of mineral dust, which makes up a large fraction of the aerosol mass. Mineral dust particles measure from about 0.1 microns (or 100 nanometers) to much larger particles. Particles at the smaller end of this range stay aloft for 1 to 2 weeks and are transported great distances by the atmosphere. During that 1- to 2-week time period, a lot of interesting chemistry takes place on the particle's surface, and the particle transforms as it undergoes surface reactions with other chemicals that enter the environment.

Mineral dust is composed of oxides and carbonates, and, as the catalyst community has demonstrated, particulate oxides are reactive materials. As a result, a large amount of rich chemistry occurs on the surface of mineral dust particles in the atmosphere. Grassian described six different types of surface reactions and mechanisms that might be operating. "What we try to do is design laboratory studies to better understand this surface chemistry," she said, with the goal of understanding the global impacts of small particles.

Grassian's research approach involves examining the individual components of mineral dust to determine how chemistry differs among the different clays, oxides, and carbonates that occur in mineral dust. For example, her group has been studying the effect of relative humidity on the chemistry that takes place on the surface of various mineral particles. Although a great deal of research has been conducted on particle surface chemistry , she said little is known about what happens in the environment that lies between the two extremes of dry and wet, a domain in which surface-absorbed water is likely to play an important role.

In one set of experiments, for example, Grassian's group looked at the reactions of nitric acid on calcium carbonate particles at various levels of relative humidity (RH), all greater than 10 percent RH. The study showed that nitrate forms on the surface of the particles at the same time that water is absorbed on the particles, but nitrate forms only in the presence of water vapor. Microscopic images clearly show that, during the process, the particles undergo a marked change in morphology (Figure 4-5) and transform from solid to liquid. This transformation likely occurs in the atmosphere, Grassian said.

When these transformations take place in the atmosphere, they can alter the particles' impact on climate. Grassian's team has shown that as calcium carbonate particles react with nitric acid and transform into calcium nitrate particles, their absorption of water increases dramatically and the particles nearly double in size. These transformed particles are not only 100 times better at serving as cloud condensation nuclei than were the original particles, but also they become photochemically active. This increased photochemical activity increases the possibility that additional chemistry will occur at the surface of the transformed particles, leading to further changes that might influence climate in ways that are not yet understood.

Another type of chemistry that can occur on the surface of calcium carbonate particles starts with the absorption of sulfur dioxide. In the absence of water vapor, little happens when calcium carbonate particles mix with sulfur dioxide, even in the presence of oxygen. The surface absorbs sulfur dioxide, but little chemistry occurs. In the presence of water vapor, however, calcium sulfite crystals start to grow on the particles. Water vapor clearly triggers chemistry to take place on the particle surface. Grassian noted that molecular dynamics simulations of ion mobility over the surface of these particles would provide useful insights into these processes.

The results of these types of studies are now being used to help interpret measurements being made in the field. For example, field measurements in Israel and China have shown that calcium carbonate particles react with sulfur dioxide in the environment and that sulfite forms in an intermediate step that eventually leads to the production of sulfate (Laskin et al., 2005, Sullivan et al., 2006), which atmospheric chemists had not anticipated.

Complex Mineral Dusts

Grassian is working to forge even stronger links between her group's experimental work and atmospheric chemistry. Recently, she and her collaborators have begun studying complex authentic mineral dust particles from different sources. As a first step, her team conducted elemental analysis on bulk samples collected from China and Saudi Arabia. All of the dusts contain silicon, aluminum, calcium, iron, magnesium, and a few other elements, but the relative levels of these elements vary across samples.

This finding raised the question of how best to think about those particles. "Maybe we want to measure elemental compositions of single particles and then look at the particles that contain 15 percent calcium and compare them to particles with less than 15 percent calcium," Grassian said. "But what if all the calcium is on the inside of a particle that's coated by a silica shell? Then perhaps what we really want to measure is single particle surface chemistry."

In a series of experiments, Grassian took calcium-containing dust particles from several dust sources and mixed them with gaseous nitric acid. As expected from her team's earlier work, the particles reacted with nitric acid, but the reaction was not uniform when viewed using scanning electron microscopy (SEM). SEM images showed that the reaction occurred only at places on the particle surface that associated with local composition of the particle, and hydroscopic growth was complex as a result.

Natural particles are more complex not only chemically, but also morphologically. They are not all spheres, which will impact remote sensing data from which aerosol concentra-

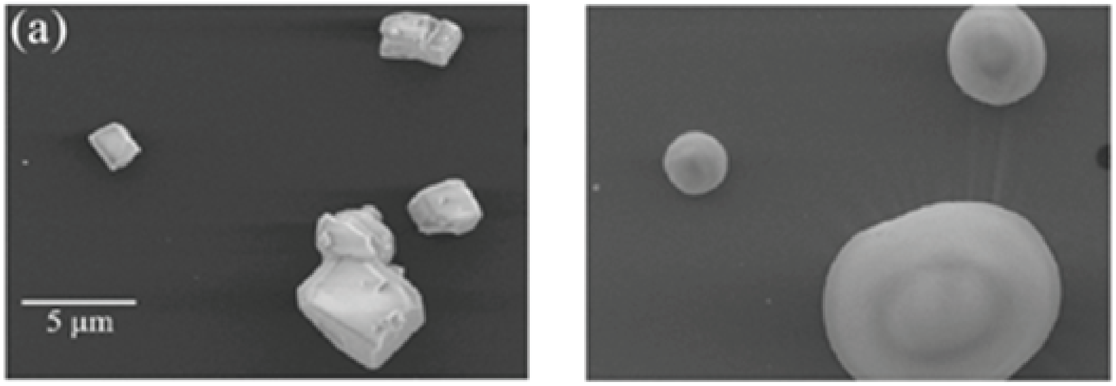

FIGURE 4-5 Calcium carbonate particles react with nitric acid in the presence of water vapor.
SOURCE: Grassian, 2010.

tions are calculated. Research is needed, Grassian said, to better understand how the complex shape distribution of natural dust particles influences optical and chemical behavior in the atmosphere.

Particle size is also heterogeneous in natural dusts, and the behaviors of particles in the atmosphere vary with their size. Particles can aggregate in the atmosphere, which impacts the particles' size, shape, and density and their available surface area, which in turn impacts their surface chemistry and their dissolution in water droplets. Dissolution will then affect aggregation.

Grassian's team has started to examine aggregation and dissolution of differently shaped and sized particles. In one study of iron nanorods and microrods, they found that isolated nanorods displayed enhanced dissolution compared to the microrods. However, in the aggregated state, nanorods were stable against dissolution, such that microrod dissolution was significantly suppressed (Rubasinghege et al., 2010). Aggregation affected not only the size of the particle, but also its chemistry.

To conclude, Grassian stated that it is important to recognize that particles are not stable entities in the atmosphere; rather they can undergo chemical and physical transformations that will impact their "climate" properties. Laboratory studies can provide insights into these transformations, but the complexity of real atmospheric dusts means that the insights may not reflect what really happens in the environment.

Discussion

In response to a comment from Abhaya Datye about the possibility that metals from catalytic converters may be getting into road dust, Grassian responded that there is evidence of those metals, including nanosized platinum particles, in road dust. She added that research is starting to look at the health effects of those metal dusts.

When asked what characterization tools she would like to have to advance her work, Grassian said she would like to perform single particle surface chemistry routinely, particularly of single particles that are components in a complex mixture. Alvarez seconded this wish, adding that he would like access to a technology capable of discerning surface properties or surface chemistries in complex matrices.

5

Modeling and Simulation of Small Particles

FROM ATOMISTIC SIMULATIONS TO HEALTH EFFECTS

Epidemiological studies, said **Angela Violi** of the University of Michigan, have demonstrated a correlation between exposure to an elevated concentration of particles and the development of fibrosis and asthma. A variety of studies has shown that smaller particles are able to penetrate and accumulate deep within the alveolar regions of the lung. Exposure is not limited, however, to the lungs, because research has shown that particles can translocate out of the lungs and circulate throughout the body, even crossing the blood-brain barrier and entering the brain.

According to data from the Environmental Protection Agency (EPA), most particulate matter (PM) in urban environments is carbonaceous (Figure 5-1), and most enters the urban atmosphere as part of diesel exhaust (EPA, 2010). Violi noted that particles from 1 to 50 nanometers in diameter represent about 1 percent of the particle mass emitted from a diesel engine, but from 35 to 97 percent of the number of particles. Current EPA particle emissions standards apply only to particles of 2.5 microns or larger, which will have no impact on the particles that are most worrisome. She added that exhaust particles are not pure carbon; they carry carcinogenic compounds such as benzopyrene and other polyaromatic hydrocarbons and thus can serve as effective delivery vehicles for dangerous compounds.

Carbon particles form during combustion, whether it is in an engine cylinder or in a candle flame. The process starts with fuel molecules that are not oxidized completely and instead react with one another to form precursor molecules, which in turn react with one another to form polyaromatic hydrocarbons over a timeframe of 10 milliseconds or so. These reactions continue, and by 50 milliseconds the molecules grow to a point that chains and agglomerates begin to form. It is this time period, when gas-phase carcinogenic species form, but before soot forms, that Violi is working to model, with the eventual goal of examining how nanoparticles interact with biological systems.

"The problem with this kind of process is the timescale," she explained. While particle formation takes place on a millisecond timescale, other chemistry that may take place on the surface of a growing particle, such as intramolecular rearrangements, can happen on the nanosecond to microsecond timescale. Modeling across both timescales is challenging.

Molecular dynamics modeling works very well for fast events, but even the biggest computers can only handle nanosecond timeframes for the complex processes involved in combustion particle formation. Continuum modeling could span the necessary timescale, but at the expense of excluding most of the chemical details. Instead, Violi's group developed a computational code that combines aspects of molecular dynamics with a kinetic Monte Carlo approach. The resulting stochastic code, which she named Atomistic Model for Particle Interception (AMPI), follows the growth of particle formation over a long timescale and large length scale and retains information on the chemical and physical properties of the system (Violi and Venkatnathan, 2006, Chung and Violi, 2007).

Using this model, Violi and her colleagues can follow particle formation as a function of fuel and have shown that particle morphology and chemical composition change dramatically even though the number of carbon atoms in the combustion products remains the same. The model, which can grow particles up to 20 nanometers in diameter, also reveals that molecular morphology affects particle morphology, which in turn affects how the particles agglomerate and whether they form block-like structures or more flaky structures.

Violi explained that AMPI can provide information not only on particle morphology, but also on hydrogen-to-carbon

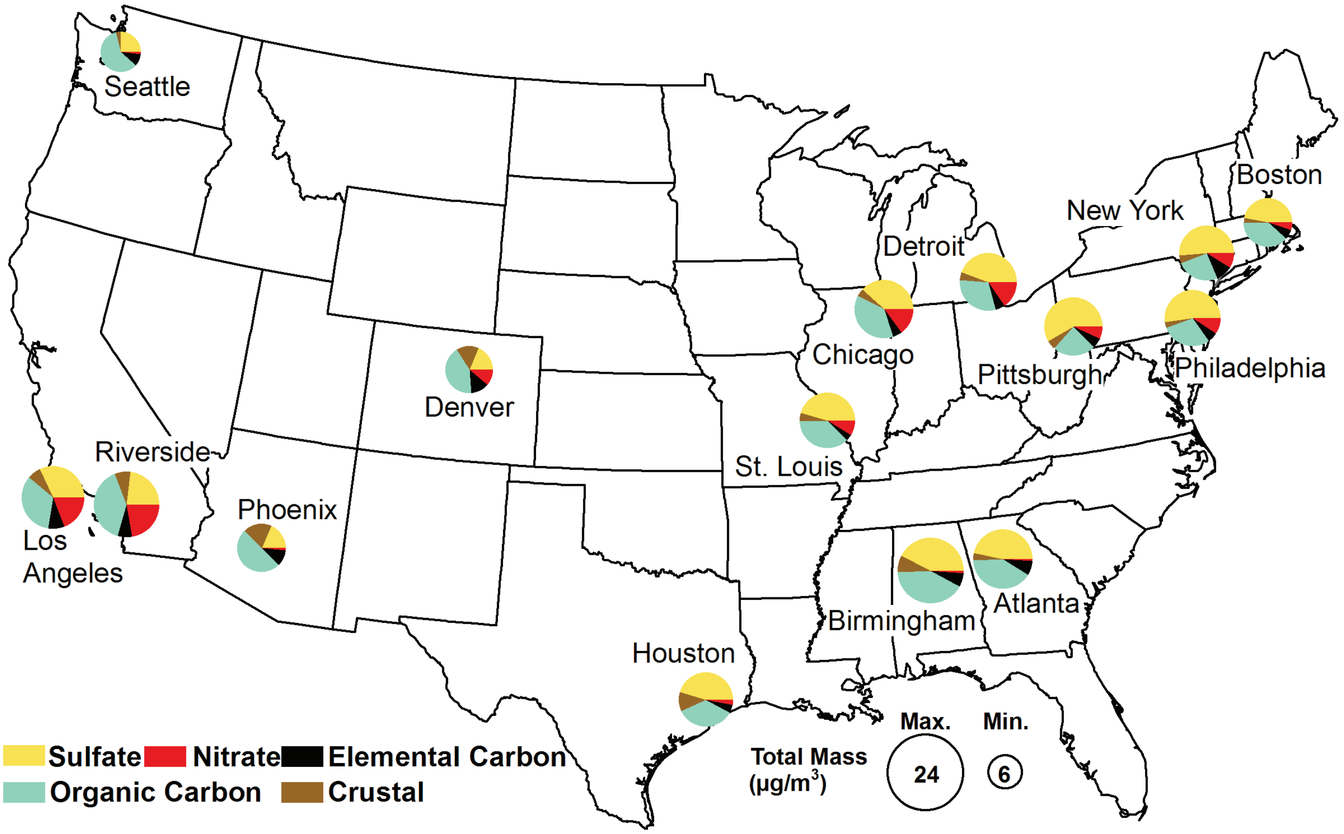

FIGURE 5-1 Four-season average of PM2.5 composition for 15 U.S. cities, 2008.
SOURCE: EPA, 2010.

ratio, free radical concentration, surface reactivity, optical properties, functional group distribution, porosity, surface area, pore size distribution, surface-averaged energy distribution, and particle density. "The whole point of this modeling approach is that the transition from gas phase to particles is very fast, and there are very few techniques—I think almost none—that can deal with the 1-to-50-nanometers range," she said. "So modeling can basically help to fill the gap in these regimes that we're interested in."

Interactions with Biology

The AMPI calculations generate a list of possible chemical structures that would be present in a carbonaceous material in the environment, but the question then becomes, how do these chemicals and particles interact with biological systems? The answer, explained Violi, is the province of nanotoxicology at the level of the individual cell, the smallest unit in a living organism, and the point of interaction between a carbonaceous nanoparticle and a cell is the cell membrane.

The cell membrane is a lipid bilayer composed of lipids, cholesterol, and proteins surrounded by water. It is a fluid system, one in which the lipids are always moving and through which diffusion can occur. Using a molecular dynamics approach, Violi's team has been able to model how carbonaceous particles of varying morphologies impact the natural diffusion of lipids that is constantly taking place in the cell membrane. Indeed, model calculations show that carbonaceous nanoparticles immediately alter lipid diffusion and that the alterations depend on the morphology of the particles (Fiedler and Violi, 2010). Because the proper functioning of the lipid membrane depends on lipid diffusion, this model suggests at least one mechanism by which these particles could cause toxicity.

Violi and her team have since used this model to test whether the decision by an international consortium of regulatory agencies, including EPA, to use C_{60} fullerenes as the only standard for toxicological testing protocols of nanoparticles in the range of 0.5-1.5 nanometers is scientifically sound. The team ran the model using the C_{60} nanoparticle to see if the results reproduced all of the characteristics seen in model runs that used carbonaceous material from combustion. The answer was no; the reason appears to be that an important parameter is surface area, and the surface area of C_{60} is small compared to that of many other carbonaceous nanoparticles.

Violi's team also modeled the interaction between carbonaceous particles and lung surfactant, a lipid-based material. They demonstrated that the particles eventually become wrapped in surfactant lipids. "The point is, even if you start with a carbonaceous material, by the time it translocates into the body it's a totally different animal," said Violi.

Discussion

In response to a question from Patricia Thiel of Iowa State University about the existence of experimental data to test the results of these modeling activities, Violi said that her team has used a differential mobility analyzer, which provides information of particle size to sample particles in actual flames. The data from those experiments validate the model in terms of particle size distribution. Currently, they do not have data on the chemical makeup of those particles. Regarding the C_{60} modeling results, her team is in the process of creating synthetic lipid bilayers and will generate diffusion data using commercially available samples of C_{60} to test their model results.

SCALING SIMULATIONS TO MODEL ENVIRONMENTAL IMPACTS

Douglas Tobias and his colleagues at the University of California at Irvine are trying to understand how the surface of a particle differs at the atomic level from the bulk of a particle and how the interface between that surface and its environment affects the chemistry of a particle. His group also is starting to explore the more coarse-grained interactions between particles and biological systems, particularly the lipid bilayer that makes up the cell membrane.

To Tobias, atomistic modeling means putting every atom of the system into the model and using molecular dynamics to solve the $F = ma$ equation for every particle in the system using a ball-and-spring model to represent atoms and bonds. The calculations continually update the positions and velocities of each atom and generate their trajectories.

The aerosol particles Tobias is interested in are typically on the order of 100 nm in size and contains too many atoms to simulate in its entirety. Because his interest lies primarily in the interface between a particle and its environment, Tobias' approach is to carve out a little chunk of the particle to create what he calls slab models (Figure 5-2). These slabs can be decorated with organics and include a variety of molecules at the interfaces.

Another type of model, used if more detail is required, replaces the ball-and-spring representation of the atoms and bonds with nuclei and electrons, and solves the electronic structure problem, producing a wave function that generates the force needed to perform ordinary molecular dynamics calculations. This type of model shows that interactions at an interface are very dynamic and occur on a timescale of a few picoseconds. Current applications for this type of model include acid-base chemistry and oxidation of halides at the air-water interface and in bulk aqueous solutions.

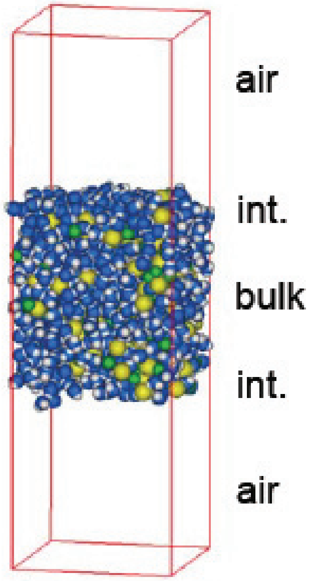

FIGURE 5-2 A "slab" model of aqueous aerosol surfaces.
SOURCE: Tobias, 2010.

Modeling larger systems, albeit with less detail, is possible using a technique known as coarse-graining, which involves lumping together certain groups of atoms that are chemically similar into so-called coarse grain beads. This method can drastically reduce the number of particles being simulated. Tobias explained how this approach was used to model a membrane lipid by reducing 138 atoms to 15 beads (Marrink et al., 2007). Coarse graining, which involves defining different types of interactions, such as polar, mildly polar, and charged, can handle mesoscopic systems over microsecond timescales with good molecular detail.

Understanding Sea Salt Aerosols

Using these modeling approaches, Tobias's group has been studying the chemistry of sea salt aerosols. Sea salt aerosol is produced when bursting bubbles shoot 100-nanometer to 100-micron droplets of sea water into the atmosphere. The droplets are primarily concentrated salt solutions consisting mostly of sodium chloride with small amounts of bromide. The latter is important because bromide is more reactive than chloride. Various field and laboratory measurements have established that these halides in sea salt can be oxidized to produce very reactive molecular halogen species (Figure 5-3). "Because of the importance of molecular halogens in the atmosphere, this chemistry is important to understand in terms of mechanisms and kinetics in order to find out if these compounds are going to be atmospherically relevant," he explained.

Tobias became involved in this research because existing kinetic models failed to reproduce the actual production of molecular chlorine from sea salt that had been measured both in the laboratory and field studies. Missing from these models, Tobias said, was surface chemistry that would make the process heterogeneous rather than homogenous.

Using a molecular dynamic simulation of a concentrated sodium chloride solution, Tobias's modeling studies surprisingly revealed that chloride anions rose to the surface of the salt solution while sodium tended to stay beneath the surface. Following the extent of surface exposure of the chloride anions in time showed that 12 percent of the droplet surface was covered by chloride anions, a finding that contradicted more than a century's worth of conventional wisdom about the behavior of halide ions at an air-water interface; that is, the ions should stay inside the solution. What appears to happen, however, is that sodium and fluoride ions are repelled from the interface while chloride ions adsorb to the interface. Bromide and iodine ions, meanwhile, also concentrate at the surface and act as surfactants (Jungwirth and Tobias, 2001).

"What we've seen is that anion adsorption increases with ion size and polarizability," said Tobias. "These are actually important concepts for understanding the behavior of ions near interfaces." And, in fact, this basic picture of increasing anion adsorption with the halide mass has recently been confirmed by x-ray photoelectron spectroscopy (Ghosal et al., 2005).

The next step in Tobias's modeling effort was to insert hydroxyl radical. The model shows that hydroxyl radicals also accumulate at the air-water interface and frequently encounter chloride ions. Quantum chemical electronic structure calculations and molecular dynamics simulations suggest that a mechanism based on the formation of a hydroxyl radical-chloride complex is plausible. When this mechanism is then used to refine the original model, it accurately reproduced the observed production of chlorine from sea salt (Knipping et al., 2000).

These models are not just of theoretical use, noted Tobias. When the sea salt reaction is included in airshed models of the South Coast Air Basin of California, which are used to calculate regional ozone levels in the Los Angeles Basin, the adjusted models predict that ozone levels will increase over most of the basin, and that some regions will experience quite significant increases at certain times of the day (Knipping and Dabdub, 2003).

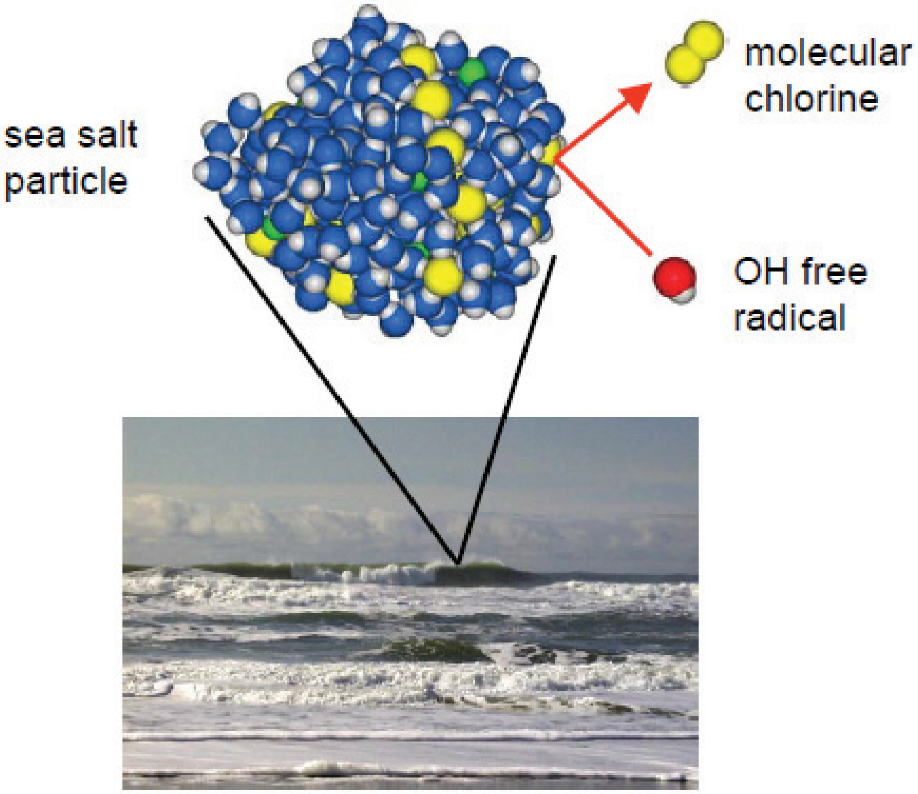

FIGURE 5-3 Sea salt particles are primarily concentrated sodium chloride, but also contain reactive species such as molecular chlorine.
SOURCE: Tobias, 2010.

Small Molecule Interactions with Biological Structures

Recently, Tobias has become interested in modeling how particles traverse membranes as an approach to understanding how particles may cross the blood-brain barrier via a passive transport process. Preliminary work using coarse-grained molecular dynamics modeling showed that a spherical, nonpolar nanoparticle can easily pass through the lipid bilayer of a larger vesicle. In this simple model, the highly curved surface of the vesicle likely plays an important role in facilitating the easy passage of the inert nanoparticle through the membrane.

His group is now working on more systematic studies to determine which particle properties actually determine its ability to cross membranes. This effort has so far shown that particle polarity is one feature that exerts a strong influence on a particle's ability to enter and cross membranes. Tobias plans to explore how variations in size, shape, and surface chemistry of a particle impact membrane permeability. He also plans to examine the effect on passive transport that results from changing membrane composition and adding lipid-embedded proteins to the lipid bilayer. As a closing comment, he briefly described atomistic modeling work performed by another group that showed that C_{60} fullerenes are capable of entering the pore of a potassium channel and becoming lodged there, blocking the channel and shutting off potassium ion flow (Kraszewski et al., 2010).

Discussion

In response to a comment by Steve Schwartz about the presence of organic material on the surface and the fact that this material can form a concentrated film on the surface of sea salt particles, Tobias said that his group has modeled particles that include a surfactant layer (Figure 5-4). The calculations show that gases can get stuck in the surfactant layer and therefore undergo additional collisions with the reactive species in solution. In that sense, the surfactant layer can act as a barrier to exclude gases from the initial sea water droplet, but it can also enhance reactivity by trapping those gas molecules that do enter the droplet. Molecular dynamic simulations suggest that these two competing processes actually balance each other out, with the collision rate between reactive trace gases and ions in solution being very similar with and without the surfactant layer. In response to a second question from Schwartz, Tobias stated that the dynamic simulations include evaporation.

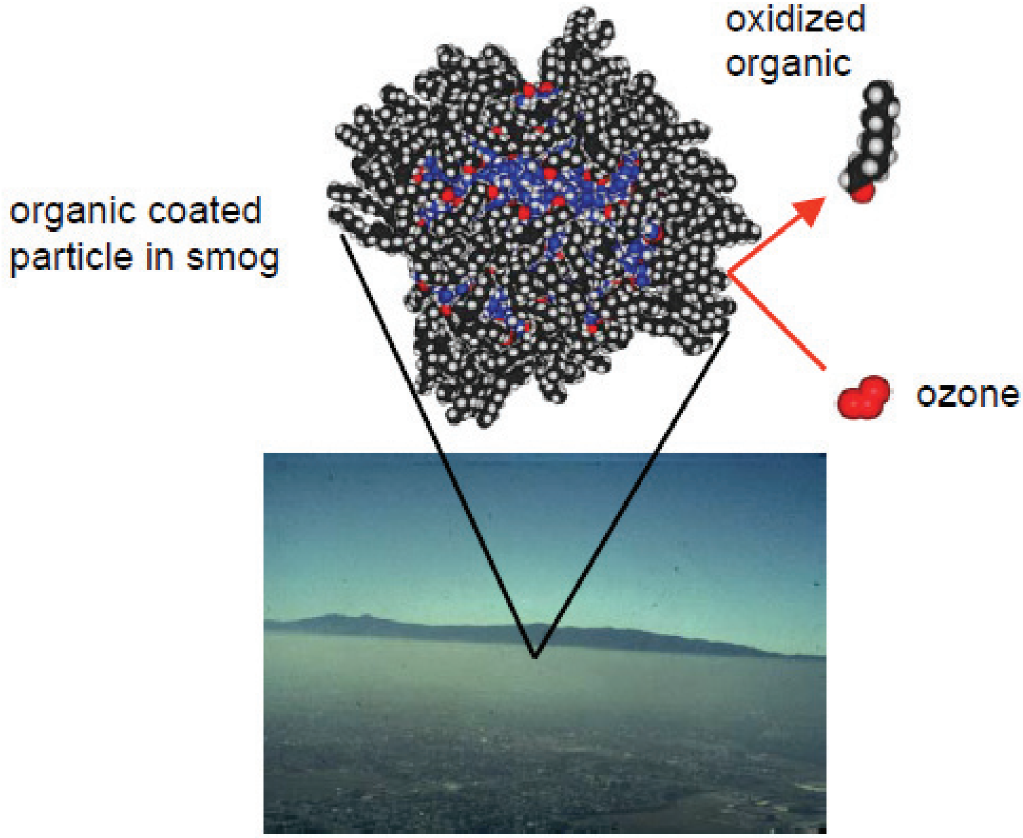

FIGURE 5-4 Sea salt particles coated with organic material in smog can lead to an increase in ozone levels.
SOURCE: Tobias, 2010.

OPEN DISCUSSION

In response to a question from Barbara Finlayson-Pitts about whether the soot models account for the complex organic functionality found on the surface of soot particles, Violi said that the modeling code she described tracks all of the surface chemistry and all of the functional groups and reactive sites on a particle's surface. The models also reproduce the finding that radical species exist on the surfaces of soot particles.

Mort Lippmann commented that he was encouraged that modeling efforts are being directed at aqueous droplets such as hygroscopic sea salt because liquid microdroplets are very important from a health perspective. He added, however, that he would like to see more work on droplets as well as on particles other than carbon because metal-containing nanoparticles are probably a bigger issue for human health. Rhonda Stroud remarked that looking at liquid particles is a challenge because many of the tools available today are geared toward studying solid materials. However, efforts are under way to design microfluidic cells for electron microscopy instruments that may be useful for studying soft materials such as droplets.

Steve Schwartz suggested that the modeling community might want to pursue knowledge of the ice crystal habitat in clouds given the importance of ice crystals to climate. Violi agreed with Schwartz's subsequent comment that it could prove fruitful to examine the kinetics of ice crystal growth under varying conditions, and Tobias noted that the atomistic simulation community has undertaken a large effort to model ice crystal formation. Stroud added that NASA Ames has a transmission electron microscope specifically designed to take in situ measurements of ice that may provide the kind of data needed to inform and validate modeling efforts.

Schwartz reiterated his earlier comment about the importance of validating model results with experimental data, particularly those on the biological impacts of nanomaterials. Violi remarked that her team always tries to conduct its modeling work in collaboration with experimentalists. The work on lipid bilayer modeling, however, is a relatively new endeavor, and efforts are under way to develop experimental benchmarks for these models. Tobias agreed with both sets of comments and suggested some experiments that could prove useful. For example, x-ray diffraction studies on stacks of lipid bilayers could look for changes in the density distributions with and without particles. If the particles were deuterium labeled, then it would be possible to use neutron diffraction to determine the exact location of the particles and how they are distributed in the bilayer.

6

Workshop Wrap-up Session

Four workshop participants, Jennifer Sinclair Curtis of the University of Florida, Michael Postek of the National Institute of Standards and Technology (NIST), Pierre Ricou of Arkema, and Richard Conroy of the National Institute for Biomedical Imaging and Bioengineering (NIBIB) at the National Institutes of Health (NIH), were asked to provide closing comments. Chosen for their diverse perspectives, each panelist discussed what he or she heard during the workshop and what some next steps might be. The panel comments were followed by an open discussion period when all workshop participants were given the opportunity to respond to the panelists and raise additional issues.

PATH FORWARD

Jennifer Curtis heard three main topics discussed during the workshop: implications, understanding complex processes, and new characterization techniques for small particles. She said that health and environmental implications seem to motivate much of the work in characterizing and modeling small particles. Given that motivation, there is a need for greater understanding of fine particles and the dynamics of their behavior. There is another need to define the methods that are capable of distinguishing between single nanoparticles and agglomerates.

A key takeaway message for Curtis was that the modeling community faces some validation challenges related to the lack of detailed experimental data. She believed it would be useful to the field to compile a database of the available characterization techniques and their key features in terms of the type of material they can handle and the characteristics and properties that they measure. Such a database may increase the use of these powerful techniques in areas beyond those for which they were developed.

ADDRESSING COMPLEXITY

Mike Postek was struck by the obvious need to make multiple measurements on the types of complex materials that represent nanomaterials found in the real world. He noted the development of a wide range of new tools for nanomaterial characterization and the continuing advances being made with instrumentation, such as the applications of the soft x-ray tomography, the cryogenic light microscopy, aberration-corrected transmission electron microscopy (TEM) and scanning electron microscopy (SEM), and in situ TEM. He also raised the need for a database of available technologies.

Postek expressed a worry that cuts to research and development budgets, particularly in industry, are hampering technology development at a time when need in the nanocharacterization field is growing. However, he also noted that a great deal of advanced characterization technology is available at the national laboratories and at NIST, along with investigators who are more than willing to collaborate and cooperate in this area.

Modeling also touches on complexity, Postek said. Industry needs tools to model complex composites for use in high-performance applications. The potential cost savings from having models capable of predicting material performance would be huge, as it would be if models were available to predict the effect that process variables have on the properties of materials with complex surfaces and surface chemistries.

COMMON GROUND

Pierre Ricou's impression was that small-scale characterization is a focal point for many different parts of the nanotechnology world. From industry's perspective, there is a need to characterize and understand the properties of materials to create complex materials that can meet a wide range of demands. From an environmental scientist's perspective, there is a need to characterize materials to understand what happens to those materials when they enter the world outside of the laboratory or factory. Although each group is tackling different issues, they are united by a need to characterize the properties and behaviors of complex materials in complex environments.

Ricou was also impressed by the wide range of technologies that are now available for characterizing nanoscale materials. He reiterated the importance of creating a database of technologies, and he stated that instrument vendors should hear more about the challenges facing those who need to better characterize nanomaterials. He would like to see development of the ability to perform spectroscopy on dynamic systems at the nanoscale to better understand how the chemistry of a nanomaterial changes over time, which would benefit many aspects of nanocharacterization.

FUNDING OPPORTUNITIES

Richard Conroy said that he came away from the presentations with two questions:

- Should we study function first or structure first?
- Should we measure something just because we can?

This second question is particularly important from the NIH perspective, because many measurements correlate weakly with outcomes, and thus it is not always clear that the measurements are useful when considering the research that has gone into them. He added that consideration of the question of safety and efficacy is also important, in terms of the comparative effectiveness and safety of nanotechnology-based products versus bulk materials.

Conroy provided a quick overview of some of the funding opportunities at NIH. Part of NIH's current mission is to bridge the life and physical sciences, and, in that regard, he thought the nanomaterial characterization community would be interested in a number of initiatives. Most of the initiatives are funded by NIBIB or the National Institute of General Medical Sciences (NIGMS), with NIBIB focusing more on the clinical side and NIGMS focusing more on basic research. One new initiative is aimed at applying technologies from the physical sciences to life sciences problems. A significant feature of this initiative, the grant review panel includes experts from both NIH and the National Science Foundation (NSF), with the latter providing a physical science perspective to the NIH review process. A partner initiative aims to translate ideas from the physical sciences into the clinical arena.

Another NIBIB initiative is the bioengineering research partnership program that encourages investigators to form a partnership between the life and physical sciences to translate a concept, technique, or tool from the demonstration to the biomedical application phase. NIBIB also offers fellowships that are designed to create time for mid-career researchers in the physical or quantitative sciences to develop projects in the life sciences.

Conroy said that all of the other NIH institutes have similar initiatives, and NIBIB also supports Small Business Innovation Research (SBIR) grants in the area of bioengineering in nanotechnology.

OPEN DISCUSSION

Characterizing Aggregates—Trading Detail for Utility

Jim Litster said he was amazed by what he heard during the workshop about the ability to measure individual small particles. He added, however, that because the functionality of the nanoparticles in use depends very much on the structures in which they are embedded, there is still a need for techniques that are just as powerful at characterizing the state of dispersion or aggregation. Developing the techniques and instrumentation to attack that problem is the logical next step for the field.

Doug Ray agreed that there is not as much capability in the area of concentrated liquids and solids. He asked, "Is it because it is just really hard and the community is not there yet, or is it because we have elected somehow to not focus in that arena?" He does not know the answer but thinks it is an interesting question to consider.

Mark Barteau added that work in this area might focus on "diagnostic," meaning that it may not be necessary to know all the details of how nanoparticles behave in a matrix. It might be enough now to characterize these complex materials according to a certain number of reduced parameters or "lumped" parameters. He is aware of some movement in that direction, but the emphasis on incredible levels of detail and expensive instruments does not match the degree found in nanoscale imaging. He wondered, however, if looking at more complex systems at lower levels of detail that are still diagnostic might be where the field makes the biggest impact. Ray added that the atmospheric sciences are starting to move from a more detailed view to one that reduces the amount of information and creates useable models.

Conroy noted that NIH is interested in where the field is going on this matter. He believes that the relevant question relates to how much detail on specific characteristics is needed to predict biological outcomes. Ricou agreed with this idea but stressed the importance of understanding these systems in fine detail to know what is important when trying to predict relevant behavior.

Chemistry and Stability

Levi Thompson pointed out that many of the particles that were discussed at the workshop are semiconductors and wondered if the properties of those particles are influenced by exposure to light. He asked if anybody had performed the requisite studies to determine whether photocatalytic or photolytic processes are important to particle reactivity. Satya Kuchibhatia from the Pacific Northwest National Laboratory answered that his group has looked at cerium oxide nanoparticles and found that exposure to light definitely influences the transformations happening on the nanoparticles. He also explained that how a nanoparticle responds to light changes over time and that his group has noticed changes between the times when a particle is received from a vendor and when it is studied. Where the particles are manufactured also makes a difference, which is likely due to the humidity of the manufacturing location.

Finlayson-Pitts said that the field of atmospheric chemistry is starting to pay attention to the photochemical properties of nanoparticles. The photochemistry of small particles can be quite different from the photochemistry of larger particles, primarily because of differences in surface-to-volume ratios. As an example, she described differences in the photolysis of nitrate ion that occurs when it is surrounded by a solvent shell on a bulk surface compared to when it is at an interface. "The whole issue of photochemistry at interfaces is certainly one that is getting increasing attention in the atmospheric community," she said. Thomson added that researchers who study catalysis, photocatalysis, and electrocatalysis have been considering these issues for many years, and it might be an intersection that can be probed more.

What's the Focus?

One participant commented that while the presentations were very informative, there was a lack of focus in terms of an industrial driver, that is, how at the end of the day will this research help to develop new products.

Kuchibhatia and his colleagues at the Pacific Northwest National Laboratory are encouraged that the field is moving beyond the excitement of getting a good TEM image to search for details about surface chemistry with an eye on developing nanoparticles with specific properties. The goal, he said, has gone from seeing structure to combining structure with a desired chemical property. "At the end of the day, it is the chemistry that is going to make the magic, not just the structure," he said.

Postek added that a roadmap created by the semiconductor industry years ago has guided the industry since the 1980s and has allowed instrument manufacturers to build the measurement tools that the industry has needed as it meets its technology goals. Nothing like that exists for nanotechnology. He acknowledged that creating such a consortium to define what is happening in nanotechnology would be difficult given the disparate nature of this community. "Perhaps several of these kinds of consortia are needed to help shape this field and get people together to talk about what their needs happen to be," he suggested.

Rhonda Stroud believes that having a focus is great, but it does not necessarily have to be on commercial applications alone. As a civil servant, her customer is the American public, and she asks herself, "Can I justify working on space particles to the taxpayer?" She believes that the common issue is really quality of life. Everyone is producing information and products that improve the quality of life. This is what air quality, new drug treatments, and astronomy have in common. They may not all have immediate commercial applications, but they can be important to the American people nonetheless. Therefore, a roadmap should look at what the impact of knowledge as well as products will be on the average person.

A participant agreed that the ultimate goal is to serve the people, but, at the end of the day, the commercial aspect is important because it is the means to get to that goal. For example, catalysis is very important for many applications. Researchers will make useful and environmentally benign catalysts from ruthenium or rhodium. However, those materials are expensive, so in poorer countries that same reaction will be carried out without the catalyst and will use excess reagent that gets dumped into waterways because pollution control standards are lax. Ultimately, if knowledge does not make money or save money, no matter how useful it is, people will not use it.

Ray replied that while certain sectors, such as energy or pharmaceuticals, are driven by commercial interests, other sectors such as the defense industry are not. He believes that there are sectors where commercial drivers are in place and are appropriate, and there are other sectors where they are not. The nation supports research in areas such as astronomy, not for an immediate commercial benefit but for quality-of-life issues and the long-term benefits that the research might produce. Stroud pointed out that the Department of Defense does a significant amount of work on the development or the advancement of catalysts and energetic materials where the driving force is not the immediate bottom line, but the need to protect the American people.

Appendixes

A

Workshop Agenda

CHALLENGES IN CHARACTERIZING SMALL PARTICLES:
Exploring Particles from the Nano- to Microscales

October 25-26, 2010
The Washington Plaza Hotel
10 Thomas Circle Northwest,
Washington, DC 20005-4106

DAY ONE, Monday, October 25, 2010

8:00 a.m. Breakfast

8:30 a.m. Welcome & Introduction to Workshop
Barbara Finlayson-Pitts, Doug Ray, and Levi Thompson

PLENARY SESSION—WHY DO SMALL PARTICLES MATTER TO ME?
Chair, Barbara Finlayson-Pitts

8:45 a.m. **Steve Schwartz**, Brookhaven National Laboratory
Understanding the influences of atmospheric aerosols on climate and climate change and representing them in models: A tall order

9:15 a.m. **Morton Lippmann**, New York University
Human health impacts of ambient air particles

9:45 a.m. **Michael Hochella**, Virginia Polytechnic and State University
New hidden Earth: The importance of putting natural, incidental, and manufactured nanoparticles in a global and historical context

10:15 a.m. Break

10:30 a.m. **Gerry McDermott,** Lawrence Berkeley National Laboratory
Visualizing the location of small particles in cells and quantifying their effects

11:00 a.m. Open discussion
Facilitator, Levi Thompson

CHALLENGES IN CHEMICAL ANALYSIS & IMAGING OF SMALL PARTICLES I
Chair, Doug Ray

11:45 a.m. **Alla Zelenyuk**, Pacific Northwest National Laboratory
Multidimensional characterization of individual aerosol particles

12:05 p.m. **Ralph Nuzzo**, University of Illinois, Urbana-Champaign
Challenges and approaches to nanoscale materials characterization at atomic resolution

12: 25 p.m. Lunch

CHALLENGES IN CHEMICAL ANALYSIS & IMAGING OF SMALL PARTICLES II
Chair, Levi Thompson

1:25 p.m. **Lee Silverman**, DuPont Central Research
Particle characterization needs—a nanocomposite perspective

1:45 p.m. **Jim Smith**, National Center for Atmospheric Research and University of Eastern Finland
Recent progress in quantifying the chemical composition of atmospheric nanoparticles

2:05 p.m. **Abhaya Datye**, University of New Mexico
Particle design and synthesis for catalysts

2:25 p.m. **Yi Qiao**, 3M Corporate Research Process Laboratory
Nanoparticle size measurement with microfluidic channel and dielectrophoresis

2:45 p.m. Open discussion on Challenges in Chemical Analysis & Imaging of Small Particles
Facilitator, Doug Ray

3:30 p.m. Break

CHALLENGES IN CHEMICAL FORMATION, FATES, USES, AND IMPACTS OF SMALL PARTICLES
Chair, Barbara Finlayson-Pitts

3:45 p.m. **James Litster**, Purdue University
Design and manufacture of delivery forms for small particles

4:05 p.m. **Pedro Alvarez**, Rice University
Particles in the environment

4:25 p.m. **Vicki Grassian**, University of Iowa
From mineral dust to nanoparticles: Challenges in understanding surface chemistry, transformations and global impacts of small particles

4:45 p.m. Open Discussion on Challenges in Chemical Formation, Fates, Uses, and Impacts of Small Particles
Facilitator, Levi Thompson

5:30 p.m. Posters & Refreshments

7:00 p.m. Adjourn

DAY TWO, Tuesday, October 26, 2010

8:00 a.m. Breakfast

8:45 a.m. Welcome & Introduction to Workshop
Barbara Finlayson-Pitts, Doug Ray, and Levi Thompson

CHALLENGES IN MODELING AND SIMULATION OF SMALL PARTICLES

Chair, Levi Thompson

8:55 a.m.	**Angela Violi**, University of Michigan *"Nanoparticle in the environment": From molecular simulations to health effects*
9:15 a.m.	**Douglas Tobias**, University of California, Irvine *Atomistic and coarse-grained molecular dynamics simulations of small particles in environmental and biological systems*
9:35 a.m.	**Rhonda Stroud**, Naval Research Laboratory
9:55 a.m.	Open Discussion on Challenges in Modeling and Simulation of Small Particles *Facilitator, Barbara Finlayson-Pitts*
10:25 a.m.	Break
10:40 a.m.	Wrap-up "Action" Panel *Facilitator, Doug Ray* Panelists will respond to the questions: What did you hear in the workshop? What do you think are some next steps? **Lee Silverman**, DuPont Central Research **Richard Conroy,** National Institutes of Health **Jennifer Sinclair Curtis**, University of Florida **Michael Postek**, National Institute of Standards and Technology
12:00 p.m.	Adjourn
12:15 p.m.	CSR Member Business Meeting

B

Poster Abstracts

MEASUREMENTS OF NEUTRAL NUCLEATING MOLECULAR CLUSTERS IN THE ATMOSPHERE

J. Zhao,[1] F. L. Eisele,[1] J. N. Smith,[1,2] M. Chen,[3] J. Jiang,[3] M. Titcombe,[3] C. Kuang,[4] and P. H. McMurry[3]

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Atmospheric nanoparticles produced by nucleation can subsequently grow to cloud condensation nuclei (CCN) within one or two days and hence affect cloud formation, precipitation, and atmospheric radiation budgets. As an intermediate stage between molecules and nanoparticles, neutral molecular clusters are believed to play an important role in processes that lead to boundary layer nucleation. Therefore, knowledge of chemical composition, concentrations, thermodynamic properties, and evolution of neutral molecular clusters is essential to better elucidate the nucleation mechanism and to reduce the uncertainty in nucleation rates used in global climate models.

Here we present field measurements from a recently developed chemical ionization mass spectrometer (the Cluster-CIMS) designed to measure atmospheric neutral clusters (Zhao et al., 2010). The sensitivity of the Cluster-CIMS was significantly improved by using a unique conical octopole device in the first vacuum stage for transmitting and focusing ions, which was further confirmed by ion trajectory simulations using SIMION. The Cluster-CIMS was well calibrated with an electrospray coupled to a high-resolution differential mobility analyzer (ES-HDMA). The calibration showed that the Cluster-CIMS has a relatively flat sensitivity in the mass range of 190-400 amu, covering the masses of sulfuric acid clusters containing 2-4 H_2SO_4. The ion cluster formation in the atmospheric-pressure inlet was controlled by two processes: neutral ionization and ion-induced clustering (IIC), which can be differentiated from the time independency of the intensity ratio between the cluster and monomer ions. Two methods were employed to separate neutral clusters from the ion-induced clustering. The concentrations and distribution of the neutral nucleating clusters containing up to 4 H_2SO_4 are estimated from the above methods at three measurement sites (NCAR foothill laboratory, Manitou Forest Observatory, and Atlanta). Typically, the molecular cluster concentrations are well correlated with the concentrations of nanoparticles measured simultaneously during the nucleation event periods. The Cluster-CIMS was employed to measure clusters containing both sulfuric acid and amines in summer 2010 at NCAR foothill laboratory. Correlation between these clusters and nanoparticles measured by several particle counters will be presented.

Zhao, J., F. L. Eisele, M. Titcombe, C. Kuang and P. H. McMurry. 2010. Chemical ionization mass spectrometric measurements of atmospheric neutral clusters using the Cluster CIMS. *Journal of Geophysical Research* 115, D08205, doi:10.1029/2009JD012606.

EXPLORING PARTICLES FROM THE NANO- TO MICROSCALES ELECTRON MICROSCOPIC ANALYSES ON ENGINEERED AND INCIDENTAL NANOPARTICLES IN BIOSOLID PRODUCTS

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With the dramatic growth of nanotechnology, the production and use of engineered nanoparticles has been rapidly increasing for the past few years. Engineered nanoparticles that are produced and/or incorporated into consumer products will enter the environment after and/or during the term of use, which in turn has raised concerns about their potentially adverse impact on the environment. However, there has been little success with identifying nanosized engineered and incidental particles from complex heterogeneous environmental samples, limiting our understanding of their environmental fate and influence. Lack of such studies is in part due to technical challenges in discovering and monitoring the environmental occurrence of engineered and incidental nanoparticles present at trace levels. In order to overcome this problem, we looked at a "bottleneck" for engineered nanoparticles in the form of a large metropolitan wastewater treatment facility. There, nanoparticles from consumer products may concentrate especially at the end stage of treatment processes where biosolids (sludges) are generated. We looked for the presence of nanosized particles in this complex organic material using analytical high-resolution transmission electron microscopy. We found nanoparticulate silver sulfides, presumably derived from silver nanoparticles and/or ionic Ag that were reacting with reduced S species in the sedimentation processes during wastewater treatment, as well as a variety of titanium oxide nanoparticles. For both materials, their size, morphology, elemental compositions, and degree of crystallinity and aggregation state were studied in detail. The results of our work clearly show a great degree of nanoparticle heterogeneity and complexity in biosolid products. We believe that this study will help us evaluate further risks when nanoparticle-bearing biosolid products enter the soil environment through agricultural land applications.

IN SITU STUDIES OF EQUILIBRIUM AND NON-EQUILIBRIUM SMALL-PARTICLE DYNAMICS OVER EXTENDED LENGTH AND TIME SCALES USING ULTRASMALL-ANGLE X-RAY SCATTERING/X-RAY PHOTON CORRELATION SPECTROSCOPY (USAXS/XPCS)

J. Allen,[1] F. Zhang,[1] L. E. Levine,[1] J. Ilavsky,[2] A. R. Sandy,[2] and G. G. Long[1,2]

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Both scattering and imaging techniques successfully characterize the microstructures of advanced materials, including small particle systems and suspensions. Yet the dynamics of these materials, especially responses to abrupt changes in environment, largely remain elusive. X-ray photon correlation spectroscopy (XPCS) has emerged as a technique offering unprecedented sensitivity to equilibrium and nonequilibrium dynamics within material systems, including small particles. However, existing XPCS facilities are limited to microstructure length scales smaller than 50 nanometers, eliminating large classes of materials of technological importance. Recently, we have developed combined ultrasmall-angle x-ray scattering/x-ray photon correlation spectroscopy (USAXS/XPCS) to probe the slow equilibrium and nonequilibrium dynamics of optically opaque materials with features in a size range from 100 nm to several micrometers, i.e., between those of dynamical light scattering and conventional XPCS. Two examples illustrate the in situ capability of USAXS-XPCS: the equilibrium dynamics of colloidal particle dispersions at various volume concentrations as a function of temperature; and the nonequilibrium dynamics of the small particle configuration within a polymer composite, for which USAXS/XPCS reveals incipient dynamical changes not observable by other techniques.

CHARACTERIZATION OF MICRO-PARTICLE ADHESION IN PHARMACEUTICAL ENGINEERING

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The understanding of interaction forces that arise when particles and surfaces come into close contact continues to be a significant focus of research. It can benefit many areas of study particularly in the pharmaceutical, chemical, and mineral industries involving solid processing. The work presented investigates capillary condensation effect on adhesion forces between particles and surfaces as it is exposed to different levels of relative humidity. Direct force measurements between molecularly smooth surfaces seem to match accurately with conventional models, but with real particles and surfaces the forces display extreme discrepancies due to their natural heterogeneity such as roughness and uneven liquid condensate layers.

The investigations on the microscale interactions are developed for nonideal surfaces to give more significant insight on the macroscale than ideal surfaces. The results have confirmed liquid condensation is present on the surface area of tooling surface on the microscale through a phase imaging technique. This was the first time it was applied in the context of pharmaceutical manufacturing, which can facilitate the design of surfaces during processing. The traditional approach for designing processing and particle interactions heavily relied on the behavior of large amounts of particles and indirect measurements of the adhesion forces of the surface. The understanding of the interactions between single particles and tooling surfaces can provide useful information through several characterization techniques such as atom force microscopy (AFM) and scanning electron microscopy (SEM).

IMAGING SMALL PARTICLES IN CELLS USING SOFT X-RAY TOMOGRAPHY

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Soft x-ray tomography (SXT) is a new tool for imaging whole, hydrated biological specimens up to 15 microns thick with a spatial resolution better than 50 nm. In SXT, cells are imaged using photons between the K shell absorption edges of carbon (284 eV, $\lambda = 4.4$ nm) and oxygen (543 eV, $\lambda = 2.3$ nm). These photons readily penetrate the aqueous environment while encountering significant absorption from carbon- and nitrogen-containing organic material. In this energy range, referred to as the "water window," organic material absorbs approximately an order of magnitude more strongly than water, producing quantitative, high-contrast images of intact, fully hydrated cells without the need to use contrast-enhancing agents. The high penetrating power, coupled with a near absence of reflection at the interface of dissimilar materials, makes x-rays an ideal probe for studying cellular morphology. These unique imaging properties also make x-ray a powerful tool for determining the precise position of small particles with respect to cellular structures.

CHARACTERIZING MOLECULAR CONJUGATION AND AGGREGATION OF NANOSCALE PARTICLES USING COMPLEMENTARY PHYSICAL MEASUREMENT METHODS

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We present results based on complementary physical characterization methods performed under both fluid-based and aerosolized conditions in order to interrogate the molecular conjugation and colloidal stability of nanoscale particles. From the change in hydrodynamic and aerosol particle size, we can probe the formation of molecular coatings and particle aggregates. For the purpose of characterizing nanoscale gold-based platforms for cancer therapeutics, citrate-stabilized gold nanoparticles (Au-NPs) conjugated by thiolated polyethylene glycol (SH-PEG) are used as a model system. Dynamic light scattering and asymmetric-flow field flow fractionation are used to characterize particle populations under relevant fluid conditions. For comparison, atomic force microscopy and electrospray differential mobility analysis offer static imaging and dry aerosol characterization, respectively. Combining information derived from these physical-based methods, we can then analyze the molecular conformation of SH-PEG on the Au-NP surface, calculate the surface coverage of SH-PEG, and estimate the degree of aggregation and shelf life of Au-NP based products in dispersed form.

CHEMICAL IMAGING ACTIVITIES ASSOCIATED WITH NANOPARTICLES AT PACIFIC NORTHWEST NATIONAL LABORATORY

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Chemical analysis and identification through direct imaging is a powerful means to develop an atomistic understanding of scientific issues associated with knowledge gaps and problems in energy, environment, and national security. For example, identification of mechanisms associated with transformations requires the direct observation of the reactions to develop the atom-by-atom model of the structural and chemical changes. Recently we introduced a laboratory-wide chemical imaging initiative to develop the suite of tools needed for such a transformation. Central to this initiative will be development of an in situ tool suite with nanometer resolution and element specificity that will allow researchers to couple the molecular-level chemical and structural information to large-scale scientific challenges. In particular, we will develop (a) synchrotron light-source-based capabilities coupled with laboratory-based imaging capabilities for three-dimensional tomographic, structural, and element-specific interrogation at the molecular level, (b) coupled optical, electron, ion, mass, and scanning probe microscopies to understand chemical, material, and biological transformations and mechanisms, and (c) integrative hardware and software applications for real-time image reconstruction, feature extraction, and information integration. Brief descriptions of these activities will be presented along with the detailed descriptions of two to three projects related to nanoparticle characterization.

IMPORTANCE OF SYNERGISM IN ATMOSPHERIC SECONDARY ORGANIC AEROSOL FORMATION: CASE STUDY OF α-PINENE OXIDATION BY NO_3 RADICALS

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Secondary organic aerosols (SOAs) formed from the gas-phase oxidation of volatile organic compounds (VOCs) are a major component of atmospheric particles. Biogenic VOCs have been long known as SOA sources via oxidation by O_3, OH radicals, and NO_3 radicals. While these reactions are usually studied separately in laboratory controlled experiments, in the atmosphere, reaction of VOC with one specific oxidant rarely occur in isolation. We report here the oxidation of α-pinene, a well-documented biogenic emission, by NO_3 radicals with varying contributions from the O_3 reaction, where the $O_3 + NO_2$ reaction is the source of NO_3 radicals. Experiments were carried out in air using a newly developed large stainless steel flow tube. Particle concentration and chemical composition were measured simultaneously using scanning mobility and aerodynamic particle sizers, two aerosol mass spectrometers, and two integrative sampling techniques (impaction on either ZnSe discs with subsequent analysis by Fourier transform infrared spectroscopy or on quartz-fiber filters followed by liquid chromatography with UV-vis detection). Even small contributions by the ozone chemistry had significant impacts on particle formation and growth, as well as on composition. The synergism between O_3 and NO_3 chemistry is discussed.

HARD SHELL GAS-FILLED CONTRAST ENHANCEMENT PARTICLES FOR COLOR DOPPLER ULTRASOUND IMAGING OF TUMORS

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Hollow hard shell particles of 200 nm and 2 micron diameter with a 10-nm-thick porous silica shell have been synthesized using polystyrene templates and a sol-gel process. The template insures than the hollow particles are monodispersed, while the charged silica surface insures that they remain suspended in solution for weeks. When filled with perfluorocarbon gas, the particles behave as an efficient contrast agent for color Doppler ultrasound imaging in human breast tissue. The silica shell provides unique properties compared to conventional soft shell particles employed as ultrasound contrast agents: uniform size control, strong adsorption to tissue and cells immobilizing particles at the tissue injection site, a long imaging lifetime, and a silica surface that can be easily modified with biotargeting ligands or small molecules to adjust the surface charge and polarity.

CARDIOVASCULAR HEALTH EFFECTS OF PM2.5 AND NICKEL NANOPARTICLE

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It is well documented that exposure to ambient fine particulate matter (PM2.5) creates increased risks for cardiovascular disorders (CVD) in humans. However, the mechanism(s) and component(s) responsible for PM2.5-associated CVD are not known. Our recent animal studies suggest that nickel (Ni) plays critical roles in PM2.5-associated CVD. To test this hypothesis, we identified two areas, Jinchange and Zhangye, in China with comparable PM2.5 but different Ni exposures for which to investigate a variety of cardiovascular markers including reparative endothelial progenitor cells (EPCs). Ambient PM2.5 with high Ni content induced elevated systemic inflammatory markers and reduced EPCs. Additionally, we have shown that both low and high concentrations of inhaled Ni nanoparticles cause reduced numbers of bone marrow EPCs of mice as well as reduced functions of these cells and may be a mechanism by which CVDs occur. Taken together, the results of the mouse exposure bolster the findings from the human study and point toward a common cardiovascular maintenance cell population that may be adversely affected by Ni on or in PM2.5.

EFFICIENT CHARACTERIZATION OF NANOPARTICLES THROUGH AN INTELLIGENT COMBINATION OF ANALYTICAL TECHNIQUES

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"There is plenty of room at the bottom"—the visionary statement of the legendary Feynman has been realized within a decade by the researchers across the globe. The advent of "nanoparticles" and the realization of their potential applications in defense, energy, environment and health made the need for their synthesis and characterization quite essential. However, the inherently complex nature of various nanoparticles made their detailed characterization significantly intricate. Here we present two specific examples: (1) nanoparticles embedded in a matrix and (2) functionalized nanoparticles. The efforts by the team of scientists from EMSL, to utilize the combination of high-resolution analytical electron microscopy and laser-assisted 3D-atom probe tomography for the three-dimensional chemical imaging of embedded Au-nanoparticles in MgO single crystal, will be presented. Also, in order to understand the functionalized cerium oxide (ceria) nanoparticles, we are using a combination of experimental, surface analysis using electron and optical spectroscopies, and theoretical analysis of the materials system. Nonlinear optical spectroscopy techniques such as SHG, SFG along with XPS, TEM, UV-Vis, and atomistic modeling are being utilized to obtain a molecular-scale visualization of the functional group conformation on the nanoparticles, surface chemistry, and its influence on the functionality of the nanoparticles.

SIZE DISTRIBUTION MEASUREMENTS OF NEWLY FORMED 1-6 NANOMETER ATMOSPHERIC AEROSOLS

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Atmospheric aerosols influence climate and climate change on local to global scales by affecting the atmospheric radiation balance directly by scattering and absorbing incoming solar radiation and indirectly as cloud condensation nuclei. New particle formation (NPF) by photochemical reactions of gas-phase precursors greatly increases the number concentrations of atmospheric aerosols, and therefore their impact on climate. Although methods for measuring sizes and concentrations N of newly formed particles of diameter greater than 3 nm are well established, measurements of nanoparticles and neutral molecular clusters smaller than this are needed to constrain nucleation rates and to better understand nucleation mechanisms. A new instrument for "bridging the gap" in measurements from neutral molecular clusters to nanoparticles has been developed and was continuously deployed in an intensive measurement campaign at Boulder, CO, in September 2010. Size distribution measurements down to 1 nm are achieved with an electrical mobility spectrometer using diethylene glycol as working fluid (50% activation efficiency at 1.2 nm). Under conditions of rapid NPF, N ($D_p < 5$ nm) can exceed N ($D_p > 5$ nm) by more than 100 fold, greatly influencing the dynamics of the evolving aerosol.

NEW PARTICLE FORMATION FROM METHANESULFONIC ACID IN AIR

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Identifying precursors and determining rates of formation for new particles in the atmosphere is an essential step in quantifying the effects of particulate matter on human health and climate change. Sulfuric acid is well known to play an important role in new particle formation, and much work has been done to characterize its role as a particle precursor, with recent studies suggesting the involvement of both ammonia and organic amines. Methanesulfonic acid (MSA) is widespread in the atmosphere as is formed alongside sulfuric acid in the oxidation of organosulfur compounds such as dimethyl sulfide and methyl mercaptan. However much less is known about its impact on new particle formation. We report here preliminary results from laboratory studies of new particle formation and growth from the gas phase reaction of MSA with organic amines. These studies are performed using a unique flow tube system equipped with an electrical aerosol analyzer and an scanning mobility particle sizer (SMPS), which are used to measure particle size distributions as a function of time and reactant concentration at 295 K in 1 atm of air. The implications for the role of MSA in new particle formation and growth will be discussed.

INHALED NICKEL NANOPARTICLES ENHANCES PROGRESSION OF ATHEROSCLEROSIS, REDUCES VASCULAR REACTIVITY, AND ALTERS GENE ACTIVITY IN BRAIN IN A MURINE MODEL

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There is evidence that once deposition of inhaled nanoparticles (NPs) occurs, the particles can bypass clearance mechanisms and target secondary organs, such as, the cardiovascular system and the brain. Utilizing a whole-body exposure system, ApoE-/- or C57BL/6 male mice were exposed to either nickel hydroxide NPs (NHNP; 100, 150, or 900 μg/m^3) or filtered air (FA) for time periods ranging from 1 d to 5 m (5 h/d; 5 d/w). At 24-hr post exposure, tension studies were conducted to evaluate vascular function in response to a vasoconstrictors and -dilators in the carotid artery. Results indicated that arteries from NHNP mice showed statistically significant differences in contractile and relaxation responses compared to those from FA mice. Oxidative stress and inflammation in the pulmonary and extrapulmonary system indicated damage, and the degree of plaque formation was determined in the ascending aorta. In addition, three brain regions were collected (olfactory bulb, midbrain, and cerebellum) for gene expression analyses. These results suggest that both short- and long-term exposure to inhaled NHNPs can induce oxidative stress and inflammation in both pulmonary and extrapulmonary organs that can accelerate atherosclerosis in ApoE-/- mice as well as alter vascular function and brain gene expression in C57BL/6 mice.

PHYSICOCHEMICAL PROPERTY MEASUREMENTS: KEY TO ENABLING RISK AND FATE ASSESSMENT FOR ENGINEERED NANOMATERIALS

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The National Institute of Standards and Technology is actively working to address the need for physicochemical property measurements applicable to engineered nanomaterials (ENMs) by developing, standardizing, and validating transferable measurement methods, protocols, and certified reference materials. Another important component of this effort is the interrogation of structure-property relationships derived from critically evaluated experimental results. Research activities include the following: development of nanoscale reference materials for instrument and method validation, laboratory qualification, and benchmarking, and to support interlaboratory comparisons; studies to develop standardized dispersion protocols for ENMs in biological and environmental test media, and to evaluate current practices; research to assess the physicochemical stability of nanoscale Ag and Au in biological and environmental matrices; measurements to characterize and quantify the amount, conformation, and distribution of surface-bound molecular species; evaluation of methods for detection and characterization of aggregates formed in ENM dispersions; and application of synchrotron X-ray and neutron scattering methods to study ENM formation, interactions, and functionalization.

USING MASS SPECTROMETRY TO CHARACTERIZE AIRBORNE PARTICLES

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Airborne particles affect health, reduce visibility, and impact climate by scattering light and altering cloud properties, and complete particle characterization is essential to understand these impacts. Secondary organic aerosols (SOAs) are a significant constituent of atmospheric particles and are formed from the condensation of semi-volatile oxidation products. The partitioning of these semi-volatile compounds between the gas phase and particles makes characterization particularly challenging. Traditional analysis techniques involve filter-based sampling and extraction, which can introduce artifacts. In the past decade, real-time particle mass spectrometry has emerged as a powerful technique that overcomes these artifacts. However, their response to organic nitrates, which are present in SOAs, is unknown. Ambient ionization mass spectrometry has also emerged as a promising technique for particulate analysis because little or no sample preparation is needed and Fourier transform infrared (FTIR) spectra of the same sample can be obtained. We report here results from the analysis of laboratory-generated SOAs from the oxidation of several terpenes, including α-pinene, using high-resolution time-of-flight aerosol mass spectrometry (HR-ToF-AMS), atmospheric solids analysis probe mass spectrometry (ASAP-MS), and FTIR. The ability of HR-ToF-AMS, a real-time technique, to analyze organic nitrates will be explored, as will the applicability of ASAP-MS, an ambient ionization technique, to particulate analysis.

CHARACTERIZATION OF HIDDEN NANOPARTICLES-POLYMER INTERFACE IN COMPOSITES

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The interface of nanoparticles-polymer plays an important role in properties and applications of nanocomposites. However, few analytical techniques are suitable for characterizing this interface due to its small length scale and hidden natures. In this work, the hidden nanoparticles-polymer interface in composites is studied by scanning probe microscopy (SPM) and scanning electron microscopy (SEM). Specifically, electric force microscopy (EFM), a special type of SPM based on long-range electrostatic interactions, and poly-transparent SEM (PT-SEM), a newly developed SEM technique for subsurface imaging, were applied in this study. The high-resolution imaging of nanoparticles-polymer interface such as zinc oxide-polyurethane, titanium oxide-epoxy, carbon nanotube-epoxy, and carbon nanotube-polyimide was demonstrated. The effect of experimental parameters of EFM and PT-SEM on interface imaging was also discussed. In particular, EFM and PT-SEM are nondestructive techniques for the nanoscale characterization of hidden interface in both thin film and bulk samples without any sample preparations. Hence, EFM and PT-SEM will be powerful tools not only for the characterization of hidden interface in nanocomposites, but also for a broad range of other nanotechnology applications.

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Participant Biographies

SPEAKERS

Pedro Alvarez, Ph.D., is the George R. Brown Professor of Engineering and the chair of the Department of Civil and Environmental Engineering at Rice University. He received a B. Eng. in civil engineering from McGill University and M.S. and Ph.D. in environmental engineering from the University of Michigan. His research focuses on environmental sustainability through bioremediation of contaminated aquifers, fate and transport of toxic chemicals, the water footprint of biofuels, microbial-plant interactions, medical bioremediation, and environmental implications and applications of nanotechnology. Dr. Alvarez is a diplomate of the American Academy of Environmental Engineers and a fellow of American Society of Civil Engineers (ASCE). Past honors include president of Association of Environmental Engineering and Science Professors (AEESP), Honorary Consul of Nicaragua, the Malcom Pirnie-AEESP Frontiers in Research Award, the Water Environment Federation (WEF) McKee Medal for Groundwater Protection, the Strategic Environmental Research and Development Program (SERDP) Cleanup Project of the Year Award, the Button of the City of Valencia, the Collegiate Excellence in Teaching Award from the University of Iowa, the Alejo Zuloaga Medal from the Universidad de Carabobo, Venezuela, a Career Award from the National Science Foundation, a Rackham Fellowship, and best paper awards from the Environmental Protection Agency (EPA) Hazardous Substance Research Center (HSRC) for Regions 7 and 8, WEF, and the Battelle Bioremediation Symposium. Dr. Alvarez currently serves on the editorial board of *Environmental Science and Technology* and as honorary professor at Nankai and Kunming Universities in China and as adjunct professor at the Universidade Federal de Santa Catarina in Florianopolis, Brazil.

Jennifer S. Curtis, Ph.D., is a professor in the Chemical Engineering Department at the University of Florida (UF). Prior to this, she held administrative roles as department chair of chemical engineering at UF and associate dean of engineering and department head of freshman engineering at Purdue University. Dr. Curtis received a B.S. in chemical engineering from Purdue University (1983) and a Ph.D. in chemical engineering from Princeton University (1989). She has an internationally recognized research program in the development and validation of numerical models for the prediction of particle flow phenomena. She is the co-author of more than 100 publications and has given more than 160 invited lectures at universities, companies, government laboratories, and technical conferences. Professor Curtis is a recipient of a Fulbright Research Scholar Award, a National Science Foundation (NSF) Presidential Young Investigator Award, the American Society of Engineering Education's (ASEE) Chemical Engineering Lectureship Award, the Eminent Overseas Lectureship Award by the Institution of Engineers in Australia, the ASEE's Sharon Keillor Award for Women in Engineering, and the American Institute of Chemical Engineers (AIChE) Fluidization Lectureship Award. She currently serves as associate editor of *AIChE Journal* and on the editorial advisory board of *Powder Technology and Chemical Engineering Education*. She has served on the National Academy of Engineering's (NAE) Committee on Engineering Education and has participated in two NAE Frontiers of Research Symposiums (2003 and 2008). Currently, she is a board member of the National Academies' Chemical Science Roundtable, as well as the Council for Chemical Research and the American Institute of Chemical Engineers.

Abhaya Datye, Ph.D., has been on the faculty at the University of New Mexico since 1984. He is presently distinguished professor of chemical and nuclear engineering and director of the Center for Microengineered Materials. He also directs the graduate program in nanoscience and microsystems. Dr. Datye received a B.S. in chemical engineering from the Indian Institute of Technology, an M.S. in chemical engineering from the University of Cincinnati, and a Ph.D. in chemical engineering from the University of Michigan. His research interests are in heterogeneous catalysis, materials characterization, and nanomaterials synthesis. His research group has pioneered the development of electron microscopy tools for the study of catalysts. By developing model catalysts for this work, they have shown that the metal and oxide surfaces and interfaces in catalytic materials can be studied at near atomic resolution. His current work involves fundamental studies of catalyst sintering, low temperature methanol reforming into H2 for portable power applications, and synthesis of novel nanostructured heterogeneous catalysts.

Vicki H. Grassian, Ph.D., received her B.S. in chemistry from the State University of New York at Albany (1981), and she did her graduate studies at Rensselaer Polytechnic Institute (M.S., 1982) and the University of California-Berkeley (Ph.D., 1987). Dr. Grassian is currently the F. Wendell Miller Professor in the Department of Chemistry and holds appointments in the Departments of Chemical and Biochemical Engineering and Occupational and Environmental Health. At the University of Iowa, Dr. Grassian has been the recipient of a Faculty Scholar Award (1999-2001), a Distinguished Achievement Award (2002), a James Van Allen Natural Sciences Faculty Fellowship (2004), the Regents Award for Faculty Excellence (2006), and the Outstanding Graduate Student Mentoring Award (2008). In 2006, she was appointed as the director of the Nanoscience and Nanotechnology Institute at the University of Iowa by the vice president for research. Her research interests are in the areas of environmental molecular surface science, heterogeneous atmospheric chemistry, climate impact of atmospheric aerosols, and environmental and health aspects of nanoscience and nanotechnology. She has more than 180 peer-reviewed publications and 15 book chapters and she has edited 3 books, the most recent being *Environmental Catalysis* published by CRC Press in 2005 and *Nanoscience and Nanotechnology: Environmental and Health Impacts* published in 2008 by John Wiley and Sons. In 2003, Dr. Grassian received a U.S.-National Science Foundation Creativity Award, and in 2005, she was elected as a fellow of the American Association for the Advancement of Science. She was named fellow of both the Royal Society of Chemistry and the American Vacuum Society in 2010. She currently serves on the editorial boards of the *Journal of Physical Chemistry*, *Surface Science*, *Atmospheric Environment*, and *Aerosol Science and Technology*. She also serves on the Publications Committee of the American Association of Aerosol Research, Environmental Molecular Sciences Laboratory at Pacific Northwest National Laboratory Users Advisory Committee, and the Executive Committee of the Physical Chemistry Division of the American Chemical Society. She currently chairs the standing symposium Interfacial Environmental Chemistry for the Colloid and Surface Chemistry Division of the American Chemical Society and was recently elected chair of the Division to serve in 2012. In 2006, Dr. Grassian co-chaired a National Science Foundation-sponsored workshop on sustainability and chemistry. She was the primary organizer and editor of the workshop report titled *Chemistry for a Sustainable Future*. The report for that workshop was reprinted in 2009 for the National Science Foundation as a result of a renewed national interest in energy and the environment.

Michael Hochella, Jr., Ph.D., is university distinguished professor at Virginia Tech, concentrating in the area of nanogeoscience. He received his B.S. and M.S. from Virginia Tech in 1975 and 1977, respectively, and his Ph.D. from Stanford University in 1981. He has been a professor at Stanford and Virginia Tech for a total of 21 years. He has been a Fulbright Scholar, a Humboldt Award winner, and Virginia Scientist of the Year. He is a fellow of six international scientific societies including the American Geophysical Union (AGU) and the American Association for the Advancement of Science (AAAS), a Dana Medal winner (Mineralogical Society of America), and a former president of the Geochemical Society. He is currently president of the Mineralogical Society of America (MSA) as of October 2011. He has also won the Brindley Lecture Award (Clay Minerals Society) and the Distinguished Service Medal of the Geochemical Society. He has served on high-level advisory boards at the National Science Foundation and the Department of Energy. He has an h-index of 40 with more than 4,000 citations. He has raised $16.4 million in research funding. Fourteen of his former advisees are now professors at leading institutions around the world, while others hold prominent positions in publishing, national labs, and industry.

Morton Lippmann, Ph.D., is a professor of environmental medicine at the New York University (NYU) School of Medicine, where he has been a faculty member since 1967. He holds a Ph.D. (NYU, 1967) in environmental health science, an S.M. (Harvard University, 1955) in industrial hygiene, and a B.Ch.E. (The Cooper Union, 1954) in chemical engineering. He has been the recipient of numerous awards, including Stokinger and Meritorious Achievement from the American Conference of Industrial Hygienists (ACGIH), Cummings from the American Industrial Hygiene Association (AIHA), Sinclair from American Association for Aerosol Research (AAAR), Smythe from American Academy of Industrial Hygiene (AAIH), and Career Achievement in Respiratory and Inhalation Toxicology from the Society of Toxicology (SOT). Much of this research has been focused on particulate matter (PM) in ambient air, and on specific airborne agents, notably ozone, sulfuric acid, and asbestos. Dr. Lippmann is a past chairman of the ACGIH (1982-1983); past president of the International Society of Exposure Analysis (1994-1995); and past member of the EPA Science Advisory Board's Executive Committee (2000-2001), EPA's Advisory Committee on Indoor Air Quality and Total Human Exposure (1987-1993), EPA's Clean Air Scientific Advisory Committee (1983-1987), and the National Institute of Occupational Safety and Health (NIOSH) Board of Scientific Counselors (1991-1993). He has been chair of the External Scientific Advisory Committee of the Children's Health Study of air pollution effects in Southern California at the University of Southern California (1993-2003). He currently serves as chair of the External Scientific Advisory Committees of the study of the inhalation toxicology of complex air pollutant mixtures at the National Environmental Respiratory Center in Albuquerque (1997-2007) and the EPA-supported PM Health Effects Research Center at Harvard. He has also chaired National Research Council committees on the Airliner Cabin Environment and the Health of Passengers and Crew and on Synthetic Vitreous Fibers, and he served on NRC Committees on Measurement and Control of Respirable Dust in Mines, Indoor Pollutants, Toxicity Data Elements, and In-Vivo Toxicity Testing of Complex Mixtures. His publications include more than 300 research and review papers in the scientific literature and 2 reference texts on environmental health science.

JIM LITSTER, PH.D., holds a joint appointment as professor of chemical engineering and professor of industrial and physical pharmacy at Purdue University, where he is a research thrust leader in the NSF-funded Engineering Research Center for Structured Organic Composite Systems (CSOPS). Prior to his appointment in 2007, he spent 20 years at The University of Queensland (UQ), most recently as head of the School of Engineering (2005-2007) and director of the Particle and Systems Design Centre (2001-2007). Dr. Litster is an internationally recognized leader in particle science and technology. He has a Ph.D. from The University of Queensland and spent several years working for BHP at its Newcastle Research Laboratories. From 1987 till 2007 he held a faculty appointment at The University of Queensland in chemical engineering, which included 5 years as chair of the department. He also has held a regular appointment as distinguished visiting professor at the University of Delaware (2001-2005). Dr. Litster's main research interests focus on particle design and formulation engineering—the production of particles and particulate delivery forms with well-controlled size and morphology from submicron to millimeter scale. The products of interest are many and varied, including proteins and other biological materials, pharmaceuticals, detergents and consumer goods, food, ceramics and high-value materials, fertilizers and agricultural chemicals, and minerals. He is particularly well known for his work on granulation, through which he has helped move this ubiquitous and troublesome process from a black art to an engineering science. He is the co-author of the well-known text in this area, *The Science and Engineering of Granulation Processes*, and his approaches are now widely used in engineering practice in industry. More recently, with collaborators at UQ and Purdue, he has established a major research focus on the recovery and delivery of bioactives for food and pharmaceutical applications particularly by crystallization and precipitation. In 2009, Dr. Litster was awarded the Achievement Award for Excellence in Granulation Research, 9th International Symposium on Agglomeration, and he has recently been elected a fellow of the Australian Academy of Technological Sciences and Engineering.

GERRY MCDERMOTT, PH.D., is a senior scientist at the National Center for X-ray Tomography, Physical Biosciences Division, Lawrence Berkeley National Laboratory, and is also affiliated with the Department of Anatomy, University of California, San Francisco.

RALPH NUZZO, PH.D., a recognized leader in the chemistry of materials, is director of the Frederick Seitz Materials Research Laboratory and the Center for Microanalysis of Materials at the University of Illinois, Urbana-Champaign. He also serves as the William H. and Janet Lycan Professor of Chemistry and professor of materials science and engineering at the university. Dr. Nuzzo received his B.S. in chemistry from Rutgers University and his Ph.D. in organic chemistry from Massachusetts Institute of Technology (MIT). After completing his graduate studies, he accepted a position at Bell Laboratories, then a part of AT&T, where he held the title of distinguished member of the technical staff in materials research.

MICHAEL T. POSTEK, PH.D., is the chief of the Mechanical Metrology Division within the Physical Measurement Laboratory at the National Institute of Standards and Technology (NIST). He has been involved with electron microscopy for more than 30 years and micro- and nano-scale scanning electron microscope-based length metrology for more than 20 years, and he has published more than 250 papers, articles, and book chapters on this and related topics. Dr. Postek received his B.A. from the University of South Florida (1973); M.S. from Texas A&M University (1974); Ph.D. from Louisiana State University (1980); and an Executive M.S. in technology management from the University of Maryland (1997).

YI QIAO, PH.D., is currently a research specialist at the Corporate Research Laboratory, 3M Company. Dr. Qiao obtained his Ph.D. in mechanical engineering in 2006 from Northwestern University. His main research interest is in developing techniques for various industrial process measurement and diagnosis.

Stephen E. Schwartz, Ph.D., is a senior scientist and group leader at Brookhaven National Laboratory (BNL). His current research interest centers on the influence of energy-related emissions on climate, with a focus on the role of atmospheric aerosols. Dr. Schwartz is a fellow of the American Association for the Advancement of Science and of the American Geophysical Union, and he is recipient of the 2003 Haagen-Smith Award for an "outstanding paper" published in the journal *Atmospheric Environment*. In 2006 he received the BNL Science and Technology Award for distinguished contributions to the laboratory's science and technology mission. In his research at BNL, Dr. Schwartz developed methods to describe the rate of reactions in clouds that lead to production of acid rain. More recently, Dr. Schwartz has been focusing on microscopic and submicroscopic aerosol particles, which influence a variety of atmospheric processes, from precipitation to climate change. Dr. Schwartz is author or co-author of more than 100 papers published in peer-reviewed scientific journals. He was editor of *Trace Atmospheric Constituents*, published by Wiley in 1983, and was co-editor of a three volume series *Precipitation Scavenging and Atmosphere-Surface Exchange*, published by Hemisphere in 1992. He is co-author of *Sea Salt Aerosol Production: Mechanisms, Methods, Measurements, and Models—A Critical Review*, published by the American Geophysical Union in 2004. Dr. Schwartz's research has been quite influential. He served as chief scientist of the Department of Energy's Atmospheric Science Program from 2004 through 2009. He also served on the management team that developed and led the Department of Energy's Atmospheric Radiation Measurement (ARM) Program. Dr. Schwartz received his bachelor's degree in chemistry from Harvard University in 1963 and his Ph.D. in chemistry from the University of California, Berkeley, in 1968. After postdoctoral research at the University of Cambridge, England, Dr. Schwartz joined the Chemistry Department at Stony Brook University. He joined Brookhaven National Laboratory in 1975.

Lee Silverman, Ph.D., received his B.S. from MIT in materials science and engineering in 1981. He then worked for 2 years doing process development for optical waveguide materials for telecommunication at Corning. Dr. Lee then went back to MIT and graduated with a Ph.D. in ceramic science and engineering in 1987. Following graduate school, Dr. Lee started work for DuPont, where he has been for the past 23 years. At DuPont, he has worked on materials intended for uses in structural, electronic, optical, and sensing applications, as well as others. Dr. Lee is currently research manager for nanocomposite technologies in DuPont's Central Research and Development Laboratory in Wilmington, Delaware.

James (Jim) Smith, Ph.D., is a scientist and head of the Ultrafine Aerosols Research Group at the Atmospheric Chemistry Division of the National Center for Atmospheric Research (NCAR), and he is currently visiting professor of aerosol physics at the University of Eastern Finland. Dr. Smith received his Ph.D. degree in environmental science and engineering at the California Institute of Technology. His thesis research included one of the first applications of molecular modeling to the elucidation of the photo-oxidation of tropospheric pollutants, as well as in situ measurements of the evolution of the size and charge of highly charged droplets emitted from electrosprayed solutions. Dr. Smith's work at NCAR involves performing laboratory and field measurements in order to understand and quantify the mechanisms of atmospheric nanoparticle formation and growth. This research is important because the formation of nanoparticles by nucleation and their subsequent growth are poorly understood processes that have significant implications for human health and climate. Dr. Smith's accomplishments include the development of the Thermal Desorption Chemical Ionization Mass Spectrometer (TDCIMS), which 10 years after its introduction remains the only instrument that can measure the molecular composition of 6- to 30-nm-diameter particles at ambient levels. His achievements include both the development of this novel instrument and its application to address key scientific questions. His observations of the importance of organic compounds in particle formation are currently being incorporated into global climate models to achieve better estimates of the impacts of aerosols on climate. Dr. Smith is the recipient of the 2009 Kenneth T. Whitby Award, given annually by the American Association for Aerosol Research (AAAR). This award recognizes outstanding technical contributions to aerosol science and technology by a young scientist. He is active in national and international research organizations and projects. He has organized or led several workshops and field campaigns devoted to atmospheric aerosol formation and physicochemical properties, and he currently serves as a member of the board of directors of the AAAR.

Douglas Tobias, Ph.D., obtained his B.S. and M.S. in chemistry at the University of California (UC), Riverside, in 1984 and 1985, respectively, and his Ph.D. in chemistry and biophysics at Carnegie Mellon University in 1991. He received a National Research Service Award from the National Institutes of Health for his post-doctoral research in the Department of Chemistry at the University of Pennsylvania from 1991 to 1995, and he was a guest researcher at the Center for Neutron Research at the National Institute of Standards and Technology from 1995 to 1997. He was appointed to the faculty in the Department of Chemistry at UC Irvine in 1997, promoted to associate professor in 2003 and to full professor in 2005. He was elected fellow of the American Association of the Advancement of Science in 2006. His research interests include the development and application of molecular simulation techniques to the study of membrane biophysics, heterogeneous atmospheric chemistry, and the chemical dynamics of aqueous interfaces.

Angela Violi, Ph.D., is an assistant professor at the University of Michigan in the Department of Mechanical Engineering and the Department of Chemical Engineering. Her current research interests include multiscale simulation of nanoparticle growth and self assembly, applied chemical kinetics, ab initio methods for reaction chemistry, aerosols and molecular modeling of complex systems using atomistic models. She has published 28 papers in these fields in peer-reviewed journals and more than 40 conference papers and peer-reviewed proceedings. Among the awards she received is the International Bernard Lewis Fellowship from the Combustion Institute for "High Quality Research in Combustion." Dr. Violi has served as a reviewer for more than 10 journals and government foundations, such as the National Science Foundation. She received her Ph.D. in chemical engineering from the University of Naples Federico II.

Alla Zelenyuk, Ph.D., is a physical chemist with expertise in real-time characterization of physical and chemical properties of individual aerosol particles. Her current research projects include (1) development and application of unique tools to study fundamental properties and chemical/microphysical transformations of size-selected nanoparticles; (2) field studies to understand "aerosol life cycle"; (3) laboratory studies of secondary organic aerosol formation; (4) laboratory/field studies of effect of particle size, internal composition, shape, and morphology on particle hygroscopicity, cloud condensation nuclei, and ice nucleation activity used for model development; (5) formation, transformations, and properties of fractal particles, including combustion-related aerosols; and (6) multidimensional data analysis and visualization. She received her Ph.D. in chemical physics from the Moscow Institute of Physics and Technology.

WORKSHOP ORGANIZING COMMITTEE

Barbara Finlayson-Pitts, Ph.D. (NAS), is a professor of chemistry in the School of Physical Sciences at the University of California where she studies chemical reactions in the lower atmosphere to better understand air pollution in urban and remote areas. She directs AirUCI—Atmospheric Integrated Research Using Chemistry at Interfaces—a multi-investigator effort to better understand how air and water interact in the atmosphere and how those processes affect air quality and global climate change. Dr. Finlayson-Pitts has studied the effects of sea salt on urban smog formation and on remote atmospheres, as well as how chemical reactions on the surfaces of buildings and roads affect urban air quality and models of air pollution. Dr. Finlayson-Pitts received a B.S. from Trent University in 1970, an M.S. from the University of California, Riverside, in 1971, and a Ph.D. from the University of California, Riverside, in 1973. Her research interests include atmospheric, physical, and analytical chemistry.

Douglas Ray, Ph.D., is the associate laboratory director for the Fundamental & Computational Sciences Directorate at the Pacific Northwest National Laboratory (PNNL). Dr. Ray is responsible for PNNL's research programs conducted for the Department of Energy's Office of Science and for the National Institutes of Health. He directs more than 500 staff members in four research divisions: Atmospheric Sciences & Global Change, Biological Sciences, Chemical and Materials Science, and Computational Sciences & Mathematics. Dr. Ray joined PNNL in 1990. A laser spectroscopist, Dr. Ray's research interests include the effects of weak intermolecular interactions on chemical phenomena in condensed phases, at interfaces, in clusters and in supramolecular complexes. He earned a B.S. degree in physics from Kalamazoo College and a Ph.D. in chemistry at the University of California at Berkeley. Dr. Ray is a member of the American Chemical Society, American Physical Society, American Geophysical Union, and American Association for the Advancement of Science.

Levi T. Thompson, Ph.D., is the Richard Balzhiser Professor of Chemical Engineering at the University of Michigan. Other honors and awards include the National Science Foundation Presidential Young Investigator Award, Union Carbide Innovation Recognition Award, Dow Chemical Good Teaching Award, College of Engineering Service Excellence Award, and Harold Johnson Diversity Award. He is co-founder, with his wife Maria, of T/J Technologies, a developer of nanomaterials for advanced batteries and fuel cells. He is also consulting editor for the *AIChE Journal* and a member of the external advisory committee for the Center of Advanced Materials for Purification of Water with Systems (NSF Science and Technology Center at the University of Illinois) and AIChE Chemical Engineering Technology Operating Council. Dr. Thompson earned his B.ChE. from the University of Delaware and M.S.E. degrees in chemical engineering and nuclear engineering and a Ph.D. in chemical engineering from the University of Michigan. Research in Dr. Thompson's group focuses primarily on defining relationships between the structure, composition, and function of nanostructured catalytic and electrochemical materials. In addition, he has distinguished himself in the use of micromachining and self-assembly methods to fabricate micro-reactor, hydrogen production, and micro-fuel cell systems. Dr. Thompson leads a large multidisciplinary team developing compact devices to convert gasoline and natural resources into hydrogen. Recently, he was appointed founding director of the Hydrogen Energy Technology Laboratory.

D

Workshop Attendees

Andrew Allen, National Institute of Standards and Technology
Pedro Alvarez, Rice University
Trish Baisden, Lawrence Livermore National Laboratory
Mark Barteau, University of Delaware
Jonathan Bearr, Occupational Safety and Health Administration
Apurba Bhattacharya, Texas A&M
Christopher Brown, Occupational Safety and Health Administration
Scott Brown, University of Florida
Emily Bruns, University of California, Irvine
William Carroll, Occidental Chemical Corporation
Robert Celotta, National Institute of Standards and Technology
John Chen, Lehigh University
Katherine Chen, Bethlehem Steel Corp. (retired)
Tae Joon Cho, National Institute of Standards and Technology
Fan-Li Chou, U.S. Department of Agriculture
Ikenna G. Clarke, Washington, DC
Richard Conroy, National Institute of Biomedical Imaging and Bioengineering
Azita (AJ) Cuevas, New York University
Jennifer S. Curtis, University of Florida
Abhaya Datye, University of New Mexico
Matthew Dawson, University of California, Irvine
Fatou Diagne, Howard University
Patricia Downs, Occupational Safety and Health Administration
Sherrie Elzey, National Institute of Standards and Technology
Britt Erickson, Chemical and Engineering News
Heather Evans, Office of Science and Technology Policy
Gregory Fiechtner, DOE/Basic Energy Sciences
Barbara Finlayson-Pitts, University of California, Irvine
Vicki Grassian, University of Iowa
Vince Hackley, National Institute of Standards and Technology
Sharon Haynie, E.I. du Pont de Nemours & Company
Alexandra Hegji, Occupational Safety and Health Administration
Lori Henderson, National Institute of Biomedical Imaging and Bioengineering
Lee Herring, National Science Foundation
Michael Hochella, Virginia Polytechnic and State University
Kimberly Jones, Howard University
Christina Jones, Occupational Safety and Health Administration
Barbara Karn, Environmental Protection Agency
Abu Khan, U.S. Food and Drug Administration
Bojeong Kim, Virginia Polytechnic and State University
Chongai Kuang, Brookhaven National Laboratory
Satya Kuchibhatla, Pacific Northwest National Laboratory
Jim Laity, Office of Management and Budget
Eric Liberda, New York University
Morton Lippmann, New York University
James Litster, Purdue University
Kaipeng Liu, National Institute of Standards and Technology
Delina Lyon, University of Lyon, France
Matthew Martin, National Institute of Standards and Technology and University of Maryland
H. Paul Martinez, University of California, San Diego
Gerry McDermott, Lawrence Berkeley Laboratory and University of California, San Francisco
Li Mu, U.S. Food and Drug Administration
Ralph Nuzzo, University of Illinois, Urbana

Veronique Perraud, University of California, Irvine
Matthew Platz, National Science Foundation
Michael Postek, National Institute of Standards and Technology
Kevin Powers, University of Florida
Yi Qiao, 3M Corporation Research Process Laboratory
Malaisamy Ramamoorthy, Howard University
Douglas Ray, Pacific Northwest National Laboratory
Rebecca Reindel, Occupational Safety and Health Administration
Pierre Ricou, Arkema Inc.
Michael Rogers, National Institute of General Medical Sciences
Steve Schwartz, Brookhaven National Laboratory
Gary Senatore, Occupational Safety and Health Administration
Najm Shamim, Environmental Protection Agency
Lee Silverman, DuPont Central Research
Wade Sisk, U.S. Department of Energy/Basic Energy Sciences
James Smith, National Center for Atmospheric Research
Julian Taurozzi, National Institute of Standards and Technology
Theva Thevuthasan, Pacific Northwest National Laboratory
Patricia Thiel, Ames Laboratory and Iowa State University
Treye Thomas, U.S. Consumer Product Safety Commission
Levi Thompson, University of Michigan
Douglas Tobias, University of California, Irvine
De-Hao Tsai, National Institute of Standards and Technology
Maho Uchida, University of California, San Francisco
Angela Violi, University of Michigan
Stephanie Watson, National Institute of Standards and Technology
Robert Wiacek, Pixelligent Technologies, LLC
Douglas Worsnop, Aerodyne Research, Inc.
Brenda Yamen, Occupational Safety and Health Administration
Nyah Zarate, Purdue University
Alla Zelenyuk, Pacific Northwest National Laboratory
Jun Zhao, National Center for Atmospheric Research
Minhua Zhao, National Institute of Standards and Technology

E

Origin of and Information on the Chemical Sciences Roundtable

In April 1994 the American Chemical Society (ACS) held an Interactive Presidential Colloquium titled "Shaping the Future: The Chemical Research Environment in the Next Century."[1] The report from this colloquium identified several objectives, including the need to ensure communication on key issues among government, industry, and university representatives. The rapidly changing environment in the United States for science and technology has created a number of stresses on the chemical enterprise. The stresses are particularly important with regard to the chemical industry, which is a major segment of U.S. industry, in terms of trade and employment opportunities for a technical workforce. A neutral and credible forum for communication among all segments of the enterprise could enhance the future well-being of chemical science and technology.

After the report was issued, a formal request for such a roundtable activity was transmitted to Dr. Bruce M. Alberts, chairman of the National Research Council (NRC), by the Federal Interagency Chemistry Representatives, an informal organization of representatives from the various federal agencies that support chemical research. As part of the NRC, the Board on Chemical Sciences and Technology (BCST) can provide an intellectual focus on issues and fundamentals of science and technology across the broad fields of chemistry and chemical engineering. In the winter of 1996 Dr. Alberts asked BCST to establish the Chemical Sciences Roundtable to provide a mechanism for initiating and maintaining the dialogue envisioned in the ACS report.

The mission of the Chemical Sciences Roundtable is to provide a science-oriented, apolitical forum to enhance understanding of the critical issues in chemical science and technology affecting the government, industrial, and academic sectors. To support this mission the Chemical Sciences Roundtable will do the following:

- Identify topics of importance to the chemical science and technology community by holding periodic discussions and presentations, and gathering input from the broadest possible set of constituencies involved in chemical science and technology.
- Organize workshops and symposiums and publish reports on topics important to the continuing health and advancement of chemical science and technology.
- Disseminate information and knowledge gained in the workshops and reports to the chemical science and technology community through discussions with, presentations to, and engagement of other forums and organizations.
- Bring topics deserving further in-depth study to the attention of the NRC's Board on Chemical Sciences and Technology. The roundtable itself will not attempt to resolve the issues and problems that it identifies—it will make no recommendations or provide any specific guidance. Rather, the goal of the roundtable is to ensure a full and meaningful discussion of the identified topics so that the participants in the workshops and the community as a whole can determine the best courses of action.

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[1] American Chemical Society. 1994. *Shaping the Future: The Chemical Research Environment in the Next Century.* Report from the Interactive Presidential Colloquium, April 7-9, Washington, D.C.

F

References

IMPORTANT NOTE ABOUT INTERNET WEBSITES

The Internet information provided in this Summary was correct, to the best of our knowledge, at the time of publication. It is important to remember, however, the dynamic nature of the Internet. Information on websites can be transient and is not always validated or verifiable. Resources that are free and publicly available one day may require a fee or restrict access the next, and the location of items may change as menus and homepages are reorganized.

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