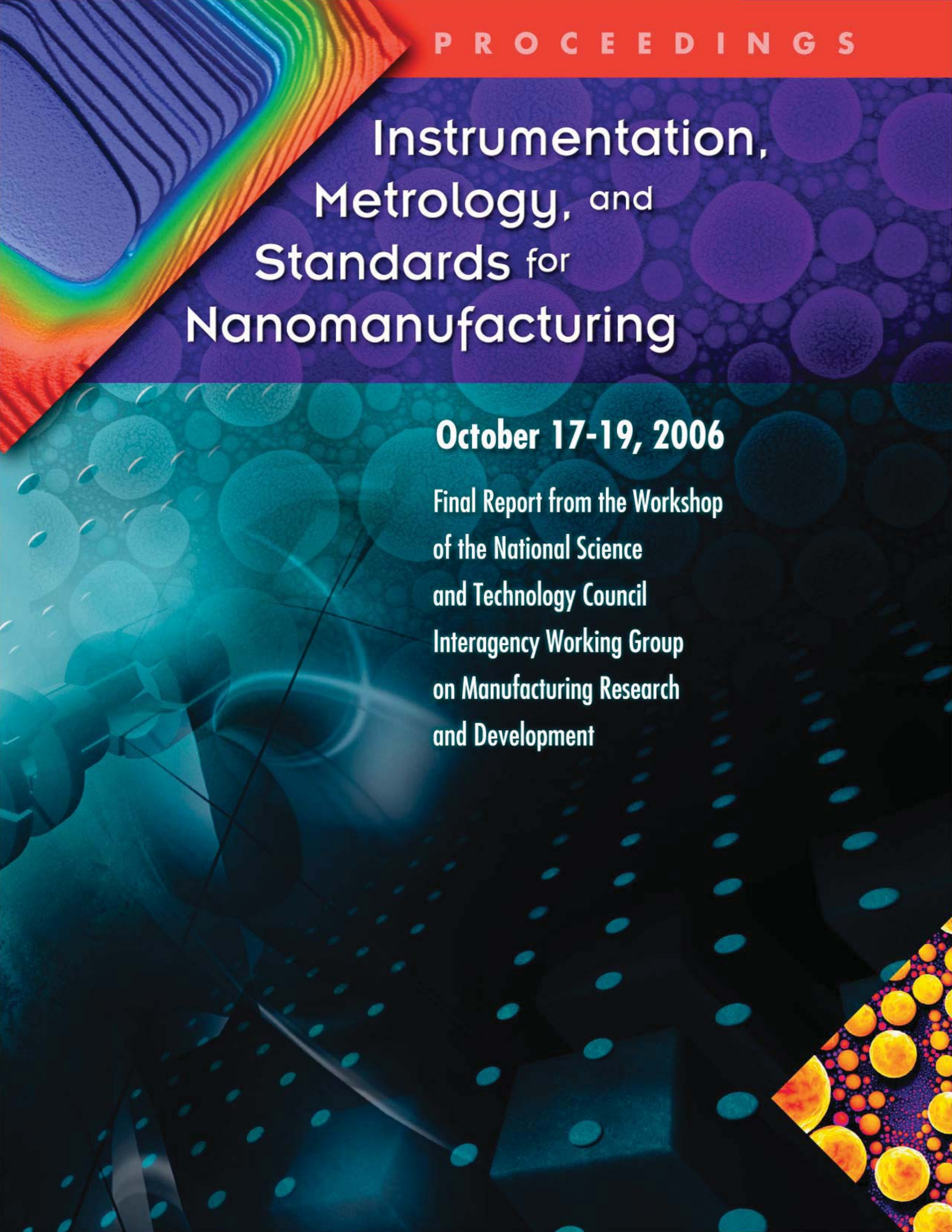


PROCEEDINGS

Instrumentation, Metrology, and Standards for Nanomanufacturing

October 17-19, 2006

Final Report from the Workshop
of the National Science
and Technology Council
Interagency Working Group
on Manufacturing Research
and Development

About the National Science and Technology Council

The National Science and Technology Council (NSTC) was established by Executive Order on November 23, 1993. This cabinet-level council is the principal means by which the President coordinates science, space, and technology policies across the Federal Government. NSTC coordinates diverse paths of the Federal research and development enterprise.

An important objective of the NSTC is the establishment of clear national goals for Federal science and technology investments in areas ranging from information technologies and health research to improving transportation systems and strengthening fundamental research. The Council prepares research and development strategies that are coordinated across the Federal agencies to form a comprehensive investment package aimed at accomplishing multiple national goals. For more information visit http://www.ostp.gov/cs/nstc.

About the Interagency Working Group on Manufacturing Research and Development

The Interagency Working Group (IWG) on Manufacturing Research and Development (R&D) serves as a forum within the NSTC Committee on Technology for developing consensus and resolving issues associated with manufacturing R&D policy, programs, and budget guidance and direction.

The chartered goal of the IWG on Manufacturing R&D, which was formed in 2004, is to identify and integrate requirements, conduct joint program planning, and develop joint strategies for the manufacturing R&D programs conducted by the Federal government. The IWG serves as a forum for the exchange and leverage of information among the participating agencies.

For more information on the IWG on Manufacturing R&D, see http://www.manufacturing.gov

About this document

This is the report of a workshop convened by the IWG on Manufacturing R&D in October 2006 addressing technology challenges and research needs associated with nanomanufacturing, with particular emphasis on instrumentation, metrology, and standards requirements. It covers issues related to nanomanufacturing of devices and products in four industrial sectors: chemicals, electronics, pharmaceutical/biomedical, and composites. In addition, the report addresses a cross-cutting environmental, health, and safety (EHS) component that was identified and discussed at the workshop. The intent of the workshop and report is to set the stage for the development of innovative solutions and promising results for the nanomanufacturing and nanometrology communities.

Cover and book design

Cover design by Beamie Young (NIST). Inset image on lower right of front cover is of nickel spheres imaged by NIST's scanning electron microscope (courtesy of Michael Postek and Andras Vladar, NIST). Book design by staff at WTEC, in consultation with NIST.

INTERAGENCY WORKING GROUP
on
MANUFACTURING RESEARCH and DEVELOPMENT

Instrumentation, Metrology, and Standards for Nanomanufacturing

Workshop Report

Compiled and Edited by:

Michael T. Postek, Kevin W. Lyons, and Mylene S. Ouimette, NIST[1, 2]

and

Geoffrey M. Holdridge, WTEC

Final Report, October 2008

Sponsors:

National Institute of Standards and Technology

U.S. Department of Commerce

National Science Foundation

Office of Naval Research

Keywords: nanomanufacturing, measurement, metrology, standards, instrumentation, nanometrology, National Nanotechnology Initiative, NNI

[1] Contributions of the National Institute of Standards and Technology not subject to copyright. Copyrights to some portions of this report (including graphics) contributed by other workshop participants are reserved by original copyright holders or their assignees, and are used here by permission or under the Government's license. Requests to use any images must be made to the provider identified in the image credits.

[2] Certain commercial equipment is identified in this report to adequately describe experimental procedures. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the equipment identified is necessarily the best available for the purpose.

ACKNOWLEDGMENTS

The Interagency Working Group (IWG) on Manufacturing Research and Development (R&D) convened the workshop on Instrumentation, Metrology, and Standards for Nanomanufacturing October 17–19, 2006, at the Holiday Inn and the National Institute of Standards and Technology (NIST) in Gaithersburg, MD. The presentations and discussions that took place at the workshop provided the foundation for this report. Thanks to the input of the participants, this report will be a valuable guide to the IWG and its member agencies. The workshop sponsors thank the principal authors of this report, who are listed on the title pages of the respective chapters. In addition, they thank all participants; a complete list of attendees is provided in Appendix B. Special thanks are extended to the members of the steering committee and the workshop technical organizing committee, listed below.

STEERING COMMITTEE

- Michael Postek, Chair (NIST)
- Kevin Lyons Co-Chair (NSF/NIST)
- James Murday and Khershed Cooper (DOD)
- Diana Bauer and Nora Savage (EPA)
- Treye Thomas (CPSC)
- Meyya Meyyappan and Raj Kaul (NASA)
- Tim Fitzsimmons, Julianne Levings, and David Prigel (DOE)
- William Chernicoff (DOT)
- Vladimir Murashov (NIOSH)
- Susan Skemp (Fellow, ASME, assigned to OSTP)
- RoseAnn Rosenthal (Ben Franklin Technology Partners)
- Ajay Malshe (University of Arkansas)

Nanomanufacturing Workshop Technical Breakout Session Leaders

Electronics

- Philip Lippel (WTEC, NNCO, and Facilitator)
- Ted Vorburger (NIST)
- Purabi Mazumdar (NIST)
- Dave Seiler (NIST)

Composites

- Clare Allocca (NIST and Facilitator)
- Stephen Gould (WTEC)
- Ted Maher (NIST)
- Tinh Nguyen (NIST)
- Vladimir Murashov (NIOSH)
- Alamgir Karim (NIST)

Pharma/Medical

- Hassan Ali (WTEC and Facilitator)
- Nicholas Dagalakis (NIST)
- Martin Fritts (SAIC)
- Anne Plant (NIST)
- Michael Gaitan (NIST)
- Ellyn Beary (NIST)
- Mylene Ouimette (NIST)
- Deb Newberry (Newberry Technologies, Inc.)

Chemical

- Geoff Holdridge (WTEC, NNCO, and Facilitator)
- Anne Chaka (NIST)
- Richard Colton (Naval Research Laboratory)
- Stephanie Hooker (NIST)
- Mark Hoover (NIOSH)
- Steve Hudson (NIST)
- Dianne Poster (NIST)
- John Henry Scott (NIST)
- Steve Stranick (NIST)

Many thanks are also due to Mary Lou Norris, then of NIST's Manufacturing Engineering Laboratory, and Stephen Gould of WTEC, who helped to coordinate the workshop, and to the conference support staff of NIST, especially Kathy Kilmer and Angela Ellis, who made sure that the meeting logistics were handled properly and efficiently.

Beamie Young is acknowledged and thanked for her graphics expertise in developing the workshop brochure, report cover, and several figures appearing in the text.

Special thanks are also due to Geoff Holdridge of WTEC and the National Nanotechnology Coordination Office (NNCO), who provided facilitation support and editorial assistance for the final report. Thanks also go to Philip Lippel of NNCO and WTEC and to the entire WTEC facilitation team—Geoff Holdridge, Hassan Ali, Stephen Gould, and Roan Horning—and to Pat Johnson of WTEC, who edited the final report manuscript.

Finally, thanks go to all the members of the National Science and Technology Council's Subcommittee on Nanoscale Science, Engineering, and Technology for their endorsement of the workshop and for their comments on the draft final report.

This workshop was convened by the Interagency Working Group on Manufacturing Research and Development of the National Science and Technology Council (NSTC), with the endorsement of and input from NSTC's Nanoscale Science, Engineering, and Technology Subcommittee. Funding for the workshop and for report editing and production was provided by the National Institute of Standards and Technology, the National Science Foundation, and the Office of Naval Research.

PREFACE

The 2004 Commerce Department report *Manufacturing in America*[1] recommended the creation of the Interagency Working Group (IWG) on Manufacturing Research and Development (R&D) to identify and integrate R&D requirements and to develop strategies for the Federal Government's manufacturing R&D programs. The IWG on Manufacturing R&D (hereafter referred to as "the IWG") reports to the National Science and Technology Council (NSTC) Committee on Technology; it was chaired at the time of this workshop by Dr. Dale Hall, the Director of the Manufacturing Engineering Laboratory at the National Institute of Standards and Technology (NIST). Its membership includes representatives from 15 executive departments, offices, and agencies of the Federal Government. These are listed below, along with the subordinate member agencies and their Internet addresses.

Objectives of the IWG on Manufacturing R&D include:

- Propose policy recommendations for manufacturing R&D
- Facilitate interagency program planning and budgeting, collaboration, coordination, and leverage
- Review agency priorities and technical issues for Federally funded manufacturing R&D
- Promote communications among the government, private sector, and academia on R&D requirements and programs

The IWG on Manufacturing R&D initially selected three technology priority areas to form the basis for a coordinated, multi-agency focus on manufacturing R&D. These topics, which were presented to the public during a public forum held by the IWG in March 2005, are each aligned with an existing national initiative:

- Nanomanufacturing
- Intelligent & Integrated Manufacturing
- Manufacturing for the Hydrogen Economy

In March 2008 under the auspices of the NSTC Committee on Technology, the IWG published the report *Manufacturing the Future: Federal Priorities for Manufacturing R&D*[2] that further articulates the Federal Government's role in each of the above areas.

For more information regarding the NSTC IWG on Manufacturing R&D, please contact the IWG Executive Secretary, Mr. David C. Stieren of the NIST Manufacturing Engineering Laboratory, at david.stieren@nist.gov.

---

[1] Available online at http://www.manufacturing.gov/report/index.asp. Additional information on the IWG and its activities is available at http://www.manufacturing.gov.

[2] Available online at http://www.ostp.gov/cs/nstc.

Agency Membership, IWG on Manufacturing Research and Development	
Department of Agriculture	- Cooperative State Research, Education, and Extension Service http://www.csrees.usda.gov/
Department of Commerce	- NIST Manufacturing Engineering Laboratory http://www.mel.nist.gov - International Trade Administration http://www.trade.gov
Department of Defense	- Manufacturing Technology Program http://www.dodmantech.com - Defense Advanced Research Projects Agency Defense Sciences Office http://www.darpa.mil/dso/
Department of Education	- Office of Vocational and Adult Education http://www.ed.gov/about/offices/list/ovae/index.html
Department of Energy	- Office of Energy Efficiency and Renewable Energy http://www.eere.energy.gov/
Department of Health and Human Services	- National Institute of Biomedical Imaging and Bioengineering http://www.nibib.nih.gov/
Department of Homeland Security	- Directorate for Science and Technology http://www.dhs.gov/xabout/structure/editorial_0530.shtm
Department of Labor	- Employment and Training Administration http://www.doleta.gov/
Department of Transportation	- Research and Innovative Technology Administration http://www.rita.dot.gov/
Environmental Protection Agency	- Office of Research and Development http://www.epa.gov/ORD/
National Aeronautics and Space Administration	- National Center for Advanced Manufacturing, Marshall Space Flight Center http://ed.msfc.nasa.gov/ncam/
National Science Foundation	- Directorate for Engineering http://www.nsf.gov/dir/index.jsp?org=ENG
Office of Management and Budget	- http://www.whitehouse.gov/omb
Office of Science and Technology Policy	- http://www.ostp.gov
Small Business Administration	- Office of Technology http://www.sba.gov/sbir/

The October 2006 Workshop on Instrumentation, Metrology, and Standards for Nanomanufacturing was attended by over 200 experts in nanomanufacturing from industry, academia, and Federal agencies (see Appendix B for a list of participants). The plenary session included invited presentations from top industry experts representing firms manufacturing nanotechnology-related products and support equipment. Reports from the National Nanotechnology Initiative (NNI) Grand Challenge workshops provided added background and context, especially the report from the NNI Interagency Workshop on Instrumentation and Metrology for Nanotechnology held on 27–29 January 2004 at NIST.[3]

---

[3] Available online at http://www.nano.gov/html/res/pubs.html.

The agenda for the workshop is provided in Appendix A. The initial presentations each day were followed by an afternoon of focused breakout sessions on four areas of application: (1) Chemicals, (2) Electronics, (3) Pharmaceuticals (Pharma/Biomedical), and (4) Composites. These facilitated sessions were held to discuss visionary goals for each area, prioritize future needs, and identify key technical barriers and challenges. Workshop discussions yielded recommendations for future research to enable the manufacture of real-world nanotechnology products, and they will help guide the IWG in its efforts to assist U.S. manufacturers in leveraging these efforts into a competitive technological advantage. The workshop concluded with an industry-led nanotechnology/nanomanufacturing stakeholder meeting, which focused specifically on predictive modeling capabilities and elements of a nanotechnology design infrastructure (see Appendix D).

A set of prioritized challenges emerged from each breakout session. These findings are expected to form the components of a set of challenges for nanomanufacturing in the areas of instrumentation, metrology, and standards development. This final report of the workshop presents the ideas that were generated by the various breakout groups as well as recommendations for future research and development. Definitions of the abbreviations and acronyms found throughout this report are provided in Appendix E.

TABLE OF CONTENTS

1. Setting the Stage

2. Stages of Technological Innovation Relevant to Nanomanufacturing

3. Instrumentation and Metrology for Chemicals

4. Instrumentation and Metrology for Nanoscale Electronics, Magnetics, and Photonics

5. Instrumentation and Metrology for Pharmaceutical/Biomedical Applications

6. Instrumentation and Metrology for Composites and Materials

7. Environmental, Health, and Safety Cross-Cut Issues for Nanotechnology

8. Conclusions

Appendices

EXECUTIVE SUMMARY

Nanomanufacturing is an essential bridge between the discoveries of nanoscience and real-world nanotechnology-enabled products; it is the vehicle by which the Nation and the world will realize the promise of major technological innovation across a spectrum of products that will affect virtually every industrial sector. For nanotechnology products to achieve the broad impacts envisioned, they must be manufactured in market-appropriate quantities by reliable, repeatable, economical, and commercially viable methods. In addition, they must be manufactured so that environmental and human health concerns are met, worker safety issues are appropriately assessed and handled, and liability issues are addressed.

Critical to this realization of robust nanomanufacturing is the development of the necessary instrumentation, metrology, and standards. Integration of the instruments, their interoperability, and appropriate information management are also critical elements that must be considered for viable nanomanufacturing. Advanced instrumentation, metrology, and standards will allow measurement and characterization of the physical dimensions, properties, functionality, and purity of the materials, processes, tools, systems, products, and emissions that will constitute nanomanufacturing. This will in turn enable production to be scaleable, controllable, predictable, and repeatable to meet market needs. In short, if a nanotechnology product cannot be measured, it cannot be manufactured effectively; additionally, if that product cannot be made safely, it should not be manufactured.

This report outlines the technology challenges and research needs associated with nanomanufacturing of devices and products in the realms of (1) chemicals, (2) electronics, (3) pharmaceutical/biomedical, and (4) composites industrial sectors. In addition, the report addresses a cross-cutting environmental, health, and safety (EHS) component that was identified and discussed at the workshop. It is hoped that this report will set the stage for the development of innovative solutions and promising results for the nanomanufacturing and nanometrology communities.

CHEMICALS

The chemical industry is already actively engaged in research and development of nanoscale technologies, and in manufacturing of nanotechnology-enabled chemical products. These are often essential to other key industries, including (although not limited to) health care, communications, food, clothing, housing, energy, electronics, and transportation. Current chemical nanotechnology products include metal, metal oxide, and semiconducting nanoparticles that are used as catalysts in chemical and energy processing; pigments for paints; UV protectants for sunscreens; and coating materials for cutting tools. Additional products include ceramics, sorbents, and membranes.

The Chemical Industry Vision2020 Technology Partnership has identified research requirements for accelerating the commercialization of technologies based on nanomaterials. The 2020 report[1] identifies several top priorities to enable the manufacturing of nanomaterials by design: the development of real-time characterization methods and tools; reference nanomaterials for property measurements to support metrology; and computational standards to improve prediction,

---

[1] *Chemical industry R&D roadmap for nanomaterials by design: From fundamentals to function*. Available online: http://www.chemicalvision2020.org/pdfs/nano_roadmap.pdf.

information processing, and transfer of nanomaterial properties among databases. These topics continue to be top priorities for the chemical industry and are cross-cutting with other industries, including the electronics industry, the pharmaceutical and biotechnology industries, and industries involving the manufacture of composites. Common chemical measurements and standards are widely needed to remove barriers to innovation in nanomanufacturing.

ELECTRONICS

The continuation of "Moore's Law"[2] in electronic information technology devices will likely rely on incorporation of nanoscale materials with new photonic, magnetic, and mechanic functionality. In addition, greater use will be made of multilayer, three-dimensional architectures. These changes will pose major challenges and opportunities with respect to characterization, metrology, and manufacturing at the nanoscale.

The introduction of new materials involving high-k dielectrics[3], low-k dielectrics, and metal gates has already introduced new failure mechanisms in the nanoscale regime. As scaling reaches its fundamental ultimate limits, new paradigms will be needed for investigating reliability mechanisms and developing new standards that can be effectively used by industry. Those new paradigms will likely involve the incorporation of magnetic and photonic materials with more conventional CMOS materials. Further to be expected is the implementation of information technologies directly into biological systems, where sensing/actuating requirements will limit encapsulation of the devices from the rather harsh (for semiconductors) biological fluid environment. Because of this increase in complexity, characterization and modeling will become even more critical factors in predicting the life span of a device or product.

PHARMACEUTICAL/BIOMEDICAL

Nanotechnology applications for new medical treatments and the production of new pharmaceuticals is one of the most promising markets for nanomanufacturing, yet it is also one that raises public health and safety concerns and is the subject of very serious regulatory restrictions. The small size and high reactivity of nanoparticles can make them the instruments of destruction for pathogenic organisms and cells that are out of control; however, these attributes can also make nanoparticles toxic to healthy tissue. Thus, they could pose a threat to human health or the environment if they escape into the air, water, or soil and humans or other biological organisms are exposed to them, or if their properties or the processes used to manufacture them are not fully understood. The pharmaceutical industry is one of the most successful and profitable of U.S. industries and has a reputation for the production of high-quality, safe products. Unfortunately, the economic risks associated with pharmaceutical development and manufacturing are very high and are expected to rise with the introduction of nanopharmaceuticals.

---

[2] "Moore's Law" is a term commonly used to describe the observation, first made by Gordon Moore of Intel in the early years of the semiconductor industry, that the number of electronic components that can be put on a single semiconductor chip has been doubling approximately every two years. See ftp://download.intel.com/museum/Moores_Law/Video-Transcripts/Excepts_A_Conversation_with_Gordon_Moore.pdf.

[3] k = dielectric constant. New semiconductor materials such as hafnium-based high-k insulators allow ten times less leakage current to escape (due to tunneling) compared to similar thicknesses of silicon dioxide; this is one of several strategies critical to continuing miniaturization of microelectronic components.

COMPOSITES AND MATERIALS

Nanoparticles and polymer nanocomposite technology comprise a broad and interdisciplinary research and development activity that has been growing rapidly worldwide since 2004. This activity has the potential to “revolutionize” the way materials are made and the range and nature of functionalities to which they may be tailored. How this nanotechnology revolution will develop, how great the opportunities that nanostructured materials and nanocomposites can provide, and how rapidly the technology will progress depend strongly on efforts to develop the relevant scientific and technological infrastructures.

The hoped-for revolution in the nanocomposite industry depends on a variety of state-of-the-art instruments, facilities, and standards for the manufacturing, testing, and characterization of these materials. The requisite instruments include those that can provide detailed information on multiple properties of nanomaterials and nanocomposites simultaneously (magnetic, mechanical, electrical, optical, etc.) and at the nanoscale. A particular requirement is for nondestructive techniques to probe the buried interfaces. Another set of tools also is needed to monitor *in situ* the fabrication and properties of nanocomposites. Federal agencies participating in the National Nanotechnology Initiative (NNI) have established over 60 centers or user facilities and related infrastructure; several of those are devoted to nanomaterials—however, none of those deals exclusively with metrologies for polymer nanocomposites, their processing, or their properties.

As in other areas of nanotechnology, research and development of standards and reference materials are essential for enabling progress in nanocomposite manufacturing technology. These standards are needed for the consistent manufacturing and reliable characterization and testing of nanocomposites. The ultimate goal will be to link key, easily controlled process parameters to nanoscale morphologies or features that define a material’s performance. In this way, the understanding of nanoscale features through highly advanced metrology will enable the creation of robust process-control parameters that ensure repeatable manufacturing processes that are cost-effective.

ENVIRONMENTAL, HEALTH, AND SAFETY ISSUES

Environmental, health, and safety issues are of concern to all industries employing or considering the use of nanotechnology-based products. Applications in the biomedical and pharmaceutical industries are among the most significant areas of concern, given that many of the products from these industries are intended to have direct contact with the human body. Participants in many of the sessions of this workshop were interested in issues associated with the potential toxicity of nanoparticles or products incorporating them. As a result, much of the discussion addressed issues related to the need for sound metrology, instrumentation, and standards for characterizing potentially toxic nanoparticles and materials containing nanoparticles.

CONCLUSION

Responding to the needs of nanomanufacturing is not straightforward, since there is no broad, unified nanomanufacturing industry at this time. In response to marketplace demands, current measurements will need to be adapted and new measurements will need to be defined and developed. Revolutionary new metrologies need to be identified and developed. Further, these instruments must be made into automated, production-worthy measurement tools for the factory floor. Hence, measurement methods to support the mass manufacture of nanotechnology-based products must be able to measure, control, and predict the nanoscale structure, performance, and properties of materials and devices over many scales reliably, reproducibly, and on the production floor in an automated, user-friendly manner. This is a daunting task, and currently the overall financial infrastructure is not in place to fund the development that needs to be done. Developing effective nanometrology is not a simple problem to solve and will require strategic alliances to be developed. The development of a National (or International) Technology Roadmap for Nanotechnology (NTRN) for Instrumentation and Metrology, similar to the current International Technology Roadmap for Semiconductors (ITRS), is a challenge and must be considered. But, unlike the ITRS, roadmapping for nanotechnology cannot be done by a single industry alone.

Finally, a major conclusion of the workshop is that there is a strong synergy between each of the breakout session findings in regard to the concern for health-related lifecycle issues in manufacturing—especially those related to the measurement of nanoparticles. There is also a strong desire to develop a “consortium” of interested industries to develop the needed research to push forward the concept of “materials by design,” including the needed instrumentation, measurements, and modeling that are necessary for success.

See Chapter 8 (Conclusions) for some additional findings and recommendations from this workshop, as well as summaries of the research needs identified in each of the breakout sessions.

1. SETTING THE STAGE

Principal Authors: Michael T. Postek (NIST) and Kevin W. Lyons (NSF/NIST)

1.1 INTRODUCTION

Nanomanufacturing is an essential bridge between the discoveries of nanoscience and real-world nanotechnology-enabled products—it is the vehicle by which this Nation will realize the promise of major technological innovation across a spectrum of products that will affect virtually every industrial sector. Manufacturing at the nanoscale is rapidly growing. In a recently released report, the Ben Franklin Technology Partners of Pennsylvania (BFTP 2007) surveyed 11 economic sectors in their region, representing 7,500 firms having a total of 420,000 jobs (2006). At the time of the study, over 25% of those jobs were being impacted by nanotechnology, and numerous commercial products utilizing nanotechnology were being produced. A *Small Times Magazine* article (January 2007) describing the manufacturing survey conducted by the University of Massachusetts Lowell in conjunction with Small Times states that "most U.S. nanotechnology industry executives said that high volume manufacturing of nano materials and products is the most important activity required for the United States to strengthen its nanotech capabilities." Quoting a number of reputable studies, an article published in *Journal of Materials* by Osman et al. (2006) observed that more than $4 billion was spent in the United States by the end of 2005 as part of the National Nanotechnology Initiative (PCAST 2005) and that:

- By the end of 2005, approximately $18 billion had been invested globally in nanotechnology by national and local governments (Cientifica 2006).
- More than $1 billion was budgeted for fiscal year 2006 for U.S. spending (PCAST 2005) and over $6 billion was projected to be invested globally in 2006 (Cientifica 2006) for nanotechnology research.
- More than 2,500 nanotechnology projects were being undertaken in the United States in 2004 (Marburger 2005).
- The popular press made more than 12,000 citations of "nanotechnology" in 2004 (Lux Research 2004).
- Nanotechnology initiatives have been established at 19 of the 30 companies listed on the Dow Jones industrial index (Baker and Aston 2005).
- More than 30 percent of nanotechnology start-up companies are focused on nanomaterials (Thayer 2003).
- $1.4 billion in revenue is estimated for nanomaterials by 2008 (Freedonia Group 2005).
- An annual growth rate greater than 30 percent is projected for U.S. nanomaterials markets through 2020 (Thayer 2003; Freedonia Group 2005).

These are impressive statistics, but this is just the "tip of the iceberg" where nanotechnology-related products are concerned. A 2007 report summarizing several 2002–2004 nanomanufacturing workshops of the National Nanotechnology Initiative (NNI) (NSET 2007a) points out that many products have already made it into the marketplace, most in the form of "first generation nano-products," but many small and large companies have "second-" and embryonic "third-" generation products in the pipeline. However, this evidence of gathering economic momentum for nanotechnology is tempered by the assessment that although the United States may have been the world leader in nanotechnology up to now, many experts regard this lead as being “imperiled” (Jacobson 2005), because investments in other parts of the world in this research area are on a par with those in the United States.. If the United States looks to maintain a leadership role in nanotechnology, there is a need for continuing support of fundamental research, infrastructure development, and effective efforts in commercialization of key processes and products.

Key Elements

It is clear that for nanotechnology products to achieve the broad impacts envisioned, irrespective of the country in which they are developed, they must be manufactured in market-appropriate quantities in a reliable, repeatable, economical, and commercially viable manner. Manufacturing a product implies that the same “nano-element” is made day after day to some acceptable level of precision at a high yield. The economies of scale resulting in the success of the semiconductor industry are a testament to this. Measurements and standards for process control and quality need to be in place to ensure that the product conforms to specification, thereby assuring the customer that the product meets expectations. Hence, instrumentation, measurement science (metrology), and standards are key infrastructural needs for nanomanufacturing.

The workshop participants identified three precepts that underlie all successful manufacturing that must also be applied to nanomanufacturing. The first is,

If a product cannot be measured, it cannot be manufactured.

The development of the necessary instrumentation, metrology, and standards is critical to the realization of robust nanomanufacturing and supports the measurement and characterization of physical, chemical, biological, and technological properties such as the dimensions, functionality, and purity of the material. In addition, this infrastructure would also address processes, tools, systems, products, emissions, and other supporting technologies that constitute nanomanufacturing. This will in turn enable production to be scaleable, controllable, predictable, and repeatable to meet market needs. This leads to the second precept,

If a product cannot be manufactured safely, it should not be manufactured.

In addition to normal measurement requirements for manufacturing, nanotechnology-based products must be manufactured so that environmental and human health requirements are met, worker safety issues are appropriately assessed and handled, and liability issues are addressed. In Roco and Bainbridge’s review of societal implications of nanoscience and nanotechnology (2001) that outlined the potential risks and benefits, the authors state that there is a need to ‘‘maximize benefit while guarding against potential harm, based on realistic assessment of technical facts in the light of human values.’’ Instrumentation required for accurate environmental monitoring needs to be developed, along with the validated protocols and standards. Thus, the third precept is,

If a product cannot be measured how would you know…

Nanotechnology involves the controlled manipulation of matter at the nanometer scale to create nanostructures with unique properties. These properties must be measured and quantified; otherwise, how would one know if they are unique or if they are safe. Through nanotechnology, it is envisioned that a dazzling array of new materials, devices, and products can be made possible, thus improving our quality of life and generating positive economic and societal effects. But to do that effectively, well-understood and well-characterized nanomanufacturing processes are needed.

Instrumentation, metrology, and standards are the key infrastructural underpinning of the emerging nanotechnology enterprise. Advances in fundamental nanoscience and ultimately manufacturing of new nanotechnology-based products all depend to a great degree on our capability to accurately and reproducibly measure the properties and performance characteristics at the nanometer scale. Both physical and documentary standards are needed to ensure product consistency worldwide. New nanotechnology-based industries that mass-produce products will require high-performance, cost-effective, reliable instrumentation and improved measurement methods that meet the requirements of effective manufacturing. Along with these comes the need for effective collection, transmission, and interpretation of measurement information and data.

As new nanostructures are fabricated, assembled, and manufactured into usable products, standardization for instrumentation and metrology will be vital for providing quality control and ensuring reproducible performance. Globally accepted standards for identification and measurement of properties and structures at the nanoscale are necessary to ensure an even playing field on which U.S. products may compete successfully in the international marketplace.

Instrumentation, Metrology, and Standards

Two previous industrial revolutions—the machine revolution at the end of the 19th century and beginning of the last century and the semiconductor revolution in the middle of the 20th century—illustrate that metrology is a key element in enabling the widespread adoption of new technologies. The same will be true for the developing nanotechnology revolution. Accurate measurement of dimensions, characterization of materials, and elucidation of structures at the nanoscale are all critical in exploratory research, in concept and prototyping, and ultimately, in manufacturing.

The currently available suite of metrology tools that has evolved over decades of scientific research is capable of meeting the needs of today’s exploratory nanoscale research. However, existing precise metrology tools are reaching their limitations for resolution, accuracy, and capability at the nanoscale; they will not meet future requirements for the manufacture of nanotechnology-based products (NSET 2006). As viable nanoscale applications emerge, revolutionary new techniques, tools, instruments, and infrastructure will be needed to support advanced research. In addition, pioneering manufacturing metrology and instrumentation capabilities must be in place for a successful nanotechnology industry to manufacture products at a commercial scale.

National Nanotechnology Initiative Program Component Areas

The National Nanotechnology Initiative Strategic Plan (NSET 2007a) devotes one Program Component Area (PCA) to the topic Instrumentation Research, Metrology, and Standards for Nanotechnology. The goal of this PCA is to advance the knowledge boundaries of instrumentation and metrology to enable the measurements that are necessary for nanotechnology. Advanced measurement knowledge is fundamental to innovation in all application areas for nanotechnology. As described in the Strategic Plan, this PCA cuts across all the NNI PCAs and is vital to the overall success of the NNI. Advances in fundamental nanoscience, design of new nanomaterials, and ultimately, manufacturing of new nanoscale products will all depend to some degree on the capability to accurately and reproducibly measure properties and performance characteristics at the nanoscale. Thus, the Instrumentation Research, Metrology, and Standards PCA relates particularly closely to the PCA on Nanomanufacturing, also included in the 2007 NNI Strategic Plan, as demonstrated in this report.

Current Situation

The semiconductor industry is already performing volume manufacturing of semiconductor chips with features well below 100 nm. The International Technology Roadmap for Semiconductors (ITRS 2005) provides a candid insight into currently available technology. The ITRS states that some metrology tools have a “resolution” that is under 1.0 nm today and calls for that resolution to fall below 0.06 nm by the year 2018. The ITRS further reports that research and measurement tools are adequate for manufacturing today, but that 5–10 years down the road, “no known solutions” have been identified for many critical metrology tasks. The semiconductor industry is primarily interested in tools capable of measuring high-value electronic parts in high-volume factories. Such tools, as currently configured, may be of limited value in other nanotechnology industries and will need to be retooled for high-volume measurements of carbon nanotubes or quantum dots, for example.

The proceedings of the 2004 NNI Grand Challenge Workshop on Instrumentation and Metrology for Nanotechnology (NSET 2006) points out that for imaging, industry currently uses evolutionary tools such as optical microscopes, scanning electron microscopes (SEMs), transmission electron microscopes (TEMs), and scanning probe microscopes (SPMs) for both research and development. However, entirely new instrumentation such as the helium ion microscope (Postek et al. 2007) is needed in order to achieve the resolution necessary for production nanomanufacturing. The helium ion microscope, once fully optimized, is expected to achieve 0.25 nm resolution, which is about four times better resolution than the current SEMs. (See the sidebar below, “Helium Ion Microscopy.”)

Helium Ion Microscopy

Helium ion microscopy (HeIM) is a new, potentially disruptive technology for nanotechnology and nanomanufacturing. Its revolutionary approach to imaging and measurements has several potential advantages over the traditional scanning electron microscope currently in use in research and manufacturing facilities across the world. Due to the very high source brightness and the shorter wavelength of the helium ions, it is theoretically possible to focus the ion beam into a smaller probe size relative to that of an electron beam of an SEM. Hence, higher resolution is theoretically possible. In an SEM, an electron beam interacts with the sample, and an array of signals are generated, collected, and imaged. The interaction zone may be quite large, depending upon the accelerating voltage and the materials involved. When the helium ion beam interacts with the sample, it does not have as large an excitation volume; thus, the image collected is more surface-sensitive and can potentially provide sharp images on a wide range of materials. The current suite of HIM detectors can provide topographic, material, crystallographic, and electrical properties of the sample.

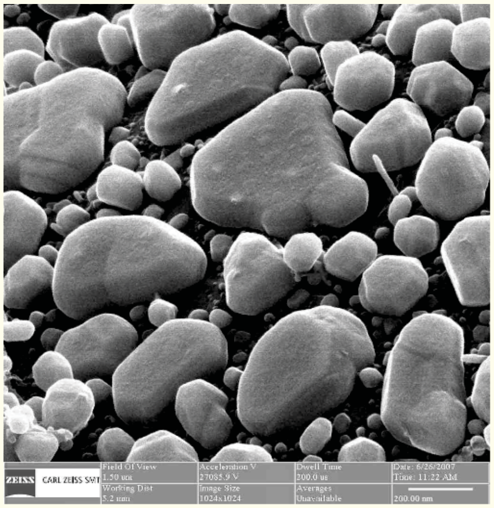


Fig. 1. Secondary electron images obtained by HIM on a gold-on-carbon sample (Field-of-view = 1.5 μm) (courtesy of Michael Postek and Andras Vladar, NIST).

Compared to an SEM, the secondary electron yield is quite high with HIM, allowing for imaging at extremely low beam currents. Also, the relatively low mass of the helium ion, in contrast to other ion sources such as gallium, results in little or no discernable damage to the sample. Because the primary

Helium Ion Microscopy

beam of a helium ion microscope is He ions and not electrons, the secondary electron contrast differs from that of a scanning electron microscope.

Potential uses of this technology for information technology devices include critical dimension measurement, defect detection and analysis, and advanced characterization of nanoscale materials. The key development has been development of field emission tips with a potentially sub-Ångstrom virtual source size, low energy spread, and high brightness. This beam can be scanned across the sample using ion optics that are well understood. Work is underway to fully understand the image contrast mechanism, because each new image provides exciting views not seen by SEM. Examples of this include observation of stains on wafers after processing.

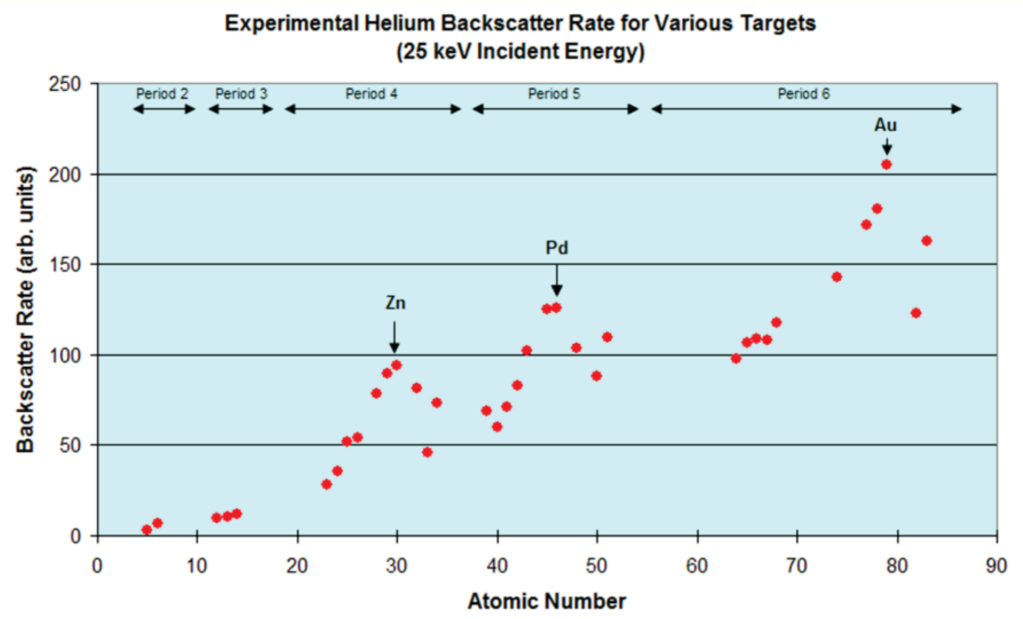
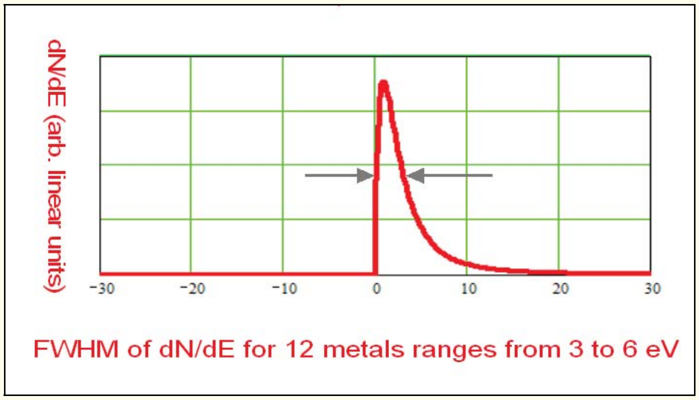


Fig. 2. Plot of the experimental helium ion backscatter intensity for zinc, palladium, and gold for an incident landing energy of 25 keV (image courtesy of John Notte, reproduced from Sijbrandij et al. 2008, accepted for publication in the Journal of Vacuum Science and Technology B*; reprinted with permission, ©2008, American Vacuum Society).*



FWHM of dN/dE for 12 metals ranges from 3 to 6 eV

Fig. 3. Secondary electron energy distribution for 20 keV He ions (courtesy of John Notte, Carl Zeiss SMT, Inc.).

Roadmapping

The semiconductor industry has realized tremendous benefits from the establishment and continuous updates of its roadmap as well as from the well-funded and organized consortia that deal with the future needs of the industry. It has made great strides in developing the supporting technology to meet the challenges and needs outlined in the ITRS. These advances have been made through the concentrated expenditures of hundreds of millions of dollars and the steady evolution of generations of instrumentation. In the field of nanotechnology, however, it is early and such an infrastructure has not yet materialized. Simply copying the ITRS process of the semiconductor industry is not viable because there is no single nanomanufacturing enterprise. "Nanomanufacturing" groups have yet to take steps to organize themselves in a manner similar to the Semiconductor Industry Association. Also, there is little focus among manufacturers about what the key products, applications, and common instrumentation and metrology needs are, and what might be the appropriate initial standards to gain maximum impact for the marketplace.

A crucial step in the path forward will be to gain consensus on what the focus areas should be for the near, mid, and long terms. Commonalities of needs among manufacturers should be identified so that research targets can be focused effectively and so that instrument manufacturers can have the appropriate tools and processes ready when needed. Specific avenues of promising research also should be identified and grouped according to near-, mid-, and long-term goals. Applications that would be affected by successful research should be identified and prioritized in terms of future potential.

The NNI workshop report *Instrumentation and Metrology for Nanotechnology* (NSET 2006) recommended that a generic technology roadmap, whether it is a national or an international endeavor, much like the ITRS, is needed to provide such focus for the many diverse efforts in nanotechnology. A National Technology Roadmap for Nanotechnology (NTRN) or an International Technology Roadmap for Nanotechnology (ITRN) for nanotechnology-related instrumentation and metrology would define where the industry wants to be in 5, 10, and 15 years, and beyond. Such a roadmap could again prove to be one of the most important driving forces in industrial and technological advancement. It should be a dynamic, living process and document, much like the ITRS, with experts coming together every two years or so to review progress and redefine goals and pathways.

Development of a national or international technology roadmap for nanotechnology for instrumentation and metrology would be difficult but must be considered. This roadmap would go beyond the topics discussed in this workshop, because it would support technology development while providing guidance to instrument manufacturers on reasonable lead times for providing needed tools. Instrument development associated with the semiconductor manufacturing industry has been an evolutionary process fueled by the defined needs of the ITRS and funded by an established industry. Currently, the emerging nanomanufacturing industry does not have sufficiently deep pockets to fund similarly high-risk development. Thus, a significant challenge is identifying and establishing funding sources for the high-risk development of a diverse assortment of needed instrumentation, some of which may need to push established technological boundaries.

1.2 THE "COMMONALITIES OF NEED" FOR NANOMANUFACTURING

A more complete understanding of the lifecycle implications of nanotechnology for the environment and human health and safety relies to a large degree on the measurement of properties at the nanoscale. Extensive discussions with the aerospace, automotive, chemical, forest products, pharmaceutical, and semiconductor industries have led to the identification of shared industrial metrology needs. Each of these industries put forth similar concerns for sustainable metrology for nanotechnology-enabled products. These—beyond specific technology-related needs—include measurements for:

- Monitoring of worker exposure to nanomaterials
- Customer exposure to nanomaterials
- Waste management
- Lifecycle planning and testing

Today, such measurements present a significant challenge for all aspects of metrology. Advanced measurement science will be necessary, for example, to detect trace levels of exposure to nanomaterials resulting from medical, occupational, environmental, or accidental release. Hence, it is essential to develop the instrumentation and metrology to accurately follow the environmental fate of nanoscale materials, develop safe nanoscale sample handling methods, and accurately measure the effects throughout the entire product lifecycle.

Metrology needs for nanomanufacturing are not trivial; measurements are needed across the entire value system[7] of the manufacturing process, from the delivery of initial raw materials by suppliers to when the final commercial product is available (see sidebar, "Commonalities of Need"). The raw materials supplier is given specifications that the customer requires; demonstrating that those specifications have been met requires measurements. Then, that customer needs to measure the incoming product to make sure it meets the required specifications or needs to be provided in-process data certifying that the material was manufactured under a controlled, approved process. That customer now becomes a manufacturer who then combines a number of raw materials together to form a product for another step in the value system. This process continues until the final product or products are generated. Measurements are needed at each stage of the process to ensure quality control and to ensure that customer specifications have been met. Measurement protocols need to be in place so that the measurements are meaningful. Measurement instrumentation needs to be in place to rapidly provide the needed data at the required precision. Standards need to be in place to ensure consistency, accuracy, and traceability of the data.

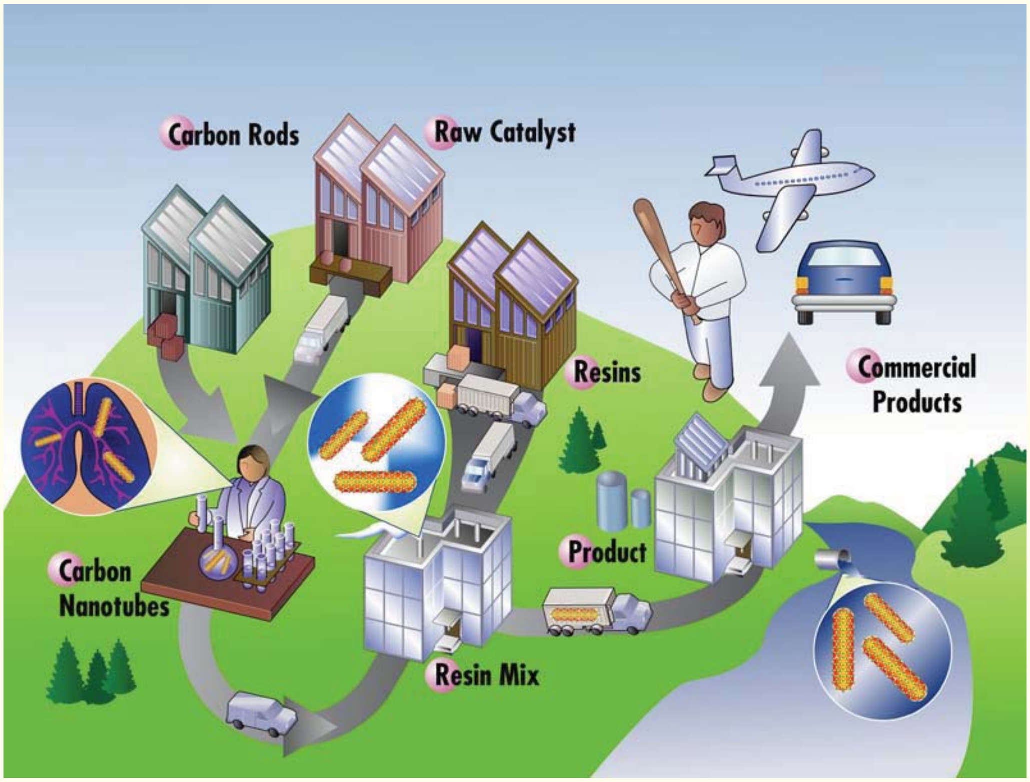
Allied Workshops

This IWG workshop report is focused on identifying the technical challenges that need to be answered, as well as the directions the manufacturing community feels it needs to take regarding instrumentation, metrology, and standards for nanomanufacturing. The starting point for this conference was a previous NNI Grand Challenge Workshop on Instrumentation and Metrology for Nanotechnology (NSET 2006), held in January 2004. The purpose of that workshop was to gain input from stakeholders in the field of nanotechnology on the capabilities that will be needed in this critical area and the R&D that will be necessary to develop those capabilities. The overall objective was to develop insights on the "hard problems" that needed to be resolved and the pathways for doing so, ultimately identifying the key elements needed for continued progress in nanoscale instrumentation and metrology. A number of other NNI workshops held between 2002 and 2004 also addressed issues related to nanomanufacturing. The findings of several of these have been published as an NNI workshop report entitled *Manufacturing at the Nanoscale* (NSET 2007b). All NNI workshop reports can be obtained from the National Nanotechnology Coordination Office (http://www.nano.gov/html/res/pubs.html).

---

[7] Adapted from Michael Porter. *Competitive advantage: Creating and sustaining superior performance*. New York: Free Press. (1998).

Commonalities of Need



(Figure is courtesy of Beamie Young, NIST.)

Example: Raw carbon rods from one supplier and raw catalyst from another supplier are shipped to a manufacturer making carbon nanotubes. Specifications are placed upon the delivery and acceptance of the raw materials, which must be documented. Measurements must be made. The carbon nanotube (CNT) manufacturer combines these raw materials in their manufacturing process to produce carbon nanotubes with certain characteristics (type, size, chirality, etc.). Process measurements assure quality, and incoming measurements assure the receiver of these goods that the carbon nanotubes meet the needs of the next operation in the value system. Each manufacturer adds value to the products; such as proprietary dispersing agents and resins combined with the carbon nanotubes to make a composite resin material that is shipped to clients who use that product to make sports equipment, automotive bumpers, or airplane component parts. Assurances of product quality specifications all require measurements. In some cases these measurements are available, and in some instances these measurements need to be developed.

1.3 SUMMARY

Responding to the metrology needs of nanomanufacturing is not straightforward, because there is no broad, unified nanomanufacturing industry at this time. Current measurements will need to be adapted, and new measurements will need to be defined and developed. Revolutionary new metrologies will need to be identified and developed. New and potentially revolutionary instruments will need to be invented. Further, these instruments will need to be made into automated, production-worthy measurement tools for the factory floor. Measurement methods to support the mass manufacture of nanotechnology-based products will need to be able to measure, control, and predict the nanoscale structure, performance, and properties of materials and devices over many scales and to do so reliably, reproducibly, and on the production floor in an automated, user-friendly manner.

This is a daunting task. Today, not only are the tools inadequate or nonexistent, but the overall financial infrastructure is not in place to finance the development of those tools. Developing effective nanometrology is not a simple problem to solve; it will require the development of strategic alliances. Nanotechnology is a new paradigm in science that has already changed the model for multidisciplinary R&D. A similar multi-industry paradigm must be developed for nanomanufacturing.

Based on the work of the earlier workshops and on industry and agency expertise, organizers of this workshop decided to focus initially on four critical application areas where advances in instrumentation, metrology, and standards are needed in order to fully realize the potential for nanomanufacturing:

1. Chemicals
2. Electronics
3. Pharmaceuticals/Biomedical (devices, etc.)
4. Composites

This report outlines the technology challenges and research needs unique to each of the above four areas, as well as cross-cutting issues, as identified by workshop participants. It is hoped that this report will set the stage for innovative solutions and promising results from the nanomanufacturing and nanometrology communities.

Nanomanufacturing: The Albany NanoTech Complex

The College of Nanoscale Science and Engineering (CNSE) at the University at Albany—the Albany NanoTech complex—is a $3.5 billion global research, development, technology deployment, and education resource supporting accelerated high-technology commercialization in nanotechnology.

CNSE is financed through more than $500 million in governmental support and over $3 billion in corporate investments; the complex houses the only fully integrated, 300 mm wafer, computer chip pilot prototyping and demonstration line within 65,000 square feet of Class-1-capable cleanrooms. Its 450,000 square feet of office, laboratory, and cleanroom incubation facilities includes capabilities for nanoelectronics; system-on-a-chip technologies; biochips; optoelectronics and photonics devices; closed-loop sensors for monitoring, detection, and protection; and high-speed communication components.

Over 1,600 scientists, researchers, engineers, students, and faculty work on-site at CNSE's Albany NanoTech complex, providing a community in which to pioneer, develop, and test new nanoscience and nanoengineering innovations in a technically aggressive and financially competitive R&D environment. Over 250 active partners encompass Federal labs, universities, and industry, including IBM, AMD, SONY, Toshiba, Qimonda, Honeywell, ASML, Applied Materials, Tokyo Electron, Freescale, Argonne National Laboratory, DARPA, and NASA. An expansion currently underway will increase the size of the complex to over 750,000 square feet, including over 80,000 square feet of Class 1 cleanroom space, to house over 2,000 scientists, researchers, engineers, students, and faculty by the end of 2008.

Through its unique model that is simultaneously supported by industry, academia, and government, CNSE's Albany NanoTech complex offers a "one-stop shop" by assisting companies to overcome technical, market, and business development barriers through technology incubation pilot prototyping and test-bed integration support, leading to target deployment of nanotechnology-based products.

1.4 REFERENCES

Baker, S., and A. Aston. 2005. The business of nanotech. *Business Week* (February 14):64–71.

Ben Franklin Technology Partners (BFTP). 2007. *Economic Analysis: Entrepreneurial development, risk capital, and technology commercialization*. Available online: http://www.benfranklin.org/news/view.asp?id=161&cid=1.

Cientifica. 2006. *Where has my money gone? Government nanotechnology funding and the $18 billion pair of pants*. White paper published by Cientifica. Available online at http://www.cientifica.com (accessed March 5, 2007).

Fredonia Group. 2005. *Nanomaterials to 2008—Demand and sales forecasts, market share, market size, market leaders*. Cleveland, OH: Fredonia Group. See also http://www.freedoniagroup.com/nanomaterials.html.

International Technology Roadmap for Semiconductors (ITRS). 2005. *ITRS 2005 Edition*. Available online: http://www.itrs.net.

Jacobson, K. 2005. Lack of manufacturing base imperils U. S. lead in nanotechnology. *Manufacturing & Technology News* 12(13)(July 8). Available online: http://www.manufacturingnews.com/news/05/0708/art1.html.

Lux Research. 2004. *The Nanotech report: Investment overview and market research for nanotechnology*, 5th ed. New York: Lux Research.

Marburger, J.H. 2005. “Nanotechnology: Government’s role.” Presentation at MS&T ‘05, Pittsburgh, PA, September 26, 2005.

Osman, T., D. Rardon, L. Friedman, and L. Vega. 2006. The commercialization of nanomaterials: Today and tomorrow. *JOM* 58(4):21–24. Available online: http://www.tms.org/pubs/journals/jom/0604/osman-0604.html.

Postek, M.T., A.E. Vladár, J. Kramar, L.A. Stern, J. Notte, and S. McVey. 2007. The helium ion microscope: A new tool for nanomanufacturing. *Instrumentation, metrology, and standards for nanomanufacturing: Proceedings of SPIE* 6648:664806-1– 664806-6 and the sidebar on pp. 4–5.

President’s Council of Advisors on Science and Technology (PCAST). 2005. *The National Nanotechnology Initiative at five years: Assessment and recommendations of the National Nanotechnology Advisory Panel*. Washington, DC: PCAST. Available online: http://www.ostp.gov and http://www.nano.gov.

Roco, M.C., and W.S. Bainbridge, eds. 2001. *Societal implications of nanoscience and nanotechnology*. Dordrecht; Boston: Springer. (Originally published by U.S. National Science Foundation, Arlington, VA.)

Sijbrandij, S., W. Thompson, J. Notte, W.W. Ward, and N.P. Economou. 2008. Elemental analysis with the helium ion microscope. *J. Vac. Sci. Technol. B* 26(6)(Nov./Dec.) In press.

Small Times Magazine. 2007 (January). “Survey says: Manufacturing, government keys to U.S. success.” http://www.smalltimes.com/articles/article_display.cfm?ARTICLE_ID=281851&p=109. (Accessed online, March 13, 2008.)

Subcommittee on Nanoscale Science, Engineering, and Technology (NSET) of the Committee on Technology of the National Science and Technology Council. 2006. *Instrumentation and metrology for nanotechnology: Report of the National Nanotechnology Initiative workshop January 27-29, 2004*. Washington, DC: NSET. Available online: http://www.nano.gov/html/res/pubs.html.

NSET. 2007a. *The National Nanotechnology Initiative strategic plan.* Washington, DC: NSET. Available online: http://www.nano.gov/html/res/pubs.html.

———. 2007b. *Manufacturing at the nanoscale. Report of the National Nanotechnology Initiative workshops, 2002–2004*. Washington, DC: NSET. Available online: http://www.nano.gov/html/res/pubs.html.

Thayer, A.M. 2003. Nanomaterials. *Chemical and Engineering News* 81(35):15–22.

2. STAGES OF TECHNOLOGICAL INNOVATION RELEVANT TO NANOMANUFACTURING

Principal Authors: Clare Allocca, Greg Blackman, Jean Dasch, Jennifer Hay, Keith McIver, and Tinh Nguyen

2.1 INTRODUCTION

By defining and addressing the needs of the four major nanotechnology-enabled product sectors, it became clear to workshop participants that defining instrumentation, metrology, and standards needs for competitive products using nanotechnologies will require addressing needs at all stages of technological innovation. An innovation continuum, defined in this chapter, is traversed by all of the technologies under study in this report; it is imperative that developers strive to be continually cognizant of the issues and needs related to all of the innovation stages. These stages are: (1) materials discovery, (2) applied research and development, (3) production, (4) market, and (5) end use. These stages, as well as the typical roles of the metrology tool providers and users at each stage, are illustrated in Figure 2.1 and are further described below.

While a majority of the discussion in this chapter is stated in terms of materials, parallel considerations are equally applicable to materials, devices, and manufacturing processes.

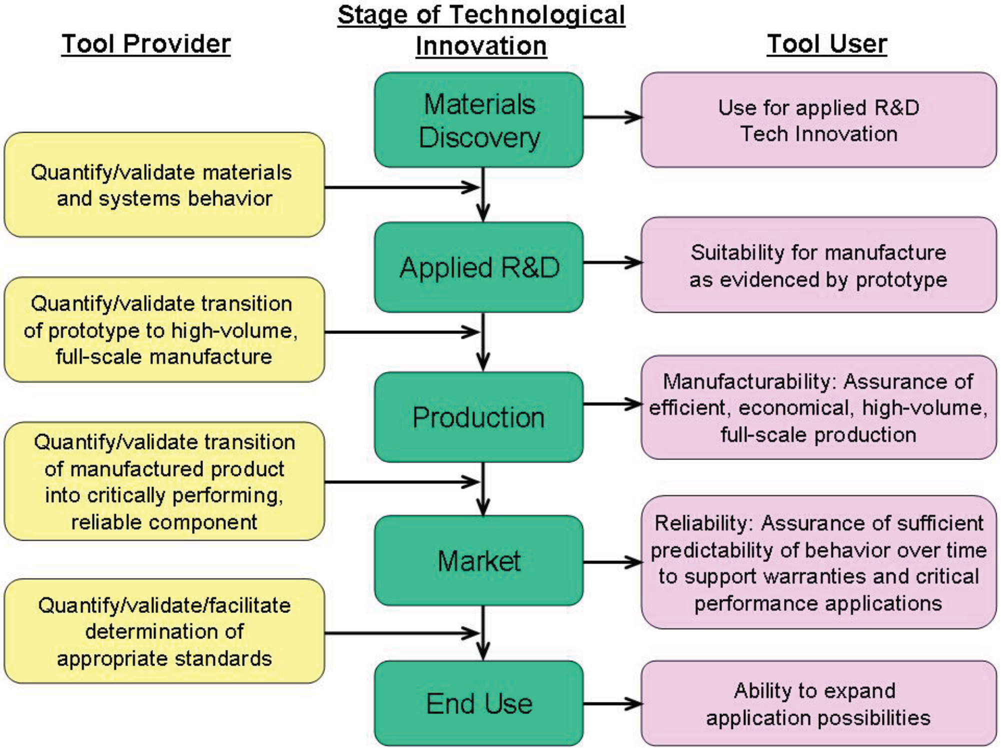


Figure 2.1. Metrology tools are critical to all stages of technological innovation for nanoscale product development and use (courtesy of Clare Allocca, NIST).

Metrology tool providers and users often vary from stage to stage in the innovation continuum, and further challenges arise based on the differing perspectives and needs of the changing players. These differing perspectives may affect definitions, requirements, and priorities that can conflict with one another. For this reason, it is extremely important for the players at each stage to understand and consider each others' concerns. Understanding of mutual concerns within their proper contexts will foster a work environment that supports a reduced product development time.

1. The ***materials discovery*** stage addresses pure research, new discoveries, and early conceptual ideas for commercial products. Fundamental knowledge and understanding is the goal. In order to proceed to the next stage, the discovery generally must be transformed into a developer's vision—that is, an idea, inspired by a problem or opportunity, that connects the discovery stage to later stages (especially to a commercial "product"). Along the development pathway, measurement and other barriers that hinder fabrication must be overcome. Material system developers must consider how this new innovation will function within a system. At this early stage the tool providers may assist in modifying existing instruments, develop new approaches for taking key measurements with existing instruments, or provide early prototype instrumentation to evaluate its effectiveness for the new application. The tool user will include research engineers, material system scientists, and developers who understand and will define the initial performance metrics for new material systems and associated fabrication processes.

2. During the ***applied R&D*** stage, effective development of tools helps to overcome barriers to the development of a prototype design or proof of concept. Some aspects of this work may be considered "precompetitive." The definition of precompetitive is variable. In general, precompetitive research can be thought of as work where companies are not concerned that their competitors have equal access to the results. In the case of the semiconductor industry, SEMATECH has successfully been able to bridge the precompetitive gap by identifying common industrial problems and developing generic solutions that benefit the entire community. At the applied stage, the tool providers have developed prototype measurement instrumentation and metrology that supports anticipated production requirements for inline and offline capabilities. The tool users will include material system developers and production engineers.

3. In the ***production*** stage, the prototype is scaled up to cost-effective production. The result is a product that is manufacturable. The impact of metrology tools to measure, monitor, and control the quality of ingredients that comprise a material system and the materials system itself becomes vital during the initial stages of manufacturing. Developing a stable, reliable manufacturing process where all the significant variables have been identified is a challenge even for normal manufactured materials, let alone ones that contain various nanoscale additives. New materials, instruments, and other process innovations that seem very promising at the lab and applied scale are often difficult to translate to a plant or production scale. The presence of defects and their inevitable impact on failure of a material are a concern at this stage. An emphasis on the quality control of materials used in the manufacturing process and the quality and reliability of the product vs. customer specifications is expected at this stage of development. As a product and its associated material system(s) transition from lab to commercial scale, the production volume increases by many times, making environmental, health, and safety (EHS) concerns even more important than at the lab stages. At the production stage the tool providers must have cost-effective, highly reliable, and automated production-hardened instruments that support the production environment and meet the quality requirements needed for the marketplace. In addition, protecting workers from potential safety and health risks must be addressed through workplace monitoring (http://orise.orau.gov/ihos/Nanotechnology/nanotech_OSHrisks.html). A 2007 planning report (http://www.nist.gov/director/prog-ofc/report07-2.pdf) studying the economic impact of measurement in the semiconductor industry found that the benefit-cost ratio was 3.3, meaning that

for every $1 invested in measurement, the industry saw a $3.30 benefit. Similar benefits should be expected for the nanotechnology sector. Tool users at this stage are the production workers; they are generally less sophisticated or educated than the users in earlier stages, so the measurement instruments must be extremely user-friendly.

4. During the ***market*** stage, metrology tools are often required to help overcome a barrier to market development and the purchasing process. This can include efforts such as proving product claims, verifying quality characteristics, and tracking worker and plant safety. Tools that are effective on the production line to make measurements in real time are refined or updated to help keep costs down and quality high. The tool users can be production workers or quality engineers. Each material system or innovation that makes it this far in the continuum will have a set of performance attributes that make it suitable for a particular market niche. There may be incumbent technology to beat, demanding accelerated tests to pass, and multiple customer specifications to simultaneously meet or exceed. Cost position relative to performance will always be a factor at this stage.

5. Finally, during the ***end use*** stage, metrology tools can help resolve disputes of claims that are reactions in the market, such as an unanticipated outcome. Alternatively, a system's requirements may change due to another developer's technology innovation (e.g., material system performance metrics were changed in response to improvements in body armor's ability to stop more-powerful bullets). As a technology innovation enters the market, it can spur the need or opportunity for a new developer's vision (next-generation products or product-development pipelines). Finally, issues of sustainability and product-centered approach to environmental protection ("product stewardship"[1]) come to the forefront during this stage.

2.2 PILLARS—COMPONENTS OF THE STAGES

The overall structure necessary to enable this multifaceted vision of successful nanotechnology product development consists of the support of three scientific disciplines, or "pillars," bound together by the metrologies needed to capitalize on the relationships among the disciplines. These disciplines are (1) modeling, (2) materials and process science and engineering, and (3) quality control and assurance, including characterization. These pillars and associated disciplines are defined in text and in the "pillars" sidebar below in terms of their relationships to nanotechnology-based product development.

Modeling

The Modeling pillar represents the theoretical understanding and/or prediction of the physical mechanisms related to the interaction of nanoscale additives with the other materials within a composite—including the effects of processing on morphology—to provide predictions of the behavior of nanotechnology-modified materials at the composite level. A key goal of modeling is to enable the performance of virtual studies to identify material combinations and morphologies that yield specific properties. This "*in silico*" approach will enable greatly accelerated development cycles by guiding the often-Edisonian (trial-and-error) approach to nanotechnology-enabled product development and manufacture. The modeling pillar will be intimately integrated with materials and process developments to improve model accuracy and processing parameters (i.e., quality control). Key to robust model development is characterization via the necessary validation through materials testing supported by appropriate instruments and measurement methods.

---

[1] See the EPA website on product stewardship, http://www.epa.gov/epr/.

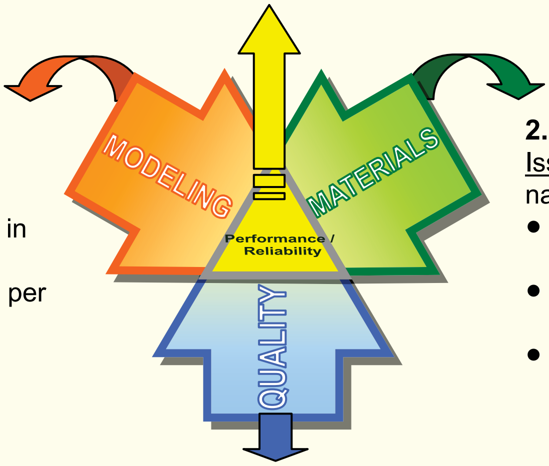
Three Disciplinary Pillars for Effective Development of Nanotechnology-Based Products

Goal: Consistently produce material that meets targeted engineering requirements

1. Modeling

Issue: Don't understand physical mechanisms

- Model nanoscale constituent interaction in complex resin system
- Tailor material system per requirements



2. Materials/Processes

Issue: Can't control nanomaterial properties

- Dispersion/model interactions
- Validate modeling predictions
- Optimize system per requirements

3. Quality/Characterization

Issue: No standards for nanomaterials

- Establish acceptance criteria for material constituents and total system

The development of three scientific disciplines—**modeling, materials/processes, and quality/characterization**—referred to here as "pillars"—are bound together by the metrologies needed to capitalize on the relationships among the disciplines—the "glue" that binds them together. Each pillar has its own unique objectives, but all are intimately interrelated. For example, the Modeling pillar provides both predictions of the material system requiring validation of the Materials pillar and guidance for the selection of appropriate tests to characterize the material for Quality. In the fabrication of a material, noncompliant attributes (e.g., not all nanotubes are the same within the same batch) need to be identified, measured, and finally correlated back to the model; additionally, characterization of these noncompliant attributes will be used to improve material processing.

Modeling Pillar

- Objective is to provide the capability to predict material properties of the nanotechnology-modified material.
- Deliverable is a parametric model that allows for quick, variable evaluations.
- Technical approach will be to investigate nanoconstituent interactions in a complex materials system by manipulating parameters such as bond strength, volume percentage, etc.
- Investigation is of dispersion effects on the material system.
- Utilized are characterization and test data to refine models iteratively and to define new tests/test methods to provide data for further refinement.

Materials/Processes Pillar

- Objective is to consistently process and produce engineered materials.
- Deliverable is a quality-controlled manufacturing process for material systems.
- Technical approach will be to interactively work with the modeling team on manufacturing challenges by using a building-block approach to manufacturing the modeled mechanisms to achieve targeted material properties.

Three Disciplinary Pillars for Effective Development of Nanotechnology-Based Products

Quality/Characterization Pillar

- Objective is to provide the capability and criteria to quantify and measure the manufacturing processes (constituents, modifications) to ensure reproducibility.
- Deliverables are to include standards for quantifying meaningful properties at various length scales; test methods to characterize materials at the nano, process-validation, and the final product levels.
- Technical approach will be to interactively work with modeling and material teams to identify critical metrics and methodologies that are practical and relevant at various length scales and manufacturing processes.
- Metrics to determine critical parameters at the nanometer length scale shall be identified and correlated to process-control parameters to develop a quality-control methodology suitable for materials production.

Materials /Processes

The Materials/Processes pillar represents the truism that the properties of a material such as a polymer composite depend on raw materials and their processing—the actual physical form being fabricated. The complex relationships between materials and processes lead to desirable (or not-so-desirable) end-use properties. For example, processing methods can affect nanoparticle agglomeration and dispersion, rheology, polymer crystallinity, and alignment, all of which have a profound impact on properties. Failure to properly control these properties can be detrimental to the performance of a material.

Quality/Characterization

The Quality/Characterization pillar represents the application of knowledge (e.g., tools, instruments, methods, models) from the other pillars to the quantitative measurement of chemistry, structure, and properties at the nanoscale, and of dimensionality, and the linking of those measurements to processing parameters and ultimate end-use properties. The development of characterization methods will, by necessity, be dependent upon and fully integrated with modeling, materials and processing, and metrology and standards development efforts.

Metrology and Standards Development

The three disciplinary pillars described above are mutually interconnected by a fourth critical element—metrology science and standards development; together all four elements can support stable, predictable, reliable, and safe manufacture of nanotechnology-based products throughout the innovation continuum. This supports the precept of predictable, reliable manufactured nanotechnology products: *"If you cannot measure it, you cannot manufacture it."* This component of the overall innovation architecture represents the continual development of tools to enable understanding of current structures, predictions of potential structures, and development of the next generation of products based on structures. Tools must be sufficiently robust to give manufacturers confidence in the performance of their products, and further, to reflect that confidence in the form of warranties.

Metrology and standards development must consider not only the robustness of the tools being developed, but identification of the appropriate tool to enable understanding in the first place. Successful commercial products are dependent on knowledge of the relationship between a particular measure and the overall behavior of a product. It is not always feasible or even possible in a manufacturing process to control or understand every aspect of a material. For example, any nanotechnology product will naturally have a distribution of particles sizes and shapes, as well as defects and impurities. Metrology tools must be developed with this in mind. Parallel development of a “perfect sample” or standard for comparison can also lead to an understanding of the effects these inevitable anomalies have on the properties. Standards can help in the validation and understanding of limitations of and overlaps among characterization instruments, the direct connections between modeling and manufacturing, and the setting of expectations of quality for materials used in the manufacturing process.

2.3 SUMMARY

The concept of the three essential disciplinary pillars supporting nanomanufacturing—modeling, materials/processes, and quality/characterization—emphasizes the connections between the three disciplines. Each of the pillars is a discipline of its own, yet no one pillar can function independently. Without all three pillars and the “glue” of metrology and standards development holding the structure together, it will be difficult to realize the promise of novel commercial nanotechnology-based products with desirable property enhancements based on material properties at the nanoscale.

A potential application of this three-pronged foundation supporting commercial product development is the industry-proposed establishment of a targeted interinstitutional thrust for commercialization of nanocomposite materials, as described in the sidebar, “Relationship of Metrology to an Industry-Proposed Nanocomposites Thrust Area.”

Relationship of Metrology to an Industry-Proposed Nanocomposites Thrust Area

Heavy investments in nanocomposites R&D are underway in the private and public sectors as well as at national institutions, and it is evident that no one entity is robust enough to take on the challenge of commercialization of nanocomposites by itself. A nanocomposites thrust is needed to increase the solidarity among U.S. industry, government institutions, and academia and to accelerate the development of commercial nanocomposites. The goal of the thrust area is to bring together key industry partners, national labs (DOC, DOE, and DOD), and academia to provide the capability to engineer nanostructured additives that may be incorporated with other materials to create composites with targeted property improvement(s).

Three components are necessary:

- Setting standards and metrology requirements and relating these to controllable, measurable process parameters
- Calculating the sensitivities of a composite to the properties, distribution, etc., of its nanostructured constituents
- Repeatably demonstrating the enhancement of a targeted property

The nanocomposites thrust will deliver the understanding and tools necessary to begin tailoring nanomaterials, additives, and the polymeric or other matrices in a precompetitive environment. Also, it will encourage focused, application-specific demonstrations called, perhaps, “pathfinders” (as used by Boeing, Intel, and others to mean demo projects that pursue validation of concepts and methods) in order to ensure that specific industry needs are being met, thereby bridging the gap between nanomaterials suppliers and end users. The nanocomposites thrust, as a national program, will lay the foundation for researchers to adopt technological breakthroughs, thus making this research applicable to any U.S. nanotechnology product.

Industry collaboration will be in a noncompetitive environment and thus be open to all industries. The intent is to provide tools, knowledge, and standards to industry partners that can then be used in a competitive environment as each industrial entity deems necessary.

The ability to meet the goals of this nanocomposites effort will secure U.S. leadership in nanotechnology via:

- Standards
- Innovation
- Verification and validation
- Requirement-specific engineered materials

This vision is achievable through industry, government, and academic solidarity in a common goal.

3. INSTRUMENTATION AND METROLOGY FOR CHEMICALS

Principal Authors: Anne Chaka, Richard Colton, Stephanie Hooker, and Dianne Poster

3.1 INTRODUCTION

Chemistry underlies all of nanotechnology, from life science to materials to electronics. By learning to understand and control the chemistry at the most fundamental level, we will enable nanotechnology to fulfill its promise. The chemical foundation consists of:

- Bonding for different classes of systems (ionic, covalent, metallic, organic, inorganic, ceramics, semiconductors, metals, etc.)
- Non-bonded interactions
- Kinetics and dynamics
- Composition/morphology
- Self-assembly
- Chemical reactivity

The high-impact application areas in nanotechnology identified for the chemical industry are catalysis, ceramics, coatings, sorbents, membranes, high-strength materials, and composites. This chapter emphasizes the needs of the chemical industry, but it also indicates common aspects that relate to the other manufacturing sectors with respect to design, instrumentation, and production.

Due to the diversity of chemical structure and function, it is tempting to consider the full scope of chemical space. It's been estimated that there are 1040 to 10200 chemical structures of molecular weight under 500. Hence the members of the breakout group on instrumentation and metrology for chemicals concluded that it is essential to focus on classes of chemistry and classes of problems—to think in terms of a matrix of fundamental issues versus application areas that relate to them. How those classes are defined depends on the class of problem under consideration; the application determines what needs to be measured and how accurately.

3.2 VISION FOR CHEMICALS

The vision for the future in terms of nanotechnology and chemicals is to support and develop instrumentation, metrology, and standards that enable rational design and manufacture of materials through improved understanding of mechanisms, processes, and structure-property relationships at the nanometer and molecular scale. Modeling and simulation is a high-priority, cross-cutting, enabling tool for discovery, process design, and process control to enable implementation of the vision.

3.3 SCIENTIFIC AND TECHNOLOGICAL BARRIERS

The key science and technological barriers to the design and manufacture of nanotechnology-enabled products result from the inherent challenges in answering the questions, What atoms are present? Where exactly are they? What unique properties emerge as a result of a particular arrangement of atoms? How do you reliably place atoms where they need to be on a manufacturing scale? How do you track dynamics in real time? How do you measure, control, and mitigate defects? As measurement science is driven towards increasing atomic resolution, the issues of sampling and assessing the statistical significance of the measurement simultaneously with making the precise atomic-scale measurements become critically important. For example, homogeneous dispersion of carbon nanotubes in a polymeric matrix is important for determining the performance of nanocomposites and can be measured in a small region. Ensuring that distribution is uniform throughout the entire bumper of a car or the wing of an airplane, however, is not currently feasible offline in a laboratory setting, let alone in commercial production. Industry requires *in situ* tests that can be applied in the production process in order to monitor material properties in real time.

Hence one of the most significant metrology challenges in nanoscale science and technology is the three-dimensional atomic resolution of composition. Measuring average chemical composition over a region even as small as 10 nm is not sufficient. The accuracy of measurements is not known, and the problem is complicated by the fact that at the nanoscale, the very act of measurement can greatly perturb the system. Background noise is a significant issue. At this scale, environmental impacts such as vibrations and small changes in temperature and humidity can cause significant variability in a measurement. Comparing the quality of measurements taken by different instruments and laboratories has been problematic because reference materials are not available to ensure that different laboratories and techniques are looking at identical systems. In addition, a deeper understanding is needed of background noise, defects, and other external impacts that can make an ideal model differ from real-world circumstances.

Complex modeling and high-performance computing are also critical to measurement science at the nanoscale, because at nanoscale dimensions, the behavior of discrete atoms becomes crucial, and interactions between measuring devices and samples make quantitative measurements of material properties extremely challenging. The interpretation of nanoscale imaging and the modeling of microelectronic circuits are severely limited due to limitations in computational speed.

Modeling and Materials Data

Attendees at the NNI Grand Challenge workshop series of 2001–2004 (see http://www.nano.gov/html/res/pubs.html) repeatedly identified the lack of quantitative materials data and modeling techniques as a “grand challenge” for the commercialization of nanotechnology. The promise of nanotechnology lies in the potential for emergence of properties at the nanoscale that are qualitatively different from those of the macroscale. Although nanoscale property data is available for a few systems, what is lacking is a systematic investigation of the fundamentals responsible for the change in properties with size. This fundamental knowledge is essential to the design process to guide researchers in selecting a combination of elements out of the exponential number of combinations possible in the periodic table that would have a high probability of expressing a property in a desired range.

For modeling and simulation to provide guidance for the accelerated development of new designs and new applications, the results must be reliable and support a design decision. Unfortunately, as stated in the NSF blue ribbon panel report on simulation-based engineering science, “… *further development* [of verification and validation and uncertainty quantification] *will have a profound impact on the reliability and utility of simulation methods in the future*” (NSF 2006, 36). For simulations to be predictive and general, they must accurately describe interactions with atomic resolution. This accuracy is unfortunately computationally prohibitive for all but the simplest systems, even on today’s supercomputers. To treat problems of industrial relevance, approximations to the exact physical laws are introduced into models to make simulations affordable. Simulations using these approximations can yield useful results for industry *if* they have been calibrated with extensive experimental data programs. However, these models have a very limited—and typically unknown—range of applicability and cannot be generalized, transferred, or extended in a rigorous manner to novel systems and conditions so as to enable innovation, design, and better technical decision-making. In addition, better models are needed for statistical design of experiments and for incorporating feedback to and from empirical results.

Development is needed for deterministic models across the full range of time and length scales. At the smallest regime, for example, highly accurate first-principals quantum mechanical methods are a powerful means to determine composition and the placement of atoms to achieve desirable properties to enable design and interpret experimental results. Because quantum mechanics is based on first principles, it can be applied reliably to novel compositions and structure, but only in models consisting of up to several hundred atoms; fast, reliable methods are needed that can be applied to particles and nanoscale systems with thousands or even millions of atoms with variable composition and structure. These models must also incorporate long-range forces such as electrostatics or mechanical stress fields, which require integration in space over many orders of magnitude. Simulations capable of predictions over several orders of magnitude in time are required for prediction of lifecycle performance, as well as of long-term thermal and oxidative stability. To solve one single problem requires multiple modeling disciplines; integration of these disciplines is a major barrier.

In sum, the major barriers to developing quantitative multiscale simulations of interactions at the nanoscale are:

1. Shortage of systematically generated experimental data *at all relevant time and length scales* for guiding and validating model development
2. Lack of systematic methods to integrate across time and length scales spanning several orders of magnitude, even if data were available, because the *fundamentals are not sufficiently understood*
3. Need for close collaboration between experts in high-precision measurement and dedicated theorists and computer modelers

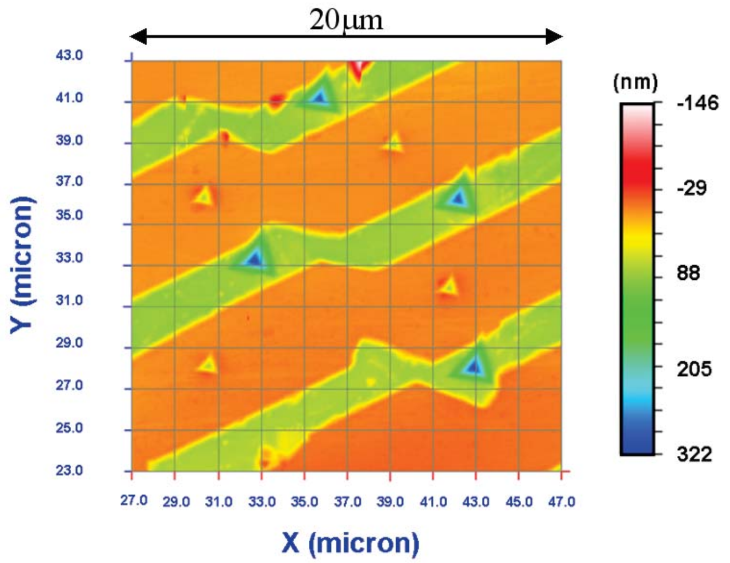
In addition, better models are needed for statistical design of experiments and incorporating feedback to and from empirical results.

Nanomechanical and Nanoscale Properties Modeling

Modeling *nanomechanical properties* is critical for the design of *all* nanodevices. For example, all nanodevices experience mechanical loads during processing and service, and quantitative predictions of failure strengths are needed to ensure reliability and maximize performance. Quantitative simulation of nanoindentation, for example, requires spanning the full range of computational techniques over six orders of magnitude from the continuum down to the electronic structure of the constituent atoms. (See the sidebar, "Instrumented Indentation Test for Hardness and Materials Parameters.") To validate the simulations and quantify the uncertainties, high-precision ultra-high-vacuum nanoindentation experiments are required that are capable of atomic-level characterization of sample and indenter tip geometries and unprecedented spatial and force resolution (picometers and piconewtons). A resulting validated sample failure models could then be used as a standard reference simulation that industry can use directly to calibrate the accuracy of their own nanomechanics modeling techniques.

Instrumented Indentation Test for Hardness and Materials Parameters

Instrumented indentation (IIT), also known as nanoindentation, employs high-resolution instrumentation to continuously control and monitor the forces and displacements of an indenter as it is driven into and withdrawn from a surface. Mechanical properties are derived from these force-displacement data. An ISO standard test method (ISO 14577) may be used to evaluate hardness and elastic modulus on a very localized scale. Submicron indentations are routine, and with careful attention, properties may be determined from indentations only a few nanometers deep. IIT has become a primary tool for examining thin films, coatings, modified surfaces, and composites. The same instrumentation used to make indents may also be used to perform other types of small-scale mechanical tests. Of particular interest is the characterization of MEMS devices such as accelerometers, RF switches, and cantilever arrays used in biological applications.



Indentations in a lamellar eutectic alloy. The primary phase is chromium silicide, Cr_3Si, and the secondary phase is a chromium-rich solid solution.

(Figure is courtesy of Jennifer Hay, Agilent Technologies.)

Large benchmark *ab initio* quantum mechanical calculations and new algorithms are needed to determine how properties and stoichiometry change with size as a function of electronic structure for classes of chemical species.

Molecular Interactions and Self-Assembly

Weak non-bonded interactions determine the structure and properties of fluids, molecular assemblies, soft materials, and biological systems, including the dispersion and aggregation of nanoparticles; self-assembly; viscosity and emulsion stability; and the structure of cellulose, proteins, and the DNA double helix. Modeling these systems in a rigorous manner requires an accurate description of the intermolecular forces that determine condensed phase properties, integrated with a proper treatment of statistical mechanics in a molecular simulation framework to capture the dynamic nature of a fluid. These forces, due to van der Waals and electrostatic interactions, are difficult to treat accurately in the bulk phase because they arise out of both short-and long-range interactions, respond dynamically to a changing environment, and are many-body in nature. Using the most accurate quantum chemistry methods, the calculation of forces scales as the number of electrons to the 7th power, so that simulations using forces calculated for each configuration of the system are impossible today. Hence, descriptions of intermolecular interactions responsible for condensed phase properties are now essentially limited to approximate models fitted to experimental data that cannot be systematically transferred, extended, or improved.

Flow Simulations

Reactive flow simulations are important for a broad range of applications, including design of chemical plants, real-time process control simulations, and vapor deposition processes. Computer simulations are only beginning to play a role because of the challenge of representing thousands of chemical species and reactions in a dynamic fluid environment. Addressing these problems requires expertise in computational fluid dynamics (CFD) integrated with expertise in chemical kinetics, quantum chemistry, and informatics to identify the essential chemistry needed to reduce a complicated mechanism to a tractable size.

Increasing computer power is necessary for more realistic simulations, but not sufficient. New algorithms need to be developed as well. For example, in the field of quantum chemistry, only some of the computational speed over the past twenty years has been due to a Moore's-law increase in computer power; improved algorithms and mathematical approaches have also contributed substantially. Moving forward requires an integrated approach that incorporates data, models, theory, and measurements to delineate the essential chemistry and physics for predictive multiscale model development with quantified uncertainty. Further, a property data project (on the scale of the Human Genome Project) is needed for mapping properties of the combination of elements in the periodic table.

Manufacturing

There is considerable "art" in the current state of nanomanufacturing, with repeatability constituting one of the greatest challenges. This is due, to a large extent, to the lack of precise control for both top-down and bottom-up nanomanufacturing processes. Even in an ideal laboratory environment, it is difficult to control the chemical composition and precise arrangement of atoms. Scale-up is problematic, and measurements made under real-world conditions do not necessarily correlate with those made in the ideal laboratory environment. Small variations in processing, composition, or defect density can dramatically change product performance. For quality control in manufacturing, it is necessary to develop the means for real-time process control. In-process tools are available to measure such parameters as temperature, gas flow, and pressure, but considerable research is required to link these macroscopic process control parameters with the resulting properties of the product. Fundamental understanding is lacking, as is the means to measure product quality analogous to what is currently possible in the semiconductor industry.

Nanotechnology also requires development of new guidelines for best practices for materials handling both during and after manufacture. New concerns have been raised with respect to environment, health, and safety (EHS) issues, as well as for stability, aging, and shelf life as compared with bulk materials. Surface structure and reactivity for nanoscale materials may be significantly different from those of bulk materials, but the differences are difficult to measure, let alone understand. Furthermore, the costs of determining optimal safe handling procedures may outweigh performance benefits and represent a barrier to development and implementation of nanotechnology.

3.4 PRIORITIES FOR R&D AND INFRASTRUCTURE INVESTMENTS

The chemical industry supplies a host of specialty and commodity products, addressing applications as diverse as microelectronics, pharmaceuticals, structural materials, and consumer products. The majority of these products utilize established materials and processing technologies; however, additional functionality is often highly desirable to customers. Due to known limitations of state-of-the-art materials, such functionality is likely to only be achieved through the development of new processing methods that provide an unprecedented capacity to tailor properties at the micro- and nanostructure levels.

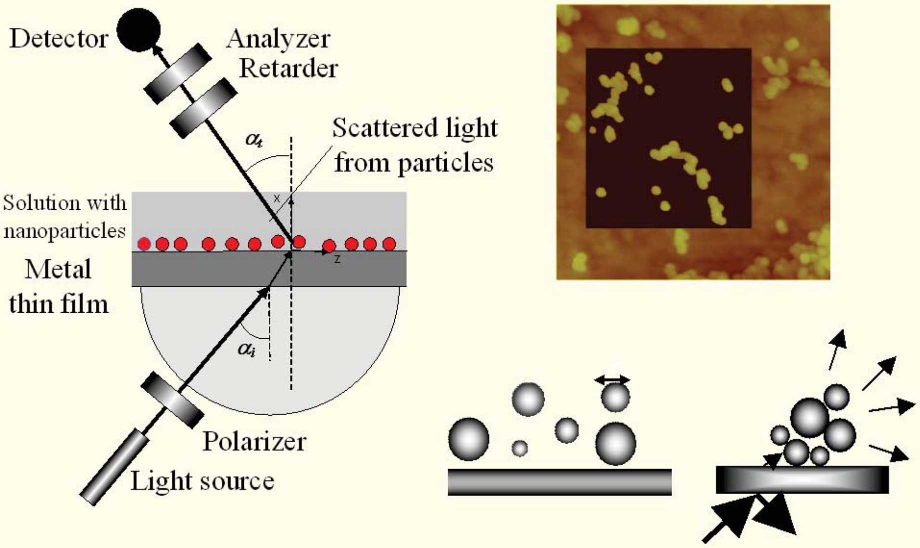
Nanotechnology is clearly emerging as one of the principal areas of R&D for the chemical industry—integrating chemistry, materials science, and in some cases, biology—to create materials with yet-undiscovered or unspecified properties that can be exploited for new market opportunities. In 2006, the global chemical industry spent approximately \$2.9 billion on nanotechnology-related R&D, an expenditure expected to grow approximately 25–30% per year until 2012 (Harper 2005). It is estimated that over 35,000 chemical researchers worldwide are directly engaged in nanotechnology-related research, the highest number of researchers of any industrial sector outside the semiconductor industry.

One of the key challenges facing these researchers is scaling from laboratory operations to volume material production while ensuring consistent quality and stability. Many exploratory synthesis routes for nanomaterials have been developed by university researchers and/or specialist companies. These efforts often utilize batch-scale processes that produce small quantities of material suitable for research purposes. As application development progresses, end users demand assurances that these new materials can be produced in substantially larger quantities with the same level of performance. However, scaling from laboratory to production without a corresponding astronomical scaling of cost is not a simple matter.

It is at this stage of development (i.e., the transition from innovation to product) where instrumentation and metrology challenges are the most critical. Considerable progress already has been made over the past decade toward new measurement technologies, accelerating progress in nanotechnology research within the chemical industry. (See sidebar, “Real-Time Characterization of Nanosize Particles and Agglomerates via Surface Waves.”) However, there are still many areas where measurement and modeling capabilities could be improved. It is here where metrology R&D at national laboratories and through university-led research can have far-reaching impact.

Significant efforts have been made to detail chemical industry needs for advanced characterization tools, documentary standards, standard reference materials, and informatics. Summaries can be found in the various publications of the U.S. Chemical Industry’s Technology Vision2020 Technology Partnership, such as the *Chemical Industry R&D Roadmap for Nanomaterials by Design: From Fundamentals to Function* (2003); *Implementation Plan for Chemical Industry R&D Roadmap for Nanomaterials by Design* (2006); and *Joint NNI-ChI CBAN and SRC CWG5 Nanotechnology Research Needs Recommendations* (2006) (see http://www.chemicalvision2020.org/library.html). This workshop examined progress toward the goals outlined in those reports, concentrating discussion primarily on those areas where continued development is still sorely needed, as indicated below.

Real-Time Characterization of Nanosize Particles and Agglomerates via Surface Waves



Reliable control of nanoparticle growth and surface assembly is a key building block in future applications of nanotechnology. There is a need for advanced tools that allow real-time, online diagnostics of chemical and physical processes important for nanoscale engineering applications, from self-assembly to nanofabrication. Applications of such a sensor will be numerous and will include electronics, bulk material fabrication, membrane synthesis, nanomechanical systems, and DNA screening (courtesy of M. Pinar Mengüç, Department of Mechanical Engineering, University of Kentucky, Lexington).

Classical light-scattering techniques cannot be adapted to determine the size, structure, and shape of nanosize particles. However, surface waves can be used to characterize nanoparticles within a few hundred nanometers of optically clean surfaces. Researchers at the University of Kentucky are using a real-time measurement tool based on surface wave scattering that has recently been designed and built, which is capable of making detailed angular scattering measurements at different polarization settings. The angular profiles of scattered surface plasmons/evanescent waves at far-field are interpreted with the use of an extensive numerical model. The model developed for this purpose is based on a hybrid approach, where the T-matrix concept is coupled with the image theory. The vector spherical harmonics are used to expand the incident and scattered fields, which are in turn related to a T-matrix. Effects of size, shape and orientation of the single and clustered particles on their scattering patterns are sorted out to distinguish particle characteristics. Additional sensitivity analyses are performed to determine the angular regimes at which the most robust measurements can be made. This information is used to monitor different agglomeration stages of self-assembled nanometer-size particles (Venkata et al. 2007; Francoeur and Mengüç 2008; Charnigo et al. 2007).

New Measurement Science to Support Advanced Chemical Manufacturing

Understanding the link between process, structure, and functionality is essential for the creation of new nanomaterials, as well as for the development and optimization of new synthesis routes (e.g., self-assembly). To accomplish this, new measurement tools are needed that range from the highly sophisticated to the relatively simple.

Sophisticated instrumentation is required to enable fundamental understanding of chemical and material behavior at the nanoscale. In particular, such tools must address surfaces and interfaces, allowing researchers to understand how materials form and react. Less complex instrumentation is needed for use in manufacturing environments for process control, quality control, material classification, and reliability testing. This instrumentation must support rapid identification of material purity and homogeneity, while remaining relatively easy to use. The two tables below list several metrology requirements associated with comprehensive characterization and process control that are considered critical for the chemical industry. It should be noted that meeting the necessary specifications for these instruments will require, in many cases, completely new approaches to chemical measurement. It is here where close collaboration between the chemical industry and metrology developers is critical to help set and share priorities and ensure that developed metrology meets broadly applicable needs.

Comprehensive Metrology Needs

- Instruments capable of 3D chemical characterization: elemental & molecular
- Platforms for simultaneously assessing multiple properties on a single sample
- Techniques that can span multiple length and time scales simultaneously
- Tools that can assess chemical reactivity at surfaces and interfaces
- Methods for measuring and visualizing chemical dynamics: time-resolved chemistry

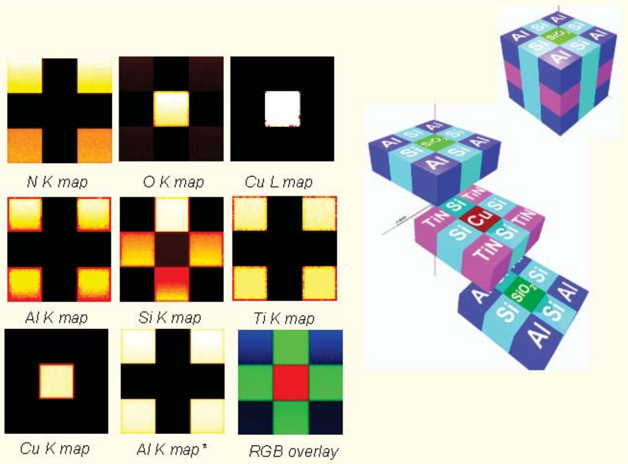
Process and Quality Control Needs

- High-throughput characterization methods, either in-process or off-line
- Techniques for materials separation, purification, and classification
- Tools to verify purity, quality, and consistency
- Tools for testing performance in real-world environments
- Instrumentation to support 3D manipulation, assembly, processing, and integration at the nanoscale

New Measurement Standards for Nanoscale Characterization

Researchers, chemical manufacturers, and product developers must be able to confidently compare and reproduce the properties of new materials before widespread application can occur. Complicating this goal is the fact that most new synthesis routes are as yet unreliable, resulting in variability that can range from slight to significant, depending on the state of process development. Known issues with material variability amplify the need for standard reference materials aimed specifically at nanotechnology. These reference materials will be used to ensure that existing and new measurement methods are properly calibrated, so that these tools can then provide meaningful feedback during material and process optimization. Ideally, an entire library of high-quality reference materials will be developed that address the full range of properties of interest for nanomaterials and the full range of material classes. (For example, see the sidebar, "Nanoscale Standards: 3D Chemical Analysis.")

Nanoscale Standards: 3D Chemical Analysis



Conceptual nanomanufacturing standard material, consisting of a multielement nanoscale "Rubik's cube." The complete structure is shown at the upper right as a large, heterogeneous cube 300 nm on a side consisting of 27 smaller, chemically homogeneous sub-cubes, each 100 nm on a side. To better visualize the distribution of elements, the cube is shown in an artificial exploded view on the lower right; although this geometry makes it easier to see the inside of the structure, no simulations are performed in this configuration. At left is an array of simulated x-ray spectral maps showing the expected data from an electron-beam elemental mapping experiment. Each map is 300 nm on a side and is labeled according to the characteristic x-ray emission line used for mapping (courtesy of John Henry Scott, NIST).

The creation of nanoscale standard materials would be of great benefit to many areas of nanoscience and nanotechnology, including nanomanufacturing. Ideally, a nanoscale standard sample would be chemically heterogeneous on the length scales of interest; well-characterized in structure, morphology, and elemental distribution; and in a physical form amenable to the characterization tools available to the industry. While the production of such a standard still presents significant manufacturability challenges and issues related to reproducibility and quality control, it is possible to simulate what such as standard might look like as well as predict its performance in some chemical metrology tools such as the electron microscope.

The "Rubik's cube" shown in the figure at left is a simulated nanoscale standard in the form of a chemically complex cube 300 nm on a side. The heterogeneous cube is composed in turn of 27 smaller sub-cubes, each 100 nm on a side. In the very center of the standard is a cube of copper metal (Cu) surrounded laterally by four cubes each of silicon (Si) and titanium nitride (TiN), a common diffusion barrier material in semiconductor devices. The two layers of sub-cubes above and below the central layer are identical; they consist of a central sub-cube of silicon dioxide (SiO_2) surrounded by four sub-cubes each of silicon (Si) and aluminum (Al).

Using a 3-dimensional Monte Carlo simulation written at NIST, it is possible to compute in detail the transport of beam electrons through this sample, accounting for material-dependent scattering cross-sections, densities, excitation thresholds, characteristic and Bremsstrahlüng x-ray generation, mass absorption coefficients, etc. This permits the simulation of high-fidelity microanalysis data of the type that would be acquired on scanning electron microscopes and transmission electron microscopes. The elemental maps shown at the left of the figure represent the calculated signals expected from an energy-dispersive x-ray spectrometer with an energy resolution of 135 eV full-width at half maximum. The gradients in the x-ray intensities seen in the maps reflect the self-absorption of x-rays on their way from the excitation volume to the x-ray detector and match quantitatively the behavior of real-world samples.

Creation of "phantom" samples such as this cubic standard block, and the generation of credible synthetic datasets, help lay the foundation for a suite of standardized physical artifacts to support the nanomanufacturing community.

Numerous hurdles must be overcome before a library of standard reference materials can be made available. First, suppliers of such materials must be found and qualified. Qualification must include extensive round-robin testing using as comprehensive a suite of analysis tools as possible. Finally, as new measurements become available, they must be tested with the standard reference materials, and rugged procedures must be developed for their use. Only by coupling standard reference materials with standard protocols can new measurement tools truly be utilized at their full potential.

Model Systems for Vastly Improved Fundamental Understanding of Nanoscale Phenomena

The chemical industry is engaging in a profusion of ongoing nanotechnology-related research activities. In some cases, this research focuses on a new synthesis route that is capable of producing a wide array of nanomaterials, perhaps with a well-defined size range. In other cases, the research focuses on a specific material such as carbon nanotubes and concentrates on controlling a particular property or degree of chemical purity. In still other cases, the research focuses on an application (e.g., catalysis), and all materials development activities are driven by performance targets.

Regardless of the driver for the research, the diversity of activities underway contributes to the market growth potential anticipated for nanomaterials. However, to truly reach the potential envisioned for innovation and new product creation, the chemical industry needs an intelligent basis for nanomaterial discovery and property tailoring. This goal is best reached through coordinated and extensive characterization of a relatively limited subset of the nanomaterial design space. Identification of a few "model systems" that are of high priority would allow for an abundance of data-gathering with direct comparison between laboratories, thereby enabling full understanding of how subtle changes in certain process parameters affect material behavior.

During this workshop, a number of potential "model systems" were identified: carbon nanotubes, ultra-thin films of SiO_2, GaN nanowires, ceramic supported platinum particles, metal oxides, and polymeric nanocomposites. To effectively evaluate any one of these systems will require a coordinated, synergistic effort across Federal agencies and in conjunction with industrial and university partners. Essential to success will be the controlled synthesis of relatively large quantities of each material; extensive round-robin characterization efforts; data mining to identify critical process and measurement parameters; and extensive computational models to extend beyond a specific material to begin to truly design-in desired behavior.

Infrastructure Needs

In addition to focused research activities, investment in nanotechnology infrastructure will also prove important for sustained product development. Much of this infrastructure relates to the ability to easily exchange data between research laboratories, simulate large numbers of experiments, mine datasets for critical information, and track progress through product databases. Traditional means of sharing data will also be important. For example, property databases and materials handbooks are needed that directly address nanomaterials. These databases will serve as critical references for material designers.

3.5 IMPLEMENTATION STRATEGIES

The development of any implementation plan or strategy takes time and resources. However, a number of industries and nanotechnology groups are actively engaged in related activities that can be leveraged. In addition, the National Nanotechnology Initiative (NNI) and its coordinating bodies are well positioned to facilitate interagency and industrial collaborations.

The NNI has designated nanomanufacturing as one of its eight program component areas (PCAs) for tracking research funding. The principal aim of the Nanomanufacturing PCA is to coordinate R&D activities that enable scaled-up, reliable, cost-effective manufacturing of nanoscale materials, structures, devices, and systems. The Nanomanufacturing PCA also involves R&D and integration of ultra-miniaturization top-down processes and increasingly complex bottom-up or self-assembly processes (NSET 2007). NIST and NSF are among several NNI participating agencies that have designated the Nanomanufacturing PCA as of "primary" interest with respect to their agencies' missions and responsibilities.

Related NIST activities that can be leveraged include the NNI workshop report on Instrumentation and Metrology for Nanotechnology NIST held on 27–29 January 2004 (NSET 2006) and ongoing NIST assessment (2007) of the U.S. Measurement System to support U.S. technology innovation.

Recommendations

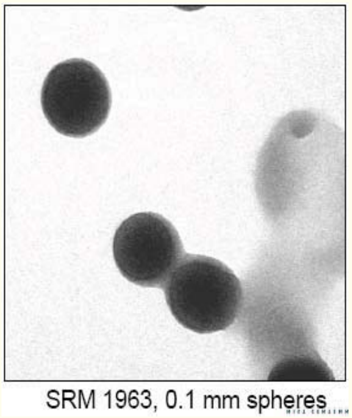
The participants recommend getting started quickly and keeping the first strategies simple. In approximate order of priority, the recommendations are as follows:

- *Define a roadmap to develop standard reference materials for nanomanufacturing*. One approach would have the government convene a meeting of all interested parties from industry, academia, government, and standards organizations. The meeting would examine and identify the most promising standard reference materials. Some attributes include materials that (a) are widely available and have known properties, (b) have the largest current and potential economic impact, (c) would provide the most meaningful data, (d) could be readily modeled, (e) would meet the requirements of potential users, and (f) are consistent with environmental, health, and safety issues.
- *Define standard operating procedures (SOPs) for the synthesis of nanomaterials and sample preparation procedures for measuring, handling, and storing these materials*. The participants also stressed the importance of identifying a core group of researchers to examine and develop standard labeling practices and Material Safety Data Sheets (MSDS) requirements for nanomaterials.
- *Develop standard meta-data formats for the capture, storage, and interpretation of raw data so that data pedigree and quality can be evaluated*. Examples from other communities include the standard crystallography structure format or the Microarray and Gene Expression Data (MGED) Society's minimum information about micro-array experiment (MIAME; http://www.mged.org/Workgroups/MIAME/miame.html). One approach forms teams of experts for different classes of measurements and instruments to develop and recommend standardized formats to journal publishers and instrument manufacturers.
- *Establish and populate a database of physical property data for nanomaterials*. One example of an existing database is the NIST Chemical WebBook (http://webbook.nist.gov/), which could serve as a starting point for this effort.
- *Provide funding and support for badly needed ("nonglamorous") systematic studies to measure the physical properties of nanomaterials.*
- *Support development of predictive multiscale models to discover new materials based on physical property data and reference materials.*

Development of Standard Reference Materials at NIST to Support Instrumentation, Metrology, and Standards for Nanomanufacturing

Standard Reference Materials (SRMs) are certified reference materials issued by the National Institute of Standards and Technology (NIST). SRMs are homogeneous, stable materials that are well-characterized for one or more chemical and/or physical properties. SRMs are designed to assist researchers, laboratories, and industry worldwide in validating analytical measurements of chemical composition or physical properties. SRMs are useful for method evaluation and are widely used for research applications, including the evaluation of sampling devices or instruments.

NIST has produced a number of particle size standards in the nanometer to micrometer size range (see table below). These are valuable for evaluating or calibrating particle size measuring instruments such as light-scattering instruments, optical and scanning electron microscopes, sedimentation systems, and wire cloth sieving devices. A number of these are polystyrene materials that consist of monodisperse latex particles that are suspended in water (see the figure below). The smallest particle size for this group of materials is on the order of 100 nm (SRM 1963). Selected non-water suspensions are also available, such as silicon nitride and zirconium oxide, with particle diameters <500 nm to 2.8 µm.



NIST particle size standards: nm-µm range (courtesy of NIST).

SRM[a]	*Type*	*Particle Diameter*[b]
1963	Polystyrene (0.5% in H_2O)	100.7 ± 1.0 nm
1691	Polystyrene (0.5% in H_2O)	269 ± 7 nm
1690	Polystyrene (0.5% in H_2O)	895 ± 8 nm
1692	Polystyrene (0.5% in H_2O)	2.982 ± 0.016 µm
1965	Microsphere Slide (10 µm Polystyrene Spheres)	9.94 ± 0.04[c] µm 9.89 ± 0.04[d] µm
1961	Polystyrene (0.5% in H_2O)	29.64 ± 0.06 µm
659	Silicon Nitride	480 nm to 2.80 µm
1978	Zirconium Oxide	330 nm to 2.19 µm

SRM 1963 Polystyrene
(0.5% in H2O), 100.7 nm

a. SRM number
b. values and uncertainties are described on Certificates of Analysis for each material at http://www.nist.gov/srm
c. hexagonal array; d unordered clusters

In an effort to meet the needs of instrumentation, metrology, and standards for nanomanufacturing, NIST is developing different types of nanoscale reference materials and smaller sized particle reference materials, including 60 nm polystyrene in water (SRM 1964 Nominal 60 nm Diameter Polystyrene Spheres) and a suite of colloidal gold materials. The three new gold sphere reference materials (RM 8011, 8012, and 8013) are nominally 10, 30, and 60 nanometers in diameter, were developed in cooperation with the National Cancer Institute's Nanotechnology Characterization Laboratory to provide researchers with one avenue to assess the quality and comparability of their performance in physical characterizations of nanomaterials. The materials are tailored for research on the biological effects of nanoparticles and will be useful in tests of the efficacy and toxicity of nanoscale particles (*in vitro* and *in vivo*).

NIST is also developing SRMs for electron and ion beam analytical imaging instruments (thin films, single-phase nanoscale particles, line width standards), and carbon nanotube materials. Information on NIST SRMs is available at http://www.nist.gov/srm.

- *Develop well-coordinated data collection activities for both the measurement results and the techniques used to collect the data*. Because nanomaterials processing is maturing at the same time as measurement methodology at this scale, it is critical that any and all data collections fully and accurately report as many conditions of growth, storage, handling, and measurement as possible. Until it is clear what parameters matter, collection and sharing of all information will be critical to further materials development. This level of data recording will require substantial commitment from the scientific community coupled with use of the best data mining tools available today.
- *Develop predictive multiscale models for process development, control, and prediction of product performance and lifecycle*. Multidisciplinary development teams should include end users. Federal agencies could play a role in coordinating integrations and access to high-end computing.
- *Develop instrumentation for real-time process development, scale-up, and control; for quality control; and for EHS monitoring and control*. The plan should be developed and coordinated with instrument developers and manufacturers early in the tool development process. Government and industry could provide access to funding for instrument demonstration projects. Procedures should be established to enable technology transfer to instrument vendors.
- *Develop nanoscale assembly and manipulation tools and processes*.
- *Develop advanced, offline materials characterization tools that emphasize ways to increase the functionality of AFM, SEM, TEM, etc*., making the tools multifunctional and capable of working with combinatorial methods.
- *Continue fundamental metrology, instrumentation, and standards work at NIST*, which provides underpinnings for coordinated interagency activities and application by industry.
- *Continue support for R&D on measurement science and novel instrumentation*.

Can a Roadmap for Success Be Outlined?

When scientists and engineers think of roadmaps, those working in the semiconductor or related industries will know about the International Technology Roadmap for Semiconductors, known throughout the world as the ITRS (http://www.itrs.net/home.html). ITRS is conducting an extensive 15-year assessment of the semiconductor industry's future technology requirements. The future needs identified by this roadmap drive strategies for worldwide research and development efforts of manufacturers, universities, and national labs. Through the cooperative efforts of the global chip manufacturers and equipment suppliers, research communities, and consortia, the roadmap teams identify critical challenges, encourage innovative solutions, and welcome participation from the semiconductor community. They actively engage with other strategic roadmapping efforts, such as those for electronics and nanotechnologies, and hold public conferences twice each year for public review and comment. By far, this roadmapping effort is the most extensive activity of its kind.

Researchers in the chemical industry may be aware of the Chemical Industry Vision2020 Technology Partnership activities (Chemical Vision2020 2003). The Vision2020 roadmap is very different in scope and function compared to ITRS, but it is, of course, pertinent to the broader scope of the chemical industry. The roadmap presents an R&D strategy to achieve nanomaterials by design. The tenets of the strategy include development of (1) fundamental understanding and synthesis, (2) manufacturing and processing, (3) characterization tools, (4) modeling and simulation, (5) environment, health, and safety protections, (6) standards and informatics, (7) knowledge and technology transfer, (8) education and training, and (9) infrastructure and enabling resources.

So what would a roadmap for instrumentation, metrology, and standards for nanomanufacturing look like? It would probably not be as specific as ITRS or as broad as Vision2020. However, because this breakout section had a *chemical* focus, there are overlaps with the chemical industry roadmap.

A roadmap for standard reference materials should begin with materials that would be relatively easy to characterize, such as simple metal and metal oxide nanoparticles. Examples would be different sizes of Au and TiO_2 nanoparticles. Adding other metals such as Pt, Pd, or Cu, and metal oxides such as SiO_2 or MoO_2 would begin to address compositional and structural complexity relevant to catalysis. An assessment would have to be made for other possible materials.

To address instrumentation for nanomanufacturing, an assessment of nanoscale imaging and manipulation instruments would be required.

Participants in this breakout session believe that if a nanomanufacturing roadmap were available, it would be used both by government (mission-oriented) agencies and by industry, and in fact, could help boost interagency and industrial coordination. Better cooperation would be possible in precompetitive areas such as instrument R&D, EHS, and infrastructure development. Instrument manufacturers would also benefit from the roadmap, and may even participate on precompetitive projects. (See the sidebar, "The Pennsylvania NanoMaterials Commercialization Center—A New Public-Private Partnership Model.")

3.6 SUMMARY

The chemical industry is actively engaged in research, development, and manufacturing of nanoscale technologies and chemical nanotechnology products. These are often essential to other key industries, including (although not limited to) health care, communications, food, clothing, housing, energy, electronics, and transportation. Current chemical nanotechnology products include metal, metal oxide, and semiconducting nanoparticles that are used as catalysts in chemical and energy processing, pigments for paints, UV protectants for sunscreens, and coating materials for cutting tools. Additional products include ceramics, sorbents, and membranes.

The Chemical Industry Vision2020 Technology Partnership recently identified research requirements essential for accelerating the commercialization of technologies based on nanomaterials (Chemical Vision2020 2003). The development of real-time characterization methods and tools; reference nanomaterials for property measurements to support metrology; and computational standards to improve prediction, information processing, and transfer of nanomaterial properties are identified in the 2020 report as top priorities to enable the manufacturing of nanomaterials by design. These topics continue to be top priorities for the chemical industry and are cross-cutting with other industries including biotechnology, pharmaceuticals, electronics, and nanostructured materials. Common chemical measurement and standards are needed to remove barriers to innovation in nanomanufacturing.

The Pennsylvania NanoMaterials Commercialization Center – A New Public-Private Partnership Model

Nanomaterials is one area of nanotechnology R&D that holds significant promise to enable enhanced features with existing products, new manufacturing processes, and unique new products never before considered. Lux Capital in its *Nanotech Report* (2004) identifies nanomaterials as one of the six key major investment themes for the next 10 years. It predicts that a number of industrial sectors that have traditionally had low growth over the past 30 years will be revolutionized by nanomaterials. These include the chemicals and basic materials industries, which include polymers, metals, alloys, and composites. This revolution will in turn have significant impact on industries that use these raw materials, such as aerospace and automotive industries, and on other industries producing a wide range of consumer goods.

Leveraging the strength of both its chemicals industries (with related polymer sectors), and its basic materials industries, the Commonwealth of Pennsylvania has developed the Pennsylvania NanoMaterials Commercialization Center (http://www.pananocenter.org/) in southwestern Pennsylvania where a number of major industry-based research and development centers for leading companies are located. Overall, the region hosts 285 polymer-based companies with employment of approximately 5,000 workers, and 75 metal-based companies. In addition, the major universities in the commonwealth are national leaders in the materials science fields. Both Pennsylvania State University and Carnegie Mellon University host National Nanotechnology Initiative-funded nanotechnology centers. Also, as pointed out in the Angle report on nanotechnology strategy (2004) commissioned by the commonwealth, the state is well-placed to attract new Federally funded nanotechnology centers, including the NSF-funded Nanotechnology Science and Engineering Centers (NSECs), and branches of the Nanotechnology Center for Learning and Teaching (NCLT).

The Pennsylvania NanoMaterials Commercialization Center has a unique approach to technology commercialization. The center was formed through the efforts and support of four key companies located in the area—Alcoa Inc., United States Steel, PPG Industries, and Bayer MaterialScience—and facilitated by the Pittsburgh Technology Council. The center capitalizes on the strengths of these four founding companies, matches their research and development expertise in nanomaterials with that of Pennsylvania's universities, and incorporates innovative technology ideas from start-ups and entrepreneurs to bridge the gaps between invention, innovation, and commercialization. In this way, the center is designed to act as both an accelerator and a facilitator of advanced nanomaterials commercialization to enhance nanotechnology-based economic development in Pennsylvania.

3.7 REFERENCES

Angle Technology Group. 2004. *Commonwealth of Pennsylvania Nanotechnology Strategy.* Sponsored by the Commonwealth of Pennsylvania. Available online: http://www.pananocenter.org/Docs/Pdf/anglereport.pdf.

Charnigo, R., M. Francoeur, M.P. Mengüç, A. Brock., M. Leichter, and C. Srinivasan. 2007. Derivatives of scattering profiles: tool for nanoparticle characterization, *Journal of the Optical Society of America A* 24(9):2578–2589.

Chemical Industry Vision2020 Technology Partnership (Chemical Vision2020). 2003. *Chemical industry R&D roadmap for nanomaterials by design: From fundamentals to function*. Available online: http://www.chemicalvision2020.org/pdfs/nano_roadmap.pdf.

———. 2006. *Implementation plan for chemical industry R&D roadmap for nanomaterials by design*. Available online: http://www.chemicalvision2020.org/pdfs/ChemInd%20Nanotech%20Impl%20Plan%209May06.pdf.

Chemical Vision2020 and the Semiconductor Research Corporation (SRC). 2006. *Joint NNI-ChI CBAN and SRC CWG5 nanotechnology research needs recommendations*. Available online: http://www.chemicalvision2020.org/pdfs/chem-semi_ESH_recommendations.pdf.

Francoeur, M., and M.P. Mengüç. 2008. "Polarized surface wave scattering for *in-situ* and online characterization of nanoparticles." Presentation at *Photonics North*, Montreal, PQ, Canada, June 2-4, 2008.

Harper, T. 2007 (April 30). "Nanotech and the chemical industry" (online business news article). MaBiCo Financial Co./Forex. Available online: http://www.mabico.com/en/news/20070430/foreign_exchange/article74463/.

Lux Research, Inc. 2004. *The nanotech report 2004™: Investment overview and market research for nanotechnology*, 3rd ed. New York: Lux Research, Inc.

National Science and Technology Council, Committee on Technology, Nanoscale Science, Engineering, and Technology Subcommittee (NSET). 2007. *The National Nanotechnology Initiative strategic plan*. Washington, DC: NSET. Available online: http://www.nano.gov/NNI_Strategic_Plan_2007.pdf.

———. 2006. *Instrumentation and metrology for nanotechnology: Report of the National Nanotechnology Initiative workshop*, January 27-29 (2004). Washington, DC: NSET. Available online: http://www.nano.gov/NNI_Instrumentation_Metrology_rpt.pdf.

National Institute of Standards and Technology (NIST). 2007. An assessment of the United States measurement system: Addressing measurement barriers to accelerate innovation. Gaithersburg, MD: NIST; Special Publication 1048. Available online: http://usms.nist.gov/usms07/index.html.

National Science Foundation Blue Ribbon Panel on Simulation-Based Engineering Science (NSF). 2006. *Revolutionizing engineering science through simulation.* Arlington, VA: NSF. Available online: http://www.nsf.gov/pubs/reports/sbes_final_report.pdf).

Venkata, P.G., M.M. Aslan, M.P. Mengüç, and G. Videen. 2007. Surface plasmon scattering by gold nanoparticles and two-dimensional agglomerates. *ASME Journal of Heat Transfer* 129:60–70.

4. INSTRUMENTATION AND METROLOGY FOR NANOSCALE ELECTRONICS, MAGNETICS, AND PHOTONICS

Principal Authors: John Carruthers, Alan Diebold, Michael Garner, Daniel Herr, James Murday, David Seiler, and Theodore Vorburger

4.1 INTRODUCTION

New nanoscale devices and structures are expected to revolutionize information technology. Realizing these advances will require accelerated development of the metrology and instrumentation needed to make reliable, reproducible measurements of material properties and device performance, as well as incorporation of devices into commercial products. This section focuses on new metrologies as well as on improvements to commercial instrumentation important to information technology devices. Relevant technology applications include the following:

- Advanced CMOS semiconductor devices (Arden 2006; Cavin et al. 2006; Hutchby et al. 2005; Zhirnov et al. 2005)
- Nanowires (Lieber and Wang 2007), molecular electronics, and other "beyond-CMOS" technologies (Brewer, Zhirnov, and Hutchby 2005; Cavin et al. 2005; Cerofolini et al. 2005; Hutchby et al. 2002)
- Quantum dots, photonic crystals, plasmonics, and other nanophotonic materials and structures (Hillmer and Germann 2003; Wong et al. 2007; Coufal and Dhar 2006)
- Nanoengineered magnetic sensors, magnetic storage, and magnetic media
- Spin electronics (Wolf, Treger, and Chtchelkanova 2006; Goronkin and Yang 2004)

4.2 VISION FOR ELECTRONICS, MAGNETICS, AND PHOTONICS

A unified vision for the future of nanoscale electronics, magnetics, and photonics is to develop (1) instrumentation and metrology capabilities for analysis of atomic-scale physical properties of nanoelectronic, nanophotonic, and nanomagnetic materials, and (2) methods to correlate these properties with device and system performance. It is envisioned that this instrumentation and metrology will support design, modeling, synthesis, and fabrication of advanced materials and devices for a variety of applications. Capabilities will include nanoscale 3D imaging, chemical analysis, dimensional measurements, *in vivo* analysis during device operation, and material manipulation in hard and soft materials. Multifunctional coupling devices will be available to link nanoelectronics, nanophotonics, and nanomagnetics, including nanoscale signal storage and processing. Advanced metrology developments will enable industry to discover and use new phenomena in materials, structures, and devices with nanometer-scale critical dimensions, where interface interactions (rather than bulk atomic behavior) dictate the collective electronic, magnetic, and photonic behavior of the structure or device. Improved resolution of measurement tools by orders of magnitude over current capabilities will make it possible to probe local behavior on the atomic and molecular scale and correlate that behavior with the macroscopic behavior of larger entities.

Nanoelectronics

In nanoelectronics, the vision includes tools that (1) can measure statistically significant information for manufacturing (e.g., average of multiple variations) and (2) are capable of point-by-point characterization (e.g., single variations across a wafer, especially at the edges, that must be analyzed). Of particular importance are physical and electrical measurements that ensure optimal nanoelectronics system operation. These include correlation of physical characterization with the electrical properties of devices; fast, noninvasive subsurface/volumetric measurement capability; and 3D-resolved, nondestructive evaluation (NDE) of chemical, physical, electrical, optical, and other properties with nanometer-resolution capability.

The semiconductor industry has already established the International Technology Roadmap for Semiconductors (ITRS); new sections cover single-electron transistors and molecular electronics. Within the ITRS, the Metrology Roadmap section discusses the metrology and materials characterization needs for advanced nonclassical CMOS and beyond CMOS, including emerging device technology. In late 2007 the ITRS included an Emerging Research Materials section in the roadmap that also includes a Metrology subsection describing the metrology and characterization needs for these materials (see http://www.itrs.net/reports.html).

Nanomagnetics

In nanomagnetics, physical measurement standards are needed to enable fabrication of magnetic structures with dimensions of 1–10 nm, to measure their chemistry and structure, to measure the magnetization vector of each atom and nanoparticle in these structures and their interactions, and to image magnetic domain structure at 1 nm resolution at high speed. The vision for magnetics is that new modeling methods will be developed that handle multiple size scales ranging from 1 nm to 1 m. Advanced measurements enabled by the above will be possible through the design of new instrumentation and/or methods that support actual operating environments and picosecond time scales. Magnetization reversal by domain processes or spin rotation methods will be observable, enabling engineering of devices for high-speed switching and sensing. This will impact a diversity of applications from biomedical detection and remediation to magnetic random access memory (MRAM), strategic sensing, and homeland security.

Nanophotonics

The nanophotonics vision includes (1) instrumentation and metrology to support the development and seamless integration of nanophotonic and nanoplasmonic materials and components into photonic, electronic, and hybrid circuits, and (2) advanced nanophotonic-based characterization tools, such as near-field scanning optical microscopy (NSOM), for nanoscale 3D imaging and spectroscopic chemical analysis. An important component of both is the rapid development of modeling capabilities critical to designing nanophotonic structures and to interpreting probe-sample interactions in photonic/plasmonic characterization techniques.

4.3 CURRENT STATE OF THE ART

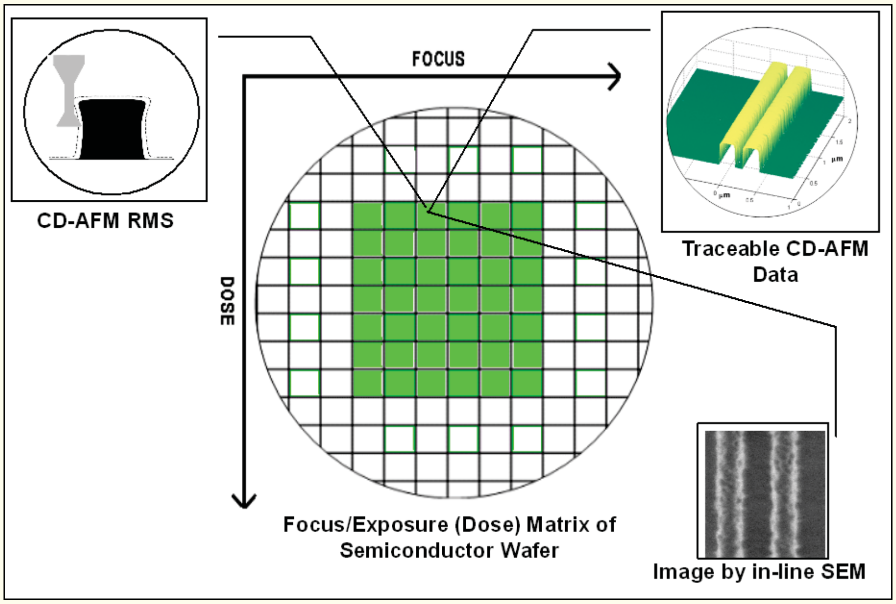
This section reviews improvements in characterization and metrology and trends in semiconductor R&D and manufacturing since the 2004 National Nanotechnology Initiative Grand Challenge Workshop on Instrumentation and Metrology for Nanotechnology. The semiconductor industry is evolving; as such, “current state of the art” is dynamic, with changes often reflected in the International Technology Roadmap for Semiconductors. The ITRS Metrology roadmap and the roadmaps for Emerging Research Devices and Emerging Research Materials provide a consensus view into future needs for measurement ranging from devices that extend CMOS technology to technologies beyond CMOS (e.g., see http://www.itrs.net/Links/2007ITRS/Home2007.htm). Several areas of recent improvement were identified at this (October 2006) workshop on Instrumentation, Metrology, and Standards for Nanomanufacturing, including the following:

- Aberration-corrected transmission electron microscopy (TEM) is commercially available and is spreading from national labs to industry. Development of the next-generation aberration correction technology is being supported by the Department of Energy Transmission Electron Aberration Corrected Microscope (TEAM) program (see http://ncem.lbl.gov/team3.htm).
- TEM use is increasing “around the fab” and in some instances is being used on the fab floor.
- The combined standard uncertainty of line width measurements performed with critical dimension atomic force microscopes (CD-AFM) is as small as 1 nm (Dixson et al. 2005; Cresswell et al. 2006; Orji et al. 2007). (See sidebar, “The SEMATECH-NIST AFM Reference Measurement System.”)
- The precision of critical-dimension scanning electron microscopes (CD-SEM) has improved to 0.2–0.3 nanometers (3 sigma) (Villarrubia, Vladar, and Postek 2005; Misumi et al. 2007).
- Laboratory versions of transmission-based, critical-dimension small-angle x-ray scattering (CD-SAXS) methods have become available and are being tested at NIST (Jones et al. 2003; see also http://polymers.msel.nist.gov/highlights/Critical-Dimension-Metrology-Nanoscale-Structures-Small-Angle-X-ray-Scattering.html).
- Optical methods are moving toward the UV with critical measurement equipment such as reflectivity measurement systems available at the extreme UV (13 nm) and commercial ellipsometry systems that extend to wavelengths of 150 nm.
- Helium ion microscopy is emerging and is in the early proof-of-concept / prototype stage (see http://www.smt.zeiss.com/nts). The image contrast from He ions is different from that of electrons and can augment the diagnostic power of imaging.
- Improvements in spin-sensitive probes such as magnetic resonance force microscopes (MRFM) and magnetic force microscopes (MFM) are being applied to semiconductor R&D (Suter 2004; Wigen, Roukes, and Hammel 2006; Huang et al. 2007).

In addition, several recent trends in measurement and processing are noteworthy:

- There are more new materials in CMOS fabrication than ever before, but their introduction into production is still a very slow/conservative process. Short product cycles support an evolutionary approach.
- Measurements for R&D and processing using scatterometry (Asano et al. 2006; Knight et al. 2006) increasingly require the use of modeling.
- Control loops will enable augmented manufacturing efficiencies, incorporating “on-the-fly” defect characterization systems.
- Atomic layer deposition is advancing rapidly and is approaching production implementation (Fahlman 2006; Lee et al. 2007; Paivasaari et al. 2007).
- Field-effect transistor (FET)-architecture sensors are rapidly developing (Tani et al. 2006; Truman, Uhlmann, and Stamm 2006; Wang et al. 2006).
- Self-assembly is closer to becoming a manufacturing reality. As one example, the Cambrios metal barrier layer self-assembly process attaches to Cu on one side, Co on other, to register layers. This technology is not in production use but is being evaluated. Another example is the application of diblock copolymers (Edwards et al. 2007; Ruiz, Sandstrom, and Black 2007).

The SEMATECH-NIST AFM Reference Measurement System (RMS)



(Illustration is courtesy of N.G. Orji, NIST.)

As information devices reach the nanoscale, challenges to the measurement of device features and the registration of those features are encountered requiring the development of new measurement techniques and tools. An atomic force microscope-based reference measurement system (RMS) was developed at SEMATECH by a joint collaboration of SEMATECH and NIST and is currently staffed on-site at SEMATECH by a NIST guest scientist.

Based on a critical dimension atomic force microscope, (CD-AFM) the RMS is used to impart traceability to dimensional measurements made in semiconductor manufacturing facilities. The types of measurements include step height, pitch, and linewidth. For linewidth, the same features measured with the RMS are measured using work-horse instruments such as the scanning electron microscope, thus enabling cross-calibration of those tools. Usually the measurements cover a series of feature sizes in a focus-exposure matrix. The RMS is capable of linewidth measurements with a standard uncertainty of 1 nm, made possible by calibration of master semiconductor features with high-resolution transmission electron microscopy.

Over the last six years, the CD-AFM-based RMS has been used to make hundreds of traceable measurements with state-of-the-art uncertainties to support projects in instrument evaluation, resist damage assessment, nano-imprint development, mask metrology development, and NIST standards development, among others.

A second CD-AFM at NIST has similar measurement capability and can be used to support the RMS at SEMATECH (Dixson et al. 2005; Cresswell et al. 2006; Orji et al. 2007).

4.4 PRIORITIES FOR R&D AND INFRASTRUCTURE INVESTMENTS

It is critical to identify the most important metrology and characterization barriers that must be overcome to continue scaling integrated circuit technology and develop new technologies to supplement CMOS. Although past documents have identified metrology capabilities needed to enable new technologies—and many of these capabilities have not emerged—the integrated circuit industry has continued to develop new technologies with higher densities without these missing capabilities. It has been able to do this through use of alternate metrology, increased use of modeling, and designs that are less sensitive to process variations. A maxim of precision engineering seems to apply here: "Design for repeatability. Accuracy can be achieved through calibration or compensation." (e.g., see The Gimbal Group 2005). However, we need to identify the capabilities that are actually crucial for future technology development and manufacturing, and an important consideration here is for metrology techniques that enable reduction of process variation.

Metrology limitations will continue to add uncertainty in the control of features and device capabilities. We need new ways to overcome these limitations; otherwise, process variations will become too large. Options include new measurement techniques, improved models of the measurement signal as a function of probe-sample interactions, and improved inline and in-tool manufacturing process control and feedback.

Further, as industry researchers seek to identify new technologies to supplement CMOS, they lack measurement tools to characterize the alternate state variables, such as spin (Wolf, Treger, and Chtchelkanova 2006) or molecular state (Reed 1999), instead of charge state in current devices. The measurement tools need to be improved to enable new device functions. Also lacking are performance metrics that enable comparison of alternative technologies to existing technologies. If new alternative technologies, such as spin state devices, are to emerge as viable devices and logic elements, new calibration and test structures must be developed to characterize the transport of alternate state properties and the interactions at contacts and interfaces within the devices that will be fabricated with features below 100 nm. In the case of molecular state devices, multiple measurement techniques must be applied to determine whether the switching is molecular or due to some other phenomenon, such as metal migration or oxidation. Thus, new measurement tools must be developed that can function at the nanometer scale and characterize alternate state properties and interactions in the materials and at interfaces.

Future R&D Directions

The semiconductor industry is already exploring beyond-CMOS devices that employ alternate state variables such as spin (Wolf, Treger, and Chtchelkanova 2006), plasmons (Hillmer and Germann 2003), orbital phase state (Tokura 2003; Saitoh et al. 2001), and optical polarization—as well as the couplings between these. However, metrology to characterize nanostructure and composition and correlate those with properties at the nanometer scale is lacking. For example, metrology is needed that can characterize dynamic changes in local dipole alignment (Duan et al. 2006), spin orientation, stress, and plasmon properties, and thus enable understanding of the coupling between those phenomena. It will be important to:

1. Understand the physical mechanisms in materials and at interfaces that change the state of the variable
2. Determine the energy required to change the state of the variable
3. Gauge the impact of defects on stability of the state

Overall, tools that can measure properties, composition, structure, and interactions at surfaces and interfaces with near-atomic resolution will be critical, as will be development of probes that couple electron microscopy to characterization of properties at the nanometer scale. Characterization of both the polarization and energy of the electrons emitted by different stimuli, such as spin-polarized photons, will provide more information than simple detection of backscattered electrons and secondaries. Thus, it will be important to explore application of new stimuli such as spin-polarized photons as a function of energy to characterize the energy required to change the spin state. Development will be needed of test structures that can be characterized during operation with multiprobe electron microscopy, and of scanning probes with atomic control of the tip and shape. Other areas of measurement need are for ways to monitor the effects of different stimuli, such as polarized photons, on the state of a functional variable to be measured.

Future nanometrology research directions for electronics, magnetics, and photonics must include development of novel scanning probes capable of characterizing alternate state variable interactions at surfaces, defect sites, and at interfaces. Research should be pursued in source probes, the physics of the source-probe-to-sample interaction, and novel detectors. There is a special need for models to enable decoupling of the probe-sample interactions from delineation of the structure and properties.

Future alternate-state devices will probably be nanometer-scale structures, so it will be important to diagnose coupling and loss mechanisms at these scales. This capability will require development of novel probe techniques that can monitor the dynamic response of multiple properties to applied stimuli. Such instruments may include the ability to apply multiple stimuli and measure the effect on several properties simultaneously.

The importance of interfaces at the nanoscale makes it mandatory to develop new capabilities to measure the structure and chemistry of interfaces and to relate these to the properties and operational performance of devices and interconnects. Some of the possible capabilities include high-resolution photoelectron emission microscopy (Kutzner et al. 1997), x-ray phase-sensitive reflection (Schreiber et al. 2000), near-field microscopy with SiC superlenses (Taubner et al. 2006), and AFM/capacitance and impedance spectroscopy (Gamry Instruments 2007).

As promising alternate-state properties emerge, it will be important to establish standards and reference materials to calibrate the measurement capabilities. Furthermore, the physical models of properties and their correlation to structure at the nanometer scale will need to be verified, and this will require experiments and simulations to be designed jointly for this purpose.

As features approach dimensions below 20 nm, self-assembly (Edwards et al. 2007; Liddle 2007; Ruiz, Sandstrom, and Black 2007) may emerge as a technique to either extend lithography or to assemble preconstructed nanostructures, creating the need to develop metrology that can characterize the control of self-assembled features and their alignment to previously fabricated structures.

Progress

Significant progress has been made both in development of new scanning probe techniques such as the conductance atomic force microscope (cAFM) (Gómez-Navarro, de Pablo, and Gómez-Herrero 2006), magnetic force microscopy (MFM), magnetic resonance force microscopy (MRFM), as well as in application of other probe techniques such as near-field scanning optical microscopy (NSOM); however, continued research in these areas is needed. MFM sensitivity has been significantly improved (Deng et al. 2004), and MRFM has been able to detect the spin of a single atom (Degen et al. 2007).

Self-assembly is being applied in technology development with atomic layer deposition techniques (Fahlman 2006; Lee et al. 2007; Paivasaari et al. 2007), and research has demonstrated the ability to align self-assembled block copolymers with top-down patterned surface layers (Edwards et al. 2007).

Understanding of plasmon physics has improved, and research progress is being made with attempts to fabricate devices (Makabe and Petrovic 2008), in addition to other ongoing progress.

Infrastructure Needs

Whereas production tools in semiconductor fabs require the highest throughput to be economical, development tools require the highest performance—e.g., resolution, accuracy, and multifunction capabilities—to be of the most use to process developers. One key infrastructure need in process development is for miniaturized instruments for process monitoring and control; along with this advanced hardware must come strategies for process control in ambiguous environments with uncertain control variables.

A second key infrastructure need is that of reference structures for metrology. (See sidebar, "Reference Measurement Scanning Electron Microscope.") This breakout group noted especially the need for structures along the lines of the Discovery Platform model (CINT 2005a; 2005b), whereby a standard wafer is fabricated with a number of structures and functions on its surface on which product designers deposit their own electronic layers, interconnects, and devices. These may include test structures with nanoscale contact resistances, and methods for simulating and designing these. Such designs should enable correlation between characterization and molecular orbital computing methods (e.g., U.S. Patent 7343277, 2008).

A third key infrastructure need is that of real-time tools for monitoring self-assembly processes, including 3D methods capable of probing through layer depths. Such tools might include the following:

- Primary inspection techniques, such as ellipsometry (Azzam and Bashara 2003) or Raman spectroscopy, which can indicate changes in an overlayer; these changes could then be assessed directly and diagnosed with analytical models
- Higher-resolution, secondary techniques such as scatterometry and *in situ* SEM or TEM (see sidebar, "Advanced Transmission Electron Microscopy")
- Registry tools to integrate bottom-up with top-down self-assembly processes

A fourth infrastructure need is for centralized facilities with experts available for enabling the development and use of exotic and emerging techniques. The expertise and equipment at these facilities could help the client determine the focus of further long-term development, which would then accelerate progress. Examples of critical infrastructural facilities would be:

- Scanning probes that enable subnanometer-scale characterization of magnetic and spin properties
- Easy-to-use modeling and computational suites with teragrid access
- Facilities to support integration of top-down/bottom-up self-assembly techniques and other mixed processes

Reference Measurement Scanning Electron Microscope

Scanning electron microscopes (SEMs) with their high throughput and excellent precision are used routinely in semiconductor production for the determination of the size of wafer and photolithography mask features. Advanced SEMs can image even the smallest-size structures that currently are used in integrated circuits and other phases of nanomanufacturing and likely will play an important role in the foreseeable future. Recent developments in this dimensional metrology technique have led to very precise tools that fulfill the precision requirements of the International Technology Roadmap for Semiconductors (ITRS). Yet even further instrument improvements are possible, especially in the area of accurate measurements.

The International SEMATECH Manufacturing Initiative (ISMI), with contributions from NIST, developed a CD-AFM Reference Measurement tool (see earlier sidebar). This tool is now available to member companies for wafer measurements and dimensional calibrations. Nevertheless, one type of tool cannot give all necessary answers; comparing measurements obtained with different methods gives better confidence in the results.

Towards that end, a new SEM-based Reference Dimensional Metrology instrument is now being developed at NIST. This instrument will allow for traceable SEM-based dimensional measurements through laser interferometry. It will be used for comparisons of the measurement results of different instruments and for calibrations of various artifacts, including wafers and photo masks. During the development of this new tool, an allowance for total measurement uncertainty will be determined. This work will explore the sources of all important measurement error components in the SEM. This will help to eliminate the largest contributors to SEM measurement errors and will facilitate faster development of better tools and standards for nanomanufacturing.

Modeled and measured library-based methods recently introduced by NIST researchers offer further advantages, as they significantly improve the precision of current measurement algorithms and lead toward improved measurement accuracy. These new methods will also provide 3D shape and size information on integrated circuit lines, contact holes, and other structures of wafers and masks. The laser interferometer-based sample stage incorporated in the instrument provides coordinate system traceability, and it makes possible compensation for stage drift and vibration. This technology could prove indispensable for future critical-dimension measurements.

Advanced Transmission Electron Microscopy

As information devices grow smaller, the presence of defects becomes a greater problem, because those defects represent a greater fraction of the atoms in the device. Further, it is clear that continuing Moore's Law will require much greater extension into three-dimensional architectures. There must be analytical tools capable of imaging devices in three dimensions. Transmission electron microscopy (TEM) in its many forms provides the high-resolution images and highest spatial resolution analysis necessary for nanotechnology R&D.

Advances in hardware and software continue to push the limits of its capability for near-atomic resolution in 3D. Aberration corrected lenses have made their way into commercial systems, and industry is beginning to apply this to solving key problems associated with the latest generation of integrated circuits as well as to R&D efforts aimed at transistors with sub-10 nm gate lengths. Both the phase contrast, high-resolution TEM and the scanning TEM have been equipped with this technology.

Scanning TEMs with aberration correction produce beams with a high angular convergence, which results in a smaller depth of focus. This greatly improves the depth resolution of images. Along with the new electron lens systems, TEMs have been equipped with energy filters that greatly improve the energy resolution of electron energy loss spectroscopy. TEM tomography also continues to advance. Applications to integrated circuit characterization and failure analysis include providing 3D views of sidewalls in vias. Image and electron diffraction simulation has become a necessary part of the characterization of nanoscale materials by TEM.

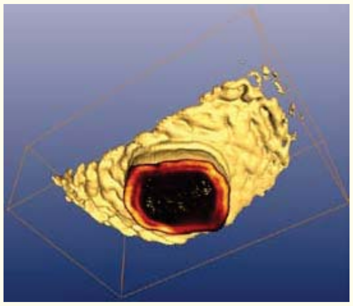


Fig. 1. Electron Tomography: 3D realization of the surface (yellow) of a vertical connection between two layers of copper metallization in an integrated circuit with cut-away showing the interior structure (red).

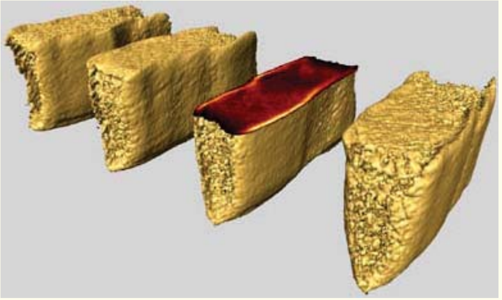


Fig. 2. Electron Tomography: Three-dimensional reconstruction of four Ta liners filled with Cu to make 90-nm-wide wires in nanoscale electrical devices.

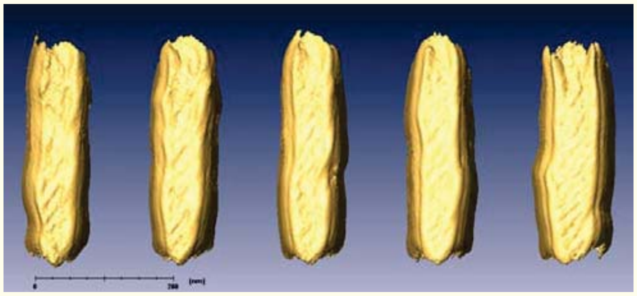


Fig. 3. Electron Tomography: Bottom view of four Ta liners filled with Cu to make 90 nm wires in nanoscale electrical wires that shows the structure's irregular surface.

(All figures are courtesy of David Muller and Peter Ercius, Cornell University.)

Existing Infrastructural Facilities

There has been a significant investment in user facilities by U.S. Government agencies:

- *NSF*: the National Nanotechnology Infrastructure Network (NNIN; http://www.nnin.org)
- *DOE:* five Nanocenters, at Lawrence Berkeley National Laboratory (LBNL), Sandia and Los Alamos National Laboratories (Center for Integrated Nanotechnologies at SNL and LANL), Argonne National Laboratory (ANL), Oak Ridge National Laboratory (ORNL), and Brookhaven National Laboratory (BNL) (see http://www.science.doe.gov/bes/User_Facilities/dsuf/nanocenters.htm)
- *NIST:* Center for Nanoscale Science and Technology (CNST; http://cnst.nist.gov), and the NIST Center for Neutron Research (NCNR; http://www.ncnr.nist.gov)

The immediate priority for the nanomanufacturing community is to ensure that these facilities meet user needs.

In addition, NSF has funded four nanomanufacturing centers that address the problems and issues associated with manufacturing at the nanoscale:

- Center for Hierarchical Manufacturing (CHM) based at the University of Massachusetts Amherst (http://www.umass.edu/chm/)
- Center for Nanoscale Chemical-Electrical-Mechanical Manufacturing Systems (Nano-CEMMS) based at the University of Illinois, Urbana-Champaign (http://www.nano-cemms.uiuc.edu/)
- Center for High Rate Nanomanufacturing (CHN) based at Northeastern University (http://www.nano.neu.edu/)
- Center for Scalable and Integrated Nanomanufacturing (SINAM) based at the University of California, Berkeley (http://www.sinam.org/)

It is a challenge to couple these centers effectively to industry. The National Nanomanufacturing Network (NNN; http://www.internano.org/), based at the Center for Hierarchical Manufacturing at the University of Massachusetts Amherst, was created in part to address this problem. Effective design and implementation of the NNN is vital if this goal is to be fully realized.

Finally, there is an increasing need to improve how we invent, develop, and use metrology tools as we move deeper into the nanoscale regime. NIST hosted the 2004 NNI Grand Challenge Workshop on Instrumentation and Metrology and established a biennial international conference series, "Frontiers of Characterization and Metrology for Nanoelectronics" (Seiler et al. 2007), to bring together top researchers from industry, universities, and government to help identify and solve new metrology challenges. Other meetings and conferences, such as the September 2007 SPIE conference on Instrumentation, Metrology, and Standards for Nanomanufacturing, are now focusing more deliberately on manufacturing issues rather than on just discovery issues, since there is now a need to demonstrate the value of the immense investments in nanotechnology by bringing nanotechnology-enabled products to market.

Barriers to Effective Use of Infrastructure

Despite the importance of extending the nanometrology infrastructure, there are barriers that can limit the use of currently available infrastructure. A critical issue for making this infrastructure available to industry and other users is understanding which facilities have the required metrology capabilities and how to access them. Improved access by researchers to such facilities could accelerate the rate of progress. However, the process to gain access to public nanotechnology facilities can be confusing because of the large number of facilities in the government, at universities, and under state control, all with different rules for engagement. An easily accessible database of the available infrastructure, including tools and experts, could help improve access to these resources. The NNN is already doing this for nanomanufacturing and could consider expanding the service to enable, among other helpful potential capabilities, multimode searching. Therefore, in order for people to learn about and use these resources it will be important to:

- Encourage development of Web-based descriptions of infrastructure, and Web-based conferences and/or training meetings
- Develop best practices for simple use agreements, intellectual property (IP) policies, and so forth

The NNN will be working with the Purdue Network for Computational Nanotechnology (NCN) on these issues and will be developing this kind of database through its website (http://www.internano.org/).

One issue that is especially acute for small businesses, which have limited financial and people resources, is protection of intellectual property. Small businesses will need help to balance control and protection of their IP against the need to enter into cooperative agreements with larger companies and public institutions. Full-cost recovery of expensive development efforts will be difficult for them without good policies or guidelines on IP.

Therefore, members of this breakout session suggest a mechanism for supporting use of NNI infrastructure that is similar to the Small Business Innovative Research (SBIR) model for research; that is, to develop a new component to SBIR programs, wherein some SBIR funding can support small business use of public facilities for proprietary research. This mode of funding can be an add-on to an SBIR grant or to an agreement between an SBIR-eligible firm and the facility. The agreement would be approved by the facility’s usual merit review process.

4.5 IMPLEMENTATION STRATEGIES

The following strategies will accelerate the development of instrumentation and metrology required for nanomanufacturing: development of nanomanufacturing measurement centers, integration of resources, training, exploitation of funding opportunities, and the creation of reference materials and measurement standards.

Consolidation of resources into centralized nanomanufacturing centers is needed to provide greater accessibility to expensive instrumentation and sophisticated metrology techniques. The measurement centers would offer expertise in specialized fields and technology capabilities such as newly developed instrumentation or test bed fabrication. Extending existing measurement and fabrication methods to support nanometer-scale samples also requires centralized expertise and equipment, especially when the cost of instrumentation is very high. The centers would require significant staffing to assist outside users in both measurement and analysis of the data and to ensure effective use of tools. University centers could be established to focus on basic R&D in instrumentation and metrology.

An important strategy will be to promote integration from the supplier to the application, in terms of equipment, education and training, and device or system support.

Funding should be accessible to interdisciplinary research groups focusing on instrumentation needs for nanomanufacturing. For example, one approach is to create separate, dedicated funding sources targeted to the development of specific new measurement tools. This could be used to encourage universities to include measurement tool development as a criterion for promotions and awarding of tenure. Another incentive to increase participation could be to create an annual award to recognize outstanding efforts in nanoscale tool development.

Reference materials and measurement standards are critical to efficient development and implementation of new measurement methods and of equipment to support nanomanufacturing. Test structures need to be developed to standardize nanomanufacturing and measurements for nanomanufacturing.

Federal Role

Federal agencies can play an important role in the development of new paradigms for information processing and storage that can be implemented with cost-effective manufacturing. This will require coordinated efforts in basic scientific discovery of novel properties of nanostructures. It is possible that only some of these data may be of use for commercial devices, yet the overall nanostructure scientific database will be enhanced. The measurement of nanoscale properties will require the discovery of new approaches for analytical tools, the engineering to make them reliable, modeling to understand their strengths and limitations, and engineering to enable their incorporation into an affordable manufacturing process. Because metrology and standards are crucial in all of the above, NIST will continue to influence development of new metrology at the nanoscale.

As noted above, NSF recently provided funding to establish a National Nanomanufacturing Network (NNN), a community-driven network that facilitates collaboration and information dissemination within the nanomanufacturing community. The NNN connects nanomanufacturing centers, projects, and experts from academic, industrial, and government institutions. It sponsors thematic nanomanufacturing workshops and other in-person activities and provides a Web-based nanomanufacturing information clearinghouse called InterNano (http://www.internano.org/). InterNano will provide information on nanomanufacturing processes, nanostructured materials, nanomanufacturing centers, experts and resources, best practices, events, and a searchable database on nanomanufacturing articles. The NNN is funded and coordinated by the Center for Hierarchical Manufacturing (the NSF Nanoscale Science and Engineering Center or NSEC based at the University of Massachusetts Amherst), in cooperation with the three other nanomanufacturing NSECs (the Center for High-Rate Manufacturing, the Center for Scalable and Integrated Nanomanufacturing, and the Center for Nanoscale Chemical-Electrical-Mechanical Manufacturing Systems) and stakeholders from NIST, DOD, DOE, NIH, NIOSH, and other institutions.

Academia Role

Over the past 50 years, universities have excelled in the discovery of new materials and their properties. This commitment to science discovery is critical in this venture, because new paradigms are needed for manufacturable devices for information processing and storage. A greater involvement of the engineering sciences is essential to the migration of newly discovered nanostructure properties into device designs and architectures appropriate for manufacturable products. (See sidebar, “Nanomanufacturing Research at the College of Nanoscale Science and Engineering.”) Scientific discovery at universities must be accompanied by close interaction with industrial scientists and engineers to enable rapid transition into innovative manufacturable technology. Since paradigm shifts are frequently enabled by the exchange of cross-disciplinary ideas, universities must be proactive in developing and participating in multidisciplinary centers and programs (NSF 2006).

Industry Role

Industry must partner with the Federal Government to ensure a robust discovery program in the universities. Otherwise, the transition of the new discoveries into technology will be too slow to continue the rate of improvement represented in the last several decades by Moore's Law.

Modeling and simulation will be a key component in the manufacturing of future information technology devices. A first step for industry will be to establish a predictive nanomaterial modeling consortium and establish a governance structure. Once this is in place, a technical advisory board can be established to identify a "pathfinder project"[1] and work with government research agencies to identify the best-in-class modeling capabilities, and develop a coordinated model-experimental validation plan with appropriate agencies. Furthermore, the consortium should work with NIST and other interested Federal agencies to form a long-term research plan that is coordinated across agencies to develop the capability to predictively model properties and biological interactions of nanomaterials (Chemical and Semiconductor Industries 2006).

Professional Society Role

As the understanding of nanostructures matures; as new discoveries are migrated toward devices, architectures, and systems; and as manufacturing at the nanoscale becomes more commonplace, it will be essential for the various professional societies' roles in nanotechnology to evolve. Greater attention must be paid to nomenclature, standards, and environmental safety and health issues. Organizations such as the Society of Manufacturing Engineers (SME; http://www.sme.org/nano) must be strongly engaged to promulgate best practices in the industrial environment.

4.6 SUMMARY

The continuation of Moore's Law in electronic information technology devices should be supported, although the approach will likely incorporate new materials with photonic, magnetic, and mechanical functionality. In addition, greater use of multilayer 3D architectures will appear. These changes will pose major challenges and opportunities in characterization, metrology, and nanomanufacturing research fields.

The introduction of new materials involving high-k dielectrics, low-k dielectrics, and metal gates has already caused new failure mechanisms in devices in the nanoscale regime. As scaling reaches its fundamental ultimate limits, new paradigms will be needed for investigating reliability mechanisms and developing new standards that can be effectively used by industry. Those new paradigms will likely involve the incorporation of magnetic and photonic materials with traditional CMOS materials. Further, one should expect the implementation of information technologies directly into biological systems (Patolsky et al. 2006; Chang et al. 2007) where sensing/actuating requirements will limit traditional encapsulation of the devices from the rather harsh (for

---

[1] The term "pathfinder" as used by Intel, Boeing, and others identifies research that is not currently part of an accepted product/process roadmap but that is relevant to the long-term goals of the roadmap. Such a project is high risk, where all the risks have been identified, and the risks must be reduced in order for project target specifications to be demonstrated. It is intended to promote validation of cutting-edge concepts and methods.

semiconductors) biological fluid environment. Because of this complexity, characterization and modeling will become even more critical factors in predicting the life of a device or product.

If successful, then:

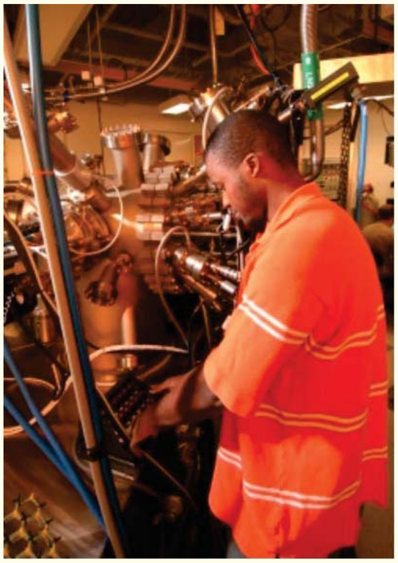
- Fewer workarounds will be necessary as process control improves
- True closed loop semiconductor manufacturing processes will be reported
- Disruptive technology will be ready for manufacturing to avoid bottlenecks in current process streams
- On-chip metrology will be distributed across the chip to adequately sample variations in the process environment without using a large area
- Real-time, in-process monitoring will be available
- Measurement technology will evolve so that it is capable of sampling smaller volumes
- Measurements will take advantage of calibrations using (atomic) crystal lattice as subnanometer height standards (ASTM standard E2530-06, 2007)
- User-friendly computation, simulation, and modeling tools will provide access to state-of-the-art codes and teragrid-level processing power

Given the uncertainties in viable information technology devices for beyond-CMOS, Federal NNI investment must continue to promote a strong discovery role.

As this workshop report shows, common themes emerge from nanomanufacturing research in disparate industrial sectors such as electronics, materials, medical, and chemical sectors. Best practices in scale-up, integration, metrology, technology transfer, and EHS are topics easily shared among diverse stakeholders, who then become more efficient in their pursuits and avoid “reinventing the wheel.” Availability of information on process capabilities, standard operating procedures, material properties, cost-benefit analyses, R&D centers and experts, education and training, safety protocols, suppliers, and manufacturing centers all help developers to make informed decisions to guide the advancement and utilization of nanomanufacturing.

To meet the identified challenges in the face of significant global competition, it will be necessary to develop an effective alliance of government members for funding and research, academic participants to cultivate innovation in science and engineering, and industrial partners to translate rapid assimilation of new knowledge and effective application into the manufacturing of affordable, competitive new technologies.

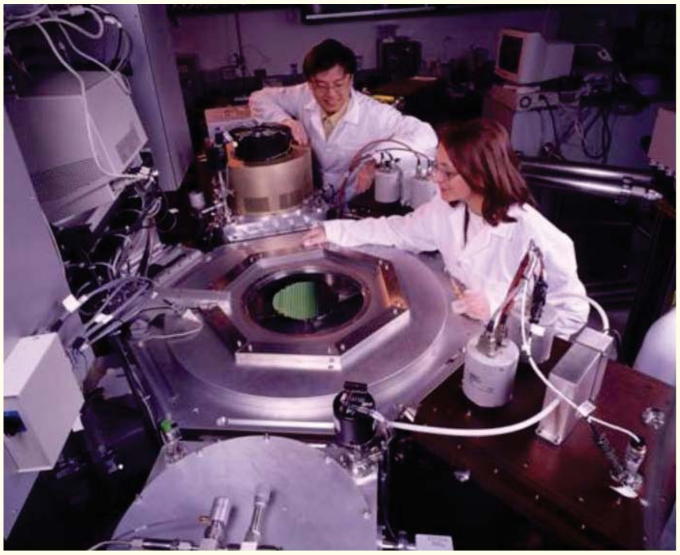
Nanomanufacturing Research at the College of Nanoscale Science and Engineering



The College of Nanoscale Science and Engineering (CNSE) at the University at Albany, State University of New York is devoted exclusively to the research, development, and deployment of innovative nanoscience, nanoengineering, nanobioscience, and nanoeconomics concepts for nanomanufacturing. In May 2006, CNSE was ranked #1 among all U.S. universities overall by *Small Times* magazine, a leading global trade publication, as the leading college in the U.S. for nanotechnology and microtechnology.

CNSE (http://cnse.albany.edu/) is located in the most advanced nanomanufacturing research complex of its kind at any university in the world. Its $3.5 billion, 450,000 square foot Albany NanoTech complex—also home to the New York State Center of Excellence in Nanoelectronics—attracts corporate partners from around the world and offers students a one-of-a-kind academic experience. CNSE has more than 250 U.S. and worldwide partners, including some of the world's largest semiconductor and semiconductor-related tool manufacturing companies.

Created in 2004, CNSE utilizes an interdisciplinary approach to education that encompasses chemistry, physics, materials science, biology, economics, mathematics, and medicine. Instead of a traditional departmental structure, CNSE has multidisciplinary "constellations." Students and faculty work cooperatively with on-site global industry partners to enable the discovery and dissemination of fundamental knowledge that will drive industry and innovation in the 21st century. As students work side by side with scientists, engineers, economists, researchers, and practitioners, the interdisciplinary approach of the constellation enhances the learning process.



CNSE offers Doctor of Philosophy (PhD) and Masters of Science (MS) degrees in both nanoscience and nanoengineering, and its "Nano+MBA" program provides dual Master's degrees in either discipline. All degree programs incorporate coursework within CNSE's constellations in nanoscience, nanoengineering, nanobioscience, and nanoeconomics.

4.7 REFERENCES

Arden, W. 2006. Future semiconductor material requirements and innovations as projected in the ITRS 2005 roadmap. *Materials Science and Engineering B-Solid State Materials for Advanced Technology* 134(2-3):104–108.

Asano, M., T. Ikeda, T. Kioke, and H. Abe. 2006. Evaluation of producer's and consumer's risks in scatterometry and scanning electron microscopy metrology for inline critical dimension metrology. *Journal of Microlithography Microfabrication and Microsystems* 5(4):043006.

ASTM standard E2530-06. 2007. Standard practice for calibrating the Z-magnification of an atomic force microscope at subnanometer displacement levels using Si(111) monatomic steps. West Conshohocken, PA: ASTM.

Azzam, R.M.A., and N.M. Bashara. 2003. *Ellipsometry and polarized light.* Amsterdam: Elsevier.

Brewer, J.E., V.V. Zhirnov, and J.A. Hutchby. 2005. Memory technology from the post CMOS era. *IEEE Circuits and Devices* 21(2):13–20.

Cavin, R.K. V.V. Zhirnov, D.J.C. Herr, A. Avila, and J. Hutchby. 2006. Research directions and challenges in nanoelectronics. *Journal of Nanoparticle Research* 8(6):841–858.

Cavin, R.K., V.V Zhirnov, G.I. Bourianoff, J.A. Hutchby, D.J.C. Herr, H.H. Howack, W.H. Joyner, and T.A. Wooldridge. 2005. A long-term view of research targets in nanoelectronics. *Journal of Nanoparticle Research* 7(6):573–586.

Center for Integrated Nanotechnologies of DOE (CINT). 2005a. CINT User Workshop January 19-21, 2005. The Discovery Platform breakout sessions (and invited speakers). See website http://cint.lanl.gov/discovery_platform.html.

———. 2005b. March newsletter. See http://cint.lanl.gov/newsletter/03052005.pdf.

Cerofolini, G.F., G. Arean, M. Camalleri, C. Galati, S. Reina, L. Renna, D. Mascolo, and V. Nosik. 2005. Strategies for nanoelectronics. *Microelectronic Engineering* 83(2-4):405–419.

Chang, C.C., K.W. Sun, S.F. Lee, and L.S. Kan. 2007. Self-assembled molecular magnets on patterned silicon substrates: Bridging biomolecules with nanoelectronics. *Biomaterials* 28(11):1941–1947.

Chemical Industry Vision 2020 and Semiconductor Research Corp. SNB Consultative WG 2 (Chemical and Semiconductor Industries). 2006. *Joint Chemical & Semiconductor Industry Research Needs for Modeling of Nanomaterials*. Available online: http://www.chemicalvision2020.org/pdfs/JointChem.pdf.

Coufal, H., and L. Dhar, eds. 2006. Materials for Optical Data (issue theme title). *MRS Bulletin* 31(4).

Cresswell, M.W., W.F. Guthrie, R.G. Dixson, R.A. Allen, C.E. Murabito, and J.V. Martinez De Pinillos. 2006. RM 8111: Development of a prototype linewidth standard. *J. Res. Natl. Inst. Stand. Technol*. 111:187–203.

Degen, C.L., M. Poggio, H.J. Mamin, and D. Rugar. 2007. Role of spin noise in the detection of nanoscale ensembles of nuclear spins. *Phys. Rev. Lett*. 99:250601.

Deng, Z., E. Yenilmez, J. Leu, J.E. Hoffman, E. Straver, H. Dai, and K.A. Moler. 2004. Metal-coated carbon nanotube tips for magnetic force microscopy. *Applied Physics Letters* 85:6263-5.

Dixson, R.G., R.A. Allen, W.F. Guthrie, and M.W. Cresswell. 2005. Traceable calibration of critical-dimension atomic force microscope linewidth measurements with nanometer uncertainty. *J. Vac. Sci. Technol*. B23:3028–3032.

Duan, C.-G., R.F. Sabirianov, W.-N. Mei, S.S. Jaswal, and E.Y. Tsymbal. 2006. Interface effect on ferroelectricity at the nanoscale. *Nano Lett*. 6:483-487

Edwards, E.W., M. Muller, M.P. Stoykovich, H.H. Solak, J.J. de Pablo, and P.F. Nealey. 2007. Dimensions and shapes of block copolymer domains assembled on lithographically defined chemically patterned substrates. *Macromolecules* 40(1):90–96.

Fahlman, B.D. 2006. Recent advances in chemical vapor deposition. *Current Organic Chemistry* 10(9):1021–1033.

Gamry Instruments. 2007 (December 28 revision). *Electrochemical impedance spectroscopy theory: A primer*. Available online: http://www.gamry.com/App_Notes/EIS_Primer/EIS_Primer.htm.

Gómez-Navarro, C., P.J. de Pablo, and J. Gómez-Herrero. 2006. Studying electrical transport in carbon nanotubes by conductance atomic force microscopy. *Journal of Materials Science: Materials in Electronics* 17:475-482. DOI 10.1007/s10854-006-8094-7.

Goronkin, H., and Y. Yang, eds. 2004. High Performance Solid State Memory Technologies (issue theme title). *MRS Bulletin* 29(11).

Hillmer, H., and R. Germann. 2003. Photonics materials for optical communications. *MRS Bulletin* 28(5):340–344.

Huang, H.S., M.W. Lin, Y.C. Sun, and L.J. Lin. 2007. Improving the spatial resolution of a magnetic force microscope tip via focused ion beam modification and magnetic film coating. *Scripta Materialia* 56(5):365–368.

Hutchby, J.A., G.I. Bourianoff, V.V. Zhirnov, and J.E. Brewer. 2002. Extending the road beyond CMOS. *IEEE Circuits & Devices* 18(2):28–41.

———. 2005. Emerging research memory and logic technologies – A critical review of the technologies based on a new relevance/ evaluation criteria. *IEEE Circuits & Devices* 21(3)47–51.

Jones, R.L., T. Hu, E.K. Lin, W.L. Wu, R. Kolb, D.M. Casa, P.J. Boton, and G.G. Barclay. 2003. Small angle X-ray scattering for sub-100nm pattern characterization. *Applied Physics Letters* 83(19):4059–4061.

Knight, S., R. Dixson, R.L. Jones, E.K. Lin, N.G. Orji, R. Silver, J.S. Villarrubia, A.E. Vladar, and W.L. Wu. 2006. Advanced metrology needs for nanoelectronics lithography. *Comptes Rendus Physique* 7(8):931–941.

Kutzner, J., R. Paucksch, C. Jabs, and H. Zacharias. 1997. High-resolution photoelectron emission spectroscopy of surface states on Ni(111). *Phys. Rev. B* 56:16003–16009.

Lee, J.H., W. Leung, J. Ahn, T. Lee, I.S. Park, K. Constant, and K.M. Ho. 2007. Layer-by-layer photonic crystal fabricated by low-temperature atomic layer deposition. *Applied Physics Letters* 90(15):151101.

Liddle, J.A. 2007. News and views: Nanostructures. *Nature Nanotechnology* 2:533.

Lieber, C.M., and Z.L. Wang. 2007. Functional Nanowires. *MRS Bulletin* 32(2):99–108.

Makabe, T., and Z. Petrovic. 2008. *Plasma electronics: Applications in microelectronic device fabrication*. Available online: http://www.physicsnetbase.com/ejournals/books/book_summary/toc.asp?id=5051.

Misumi, I., S. Gonda, O. Sato, M. Yasutake, R. Kokawa, T. Rujii, N. Kojima, S. Kitamura, R. Tamochi, J.I. Kitta, and T. Kurosawa. 2007. Round-robin measurements of 100- and 60-nm scales among a deep-ultraviolet diffractometer, a scanning electron microscope and various atomic force microscopes. *Measurement Science & Technology* 18(3):803–812.

National Science Foundation (NSF). 2006. *Investing in America's Future: Strategic Plan, FY 2006-2011.* Arlington, VA. Available online: http://www.nsf.gov/pubs/2006/nsf0648/NSF-06-48.pdf.

Orji, N.G., R.G. Dixson, A. Martinez, B.D. Bunday, J.A. Allgair, and T.V. Vorburger. 2007. Progress on implementation of a CD-AFM-based reference measurement system. *J. Micro/Nanolithography, MEMS, and MOEMS* 6(2):023002.

Paivasaari, J., J. Niinisto, P. Myllymake, C. Dezelah, C.H. Winter, M. Putkonen, M. Nieminen, and L. Niinisto. 2007. Atomic layer deposition of rare earth oxides. *Rare earth oxide thin films: Growth, Characterization and Applications* (Topics in Applied Physics Series, #106):15–32.

Patolsky, F., B.P. Timko, G.H. Yu, Y. Fang, A.B. Greytak, G.F. Zheng, and C.M. Lieber. 2006. Detection, stimulation, and inhibition of neuronal signals with high-density nanowire transistor arrays. *Science* 313(5790):1100–1104.

Reed, M.A. 1999. Molecular-scale electronics. *Proceedings of the IEEE* 87:652-658.

Ruiz, R., R.L. Sandstrom, and C.T. Black. 2007. Induced orientational order in symmetric diblock copolymer thin films. *Advanced Materials* 19(4):587.

Saitoh, E., S. Okamoto, K. T. Takahashi, K. Tobe, K. Yamamoto, T. Kimura, S. Ishihara, S. Maekawa, and Y. Tokura. 2001. Observation of orbital waves as elementary excitations in a solid. *Nature* 410:180-183.

Schreiber, F., M.C. Gerstenberg, B. Edingera, B. Toperverga, S.R. Forrest, G. Scoles, and H. Dosch. 2000. Phase-sensitive surface X-ray scattering study of a crystalline organic–organic heterostructure. *Physica B: Condensed Matter* 283:75-78.

Seiler, D.G., A.C. Diebold, R. McDonald, C.M. Garner, D. Herr, R.P. Khosla, and E.M. Secula, eds. 2007. *Frontiers of characterization and metrology for nanoelectronics*. Amer. Inst. of Physics Conference Proceedings, Gaithersburg, MD, 27-29 March 2007. New York: Springer.

Suter, A. 2004. The magnetic resonance force microscope. *Progress in Nuclear Magnetic Resonance Spectroscopy* 45(3-4):239–274.

Tani, K., H. Ito, Y. Ohno, S. Kishimoto, M. Okochi, H. Honda, and T. Mizutani. 2006. Fabrication of antigen sensors using carbon nanotube FET. *Japanese Journal of Applied Physics* 45(6B):5481–5484.

Taubner, T., D. Korobkin, Y. Urzhumov, G. Shvets, and R. Hillenbrand. 2006. Near-field microscopy through a SiC superlens. Science 313:1595 (15 September). DOI: 10.1126/science. 1131025.

The Gimbal Group. 2005 (revised 11 October). *CNC mill design*. Available online: http://www.gimbal.com.au/content.aspx?name=cnc-mill-design.

Tokura, Y. 2003. Correlated-electron physics in transition-metal oxides. *Physics Today* July:50–53.

Truman, P., P. Uhlmann, and M. Stamm. 2006. Monitoring liquid transport and chemical composition in lab-on-a-chip systems using ion sensitive FET devices. *Lab on a Chip* 6(9):1220–1228.

United States Patent 7343277. 2008 (March 11). Parallel computing method for total energy and energy gradient of non experience molecular-orbital method.

Villarrubia, J.S., A.E. Vladar, and M.T. Postek. 2005. Simulation study of repeatability and bias in the critical dimension scanning electron microscope. *Journal of Microlithography, Microfabrication, and Microsystems* 4(3):033003.

Wang, X.D., J. Zhou, J.H. Song, J. Liu, N.S. Xu, and Z.L. Wang. 2006. Piezoelectric FET and nanoforce sensor based on a single ZnO nanowire. *Nano Letters* 6(12):2768–2772.

Wigen, P.E., M.L. Roukes, and P.C. Hammel. 2006. Ferromagnetic resonance force microscopy, spin dynamics in confined magnetic structures III. *Topics in Applied Physics* 101:105–136.

Wolf, S.A., D. Treger, and A. Chtchelkanova. 2006. Spintronics: The future of data storage. *MRS Bulletin* 31(5):400–403.

Wong, H., V. Filip, C.K. Wong, and P.S. Chung. 2007. Silicon integrated photonics begins to revolutionize. *Microelectronics Reliability* 47(1):1–10.

Zhirnov V.V., J.A. Hutchby, G.I. Bourianoff, and J.E. Brewer. 2005. Emerging research logic devices. *IEEE Circuits and Devices* 21(3):37–46.

5. INSTRUMENTATION AND METROLOGY FOR PHARMACEUTICAL/BIOMEDICAL APPLICATIONS

Principal Authors: Nicholas Dagalakis, Michael Gaitan, and Mylene Ouimette

5.1 INTRODUCTION

Nanotechnology and nanomanufacturing challenges are shared across a variety of industries from electronics to chemicals. With expanding publicity regarding nanotechnology advances, public interest in these subjects has also increased. Based on a large number of recent articles in mass-circulation publications, it would appear that from both a public and political perspective, nanotechnology applications in the biomedical and pharmaceutical industries are among the most significant concerns. (Several sidebars in this chapter illustrate biomedical and pharmaceutical applications.)

Chief among the concerns in these industries is the subject of toxicity. It is well known that, as material shrinks in size to the nanoscale, the ratio between its surface area and mass increases. A material may exhibit markedly different properties in nanoscale than demonstrated in bulk-sized equivalents. These changes in properties can be very advantageous and provide results that allow for the realization and maturation of new applications. However, these changes can also result in increased toxicity (Karakoti, Hench, and Seal 2006).

Typically, toxicity is measured as a function of mass, but when a material is reduced to the nanoscale, this metric is no longer valid or reliable. In biomedical and/or pharmaceutical applications, nanoparticles may be ingested, inhaled, injected, or absorbed through the skin into the body. Researchers express most concern regarding the behaviors and attributes of free nanoparticles.

It should be noted that the combination of participants in this particular session of the workshop were particularly interested in potential toxicity issues. As a result, much of the discussion addressed issues related to the need for sound metrology, instrumentation, and standards for characterizing potentially toxic nanoparticles in biomedical and pharmaceutical applications.

5.2 VISION FOR PHARMACEUTICAL/BIOMEDICAL

The issues of health and toxicity of nanomaterials and nanoparticles is a highly visible public concern and, consequently, a political issue as well. There are significant benefits to developing a greater infrastructure in nanomanufacturing instrumentation, standards, and metrology. For example:

- The pharmaceutical industry is a major contributor to the U.S. economy in terms of job creation, revenue, R&D spending, and tax revenue (Ernst and Young 2000). According to U.S. Census Bureau figures (2006), the pharmaceutical industry nominally employs 292,000 employees at an annual cost of $14 billion. Improving the efficiency with which the industry operates allows for growth in revenue and applications, contributing to a more robust economy.

Of Silver, Lining, and Clouds

Silver is a soft, white, lustrous, transition metal with widespread commercial applications and a long and positive association with medicine. Hippocrates wrote that silver had beneficial and anti-disease properties. Silver vessels were used by the Phoenicians to store water, wine, and vinegar to prevent spoilage. In 1893 the botanist von Nageli discovered that minute concentrations of silver have antimicrobial properties. During World War 1 and after, silver was used to treat infections until replaced by antibiotics.

Silver ions are today a significant resource for topical therapy by virtue of their antiseptic properties (Berger et al. 1976) and low toxicity to mammalian cells (Dietch et al. 1983). Of special importance is silver's role in burn treatment, where clinical practice is dependent on local as opposed to systemic drug treatment. Silver is also being researched as a first-line defense against "super-bug" methicillin-resistant staphylococcus aureus (MRSA), which is resistant to penicillin and other common antibiotics and hospitalizes 100,000 people annually. The Centers for Disease Control and Prevention (CDC) estimates that 2 million U.S. patients a year acquire hospital-related infections. These infections cost an average of $47,000 per patient annually and cause 90,000 deaths per year. The added cost to hospitals is $4.8 billion annually in extended care and treatment.

In December 2005 the FDA approved the application of silver nanoparticle coatings to render existing medical devices impervious to infection-causing bacteria. The application can be applied to any device without altering the device's form or original properties, and this is expected to have a significant impact on the battle against hospital-related infection. The approval was given to I-Flow Corporation's ON-Q Silversoaker™ regional anesthesia delivery catheters (see figures at right). The catheters are treated with AcryMed Inc.'s SilvaGard™ nanoparticle coatings.[1] For updated information on silver nanoparticles, their applications, and related EHS research findings and regulatory issues, see: http://www.nsec.wisc.edu/NanoRisks/NS--SilverParticles.php.

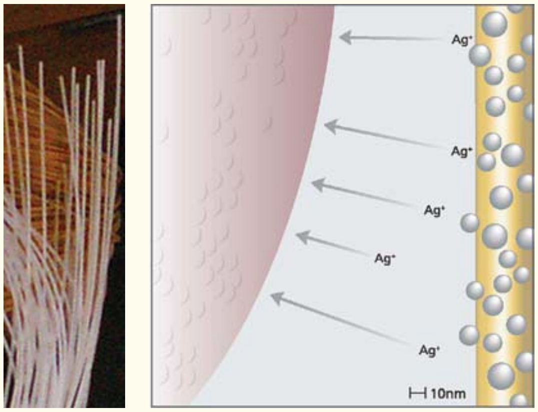


Fig. 1. (Left) Nylon catheters/tubing for medical device assembly. Fig. 2. (Right) Antibiotic effect: bacterium attacked by silver ions released by AcryMed's SilvaGard™-coated tubing (both figures courtesy of AcryMed).

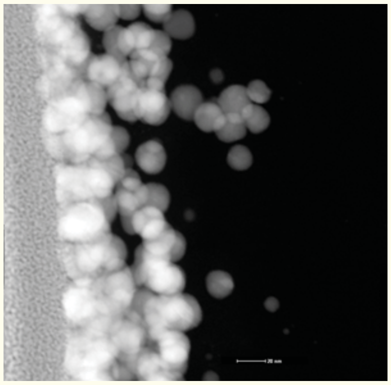


Fig. 3. High-angle, dark field, scanning-transmission electron microscopy image, showing round [white] silver nanoparticles on the surface of the nylon tubing on the left (courtesy of FEI Co.).

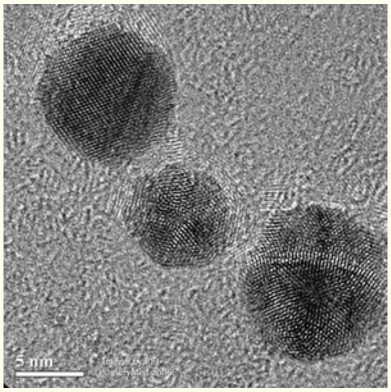


Fig. 4. Atomic-resolution image of 3 silver particles in size range of 7-10 nm (courtesy of FEI Co.).

---

[1] *Note: I-Flow Corporation acquired AcryMed, Inc., in February 2008.*

- The ability to conduct early self-diagnosis will increase the efficacy of medical treatments, potentially even increasing the prevention of disease occurrences. In addition, nanomanufacturing improvements can offer improvements in medical treatments by lowering toxicity levels.
- Homeland security and bioterrorism are of grave concern to both U.S. policymakers and citizens. Advances in biotechnology nanomanufacturing will allow for development of effective biosensors.

Perhaps of even greater significance is the need to maintain U.S. leadership in nanotechnology. Many leading research organizations advocate that the United States must facilitate the development and implementation of nanotechnology standards and metrology techniques. According to an IEEE-USA position statement originally issued in 2003 and updated in 2008 (IEEE USA 2008), "…[I]t is imperative for the U.S. Government, through its scientific arms, to drive not only the international standard measurement and nomenclature [efforts], but also lead the establishment of a program that guides researchers in developing quality methodologies to provide a fundamental understanding of the exact nature of the novel properties of the nanomaterials."

Governmental efforts in Japan, the Republic of Korea, and the United Kingdom are focused on increasing the rate at which these countries consider nanotechnology standardization needs and issues (Park 2004; Royal Society and Royal Academy of Engineering 2004; Fujimoto 2005; Shindo 2005). The U.S. pharmaceutical industry is particularly aware of this need, because U.S.-developed products are held to a higher standard than some international counterparts. A lack of uniform international standards in such areas as toxicity could undermine the domestic economic benefit of advances in nanotechnologies. The United States must take the lead to remain globally competitive.

5.3 CURRENT STATE OF THE ART

The current state of the art in nanomanufacturing in the pharmaceutical industry is quite varied. As of late 2005, approximately 15 nanomedicine applications are in the developmental pipeline and in various stages of approval by the FDA. Two are currently in the marketplace. Some approaches use nanoscale coatings on capsules and tablets to deliver drugs directly where they are needed within the patient's body. These applications highlight a promising trend in the rate of development of nanomedicine concepts.

As research advances progress in the area of nanomedicine, there is an increasing awareness of potential toxicity issues and an increased need for greater understanding of these issues. Interagency coordination within the government is beginning to foster dialogues about these concerns. Increased sharing of data and knowledge regarding varying aspects of toxicity will occur as a result of this coordination. These collaborative and cooperative relationships must continue to mature and evolve in order to further the development of the knowledge base.

Despite recent progress in the area of nanomanufacturing, the current state of pharmaceutical industry resources are inadequate to make the transition to the next level of technological advancement. For example, significant advances in systems biology are required in order to realize the full potential of personalized medicine (Arnaud 2006).

Determining Single-Particle Macromolecular Structures: the "Spy" that Came in from the Cold

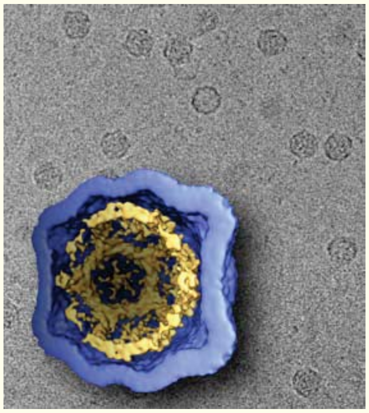


Fig. 1. Background: Cryo-TEM image of Cow Pea Mosaic Virus particles suspended in vitrified water; Foreground: 3D computer reconstruction of virus, created from the projected 2D TEM virus images.

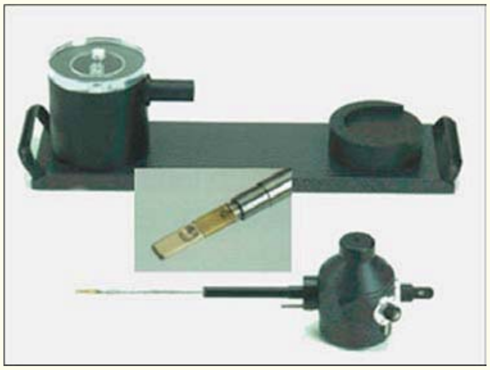


Fig. 2. Cryo-TEM cryostat used to load sample, holder tip where cryo sample is inserted; cryo-cooled sample holder.

Fig. 3. Cryo-TEM with loaded side-entry cryo sample holder.

The benefits of x-ray crystallography to study proteins are its relative simplicity and atomic-level resolution; its weakness is the need to have the protein in the form of a high-purity, single crystal. This sample requirement is a restriction because the process of crystallization may significantly alter the form and properties of the molecule in its natural aqueous environment and thereby make it impossible to track the various functional conformation states of the molecule. An additional limitation is that many macromolecules and their constituent proteins cannot be crystallized.

Cryo-transmission electron microscopy is one of the few techniques capable of visualizing large, dynamic molecules. The technique is uniquely suited to obtain three-dimensional images of molecular machines in different functional states, as it does not require crystals. In single-particle electron cryo-microscopy, biomolecules in solution are quick-frozen on a thin carbon substrate. The rapid freezing imprisons the complex in vitreous ice, a glassy noncrystalline form of ice, thus preserving the protein's native structure. Using an electron microscope with a low-intensity beam to avoid damaging the molecules, these randomly oriented particles can be recorded.

The cryo-electron microscope obtains images of thousands of captive protein complexes. Computer image analysis is then applied to reconstruct a 3D model from a selection of the differently oriented 2D images. If all particles in the sample are in the same conformational state, the 3D density map can be interpreted as a meaningful "3D snapshot" of the macromolecular machine along its dynamical course. Since the resolution of these density maps is approaching 6 Å, methods of docking and fitting are required to interpret each map in terms of the underlying atomic structures obtained by x-ray crystallography.

(All three images are courtesy of FEI Company.)

5.4 PRIORITIES FOR R&D AND INFRASTRUCTURE INVESTMENTS

Numerous barriers have been identified that prevent and delay the introduction and safe use of pharmaceuticals based on nanotechnology, as outlined below.

Economic Risk

Producing a new pharmaceutical is very risky. The perception exists that nanotechnology-based pharmaceuticals will have a much higher risk probability. This perception makes funding more difficult and expensive. There is a need for inexpensive, accurate, and reliable instruments that can measure the properties of nanoparticles used for pharmaceuticals and standard preparation procedures, in order to reduce cost, variability, and contamination.

Protein Chemistry

Nanobiology must operate at the peptide level. Understanding protein chemistry is a huge problem. How can nanotechnology address the protein binding control and functioning issues? There is a need for instrumentation for real-time protein binding and control.

Nanotechnology Product Knowledge

Most manufacturers have not fully characterized their nanotechnology-based products. Most nanoparticles used for pharmaceutical preparations are depicted in the promotional literature as perfect spheres covered by medicinal molecules distributed uniformly around the outer surface of the sphere at the density needed for their function. New studies have revealed that in reality these nanoparticles have irregular shapes and that the distribution of the medicinal molecules can vary widely from one particle to another. Furthermore, the crystalline structure of the nanoparticles can vary within the particle itself, depending on the manufacturing process used.

Such variations can be critical in the case of nanoparticles used for medical applications. Examination of nanopharmaceutical samples submitted to the FDA has revealed significant disparity in the shape and number of drug-carrying molecules from one nanoparticle to another. A patient who is treated with pharmaceuticals based on molecules attached to the external surface of nanoparticles might receive an unpredictable amount of this medicine, depending on the distribution of the molecules on the particle surface. This is a significant problem and threatens failure for a most important application of nanotechnology.

Common Vocabulary

There is a lack of common vocabulary (ontologies) for the accurate description of medicinal nanoparticles: their shape, crystalline structure, chemical composition, properties, etc. These ontologies need to be fully developed.

Scale-Up

When an application for the approval of a medicine still in the preclinical stage is submitted to the FDA, it requires that the applicant submit one milligram of the medicine material for examination. Most applicants requesting approval of nanotechnology-produced medicines are unable to meet this requirement. The transition from research sample preparation to safe and reliable mass production is particularly difficult for these types of substances. Issues of scale-up for nanotechnology products are common across all industries and sectors yet may be even more an issue in this segment. These challenges can slow technology development and provide cost increases that translate into production charges.

National Characterization Facility

Currently, most manufacturers of nanotechnology-generated pharmaceuticals do not have the expertise or the means to conduct preclinical characterization of their products. A national facility could undertake that responsibility. The National Cancer Institute (NCI), working in concert with NIST and FDA, established the Nanotechnology Characterization Laboratory (NCL) to help address that need. NCL performs preclinical efficacy and toxicity testing of nanoparticles, serving as a national resource and knowledge base for all cancer researchers to facilitate the regulatory review of nanotechnologies intended for cancer therapies and diagnostics. By providing the critical infrastructure and characterization services to nanomaterial providers, the NCL can accelerate the transition of basic nanoscale particles and devices into clinical applications. As part of its assay cascade, the NCL will characterize the physical attributes of nanoparticles, their *in vitro* biological properties, and their *in vivo* compatibility using animal models. The time required to characterize nanomaterials from receipt through the *in vivo* phase is anticipated to be one year (NCI/NCL n.d.).

5.5 IMPLEMENTATION STRATEGIES

The Pharma/Biomed breakout group recognized a number of potential benefits of nanotechnology to nanomedicine, which include superior early-stage detection and new and improved therapies based on targeted drug delivery and personalized treatments. The discussion focused on new nanoparticle-based detection therapies and the rapid growth of requests for testing and FDA approval. It was recognized that a major “show stopper” for advances in nanoparticle-based nanomedicines is the production of highly uniform nanoparticle formulations in sufficient quantity for the early tests. There is a high cost barrier for manufacturing high-quality monodisperse formulations in required quantities, typically at the microliter level.

Recommendations

The Pharma/Biomed breakout group developed four principal recommendations for relevant instrumentation, metrology, and standards for nanomanufacturing:

- Develop characterization methods and standard reference materials for nanoparticle type, size, shape, and charge
- Develop methods for high-quality (monodisperse) nanoparticle manufacturing
- Perform toxicological studies for nanoparticles by type, size, shape, and charge
- Develop new computer models for design and functionalization of nanoparticles

Federal Role

The Federal Government through its programs should promote effective teaming between academia and industry. Methods for nanoparticle formation and characterization, as well as the results of toxicological studies, should be developed and made available in the public domain. Standards and standard reference materials should be developed and made available as well. Nanoparticle toxicology and safe practices should be developed in partnership with academia and industry. Additional issues related to the Federal role are similar to those discussed in other chapters of this report.

Academia Role

Universities should perform basic research on nanoparticle structure and function, and develop computer computational methods and models for nanoparticle design and functionalization.

Industry Role

Industry should team with government and academia to identify needs and promote research, standardization, and policies that facilitate rapid and safe commercialization of nanoparticle diagnostics and therapies.

5.6 SUMMARY

Nanotechnology applications for new medical treatments and the production of new pharmaceuticals is one of the most promising markets for nanomanufacturing, but also one that raises concerns and is the subject of very serious regulatory restrictions. The small size and high reactivity of nanoparticles can make them the instruments of destruction of pathogenic organisms and out-of-control cells, but also the toxic killers of healthy tissue if they escape into the air, water, or soil, or if they are the result of defective pharmaceutical manufacturing. The U.S. pharmaceutical industry is one of the nation's most successful and profitable industries and has a reputation for the production of high-quality safe products. Unfortunately the economic risk of pharmaceutical development and manufacturing is very high and is expected to rise with the introduction of nanopharmaceuticals.

There are several ways to address these problems:

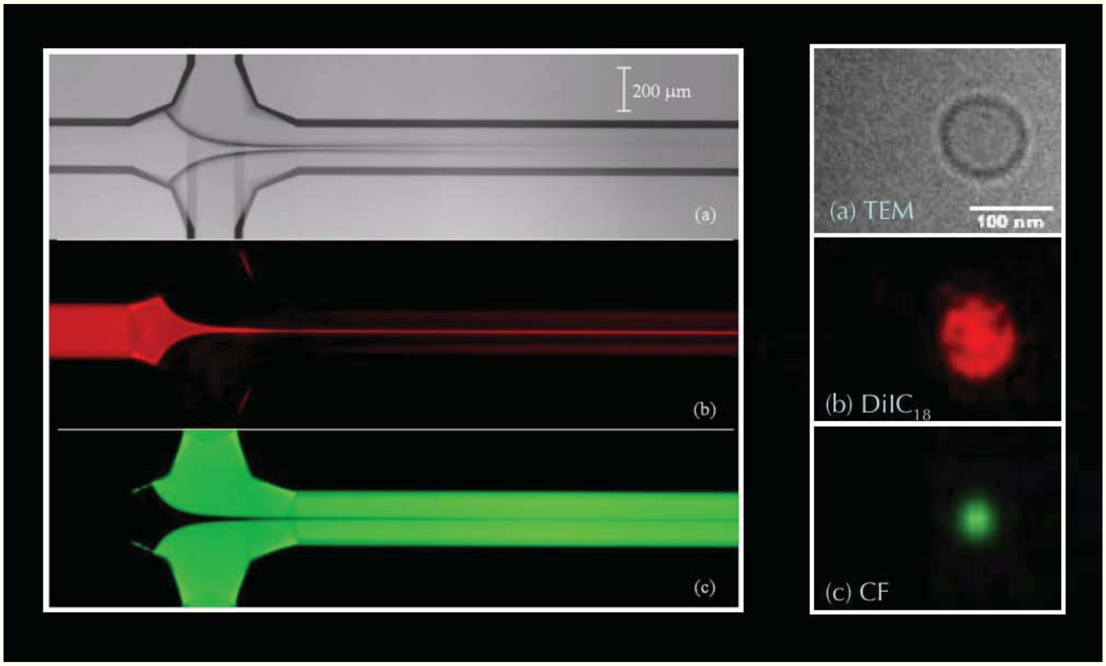
- Creation of internationally accepted and practiced standards
- Development of real-time protein binding and control instrumentation
- Development and validation of innovative new nanometrology instruments and methodologies
- Creation of a common vocabulary, or ontology, for accurate and consistent description and characterization of medicinal nanoparticles, including their shape, crystalline structure, chemical composition, properties, etc.

The transition from research sample preparation to safe and reliable mass production is particularly difficult and risky for nanopharmaceuticals. Therefore, precautions should be taken to prevent a highly publicized failure that would tarnish the reputation of the entire nanotechnology-based manufacturing enterprise, potentially halting nanotechnology research, development, and commercialization for many decades.

Microfluidic Methods for Nanomanufacturing of Nanoparticle Formulations

There is growing interest in development of "smart" nanoparticle formulations for targeted delivery of imaging agents and therapeutic compounds, but a barrier to progress is the cost of manufacturing promising new formulations in sufficient quantity and quality for efficacy and toxicology testing. Current methods for nanoparticle formation produce nanoparticle distributions that have a large variation in size, whereas the requirements for testing are for particles that are virtually all the same size. In order to produce formulations that meet the size requirements, researchers must contend with the tremendously high cost of filtering and sorting the particles and keeping only those with the desired size, even for the relatively small microliter volumes that are required.

Improvements in nanoparticle nanomanufacturing based on better understanding of the nanoparticle formation process are required in order to solve this problem. Microfluidic-based methods offer an opportunity to solve it by producing highly uniform particle formulations and also enabling the direct observation of the formation process. Fluid flow in the microfluidic environment is laminar, meaning that there is no turbulence, and so all the nanoparticles formed in this process experience the exact same conditions. In addition, microfluidic devices can be made on flat surfaces like a microscope slide so that formation of nanoparticles can be observed using a microscope.



Panels (a), (b), and (c) on the left are optical micrographs of fluid streams flowing in a microchannel imaged with white light, and red and green filtered light, respectively. The fluid streams are injected in the left-side, top and bottom channels and flow into the longer channel to the right. The center stream, where the nanoparticles are formed, is pinched down to a very narrow width. The panels to the right are images of liposomes that are formed using this method (Jahn et al. 2004; image ©2004, American Chemical Society; used with permission).

5.7 REFERENCES

Arnaud, C.H. 2006. Systems biology's clinical future. *Chemical & Engineering News* 84(31):17–26.

Berger, T.J., J.A. Spadaro, S.E. Chapin, and R.O. Becker. 1976. Electrically generated silver ions: Quantitative effects on bacterial and mammalian cells. *Antimicrob. Agents Chemother*. 9(2):357–358.

Dietch, E.A., A.A. Marino, T.E. Gillespie, and J.A. Albright. 1983. Silver-ion: A new antimicrobial agent. *Antimicrob. Agents Chemother*. 23:356–359.

Ernst & Young Economics Consulting and Quantitative Analysis. 2000. *The economic contributions of the biotechnology industry to the U.S. economy*. Prepared for the Biotechnology Industry Organization (BIO). Available online: http://www.bio.org/speeches/pubs/ernstyoung.pdf.

Fujimoto, T. 2005. The development and spread of nanotechnology and related measurement standards. *AIST Today* (Int. Ed.) 15:13. Available online: http://www.aist.go.jp/aist_e/aist_today/2005_15/pdf/2005_15_p13.pdf.

IEEE-USA. 2008. Nanotechnology research & development (2003 position statement updated June 2008). Available online: http://www.ieeeusa.org/policy/positions/nanotechr&D.pdf.

Jahn, A., W.N. Vreeland, M. Gaitan, and L.E. Locascio. 2004. Controlled vesicle self-assembly in microfluidic channels with hydrodynamic focusing. *JACS* 126(9):2674–2675.

Karakoti, A.S., L.L. Hench, and S. Seal. 2006. The potential toxicity of nanomaterials – The role of surfaces. *Journal of Medicine* 58(7):77–82.

National Cancer Institute Nanotechnology Characterization Laboratory (NCI/NCL) homepage http://ncl.cancer.gov/. N.d. Accessed May 2008.

Park, C.H. 2004. Standardization policy in Korea. *Standardization News* 32(5):32–35.

Royal Society and Royal Academy of Engineering. 2004. *Nanoscience and nanotechnologies: Opportunities and uncertainties*, London: The Royal Society & The Royal Academy of Engineering. Also available online: http://royalsociety.org/landing.asp?id=1210 and http://www.raeng.org.uk/policy/reports/.

Shindo, H. 2005. Nanotechnology standardization in Japan. *Standardization News* 33(7):36–39.

U.S. Census Bureau. 2006. *Statistical abstract of United States 2006*. Available online: http://www.census.gov/compendia/statab/2006/2006edition.html.

6. INSTRUMENTATION AND METROLOGY FOR COMPOSITES AND MATERIALS

Principal Authors: Clare Allocca, Greg Blackman, Jean Dasch, Jennifer Hay, Keith McIver, and Tinh Nguyen

6.1 INTRODUCTION

There is great interest in nanotechnology throughout the international community; large R&D investments are being made around the world. In a series of industry, government, and academic meetings and workshops, nanocomposites, in particular, have become a common theme. The allure of nanocomposites is the expectation of dramatic improvements in properties in areas important to such varied industries as aerospace, automotive, semiconductor, plastics, and chemicals. It is hard to find a company serving any of these market segments that is not working in the area of nanocomposites. Yet, despite the extensive resources devoted to research and development, the actual number of success stories where a new nanoscience-enabled material has moved from research to a commercial product remains low.

Nanocomposite

A nanocomposite is a multicomponent material system including at least one type of nanoscale particulate or additive that is compounded, mixed, combined, or assembled with an appropriate matrix to produce a material with new properties. These enhanced properties in turn may enable products such as lighter aircraft, more-impact-resistant automotive bumpers, or modified lumber with resistance to environmental elements.

6.2 VISION FOR COMPOSITES AND MATERIALS

The goal of the Composites and Materials breakout session at this workshop was to help lay the groundwork for the next ten years. The session participants' vision for composites and materials is to ultimately enable industry to add nanomaterials to its products in a manner that is consistent, safe, and dramatically enhancing to product performance. Toward this end, the following key criteria need to be fulfilled:

- *Reliable and accurate modeling,* Modeling research must reach a level of maturity in 10 years where one can predict product performance based on the nanomaterial's fundamental parameters. Precursors to such confidence will be significant advancements in multiscale modeling.
- *Characterization instrumentation/techniques/protocols providing quality control.* Characterization techniques must progress to the stage where they will ensure the behavior of nanocomposite materials in practice.
- *Materials synthesis and processing techniques that are reproducible and tailored to the end-product.* Processing technologies will have developed to the point where marketing and manufacturing personnel can create a simple bill of materials and warranty the items with confidence that they contain reliable nanomaterials.

- *Nanometrology tools to validate and integrate all of the above.* Nanometrology is the "glue" binding all of these efforts; it will allow the required level of quality control needed in a rigorous nanomanufacturing environment. Proven links will exist between process control and the desired nanotechnology products. Of particular interest are tools with refined measurements of dispersion and interfacial bonding within the nanocomposite matrix. Specifically, NIST will have a measurement toolbox available for high-end measurements, and industry will have the essential tools in its nanomanufacturing environment for quality-control metrology.

Executing this vision will enable new, perhaps even unforeseen, technical capabilities within ten years. Coupling this vision with the convergence of nano-, bio-, info-, cogno- (NBIC) technologies could offer a veritable whole new technological toolbox for mankind (Roco and Bainbridge 2003; 2006). Certainly the industry sectors of electronics, biotechnology, building materials, aerospace, automotive, and textiles are open for dramatic improvements in product quality. As Dr. Richard Feynman said so aptly in his seminal 1959 talk, "… I am not afraid to consider the final question as to whether, ultimately—in the great future—we can arrange the atoms the way we want; the very *atoms*, all the way down! What would happen if we could arrange the atoms one by one the way we want them..." (Feynman 1959).

The future awaits us—can we deliver?

6.3 APPLICATION OF THE "PILLARS" TOWARDS ACHIEVING THE VISION

The overall structure necessary to enable the vision described above involves the development of three disciplines bound together by the metrologies needed to capitalize on the relationships among the disciplines. These "three pillars"—modeling, materials, and quality/characterization—are discussed in Chapter 2 as they apply to nanomanufacturing broadly. Their application to manufacturing of nanocomposites is summarized below and expanded upon in the following sections.

Modeling

Nanocomposite materials are complex systems where the property of the bulk material is influenced by a multitude of variables that operate at different length scales. There is a lack of fundamental theoretical understanding of the important variables connecting structure and chemistry of nanomaterial additives to performance properties. Sometimes it is even difficult to know what variables are important for a given performance characteristic. This lack of understanding leads to development based on trial and error and inhibits the timely development and commercialization of these materials.

Computational models correlated with experimental characterization are keys to maturation of this field and essential in guiding discovery, synthesis, process design, and process control for scaled-up manufacturing of commercial quantities of nanocomposite materials. Computational models for nanocomposites serve as tools for quantitative analysis of nanocomposite bulk material properties vs. nanoparticle synthesis/structure, interfacial properties, inclusion methods, matrix properties, and other relevant variables. The tool suite should provide predictive capability for correlating electrical, thermal, mechanical, and acoustic properties to the synthesis, manufacturing-processes, and quality-control (QC) metrics. The suite should support characterization at the element level to help develop QC testing plans and at the composites-structure level for design purposes. The modeling framework should enable integration of models at various length and time scales. It would provide integration to the end user's bulk material design tools to provide the end user with the ability to model the interaction of nanoparticles in a composite system and the ability to predict the end state of performance parameters such as electrical, thermal, mechanical, and acoustic properties.

Characterization

Characterization establishes the tools and methods needed to answer questions about structure and chemistry of various additives, their influence on matrix properties, and eventual performance attributes of nanocomposites at all stages of technological innovation—"If you cannot measure it, you cannot manufacture it." During the R&D stage, this pillar refers to the measurement and characterization tools needed to establish sufficient understanding to create a prototype (e.g., mechanical testing and microstructure evaluation at the nanoscale). During production/manufacturing, this pillar provides tools to ensure a cost-effective manufacturing process. Examples might include measurements of quality, closed-loop control of a manufacturing line, and other methods to aid in the establishment of "acceptable" vs. "unacceptable" products. During the market and end-use stages, this pillar provides inspection methods, standards, nondestructive quality measurements, indicators of attribute thresholds, methods for failure analysis, and other measurements. A principal goal is to establish quality standards for nanostructured materials and their interaction with a polymer or blend, and provide the capability to measure at the nanoscale.

In nanoparticle- and nanocomposite-based materials and devices, characterization needs begin with the individual components; the critical issues are the distribution of shape, size, surface charge, and chemical functionality within a batch and variation from batch to batch. The barriers to technology advancement revolve around the need for cost-effective manufacturing so that the advantages and opportunities provided by the nanoparticles are realized. To achieve this goal, a thorough characterization of the nanoparticle, the changes in the matrix induced by the nanoparticle, and the interaction between the two is necessary. For example, it is common to treat the nanoparticle with a molecular sizing agent to improve dispersion or compatibility with the matrix and to bind it in place for a more mechanically robust material. Despite the importance of this molecular-scale interaction, developers still do not have general tools that will answer the question of whether there is a chemical bond formed between nanoparticle and the linker molecule or between the linker molecule and the matrix. Tools will also be required for characterizing the properties of nanoconstituents that are grown *in situ* rather than through blending, dispersion, and the like. This would include dynamic measurements such as growth rates during synthesis.

Another area for particular emphasis is to facilitate or enhance the interaction between experiment and modeling. This feedback loop is currently ineffective. Both communities would benefit from a closer interaction, and the commercialization of nanocomposite materials would be accelerated as a result.

Materials and Processing

Nanomanufacturing processes are used for a range of related purposes in product realization, from synthesis of nanoscale building blocks to their integration across multiple scaling boundaries. Typically, during controlled nanomanufacturing, the objectives are to predict the outcome of the designed supply-chain flowchart (protocol), to produce the product efficiently using environmentally sustainable routes and at low cost, and to realize application-specific nano-integrated product systems. Product systems are either new application concepts or improved current products made by adding value through new and/or improved functions in existing products. Integration of material-and-process monitoring tools during nanomanufacturing is vital for achieving predictability in the supply chain.

Nanomanufacturing processes that are used to fabricate nano-integrated materials and systems can be classified into three sets of processes: (1) top-down (where one starts with a microcrystalline raw material), (2) bottom-up (where one starts with atomic or molecular building blocks and their assemblies), and (3) their hybrids. During processing, raw nanomaterials are compounded, mixed, extruded, sprayed, molded, baked, etc., to produce the final part. For a normal manufactured material or composite, decades of experience help guide the selection of processing conditions to achieve the required properties. However, even for modern composite materials, the connection between processing and the resulting material properties is not always clearly understood.

Examples of such processes are equal-channel angular extrusion, mechanical ball milling, colloidal chemical synthesis, electrostatic coating, chemically and physically reactive vapor deposition, molecular-beam epitaxy, and other related processes. In the supply chain of nanomanufacturing a product, one integrates steps from synthesis of nanoconstituents to their functionalization and/or deagglomeration, assembly, sintering, and delivering application-specific design, either by casting, forging, lamination, coating, machining, etc. Process scale-up, environment safety, worker training, and related issues are other key points when considering materials and processes.

The final properties of nearly any manufactured part depend on both the quality of the initial materials and the processing steps used to create it. A material will start with a certain set of properties—size, surface chemistry, morphology, color, and shape—but the manufacturing process is often dynamic and can cause dramatic changes to the initial state.

As the size of a nanoparticle additive gets smaller, more and more of the atoms are on the surface. This presents a significant quality control problem. Trace impurities that might be negligible on bulk or macroscale additives can now adversely affect the material’s fundamental properties. The problem affects all stages of technological innovation. It can manifest itself by causing irreproducible results in early R&D efforts all the way to sudden inexplicable shifts in performance of the final nanocomposite part. Efforts to understand and minimize variability in nanoparticle key characteristics will lead to much more robust and reliable manufacturing processes.

If the promise of reliable nanocomposite products is to be realized, it will be necessary to develop tools and accepted methods to evaluate and certify the quality and specifications of standard nanoparticle additives. Careful experiments closely coupled to theory and modeling are required to make connections between the various processing methods and final properties.

Metrology and Standards Development: Integration

Nanocomposites are expected to “revolutionize” the way materials are made and the range and nature of functionalities to which materials may be tailored. Realizing these advances will require accelerated development of metrologies (measurement science) and standards needed to make accurate and reproducible measurements and modeling of nanocomposites’ properties and performance. Unifying the three disciplinary pillars of nanotechnology-based manufacturing are the tools, metrologies, and standards to support the varied research and development on processing, modeling, and characterization of nanocomposites. Advances in metrologies and standards needed for nanocomposites include:

- Establishment of metrological and predictive capabilities and globally accepted standards for manufacturing, modeling, and measurements of nanocomposites and their properties
- Accurately and reproducibly measuring and predicting the dimension, structure, and chemistry of nanoscale additives, their interactions with the matrices, performance properties, and environment and health effects of nanocomposites

- Development of instrumentation, metrologies, and models for reliably quantifying the dispersion of varied-shape nanoparticles in polymer matrices
- Development of metrologies and models for effectively assessing the properties and adhesion of nanoparticle/polymer interfaces and interphases
- Providing accurate measurement at the nanometer scale and to relate such measurements to macroscale properties

6.4 CURRENT STATE OF THE ART

Modeling

Currently, various research projects addressing modeling of nanostructured materials are funded by the government and are being executed by universities, government research labs, and small companies. Generally speaking, these efforts—as valuable as they are in improving fundamental understanding of the phenomena under investigation—are not directed and guided towards design and scale-up of the manufacturing capability for producing nanocomposites with targeted property goals. The issue of bridging length scales is still unresolved, limited by currently available computing power as well as by the lack of suitable numerical methods to enable model creation and the development of efficient algorithms. Most studies are focused on a single scale with homogeneous descriptions of the phenomena. Moreover, minimal coordination between modelers and experimentalists exists, which means that an important feedback loop is absent from the present efforts. This has resulted in insufficient or poor integration of experimental results, modeling calculations, and physics/chemistry-based models.

Characterization

Carbon nanotube characterization is notoriously difficult because the lack of quantitative metrics for characterization makes it difficult to optimize synthesis. Moreover, the impurities and the diversity in nanotube and nanoparticle structures (length, diameter, and chirality) prevent the development of simple characterization strategies.

Materials and Processing

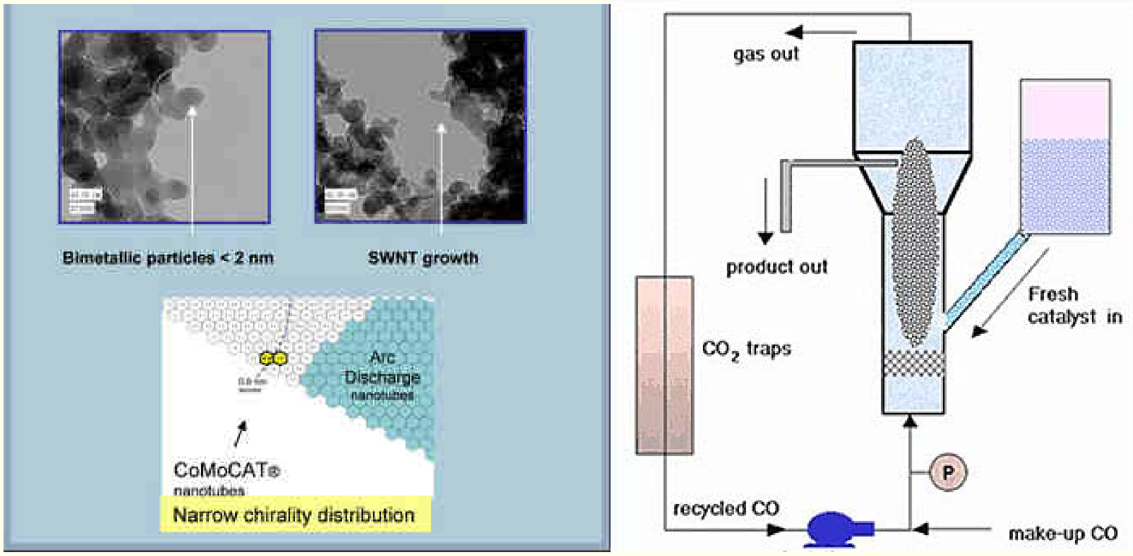
Nanomanufacturing of composites and materials can currently be divided into two categories: (1) *bottom-up*, whereby the nanostructured constituents are controlled at the nanoscale via self-assembly, directed assembly, nanolithography, or nanomanipulation; and (2) *top-down*, where the nanoscale additives are incorporated into traditional manufacturing processes, such as extrusion, molding, or casting. The practical tradeoff between these two groups is either high-precision placement with an impractical time scale to manufacture a consumer product, or low-precision placement with a high rate of manufacture that requires exploring a large combinatorial space to identify a superior-performing nanocomposite.

Recent advances in the synthesis and production of constituent nanomaterials have, for the first time, provided sufficient quantities for manufacturing trials beyond the bench scale. The first wave of products marketed as nanocomposite products is beginning to reach consumers through carbon nanotube-“enhanced” baseball bats, nanocoatings imparting stain resistance to clothing, and nano-inked pharmaceuticals to combat counterfeiting. Many of these achievements have been through the “top-down” approach where trial and error has led to the discovery of nanocomposites that afford enhanced product performance. Additional nanocomposite-enabled products that have made it through to the marketplace include reduced-weight and increased-strength automotive bumpers and bedliners, high-strength nanocomposites for sporting goods, and layered barrier materials.

Some nanoparticle additives are more problematic than others. Intense research into the use of carbon nanotubes (CNT) as additives has only resulted in a few notable nanocomposite successes (conductive polymers for fuel lines in automotive applications; high-strength, high-modulus materials for sporting goods). (See sidebar, "Large-Scale Nanomanufacturing of Carbon Nanotubes.") Plaguing researchers in this area are inconsistency in cost and availability of raw materials, variability in the CNT manufacturing processes, difficulties in purification and de-agglomeration, and challenges in producing strong CNT/matrix interactions.

Large-Scale Nanomanufacturing of Carbon Nanotubes

SouthWest Nanotechnologies, Inc., has developed a unique catalytic method that produces single-wall carbon nanotubes of high quality at very high selectivity and with a remarkably narrow distribution of tube diameters.



Selective synthesis of single-walled carbon nanotubes and the fluidized bed process for scalable nanomanufacturing (courtesy of D.J. Arthur, SouthWest Nanotechnologies, Inc.).

The CoMoCAT® process can grow significant amounts of single-wall nanotubes in less than one hour, maintaining a selectivity rate of better than 90 percent. Two of the unique characteristics of the CoMoCAT® process is that it is readily scalable and that its intrinsic high selectivity is preserved as the reactor size is scaled up. These characteristics impart to the single-walled carbon nanotube (SWCNT) product the dual benefit of lower cost and high product quality. This process is based on original work conducted by the research group of Prof. Daniel Resasco at the University of Oklahoma.

The tendency of CNTs to agglomerate is a particularly serious problem for nanocomposite manufacturing, because it significantly decreases the aspect ratio and mechanical properties. Good dispersion of CNTs in a polymer matrix is critical for effectively enhancing the performance of polymer/CNT nanocomposites. Today, the most common method for achieving good dispersion of CNTs in polymer matrices is either through chemical functionalization of CNTs or by surrounding them with dispersing agents such as polymers and surfactants (Tasis et al. 2006; Du and Winey 2006). Chemical functionalization allows CNTs to be more readily wetted by, and form covalent bonds with, the matrices, resulting in increased interfacial strength and stress transfer efficiency in the nanocomposites.

Polymer/CNT nanocomposites are fabricated by mainly two common methods, solvent casting and melt mixing. Solvent casting, including spin casting and drop casting, involves preparing CNT suspension in polymer solution, usually with a large excess of solvent, and then allowing the solvent to evaporate to produce a polymer/CNT nanocomposite film. The dispersion is usually facilitated through sonification or/and mechanical mixing. However, without an effective functionalization method or the presence of a suitable dispersant, solvent casting can allow the CNT to reaggregate. The melt mixing method uses high temperatures and shear force to debundle the CNTs. In this method, the increase of viscosity apparently restricts Brownian motion and sedimentation of the CNT, preventing CNTs from agglomeration.

The cost of nanoparticle additives will always to some extent limit their use to high-value applications. As cost comes down and as the number of successes increases, there will be more confidence on the part of companies involved in nanocomposite manufacturing. However at the present time, it is sometimes difficult to produce enough nanocomposite materials for adequate performance and reliability testing. A common strategy is to produce micro- or mini- batches of materials and develop surrogate microscale tests of performance. There is risk in this approach, due to inevitable difficulties in scaling-up the manufacturing process and uncertainties in interpretation of nanoscale measurements and their relationship to macroscale and performance properties.

Finally, product stewardship issues need to be addressed so that nanocomposite materials are synthesized, manufactured, shipped, marketed, and recycled or destroyed in an environmentally sound and safe manner. Some companies have been proactive in this regard and are working with government regulatory agencies, nongovernmental organizations, and academic institutions to develop frameworks for responsible handling and use of nanoparticle-enabled materials.

Materials and processing parameters will need to be established for the end-goal of successful implementation of nanocomposites within the industrial community. A suite of capabilities within the nanomanufacturing environment will need to include issues such as robust models for the prediction and iterative improvement of composites toward a desired product form, instruments and protocols for nanometrology of the raw and final form nanocomposites, and process materials synthesis for the production of a range of products.

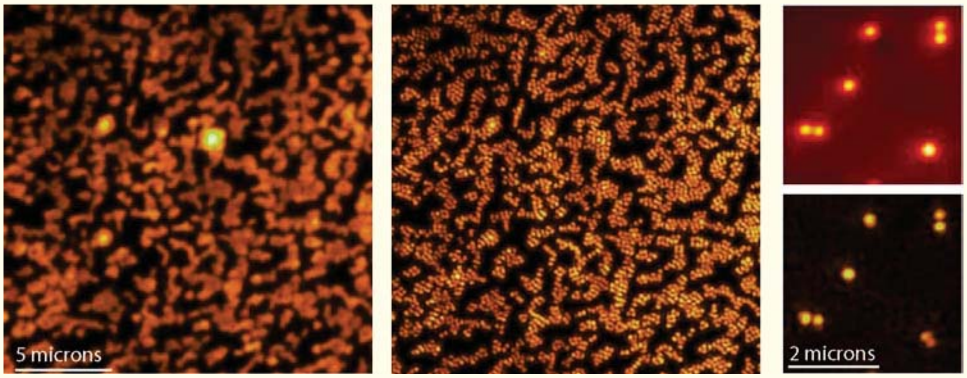
Metrology and Standards Development

In the 2004 NNI Grand Challenge workshop devoted to instrumentation and metrology of nanostructured materials (NSET 2006), the participants articulated a vision of the ultimate metrology instrument: “a suite of tools and techniques that will allow a detailed characterization (structure, function, and chemistry) of complex 3D nanostructures…” (Vaia and Wagner 2004). There is still no single instrument that can do everything, but some instruments are getting closer to this vision. Current state-of-the-art x-ray microtomography can provide nondestructive 3D images of composite materials with a resolution down to ~60 nm. Specialized instruments at beam lines can use certain x-ray-absorption lines to obtain some chemical information as well.

Nano-Optics for Chemical and Materials Characterization

Light microscopy is a widely used analytical tool because it provides nondestructive, real-time, three-dimensional imaging with chemically-specific contrast. However diffraction limits the resolution of these microscopes to >200 nm, which reduces their utility for the study of nanoscale materials. Recently, several superresolving microscope techniques have achieved sub-100 nm resolution by modifying a microscope's illumination or excitation beam structure and phase. The stimulated emission depletion (STED) technique allows scanning fluorescence microscopy to achieve 30 nm resolution by limiting fluorescence emission to a small region formed by the intersection of two laser foci (Westphal, Kastrup, and Hell 2003).

A complementary approach illuminates the sample with a fine grid pattern to generate moiré patterns. This illumination pattern causes small features to generate a low-frequency fringe pattern that is large enough to be observed by the microscope. Through computer processing, the original object can be reconstructed with a significant resolution enhancement. When combined with nonlinear optics, this approach achieves <50 nm resolution (Gustafsson 2005). Since these fluorescence techniques were developed for use in microbiology, a key challenge is to take the resolution-enhancing features and apply them to contrast mechanisms like reflectance and vibrational spectroscopy (e.g., Raman and CARS [coherent anti-Stokes Raman]) that provide morphological and chemically specific imaging for materials science. Currently, research is focused on the use of programmable optical elements to create the necessary illumination patterns for these contrast mechanisms.



Left and Center: Conventional and superresolved fluorescence images of 200 nm diameter particles. Right: Close-up comparison of individual particles in a conventional micrograph (top) and in the superresolved micrograph (bottom) (courtesy of M.R. Beversluis and S.J. Stranick, NIST).

In this discussion of metrology and characterization standards it is necessary to include a description of the current state of the art for nanoscale measurements. Nanoscale measurements can be divided into two families: (1) nanoscale measurements that examine ensembles of nanoconstituents and, (2) nanoscale measurements that examine nanoconstituents individually. Appendix C to this report includes two tables, one for each family of measurements that describe many of the characterization techniques in current practice and what information they provide.

Given the techniques listed in Appendix C, we must now ask the questions: what properties of nanocomposites need to be measured and what tools are we missing to make these measurements? Or how might current tools improve to address specific gaps?

Nanocomposites often have complex three-dimensional structures where the dispersion and interfacial interactions between the nanoconstituents and the matrix dominate the properties of interest. Current characterization and metrology tools cannot sufficiently address dispersion, interfacial interactions, and interphase properties.

6.5 SCIENTIFIC AND TECHNOLOGICAL BARRIERS

Modeling

Fundamental Understanding of Nanoscale Phenomena

As previously described, there are multiple gaps that affect the understanding of synthesis/manufacturing process, material structure, quality, and property estimation of nanostructure systems. Furthermore, the interfacial properties of nanoparticles and the host matrix are not fully described. There are also deficiencies in understanding the electronic, thermal, and acoustic transports across interfaces. Mechanical strength, fracture mechanics, as well as damage tolerance are of paramount importance for end users such as the aerospace industry. These gaps occur within the simulation methods in terms of their scope, time and length scales, and between the simulation and the physical systems in terms of the performance and end-use properties.

Validation and Qualification

The limitations of current instrumentation are barriers to verification, validation, and qualification of computational models. Specifically, the lack of instrumentation with sufficient temporal and spatial resolution impacts the validation and qualification of nanomaterial with less than 100 atoms and sub-picosecond dynamics. The lack of *in situ* instrumentation limits the development of computational models to analyze the manufacturing process and predict the outcome in industrially relevant systems. The lack of metrology and characterization models also contributes to a deficiency in validation techniques, as discussed below.

Algorithms and Computational Methods

Current computational methods and algorithms are not efficient in addressing nanocomposite modeling across multiple length and time scales. There is a lack of widely held common integration tools for quantum, atomistic, meso, and macro or finite element length and time scales. Given the current level of available computing power and resources, algorithm efficiency is a barrier in the fundamental development and maturation of computational models. In addition, a collaborative, integrative environment does not exist where the infrastructure allows for efficient collection of experimental data from disparate sources and subsequent correlation with model outputs.

Characterization

For nanomaterials research, there is a need for development of standard characterization methods unique to each class of material: nanotubes, platelets, fibers, and nanoparticles. Currently there is a lack of reliable metrics for measurement of dimensions and of electronic and optical properties. Metrologies that will rapidly measure large numbers of particles (hundreds or thousands) will allow accurate statistics of particle distributions to be obtained.

Critical nanocomposite characterization needs include the ability to measure:

- Dispersion of nanomaterials
- Interface-bonding strengths
- Carbon nanotubes: chirality, purity, and agglomeration metrology

Materials and Processing

The chief perceived advantage of nanotechnology in composites has been that, when effective, the incorporation of nanoparticles/nanoconstituents into a composite can produce benefits that are significantly beyond what a standard rule-of-mixtures calculation would predict. These larger-than-expected benefits generally arise from effects that occur at length scales below those of continuum mechanics where principles such as the rule of mixtures apply. In order to characterize the effects of nanocomposite combinations, it has become increasingly important to be able to reliably and accurately measure materials distributions, morphologies, interactions, etc. At present, accomplishing these needs require measurements at the nanoscale using tools like TEM, high-resolution SEM, and others, and the development of physics-based models that will augment data collection from measurement techniques and allow for greater characterization of behaviors and properties.

In order to achieve the full benefits of nanotechnology in composite materials (“nanocomposites”) it will be necessary to be able to translate the constituent material properties, the composite material morphologies, and the nanocomposite properties into parameters that lead to the performance levels desired. Providing these links will require advanced metrology techniques and improved materials models. Data needs to be gathered for key end-use properties (e.g., strength, stiffness, toughness, etc.) and related to the observed nanoscale properties and input into improved models. Ultimately, it should be possible to identify which nanoscale properties lead to improved macroscale properties and to build models to apply the specific knowledge gathered from a particular materials system more generally.

To transition this knowledge to large-scale production, fabrication processes must be repeatable such that constituent materials as well as their incorporation into nanocomposites can be replicated in a continuous process. In order for the processes to be repeatable, those process-control parameters that affect the constituents or the composites must be identified and their sensitivities quantified. Models may need to be built to perform sensitivity analyses.

Metrology and Standards Development

The incorporation of nanofillers (whether tubes or plates) having nanoscopic dimensions, extreme aspect ratios, and varied chemical and physical properties in a matrix produces many interrelated characteristics that are clearly distinguished from classic filled systems. These include low percolation threshold (0.1-2 %vol.), large number of density of particles per volume, (10^6–10^8 particles/μm^3), extensive interfacial area per volume (10^3–10^4 m^2/ml), and short distances between particles (Gou and Lau 2005). These characteristics greatly control the properties and performance of a nanocomposite and present many metrological challenges for processing, modeling, and characterizing these complex materials.

Table 6.1 lists some of the key scientific and technical barriers for metrology and standards.

Table 6.1
Key Scientific and Technical Barriers to Metrology and Standards for Nanocomposites

Metrology	Scientific and Technical Barriers
1. Modeling	1. Absence of tools to bridge time and length scales for nanoscale modeling and simulation 2. Deficiency of optimally fast methods for calculating large number of atoms to predict structure and properties of nanomaterials and nanocomposites 3. Lack of capability for formal statistical uncertainty analysis of modeling and simulation for nanoscale structures and properties 4. Lack of methodology for systematic intercomparison of codes used for verification and validation 5. Tools for modeling and simulation are often difficult to use 6. Lack of methods to integrate and analyze large datasets 7. Ineffectiveness of deconvolution techniques for analyzing nanoscale and atomic data
2. Characterization	1. Lack of instrumentation for mapping chemical composition and defects in the interfacial region of nanocomposites at the nanoscale 2. Lack of capability for providing quantitative mechanical properties at nanoscale spatial resolution (<100 nm) 3. Lack of instruments for simultaneously measuring properties of nanocomposites 4. Nonexistent standards and reference materials for measuring and assuring nanocomposites' properties 5. Slow speed of measuring and data acquisition for nanoscale measurements 6. Inadequate understanding of nanoscale and heterogeneous microstructure of nanocomposites. 7. Lack of instruments to provide real-time data from the nanoscale to the microscale 8. Nonexistence of instruments and standards for quantifying dispersion of nanofillers in matrices in solid state
3. Materials and Processing –Chemical composition and physical properties	1. Lack of chemical composition, reactive sites, and defect distribution on nanofiller surfaces 2. Inconsistency in morphology, shape, properties of nanofillers (e.g., resulting from poor understanding and control of the synthesis) 3. Lack of 3D data of both chemical and physical properties of nanofillers 4. Insufficient knowledge about structure, morphology, and shape of nanofillers
–Interfacial properties, molecular interactions, and wettability	1. Buried interfaces/interphases, small dimensions 2. Lack of nondestructive measurement methodologies 3. Presence of dynamic and unstable interfaces 4. Poor understanding of the contributions of different interactions, i.e., van der Waals, electrostatic, hydrogen bonding, covalent 5. Lack of metrology to accurately measure the wetting characteristics of nanofillers by matrices 6. Lack of tools to detect and quantify specific, interactive sites between nanofillers and matrices 7. Insufficient understanding on the role of interfaces in processing properties 8. Non-existent protocols and standards for quality control of nanocomposite processing 9. Visualization of small particles (<100 nm) with nondestructive method
–Dispersion	1. Nonexistent techniques for examining and quantifying dispersion of nanofillers in liquid phases 2. Lack of reference materials 3. Scalability from laboratory to commercial production

6.6 PRIORITIES FOR R&D AND INFRASTRUCTURE INVESTMENTS

Modeling

Computational models will support end users from many industries in the design of materials, structures, and systems and will significantly aid in establishing quality-control criteria. These tools will also lead to faster qualification and, ultimately, to certification by analysis. In support of structures design, the future toolbox will offer the user the ability to predict the material properties for a given combination of material constituents and process parameters.

Each stakeholder along the value chain will benefit from predictive models in various ways. The nanoparticle suppliers will benefit through improved understanding of the synthesis environment, growth process, structure, and final properties of the nanoparticles. Further, it will aid them in the analysis of the surface chemistry and functionalization of the nanoparticles. These features will allow for the development of robust, measurable process-control parameters in nanoparticle manufacturing.

Ultimately, computational models will allow downstream nanocomposites manufacturers to correlate nanoparticle-supplier data with experimental data and quantitative physics-based analysis of the composite-material production process to establish process-control variables and quality-control criteria for the nanocomposites. This will ultimately lead to an optimized solution among competing properties to permit design trade studies to be conducted virtually for materials systems where such trade studies are not possible today.

It is recommended that a coordinated effort between industry and government be developed to further “pathfinder” (see Chapter 4) or other pilot programs in which computational modeling and experimental characterization are exercised around selected material systems of highest priority to end users in industries such as aerospace, chemical, automotive, and forestry and paper products. This collaborative R&D will involve the government to a greater degree in precompetitive research, whereas in the later stages of R&D, companies will take the lead in competition with each other to produce products.

R&D priorities can be divided in two categories based on development and validation:

1. Algorithms

- Research should be directed at developing computationally efficient algorithms for nanoparticles that predict synthesis from nucleation to full growth as a function of process variables/metrics. These algorithms would be drawn from the areas of quantum physics, chemical simulation, statistical simulation, and finite-element simulation. In addition, efforts should be put towards correlating structural measures to mechanical, electrical, acoustic, thermal, and toxicity properties and quality metrics. Also research should be focused on linking together simulations of varying lengths and time scales.
- Numerical methods and algorithms need to be developed to describe surface chemistry, the interfacial properties between nanoparticles, the interfacial properties between nanoparticles and the host matrix, and the impact of functionalization on the desired properties. Numerical methods also need to be developed that link the design parameter requirements with these nanoscale properties.
- There is a great need to develop numerical model reduction methods that in turn decrease the demands on processing resources and make the models compatible with commonplace platforms. Such approximations or reduced models, based on neural net, Bayesian, or

evolutionary algorithms, among other solutions, will be crucial to model development. More efficient algorithms will make predictive models viable tools in the hands of designers and end users of nanocomposites.

- Optimization techniques such as tree searches or pareto-optimization methods and their associated algorithms will need to be developed to allow the end user to optimize the bulk material design when dealing with many complex competing properties. As an example, while a structure may need to meet a certain level of conductivity, its strength, modulus, and damage tolerance should not be compromised in order to obtain the improved conductivity.

2. Framework/Architecture

- Efforts need to be directed towards development of a collaborative framework/architecture that enables the integration of quantitative models and experimental data for the validation and development of metrology and standards. The predictive-modeling framework enables experimentalists and theoreticians to work in parallel and streamline the creation of metrology and standards.
- The architecture for integration across multiple time and length scales is essential for making the tool useable in the hand of designers and material end users.
- There is a need to support nanocomposites data management through the development of metrology databases related to the manufacturing and experimentation process and to make the data available for the application of various data mining and statistical analysis and image-processing tools.

The infrastructure investment in support of computational modeling should be centered on two goals: enhanced accessibility and creation of a common development environment. To enhance the visibility and streamline remote access to the available published codes (national and international), it is recommended that a coordinated effort between industry, academia, NIST, DOE, NASA, and DOD be established to develop a single point of entry for remote access, searching, viewing, and uploading of the published computational algorithms. Such capability will greatly enhance the visibility of the available codes and reduce redundant and duplicate efforts. To expedite the development and maturation of computational models, investments need to be directed towards developing common data management and integration architectures as summarized below:

- Use and enhancement of collaborative computing environments for exchanging disparate data across multiple agencies, universities, commercial modeling organizations, and industrial users to accelerate maturation of the computational predictive models
- Standards for interoperable data from experimental, process, and computational models
- Infrastructure for management of data from experimental, process, and numerical analyses

Characterization

Critical overarching R&D issues for characterization of nanomaterials include the following:

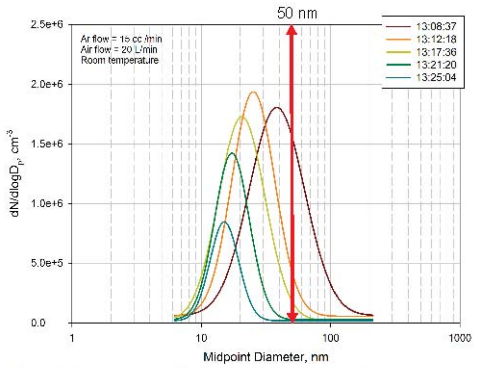
- Environmental, health, and safety (EHS) issues
- Modeling
- Insufficient funding for small businesses to develop new characterization techniques (more funding infusion needed for SBIR/STTR, BAA, etc., across multiple Federal agencies)

Real-Time Characterization Project Addresses a Priority Need in Nanomanufacturing

A key need identified by both the chemical and semiconductor industries is the capability for real-time characterization of nanoparticles smaller than 50 nanometers during synthesis processes (Chemical Vision2020 2003; 2006). According to the industry experts, the techniques currently used in commercial processes either lack the accuracy needed, or are not suitable for in-plant operation. Thus, there is often an inadequate ability to monitor and control production processes for nanoscale materials, resulting in variability in product quality.

The Industrial Technologies Program (ITP) of the Department of Energy's Office of Energy Efficiency and Renewable Energy has recognized the emerging needs in nanomanufacturing and has initiated projects to address the need for real-time characterization. In a recent project, a multidisciplinary team at Oak Ridge National Laboratory was assembled to work with industry to demonstrate a promising technique on systems characteristics of industrial processes.

The work was focused on validating the capability of a differential mobility analyzer (DMA) for real-time process characterization. This technique, which has been used broadly in aerosol science and in scientific research on the nanoparticles synthesis (Kim and Zachariah 2005; 2006), employs the deflection of charged particles in an electric field to segregate particles in a gas stream. A commercial DMA was used to sample and characterize the nanoparticles produced in two different types of gas-phase processes: a chemical vapor deposition process for production of metal-oxide particles, and a laser-ablation process for synthesis of carbon nanomaterials. The potential capability of the analyzer to provide real-time data on the variation of the particle size distribution was demonstrated. The results indicated promising opportunities for rapid detection of process transients and for the use of the instrument in process development (Cheng, Ford, et al. 2007; Cheng, Lee, et al. 2007). The success of this industry-national laboratory collaboration in translating advancements from scientific fields to industry to address an urgent, widespread need in nanomanufacturing indicates the value of such efforts.



Real-time sampling and analysis detected a shift in particle size distribution in the sub-50nm range during a transient in process conditions.

Mengdawn Cheng of ORNL and Emory Ford of Materials Technology Institute operate a differential mobility analyzer.

(Images are courtesy of U.S. Department of Energy, Oak Ridge National Laboratory.)

- Better understanding within the United States of other metrology activities overseas and coordination with such international R&D
- Framework to characterize changes in the matrix due to addition of nanoparticles (interphase) such as the creation of new crystal morphologies, distortions in polymer chain conformation, or mobility

- Framework to characterize the changes to composite properties upon addition of nanoparticles (rheology, strength, toughness, conductivity, permeability) with the size, interfacial chemistry, and intrinsic properties of the nanoparticles
- Framework to characterize how the changes in matrix structure and composite properties affect the performance of the composite in applications (product stability, processability, spreadability, vapor-barrier properties, heat deflection, etc.)
- Framework to characterize nanoparticles that are introduced directly into a fibrous preform independently from the matrix via processes such as chemical vapor deposition and to link these characteristics to resultant composite properties
- New instruments or combinations of instruments to evaluate dispersion of nanoparticles during synthesis, throughout the manufacturing process, and into the final manufactured part
- New instrumentation to characterize the adhesion between the matrix and the nanoparticle, measurement methods for stress transfer, and kinetics
- New instrumentation to ascertain the complex relationship between processing, rheology, and final properties (such as conductivity)
- Design of cost-effective strategies to manufacture materials with existing equipment in which sizable capital expenditures have been made
- New instrumentation to locate, analyze, and eliminate nanoscale imperfections or defects prior to the failure of the manufactured part
- New solution-based metrologies to disperse nanoparticles so that advanced characterization studies can be carried out
- New standard nanostructured materials that will facilitate cross-laboratory comparisons and trade, and serve as the basis of testing for environmental, health, and safety effects

Materials and Processing

The long-term goal for research and development in technologies for nanocomposites is to make these materials readily and affordably available to end users for a wide variety of applications. In order to reach this goal, links must be established between laboratory-scale fabrication and measurement techniques and large-scale production and industrial process-control methods. Investments in infrastructure should be guided by this principle.

It is critical to create a dataset for developing the understanding and the modeling necessary to move technologies from the laboratory to the production floor. In the early stages of research and development, metrology and modeling at the nanoscale will be paramount. These efforts, in general, are best handled at academic and government labs, with guidance from industrial partners to maximize the impact of these studies. Furthermore, key industrial partners will be needed to fabricate the materials necessary for the early study phases, while other industrial partners will be needed to establish the suitability of the materials and processes for transformation into product forms.

Metrology and Standards Development

The goal of R&D investment in metrology and standards development is to create the basis for accurate and reproducible measurements and reliable predictions of the properties, performance, and health effects of nanocomposites. The following investment areas will support this accomplishment:

- Improved or new instrumentation and methods for measurements of dimensions at sub-nanoscale and chemical composition at nanoscale spatial resolution; these metrologies are applied for both nanomaterials and nanocomposites
- Tools for online measurement and quality control of nanocomposites processing, e.g., measuring changes in rheological, dispersion, or optical (spectroscopic) properties
- Advanced instruments for characterizing nanocomposites properties *in situ* and nondestructively at the nanoscale spatial resolution
- Metrologies for measuring the nanoparticle/matrix interfacial properties and adhesion at the nanoscale spatial resolution
- Instrumentation and methods to measure accurately the dispersion of nanofillers in the matrices in both solution and solid states
- Methodologies for accurately measuring and predicting the properties and long-term performance of nanocomposites
- Protocols and methods for reliably measuring the effects on human health and the environment of products produced during burning and degradation
- Calibration and reference materials for nanocomposite testing
- Development of a set of standards strictly used for the processing, characterization, and modeling of nanocomposites

6.7 IMPLEMENTATION STRATEGIES

Nanocomposites research and development is still in its nascent stage, and the problems associated with the metrology and standards for these materials are extremely challenging; no individual organization can adequately solve them. Therefore, an effective partnership among government, academia, and industry is essential for addressing the metrology and standards issues in the manufacturing, characterization, and modeling of nanocomposites.

Federal Government Role

The Federal Government should provide two principal roles: coordination and fundamental characterization. Coordination, in this case, means providing the structure to enable the clear flow of information between partners in order to take full advantage of the contributions of the partners. The coordination role is principally an administrative one, but it needs to be tied closely to the Government's own role in technology development, which will principally be provided through the Government laboratories. The laboratories are unique national assets that possess metrology equipment not generally available to either academia or industry, and these should be leveraged heavily to provide data and methods to the other partners. Since metrology research and standards development often require long-term funding, highly-specialized human resources, and sophisticated and expensive instruments, the Federal Government will remain an important partner, along with industry and academia, in this effort. The roles of the Federal Government and its laboratories include the following:

1. Creating a roadmap on metrology and standards that addresses the industrial needs, and bringing appropriate parties, e.g., industry, academia, Federal agencies, to the table. In the past, the Federal Government has taken the lead in organizing technical conferences and focus workshops with industry, academia, and stakeholders to refine R&D direction and to direct resources. Specific gaps and barriers should be identified in both research and resources. Free exchange of information should be ensured for evolution of all issues related to metrology and

standards for nanocomposites (i.e., processing, characterization, models, performance, health, and environment).

2. Fostering/providing a mechanism to identify and undertake critical metrology and standards research activities that will advance research in, for example, characterization, service life prediction, databases, etc., of nanocomposites. One effective mechanism is the formation of government/industry/university consortia, which takes advantages of the stable funding, specialized human resources, advanced facilities, and highly-specialized and expensive instruments at the national laboratories. This type of platform is also effective for incorporating inputs from industry and information exchanges.
3. Funding precompetitive research and advanced research facilities in areas such as metrologies and standards for subnanoscale measurement, chemical composition at nanoscale spatial resolution, interface/interphase characterization, stress transfer, and dispersion of nanomaterials in polymer nanocomposites. The Government can also assist industry and university in identifying funding sources, e.g., the Small Business Innovation Research (SBIR) program.
4. Providing/fostering the formation of highly skilled teams to allow effective collaboration between researchers of different disciplines. R&D in nanocomposite metrologies and standards requires a strong collaboration between materials scientists, chemists, physicists, computer scientists, engineers, and modelers.
5. Providing leadership in standardization activities. An agency such as NIST, which is active in standards activities and familiar with the standardization process, should continue its work to foster the development of standards, protocols, and reference materials for the nanocomposite communities.
6. Assisting industry and universities in identifying research capabilities and facilitating access to national laboratories that are conducting metrology and standards research for nanomaterials, nanomanufacturing, and nanocomposites.
7. Providing guidance in defining precompetitive research and collaborations, and protecting exchange and publication of intellectual properties. For example, NIST’s CRADA (Cooperative Research and Development Agreement) office and legal department have extensive experience in this area and can provide such guidance.
8. Promoting international collaboration on development of metrologies and reference materials, standardization of test methods, and data analysis methodologies.

Role of Academia

Academia can and should play a key role in the development of fundamental understanding of nanocomposites and should also serve as a source of breakthrough innovation. In both these cases, academia’s focus should be on small-scale testing, evaluation, and characterization, coupled with the development of models based on these results. New fundamental understanding should also be verified through tests that may lead to innovative fabrication and characterization techniques that can be leveraged through other length scales. In all its activities (as with the other partners below) it is essential that the knowledge and data created within academia be clearly and regularly communicated with its government and industrial partners to provide a robust feedback mechanism to maximize the benefits to all partners. Metrology development relies on sound understanding of many physical and chemical phenomena of materials and their interactions. Academia’s roles in this area, therefore, will embrace:

1. Conducting focused research to provide the fundamental understanding of complex properties and behaviors of nanocomposites and their components (e.g., mechanism and modeling of interfacial properties and adhesion) to the government/university/industry collaborative effort.
2. Developing innovative techniques and methods for assessing and characterizing nanoscale properties. As part of consortium activities, these useful techniques and methods could become specifications and standards.
3. Assisting in providing graduate students and postdocs to work in the consortia or at national laboratories conducting metrology research on nanocomposites.

Industry Role

Industry plays one or more of three roles: those of innovator, supplier, and customer. In certain cases industry may play all three roles—especially with emergent materials and processes, as has been the case in the electronics and biotech industries. In its role of innovator, industry may be able to handle the role of fundamental characterization in some cases, but, in general, these will be done in conjunction with other partners, be they in academia, government, or other companies.

The role of supplier applies equally to nanoparticles, composite materials, parts, and assemblies. Most industry partners will act in the role of supplier where materials inputs are provided to them to combine into value-added products. In order for nanomaterials to achieve more rapid transition to such products, robust quality-control systems for these materials and their associated processes will have to be developed. In the case of nanocomposites, the investment required for speedy transitions are generally larger than would make sense for an acceptable rate of return, so that implementations of new technology will occur later rather than earlier unless other resources are brought to bear.

In these cases, industry's role becomes that of the technology consumer and provides the requirements needed to transition the technology to an end use. In this role, industry serves as the partner in the academia-government-industry triangle that provides direction and feedback to developers to make technology transitions both more likely and more rapid. Industry's role will also require that it provide some its own investment by providing both funds and innovative ideas.

Metrology and standards development for nanocomposites are aimed to principally serve various sectors associated with this industry, including instrument manufacturers, materials suppliers, and materials users. Therefore, the success of an implementation strategy for nanocomposite metrology and standards largely depends upon the industry's desire and efforts in this area. The industry role will encompass:

1. Providing inputs on the critical needs of these industrial sectors, e.g., standards, calibration, and reference materials for advanced instruments, standards for testing the performance of nanocomposite products, and standardization of statistical analysis for nanoscale data.
2. Providing quality materials and samples needed for testing, demonstration, and validation of metrologies and models.
3. Actively working with government and standards organizations to standardize methods and specifications for materials, processing, and characterization of nanocomposites (e.g., round-robin testing).
4. Contributing funding, intellectual property (e.g., models, software), and human resources (e.g., research associates) to centers or consortia conducting research on metrology and standards for nanocomposites.

6.8 SUMMARY

In conclusion, nanoparticles and polymer nanocomposite technology comprise a broad and interdisciplinary research and development activity that has been growing rapidly worldwide in the past few years. It has the potential to "revolutionize" the way materials are made and the range and nature of functionalities to which they may be tailored. How this nanotechnology revolution will develop, how great the opportunities that nanostructured materials and nanocomposites can provide, and how rapidly the technology will progress depend strongly on the efforts to develop the scientific and technological infrastructures outlined here.

The hoped-for revolution in the nanocomposite industry depends on a variety of state-of-the-art instruments, facilities, and standards for the manufacturing, testing, and characterization of these materials. These instruments include those that can measure multiple properties simultaneously (magnetic, mechanical, electrical, optical, etc.) at the accuracies required for nanomaterials and nanocomposites. A particular desire is nanoscale nondestructive techniques to probe the buried interfaces. Another set of tools also is needed to monitor *in situ* the fabrication and properties of nanocomposites.

For facilities, NNI agencies have established over 60 centers or user facilities and related infrastructure; several of those are devoted to nanomaterials. However, none of those deals exclusively with metrologies for polymer nanocomposites, their processing, or their properties.

With respect to standards, as in other nanotechnology areas, research on development of standards and reference materials is essential for advancing nanocomposite technology. These standards are needed for the consistent manufacturing and reliable characterization and testing of nanocomposites. The ultimate goal will be to link key, easily controlled process parameters to nanoscale morphologies/features that define a material's performance. In this way, understanding of nanoscale features through highly advanced metrology will enable the creation of robust process-control parameters that ensure repeatable manufacturing processes that are cost-effective.

The combination of nanoscopic dimensions, multiple shapes, extreme aspect ratios, and large, buried filler-matrix interfaces residing in nanostructured materials and nanocomposites has brought opportunities but also has raised many scientific and technological challenges. Further, the transformation of materials at the nanoscale to reliable, larger-sized composites poses many issues in both manufacturing (processability and quality control) and performance assessment (test methods and quality control).

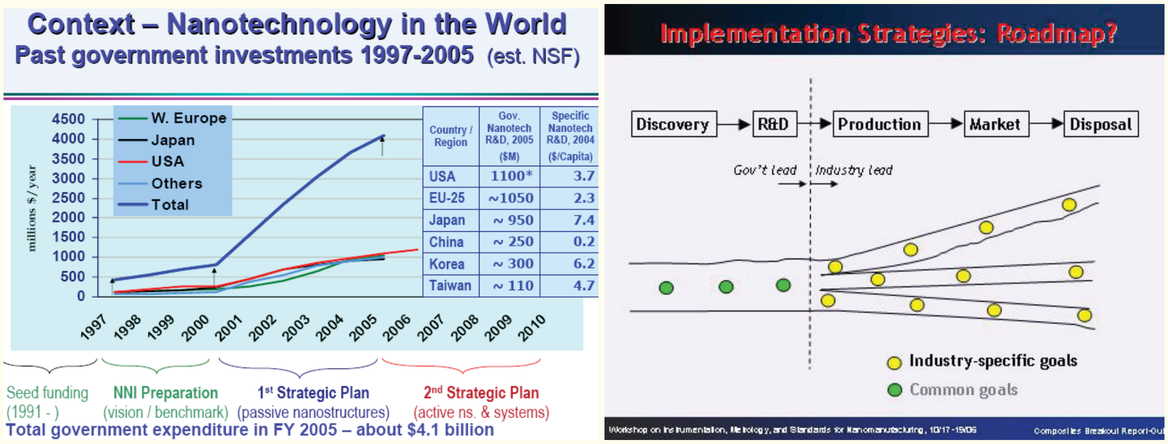
The development of nanotechnology for nanocomposites and the scientific data generated from it are only in the initial stages. Therefore, one important effort in the scientific investment is the development, compilation and integration of available sound models, materials, and processing methods that can be applied to produce nanocomposites with desired properties and performance levels, so as to create a "toolbox" that enables these developments to happen more rapidly, more cost-effectively, and more robustly. For example, the topological similarities between nanocomposites and other mesoscale polymer systems, such as block copolymers, semicrystalline polymers, and colloids, provide good guidance toward understanding the role of processing on structure and properties.

The Global Perspective on Nanomanufacturing

In recent years, nanomanufacturing has become an increasingly international activity; globally, there are now some 44 major nanotechnology consortia (*Nanotechnology Now* 2008). The graphic below further elucidates the high levels of global investment in recent years. European researchers and industry have intense activities driving a nanometrology roadmap. Asia continues to build on its prowess from its well-established semiconducting and electronics sectors: "Nanotechnology is being touted as the "next big thing" across the region, and the feverish pace of research among its many domains, across the region, certainly drives home the point" (Frost and Sullivan Research Service 2005).

If the United States truly wants to lead the world in nanomanufacturing in the near and far future, we will need to continue to forge new alliances with our colleagues overseas. One means toward building these new partnerships is to make a survey of existing nanomanufacturing roadmaps and activities from an international perspective. We could then identify the key contact points to approach and begin establishing new relationships with overseas colleagues to accelerate the acceptance of U.S. industry-initiated roadmaps in the international community.

Ultimately, it is recommended to build upon such alliances to create an international nanomanufacturing roadmap comparable to the International Technology Roadmap for Semiconductors (ITRS) of the semiconductor industry (http://www.itrs.net/reports.html). As illustrated below, precompetitive research problems would need to be agreed upon, collaboratively researched, and solved by a unified consortium led by the government. This groundwork effort would be followed by execution of industry-specific goals toward product commercialization.



Context – Nanotechnology in the World

Past government investments 1997-2005 (est. NSF)

Country / Region	Gov. Nanotech R&D, 2005 ($M)	Specific Nanotech R&D, 2004 ($/Capita)
USA	1100*	3.7
EU-25	~1050	2.3
Japan	~ 950	7.4
China	~ 250	0.2
Korea	~ 300	6.2
Taiwan	~ 110	4.7

Total government expenditure in FY 2005 – about $4.1 billion

Implementation Strategies: Roadmap?

Workshop on Instrumentation, Metrology, and Standards for Nanomanufacturing, 10/17-19/06

Composites Breakout Report-Out

(Left) worldwide government investments in nanotechnology; (right) implementation strategies (Roco 2005; courtesy of Mihail Roco).

Another critical investment is integrating modeling and simulation into the research and development of nanocomposites. Experimental data in the absence of models and robust process controls will not suffice. Experimentally verified multiscale modeling and simulations of nanostructured materials and their composites across the hierarchy of length scales from atomic to mesoscopic to macroscopic must be utilized to guide the manufacturing and performance. Reliable models based on scientific theories will be needed to interpret measurement results, and simulations will be needed to validate experimental results or to stand in for measurements not yet possible. Complete integration of physical, chemical, and process parameters during manufacturing is also essential to producing nanocomposites reliably on a large scale.

A broad-based consortium comprising government agencies, academia, and industrial partners will be needed to identify and overcome precompetitive issues that would otherwise create barriers to the effective execution of a national nanotechnology strategy for nanomanufacturing. No single company, university, or government agency can address these problems in an effective manner without leveraging the cooperation of other members. International activities (see sidebar, "The Global Perspective on Nanomanufacturing") are also important to fold into national activities to avoid unnecessary duplication of R&D.

6.9 REFERENCES

Chemical Industry Vision2020 Technology Partnership (Chemical Vision2020). 2003. *Chemical industry R&D roadmap for nanomaterials by design: From fundamentals to function*. Available online: http://www.chemicalvision2020.org/pdfs/nano_roadmap.pdf.

———. 2006. *Implementation plan for chemical industry R&D roadmap for nanomaterials by design*. Available online: http://www.chemicalvision2020.org/pdfs/ChemInd%20Nanotech%20Impl%20Plan%209May06.pdf.

Cheng, M.-D., E.A. Ford, D.W. DePaoli, E.A. Kenik, and P. Angelini. 2007. On-line real-time characterization of engineered nanomaterials for nanomanufacturing applications. *Industrial and Engineering Chemistry Research* 46:6269–6272.

Cheng, M.-D., D.-W. Lee, B. Zhao, H. Hu, D.J. Styers-Barnett, A.A. Puretzky, D.W. DePaoli, D.B. Geohegan, E.A. Ford, and P. Angelini. 2007. Study of formation and production of carbon nanohorns using continuous in-situ characterization techniques. *Nanotechnology* 18(18):185604.

Du F., and K. Winey, 2006. Nanotubes in multifunctional polymer nanocomposites. In *Nanotubes and nanofibers*. Y. Gogotsi, ed., New York: Taylor and Francis, pp 179-197.

Feynman, R. 1959. "There's Plenty of Room at the Bottom." Presentation at the American Physical Society annual meeting, December 29, 1959. A transcript is available online: http://www.its.caltech.edu/~feynman/plenty.html.

Frost and Sullivan Research Service. 2005. Nanotechnology Developments in Asia (Technical Insights). Available online: http://www.frost.com/prod/servlet/report-brochure.pag?id=D328-01-00-00-00.

Gou M.J., and K. Lau. 2005. Modeling and simulation of carbon nanotube/polymer composites. *In Handbook of theoretical and computational nanotechnology,* M. Rieth and W. Schommers, eds. Vol. 1, Chapter 66, pp 1–33. American Scientific Publishers.

Gustafsson, M.G.L. 2005. Nonlinear structured-illumination microscopy: Wide-field fluorescence imaging with theoretically unlimited resolution. *Proc. Natl. Acad. Sci USA* 102:13081–13086.

Kim, S.H., and M.R. Zachariah. 2006. In-flight kinetic measurements of the aerosol growth of carbon nanotubes by electrical mobility classification. *J. Phys. Chem. B* 2006(110):4555–4562.

———. 2005. In-flight size classification of carbon nanotubes by gas phase electrophoresis. *Nanotechnology* 16: 2149-2152 (2005).

Nanoscale Science, Engineering, and Technology Subcommittee (NSET), Committee on Technology, National Science and Technology Council, 2006. *Instrumentation and metrology for nanotechnology: Report of the National Nanotechnology Initiative workshop*, January 27–29, 2004. Washington, DC: NSET. Available online: http://www.nano.gov/html/res/pubs.html.

Nanotechnology Now. 2008. International nanotechnology programs. (Accessed May 2008; last updated 29 March 2008.) 7thWave, Inc. Available online: http://www.nanotech-now.com/international.htm.

Roco, M.C. 2005, International perspective on government nanotechnology funding in 2005. *J. Nanoparticle Research* 7(6):707–712.

Roco, M.C., and W.S. Bainbridge, eds. 2003. *Converging technologies for improving human performance: Nanotechnology, biotechnology, information technology and cognitive science*. Dordrecht, Boston:

Kluwer Academic Publishers (Springer), Low-resolution PDF copy available online: http://www.wtec.org/ConvergingTechnologies/.

———. 2006. *Managing nano-bio-info-cogno innovations: Converging technologies in society*. Dordrecht, the Netherlands: Springer. Low-resolution PDF copy available online: http://www.wtec.org/ConvergingTechnologies/).

Tasis, D., N. Tagmatarchis, N. Bianco, and M. Prato. 2006. Chemistry of carbon nanotubes, *Chem. Rev*. 106(3):1105–1136.

Vaia R.A., and H.D. Wagner. 2004. Framework for nanocomposites. *Materials Today* (November):32–37.

Westphal, V., L. Kastrup, and S.W. Hell, 2003. Lateral resolution of 28 nm (lambda/25) in far-field fluorescence microscopy, *Appl. Phys. B-Lasers Opt.* 77:377–380.

6.10 BIBLIOGRAPHY

Ajayan, P.M., and J.M. Tour. 2007. Nanotube composites. *Nature* 447:1066–1068.

Baur, J., and E. Silverman. 2007. Challenges and opportunities in multifunctional nanocomposite structures for aerospace applications. *MRS Bulletin* 32(April):328–334.

Breuer, O., and U. Sundararaj. 2004. Big returns from small fibers: A review of polymer/carbon nanotube composites. *Polymer Composites* 25:630–645.

Coleman, J., U. Khan, W. Blau, and Y.K. Gun'ko. 2006. Small but strong: A review of mechanical properties of carbon nanotubes–polymer composites. *Carbon* 44:1624–1652.

Krishnamoorti, R. 2007. Strategies for dispersing nanoparticles in polymers. *MRS Bulletin* 32(April):341–347.

Moniruzzaman, M., and K.I. Winey. 2006. Polymer nanocomposites containing carbon nanotubes: Review. *Macromolecules* 39:5194–5205

Ray, S.S., and M. Okamoto. 2003. Polymer/layered silicate nanocomposites: A review from preparation to processing. *Progress in Polymer Sci.* 28:1539-1641.

Schadler, L.S., S.K. Kumar, B.C. Benicewicz, S.L. Lewis, and S.E. Harton. 2007. Designed interfaces in polymer nanocomposites: A fundamental viewpoint. *MRS Bulletin* 32(April):355–340.

Sheng, N., M.C. Boyce, D.M. Parks, G.C. Rutledge, J.I. Abes, and R.E. Cohen, Multiscale Micromechanical Modeling of Polymer/Clay Nanocomposites and the Effective Clay Particle, *Polymer* 45 (2004) 487–506.

Thostenson, E.T., C. Li, and T.-W. Chou. 2005. Nanocomposites in context: Review. *Composites Sci. Technol.* 65:491–516.

Wagner, H., and R A. Vaia. 2004. Issues at the interface. *Materials Today* (November):38–42.

Winey, K.I., and R.A. Vaia. 2007. Polymer nanocomposites. *MRS Bulletin* 32(April):314–321.

7. ENVIRONMENTAL, HEALTH, AND SAFETY CROSS-CUT ISSUES FOR NANOTECHNOLOGY

Principal Authors: Mark D. Hoover and Dianne Poster

7.1 INTRODUCTION

A common and fundamental theme among all nanomanufacturing sectors represented at the workshop is the need to develop and provide a practical and essential array of instrumentation, metrology, and standards to understand and manage environmental, health, and safety (EHS) issues. The chemicals, electronics, pharma/biomedical, and composites/materials breakout sessions identified broad needs for fundamental nomenclature, metrology, instruments, and standards to support scientifically sound and technically defensible approaches to EHS issues. The natural synergies and cost-efficiency benefits of developing both effective nanomanufacturing quality and effective EHS protections should be recognized and pursued as essential to success in both areas.

Recent documents that have focused on research needs for EHS of nanomaterials include the report published jointly by the Chemical Industry Vision2020 Technology Partnership and the Semiconductor Research Corporation on chemical and semiconductor industry research recommendations on EHS of nanomaterials (Chemical Vision2020 n.d.), and reports from the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council's Committee on Technology that identify EHS research, information needs, and strategies related to understanding and managing potential risks of engineered nanoscale materials (NSET 2006; NSET 2008).

7.2 VISION FOR A GENERAL EHS APPROACH

The web document “Approaches to Safe Nanotechnology: An Information Exchange with NIOSH” (draft for public comment) (NIOSH 2006) reviews what is currently known about nanoparticle toxicity and control. It serves both as a starting point and as a request from NIOSH to occupational safety and health practitioners, researchers, product innovators and manufacturers, employers, workers, interest group members, and the general public to exchange information that will ensure that no worker suffers material impairment of safety or health as nanotechnology develops. Opportunities to provide feedback and information are available throughout the document.

There are already practical and achievable strategies to provide safe nanomanufacturing such as through assessing and managing occupational exposures (Bullock and Ignacio 2006; ILO 2005; Shulte et al. 2008), as shown in Figure 7.1. However, the critical challenge for nanomanufacturing is providing a sound, practical, and affordable scientific basis for answering three basic questions:

- What are the characteristics of the material to which exposures may occur?
- What are the potential magnitudes of the exposures?
- Are the exposures acceptable?

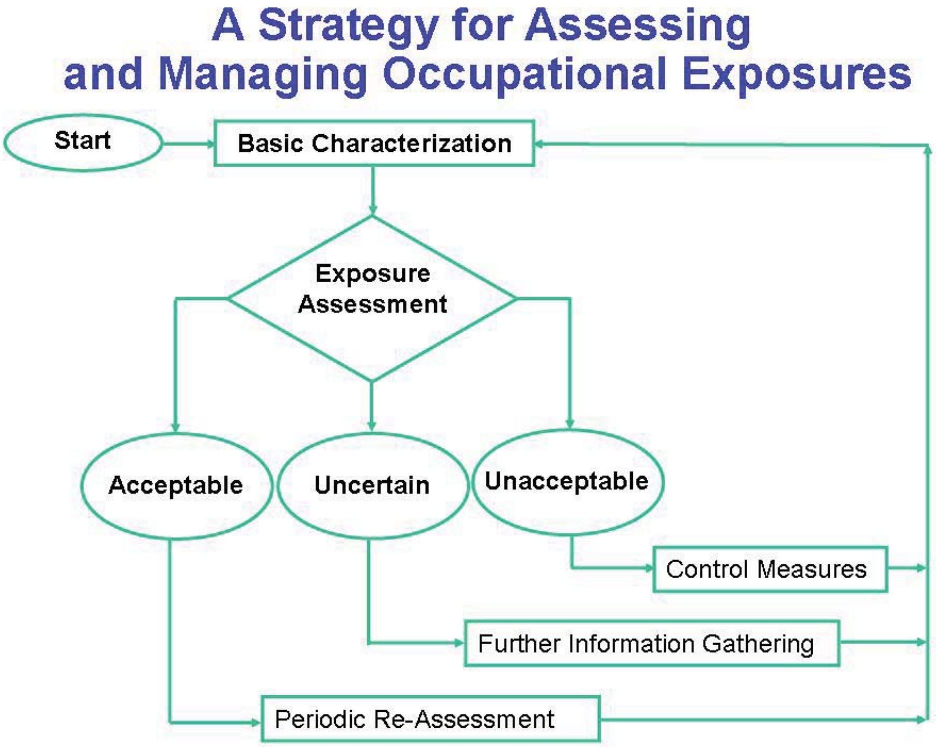
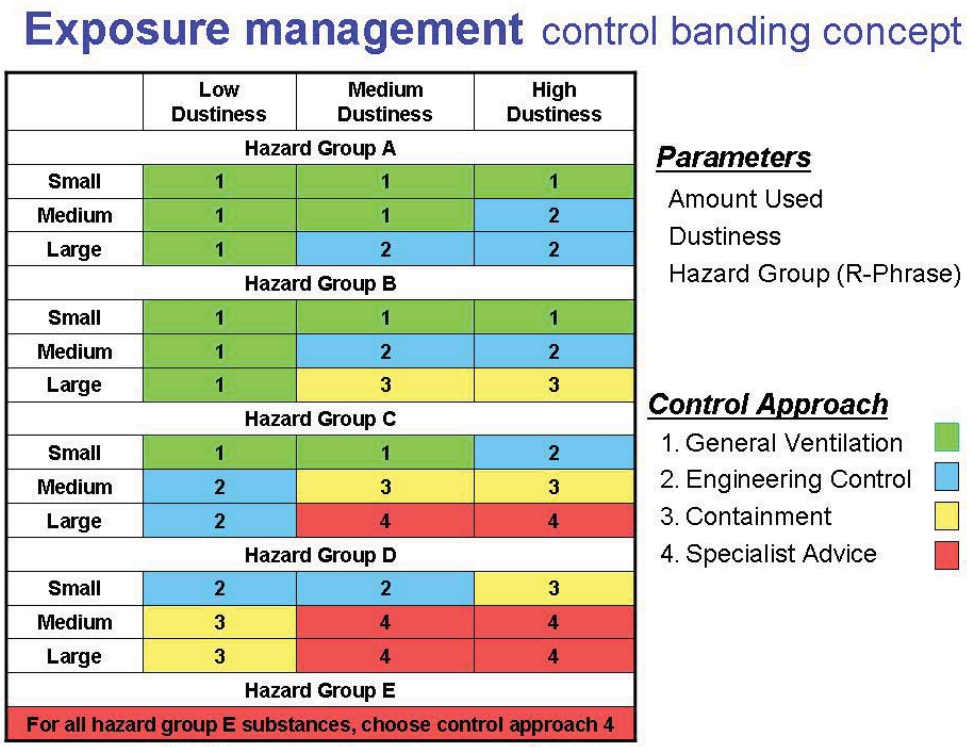


Figure 7.1. Example of a basic strategy for assessing and managing occupational exposures (Bullock and Ignacio 2006; ©2006, used with the permission of the American Industrial Hygiene Association [2008]).

As illustrated in Figure 7.2, it appears both feasible and necessary to adopt a graded approach to applying general ventilation, engineering controls, containment, and specialist advice to managing potential exposures to different amounts of materials having a range of dustiness and potential toxicity characteristics. The concept of "Control Banding for Safe Nanotechnology" may be both practical and necessary. Additional information about control banding, including its historical development in the pharmaceutical industry, can be found at the website on the Control of Substances Hazardous to Health (COSHH) of the United Kingdom's Health and Safety Executive (http://www.coshh-essentials.org.uk). Further information is also available from the website of the National Institute for Occupational Safety and Health (NIOSH) (http://www.cdc.gov/niosh/topics/ctrlbanding/).

As illustrated in the example classification scheme shown in Figure 7.3, ability to apply a control banding approach, as well as more extensive exposure assessment and risk management, will require some type of science-based classification scheme for nanomaterials. The scheme in Figure 7.3 includes the basic concepts of nanoparticle shape, composition, degree of agglomeration, and functionalization. To validate the control band assignments it will be key to provide the details of such a scheme, the tools to assign materials to the classes, and the detailed toxicology and risk management case studies.

Finally, as Figure 7.4 illustrates, success in providing safe nanomanufacturing will depend on our ability to bring to bear all the essential elements of a comprehensive industrial hygiene program. In addition to providing effective exposure assessment and control for the nanoscale aspects of nanomanufacturing, this will require a harmonized and seamless inclusion of the full spectrum of health risks associated with manufacturing.



Exposure management control banding concept

	Low Dustiness	Medium Dustiness	High Dustiness
Hazard Group A			
Small	1	1	1
Medium	1	1	2
Large	1	2	2
Hazard Group B			
Small	1	1	1
Medium	1	2	2
Large	1	3	3
Hazard Group C			
Small	1	1	2
Medium	2	3	3
Large	2	4	4
Hazard Group D			
Small	2	2	3
Medium	3	4	4
Large	3	4	4
Hazard Group E			
For all hazard group E substances, choose control approach 4			

Parameters

Amount Used
Dustiness
Hazard Group (R-Phrase)

Control Approach

1. General Ventilation 🟩
2. Engineering Control 🟦
3. Containment 🟨
4. Specialist Advice 🟥

Figure 7.2. Illustration of the concept of control banding to apply a graded approach of general ventilation, engineering controls, containment, and specialist advice to manage potential exposures to different amounts of potentially toxic materials with a range dustiness and toxicity characteristics (courtesy of NIOSH; see also ILO 2008; Shulte et al. 2008).

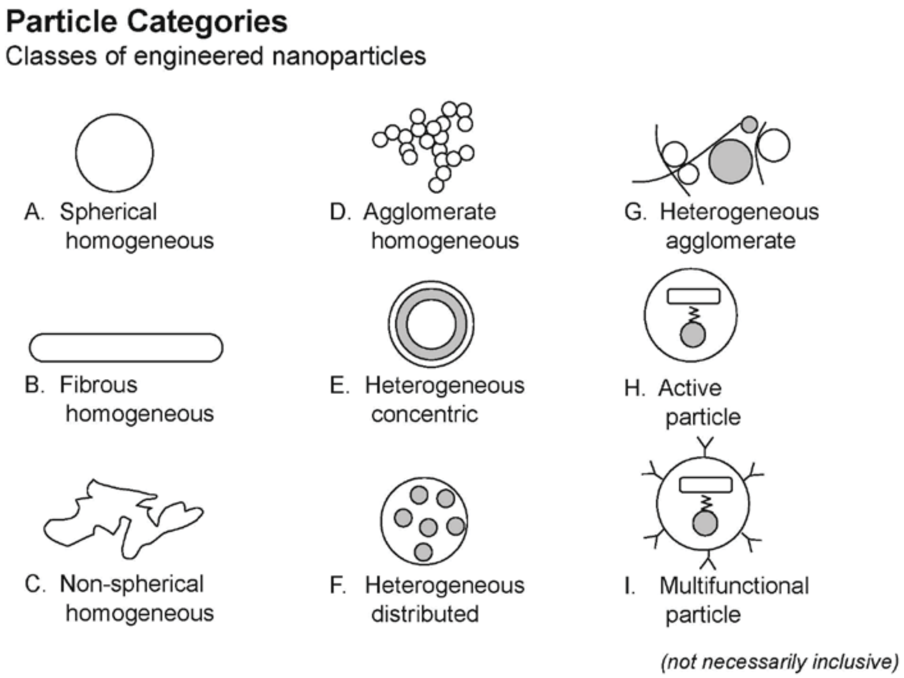


Figure 7.3. Illustration of a categorization scheme for engineered nanoparticles (courtesy of Andrew Maynard, Woodrow Wilson International Center for Scholars; Maynard 2005; see also Maynard and Aitlen 2007).

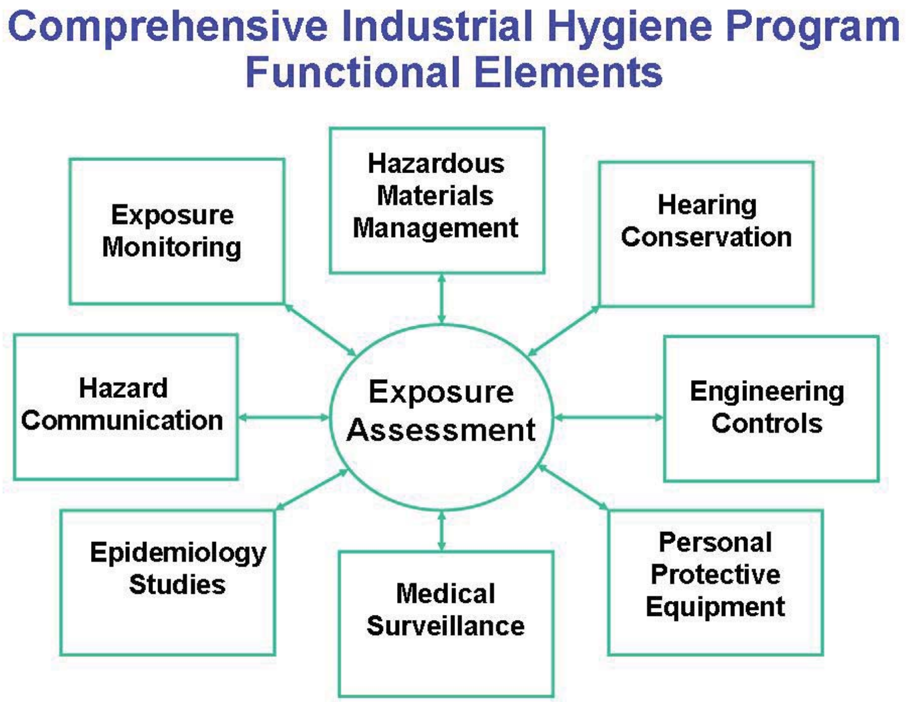


Figure 7.4. Illustration of essential elements of a comprehensive industrial hygiene program that can provide for effective exposure assessment and control in nanomanufacturing. Note that the illustration includes the inherent inclusion of the full spectrum of health risks associated with manufacturing (courtesy of Mark D. Hoover, NIOSH).

7.3 SPECIFIC EHS ISSUES FOR NANOMANUFACTURING

EHS concerns regarding nanomaterials are a large barrier for the commercialization of many nanotechnologies, particularly from the perspective of manufacturing safety and product lifecycle safety. EHS is an area where there is an opportunity for mutually beneficial, precompetitive research and development across all nanomanufacturing sectors. Critical to this effort is the development of a traceable measurement infrastructure and metrology that will enable the fate of nanoparticles to be tracked from their point of production, including as raw materials, to their end of use and disposal, either in raw form or in a product. This requires cross-cutting EHS efforts focused on research and development of instrumentation and analytical methods applicable to the nanoscale size-regime.

Existing instrumentation and analytical methods currently used for the determination of macroscale metrics, such as the amount or distribution (mass or volume), may need to be altered for nanomaterial assessments. Similarly, it may be necessary to modify existing instrumentation for the determination of the physical and chemical characteristics of nanoscale materials, or new instruments and approaches may need to be developed. Characteristics include purity, particle size and distribution, shape, crystal structure, composition, surface area, surface chemistry, surface charge, surface activity, and porosity. However, the product or its application ultimately determines what needs to be measured and how accurately.

A wide range of harmonized tools and methods are especially needed for the determination of such metrics and properties, particularly from a manufacturing perspective. Harmonized efforts will enable the measurements to be comparable from one source to the next. Moreover, representative reference species from broad classes of nanomaterials, both in pure and altered states (such as in solution, or environmental and biological media) are necessary in order to develop and evaluate measurement and characterization approaches. For example, portable particle monitoring technologies are currently in use for monitoring nanoparticle release in the manufacturing environment. However, the effects of nanoparticle size, shape, chemical composition, and surface chemical functionality on the performance of these devices have not been rigorously examined, largely due to the lack of well-defined nanoscale reference materials. Widespread EHS measurement and standards needs for chemical or physical property assessments of nanomaterials in nanomanufacturing are highlighted below.

Detection of Nanomaterials

Methods for identifying and accurately measuring the amount and type of nanomaterials in a manufacturing environment are not well developed. Moreover, such methods are lacking for identifying and assessing critical parameters related to nanomaterials in biological systems and the environment. The presence of materials in such media must be measured, as well as their fate and transport. Detection of nanomaterials is a key, fundamental measurement need for all of the industrial sectors represented at the workshop and is critically linked to chemical and physical property measurement needs. Methods are needed for detecting not only single particles but also particle populations and distributions. By-products and altered forms of materials, which may occur during the manufacturing process or during a material's biological or environmental residence time, also should be considered.

Purity and Homogeneity in Nanomaterials

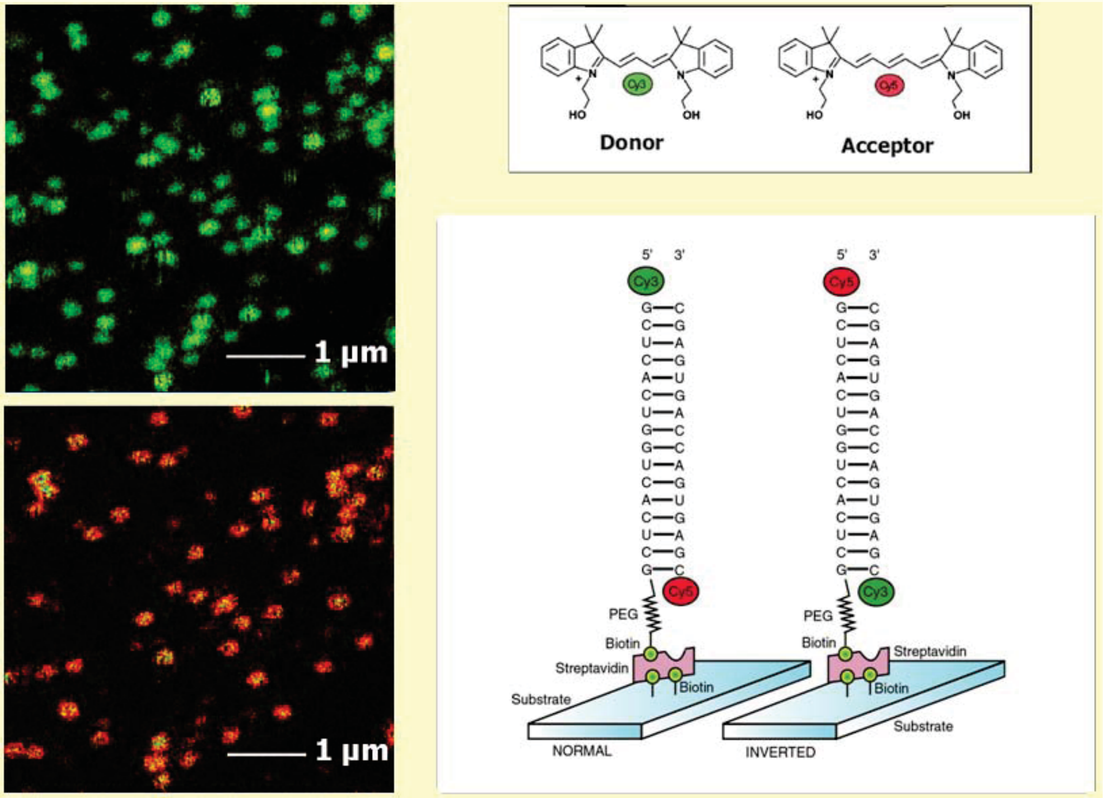
Purity and batch-to-batch variation in nanomaterial production are not well understood and are difficult to monitor in real time. As such, the ability to assess homogeneity in manufactured nanomaterials is lacking. For example, in-process tools are available to measure temperature, gas flow, pressure, and related properties, although such capabilities need to be linked to resulting properties of the products, such as the presence of defects. A range of optical methods, including photoluminescence, absorption, and Raman spectroscopies, may be applied to assess nanomaterial purities, although challenges still exist. For example, the presence of possible contaminants and by-products produced during nanomaterial syntheses may be determined through the use of analytical electron microscopy, field-emission scanning electron microscopy, or environmental scanning electron microscopy. However, microscopy approaches are dependent on statistics, and efficiencies change depending on the information needed (i.e., population or single-particle information). Contaminant concentrations associated with materials may be determined using instrumental neutron activation analysis, inductively-coupled plasma mass spectrometry, liquid chromatography mass spectrometry, gas chromatography mass spectrometry, x-ray microanalysis, and possibly capillary electrophoresis. However, modifications or enhancements to these methods may be necessary to apply them to nanomaterials. Also, validated measurement methods to assess purity of nanomaterials or to compare manufactured materials from different vendors are sparse or entirely lacking.

Single-Molecule Optical Measurements

Understanding the action of nanoparticles or biomolecules ultimately involves understanding the structure and dynamics of individual particles or molecules. The ability to measure individual molecules or bioreactions is a relatively new technology for which the metrology is still in its infancy.

Single-molecule optical measurements eliminate waste of expensive resources and reduce to a minimum the need to deal with harmful or toxic substances. Significant reductions in time and costs can be realized by using single molecule measurement techniques to replace laboratory processes that require amplification such as polymerase chain reaction (PCR). Reduction in costs and damage to the environment can be achieved by minimizing the use of expensive chemical reagents, which may pose significant health hazards when used in greater than trace quantities.

Metrology issues involve data acquisition and analysis as well as sample preparation and handling. Isolation, immobilization (when necessary), and chemical labeling of the species under investigation are the primary technical challenges facing industry regarding the use and reliability of single-molecule measurements. Modeling and data acquisition protocols for quantitative interpretation of fluorescence resonance energy transfer (FRET) are under development at NIST and elsewhere. Nanoencapsulation and labeling schemes that are minimally perturbative to a single molecule or a single nanobiosystem such as a molecular complex, virus, or organelle are also in the development phase. A good nano-encapsulation system will not change the functionality of the molecule or nanobiosystem under study.



Right: Schematic of RNA molecule attachment to glass surface showing placement of tether and dyes. Left: Donor (top) and acceptor (bottom) images of slide with attached RNA molecules. The green/red spots are individual donor/acceptor molecules. The ratio of donor to acceptor signal can be used to extract the probability of fluorescence resonance energy transfer, which in turn can be used to elucidate structure, kinetics, and dynamics (courtesy of NIST and Lori Goldner, University of Massachusetts).

Particle Size and Size Distribution of Nanomaterials

Rapid, statistically valid, methods are lacking for the measurement of the particle size and particle-size distribution of manufactured nanomaterials. Development of analytical tools for the characterization of nanoparticles by electron-beam analysis methods is needed to determine the true size, and in-process capability is needed. Improved measurement methods for particles that are less than 5 nm are critical for nanomanufacturing. Optical microscopy and spectroscopy may be feasible for nanomaterial characterization at <100 nm resolution using super-resolution optical microscopy. Methods that may have sufficient particle number sensitivities for the characterization of the size and number distribution of nanoparticles include differential light scattering, analytical ultra centrifugation, ion mobility classification, scanning tunneling microscopy, atomic force microscopy, and small angle scattering using x-ray or neutron sources. Development of automated microscopic methods for the rapid analysis and screening of a large number of nanomaterials is critical for nanomanufacturing. Correlations of electron microscopy with other size-measurement techniques, such as differential light scattering or field flow fractionation, would likely be useful for nanomanufacturers. In addition, separation techniques, such as liquid chromatography, size-exclusion chromatography, capillary electrophoresis, field flow fractionation, or microfluidic techniques, may be applicable to the determination of the size-distribution of manufactured nanoparticles at both the bench or preparative scale, the latter being preferred for manufacturing or process control.

Shape, Structure, and Surface Area of Nanomaterials

Many challenges exist for the determination of the shape, structure, and surface area of particles associated with nanomaterial production. Moreover, these characteristics are often required during manufacturing for not only large populations of nanoparticles but also for single particles. Conventional electron microscopy is not fast enough to provide population statistics necessary to sufficiently characterize the structure of nanomaterials. Single-atom analytical capabilities need to be developed as a primary calibration method and may be possible with aberration-corrected analytical electron microscopy. Aggregation of particles associated with nanomaterials may likely be determined using ion mobility mass spectrometry, although this has not been critically explored or evaluated, particularly for inline or in-process applications. Surface areas may be determined using classical BET (Brunauer, Emmet, and Teller) techniques, although these may need to be modified for accurate characterization of nanomaterials. Rapid, automated techniques are currently lacking for the determination of those metrics that are applicable during and after the production of nanomaterials.

Chemical Composition (Internal and External) of Nanomaterials

Existing methods for the accurate determination of the chemical composition of materials may need to be modified or enhanced in order to be applied to nanomaterials. For example, the Materials and Composites breakout group specifically identified the lack of instrumentation for mapping chemical composition and defects in the interfacial region of nanocomposites at nanoscale. New methods may be necessary, and application of such methods during manufacturing needs to be explored. A novel method for determining the core atomic composition as well as ligand composition and surface reactivity may be single-particle mass spectrometry. Three-dimensional chemical characterization of nanoparticles at the 1-nm resolution level is necessary for the accurate assessment of the chemical composition of nanoparticles. Applicable techniques include secondary ion mass spectrometry, x-ray photoelectron spectroscopy, Auger-electron spectroscopy, analytical electron microscopy, and x-ray microanalysis. Aspect ratios and chirality of nanomaterials may be determined by electron and optical microscopy, gas chromatography mass spectrometry, and liquid chromatography mass spectrometry. The surface charge of nanoparticles may be determined by using zeta potential measurement techniques, although standard operating procedures are lacking. Extremely fast techniques and harmonization of multiple methods are necessary for nanomanufacturing applications and need to be explored.

Modeling of Nanomaterial Interactions and Characteristics

A key area often overlooked for addressing EHS and measurement issues is the development of atomic-scale modeling efforts with respect to nanomaterials. These approaches can provide fundamental insight into their stability, an important issue in sample handling and processing. Atomic-scale modeling efforts may also assist with determining surface and material interactions such as metal-metal, ligand-metal, and ligand-ligand interactions. In addition, physical and chemical properties of nanomaterials may be computed using atomic-scale models. These results could enhance, advance, and guide experimental characterizations of the materials. Computational efforts are necessary to provide fundamental information for nanometrics and method development for nanomanufacturers.

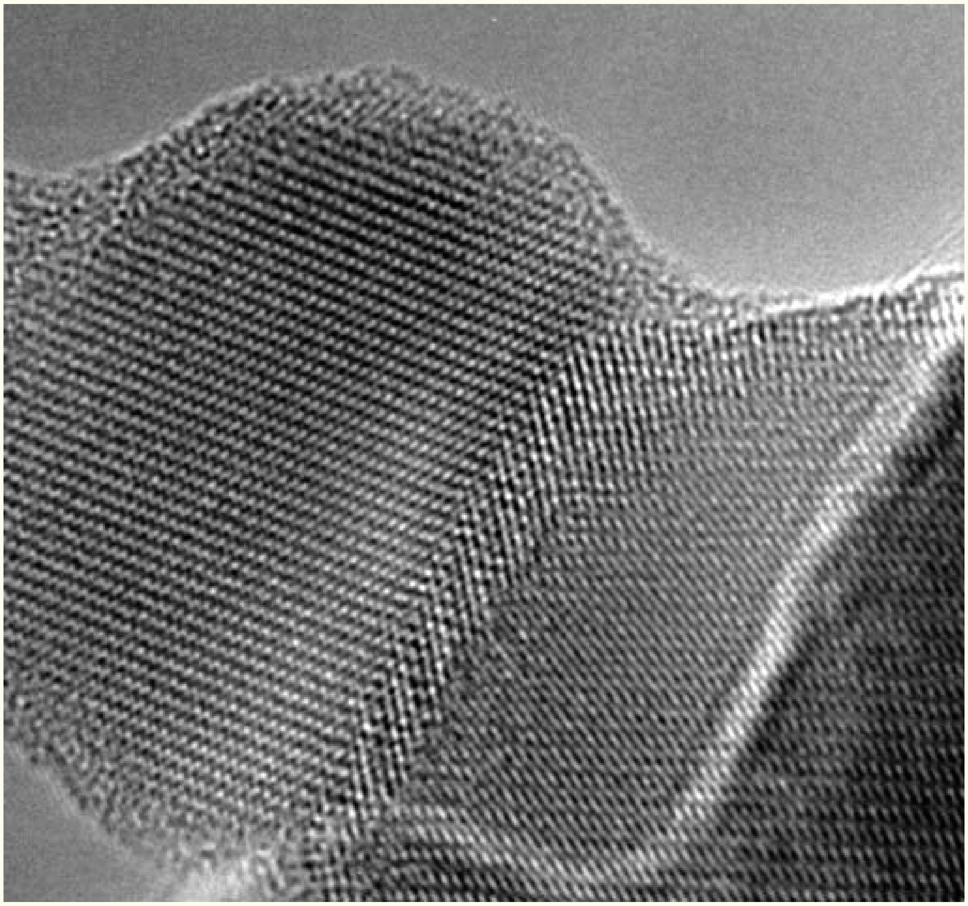
Nanoscale Reference Materials

Nanomaterial and nanoparticle reference materials of different media, size, chemical composition, surface chemical functionality, shape, and charge will enable traceability, calibration, and validation of measurement tools used in nanomanufacturing process monitoring and EHS applications. Media to consider include not only single-phase nanoparticles but also more complex systems where surfaces may be modified or enhanced. Carbon nanotube materials and nanogold materials are currently under development. The next generation should likely consider particle-based sunscreens, nanosilver, a suite of metal oxides, and possibly a composite of some type for the materials/composite industry. In particular, the need to define a roadmap for reference materials is clear. The interested parties should examine with respect to EHS issues, (a) widely available materials, (b) which materials have largest current and potential economic impact; (c) information already available; and (d) communities, users, and their requirements.

Microfluidics for EHS

Microfluidic methods for nanomanufacturing may provide avenues to assess EHS aspects of nanomaterials. In particular, such methods offer an opportunity to produce highly uniform particle formulations and enable direct observation during the formation process. Production of nanoparticles under such conditions may enable nanoparticle formulations for targeted delivery of imaging agents and therapeutic compounds produced in enough quantity and quality for efficacy and toxicology testing. Current methods for such nanoparticle formations produce nanoparticle distributions that have a large variation in size. Fluid flow in the microfluidic environment is laminar, meaning that there is no turbulence, so all the nanoparticles formed in this process see the exact same conditions, and very uniform particle distributions may be produced. In addition, microfluidic devices can be made on flat surfaces like a microscope slide so that formation of nanoparticles can be observed using a microscope, thereby enabling direct observation of the product. Real-time observations are lacking in many nanomanufacturing processes today, and this approach could be a feasible solution to such a need.

Nanoparticle Characterization by TEM



Energy-filtered transmission electron micrograph of two Tb-doped yttrium nanoparticles caught in the act of coalescence. The regular array of atom columns is clearly visible in each (crystalline) particle's center, while less ordered regions appear at the particle surfaces and the inter-particle interface. The entire field of view is about 12 nm (courtesy of John Henry Scott, NIST).

Transmission electron microscopy (TEM) is a powerful characterization tool for probing the atomic-scale structure and chemical heterogeneity of nanomaterials. Using electron beams typically ranging from 80 keV to 400 keV in energy, a wide variety of nanosamples can be imaged with a lateral spatial resolution well below 1 nm. All TEM instruments can be operated in a mode analogous to light microscopes, illuminating a wide analysis region with a broad, uniform electron beam and using electron lenses to project a magnified image on an area detector such as a CCD camera. Many modern TEMs can also be operated in a focused-probe mode (scanning transmission electron microscopy, STEM), where a small electron spot is rastered across the sample. Because STEM mode allows the beam to be stopped on a region of interest and chemical spectroscopies to be engaged, it is preferred for most analytical work.

The chief drawbacks to TEM are the need for very thin samples, often less than 100 nm, and the need to examine samples in a high vacuum environment. This last requirement, when coupled with the tendency for soft/organic materials to sustain damage under electron bombardment, is the chief difficulty in applying TEM analysis to nanobiological samples. Despite these barriers, innovative sample preparation techniques and clever experimental design have permitted TEM to make significant contributions to the characterization and visualization of these soft materials.

7.4 IMPLEMENTATION STRATEGIES

Nanoparticles and polymer nanocomposite technology comprise a broad and interdisciplinary research and development activity that has been growing rapidly worldwide in the past few years. Similar to other industries, the success of the nanocomposite industry relies on its ability to produce products that demonstrate high performance, are safe to fabricate and use, and cause no harmful effects to the environment. In addition to technical research and development challenges, EHS is a major cross-cutting issue. The goal is to protect workers as they produce and handle nanomaterials and members of the public as they use nanomaterials. A further goal is to prevent the dispersal of nanoparticles into the environment. Environmental topics necessary to consider, for example, include the effects of nanocomposite products when such products are disposed of in landfills. Products may be generated from mechanical erosion, thermal- and photodegradation, and burning of polymer nanocomposites. EHS issues that arise during manufacturing of composites and materials include the need to address pertinent chemical and particle-size information about nanoparticles in a product and the need to know stages and behavior of nanoparticles during processing so that appropriate engineering and environmental controls can be identified and implemented. In addition, it is necessary to monitor levels of nanoparticles in the indoor and outdoor environment, and the appropriate instrumentation and methods must be available to conduct such monitoring.

Implementation strategies are linked to the industry sector being impacted. For example, the semiconductor industry is exploring potential applications of nanoparticles with unique properties for application as device or interconnect elements in future integrated circuit technologies. These applications are currently over ten years from potential production applications but are in research. These approaches would need robust, compact, mobile metrology to monitor potential exposure of workers to nanoparticles and quantify particle size distributions and critical properties.

At one end of the spectrum, the semiconductor industry and others currently have the need for metrology that can detect and quantify nanoparticle distributions and properties critical to EHS in both air and liquids in a manufacturing environment. Although airborne nanoparticle monitors are available now for use in laboratories, they need to be more robust and mobile so they can monitor particles at nanoparticle process equipment during operation, especially when maintenance is being performed, and validate that personal protective equipment is effective in preventing worker exposure. Further, characterization of the critical properties that impact biological response is needed in order to establish effective metrics of dose and enable the metrology to monitor these properties and translate to an effective exposure dose to workers. In the case of nanoparticles in liquids, metrology would need to be established to monitor nanoparticle distributions in high and low concentrations as waste liquid is being processed. Further, as conventional semiconductor processing continues to reduce feature sizes, nanoparticles may be introduced into process chemicals making it necessary to monitor for nanoparticles at the process tools, including airborne, and liquid-based in the waste stream, as mentioned above.

On the other hand, the auto industry is at the end of the nanomaterial value chain. This industry does not itself directly produce nanoparticles, nor does it incorporate nanoparticles into products. Rather, this industry purchases vehicular components that contain nanoparticles. As time goes on, the list of nanomaterials in use on vehicles is increasing as engineers search for lighter-weight, yet stronger, materials. Some vehicle components that make use of nanotechnology today include tires, paints, bumpers, tribological coatings, and catalysts.

The growth of nanomaterials use within automotive vehicles is increasing faster than procedures are being formulated to address environmental, health, and safety concerns. It is not known if nanomaterials are being handled, because a Material Safety Data Sheet does not necessarily include information on whether nanoparticles are contained in a component. When it is not known if nanoparticles are present, then the next issue is whether nanoparticles are released during the processing of that part. As an example, are nanoparticles released to the air when paints containing nanoparticles are sprayed onto the car body? Or are nanoparticles mechanically generated when a nanocomposite truck bed is assembled onto the car body? Studies are just beginning on such topics.

Manufacturing plant air needs to be monitored for particle concentration and size characteristics to determine if nanoparticles are released during manufacture. If nanoparticles are found to be present in plant air, it is imperative to consider whether the plant's conventional air handling and conditioning system is effective against nanoparticles and whether it protects the workplace environment.

The comments above relate to nanomaterials and manufacturing issues. A complete lifecycle analysis should also consider the possible release of nanomaterials to the environment during product use and at the end of life. For instance, are carbon black nanoparticles in tires released to air, water, and/or soil systems as cars are driven on the road? When a truck is recycled and plastics are shredded, are carbon nanotubes released from the nanocomposite truck bed? When there is an accidental fire in a home containing products with nanoparticles, are the nanoparticles released to the environment?

At this time, there are more questions than answers concerning EHS and nanomaterials. Luckily, many industries have prior EHS experience in these areas, since workers are already protected against some types of small particles. But it is necessary to take a closer look at nanoparticles to ensure that all workers as well as the public and the environment are protected.

Turning to the chemical industry, it is actively engaged in the research, development, and manufacturing of nanoscale technologies with sustained economic and societal benefits. Chemical nanotechnology products have a technological and economic ripple effect because they are essential to other key industries, including health care, communications, food, clothing, housing, energy, electronics, and transportation. The Chemical Industry Vision2020 Technology Partnership has published a report outlining the joint chemical and semiconductor industry research recommendations on EHS of nanomaterials (Chemical Vision2020 n.d.). Also, in addition to the chemical and physical metrology needs highlighted above, the chemical industry needs better high-throughput characterization tools for EHS assessments of nanomaterials—either in-process or offline—for measurements in real-world manufacturing conditions; tools for measurements that can span multiple length and time scales simultaneously; tools for understanding chemical reactivity at system interfaces; and tools for measuring and visualizing chemical dynamics.

The Nano Risk Framework

The Environmental Defense Fund and DuPont have developed a framework for the responsible development, production, use, and end-of-life disposal or recycling of engineered nanoscale materials—that is, across a product's lifecycle. The "Nano Risk Framework" offers guidance on the key questions an organization should consider in developing applications of such materials, and on the critical information needed to make sound risk evaluations and risk management decisions. The framework allows users to address areas of incomplete or uncertain information by using reasonable assumptions and appropriate risk management practices. Further, the framework describes a system to guide information generation and update assumptions, decisions, and practices with new information as it becomes available. And the framework offers guidance on how to communicate information and decisions to stakeholders. The framework consists of six distinct steps. It is designed for iterative use as development advances and new information becomes available.

Step 1. Describe Material and Application. This first step is to develop a general description of the nanomaterial and its intended uses, based on information in the possession of the developer or in the literature. These general descriptions set up the more thorough reviews, in Step 2, of the material's properties, hazards, and exposures. The user also identifies analogous materials and applications that may help fill data gaps in this and other steps.

Step 2. Profile Lifecycle(s). The second step defines a process to develop three sets of profiles—of the nanomaterial's *properties*, inherent *hazards*, and associated *exposures* throughout the material's lifecycle. The properties profile identifies and characterizes a nanomaterial's physical and chemical properties. The hazard profile identifies and characterizes the nanomaterial's potential safety, health, and environmental hazards. And the exposure profile identifies and characterizes the opportunities for human or environmental exposure to the nanomaterial—including exposure through both intended use and accidental release.

Step 3. Evaluate Risks. In this step, all the information generated in the profiles is reviewed in order to identify and characterize the nature, magnitude, and probability of risks presented by this particular nanomaterial and its anticipated application. In so doing, the user considers gaps in the lifecycle profiles, prioritizes those gaps, and determines how to address them—either by generating data or by using, in place of such data, "reasonable worst case" assumptions or values.

Step 4. Assess Risk Management. Here the user evaluates the available options for managing the risks identified in Step 3 and recommends a course of action. Options include engineering controls, protective equipment, risk communication, and product or process modifications.

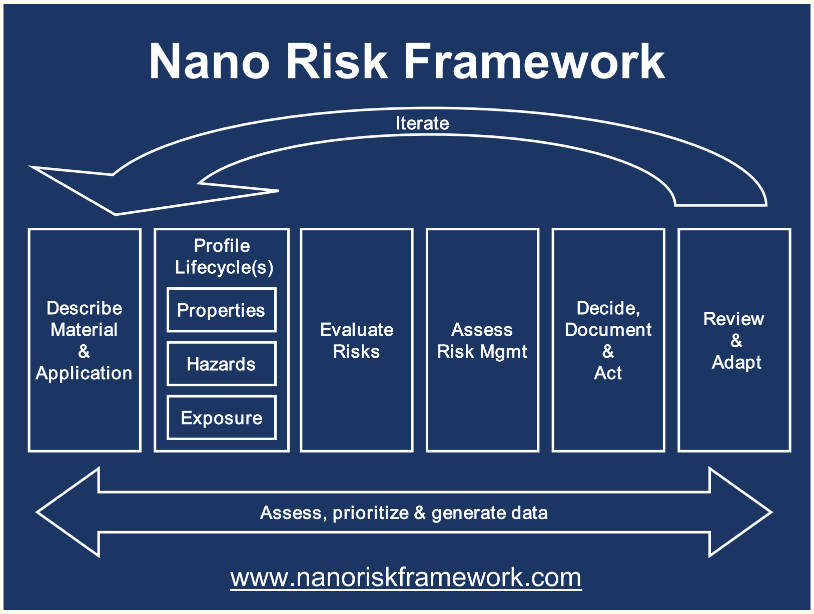
Step 5. Decide, Document, and Act. In this step, appropriate to the product's development stage, the user consults with the appropriate review team and decides whether or in what capacity to continue development and production. Consistent with a transparent decision-making process, the user documents those decisions and their rationale and shares appropriate information with the relevant stakeholders, both internal and external. The user may also decide that further information is needed and initiate action to gather it. And the user determines the timing and conditions that will trigger future updates and reviews of the risk evaluation and risk-management decisions for the nanomaterial or nanomaterial-containing product. An output worksheet for documenting information, assumptions, and decisions is provided in the appendix of the framework (see http://www.nanoriskframework.org).

Step 6. Review and Adapt. Through regularly scheduled reviews as well as triggered reviews, the user updates and re-executes the risk evaluation, ensures that risk-management systems are working as expected, and adapts those systems in the face of new information (e.g., regarding hazard data) or new conditions (such as new or altered exposure patterns). Reviews may be triggered by a number of situations (development milestones, changes in production or use, or new data on hazard or exposure,

The Nano Risk Framework

for example). As in Step 5, the user not only documents changes, decisions, and actions but also shares appropriate information with relevant stakeholders.

Through these six steps, the Nano Risk Framework seeks to guide a process for risk evaluation and management that is practical, comprehensive, transparent, and flexible.



The framework, an editable version of the framework's output worksheet, and case studies demonstrating its implementation on a variety of nanomaterials and applications are available for download at http://www.nanoriskframework.com (courtesy of Environmental Defense Fund).

Coordination with Other EHS and Roadmap Initiatives

As mentioned earlier in this chapter, there have been a number of reports stating the importance of continued and increasing research regarding potential EHS implications of nanomaterials. Three key reports are the Chemical Industry Vision2020 Technology Partnership report (n.d., ~2005), the U.S. National Nanotechnology Initiative (NNI) document that identifies EHS research and information needs (NSET 2006),[10] and the NIOSH Web document "Approaches to Safe Nanotechnology: An Information Exchange with NIOSH" (NIOSH 2006). It is hoped that these documents will assist industry in ensuring that proper precautions and measures are followed to ensure that no worker suffers material impairment of safety or health as nanotechnology develops. Coordination with the Federal and academic research communities and international standards development organizations is also essential to strengthen and fortify EHS efforts in nanomanufacturing. An example of a coordinated approach toward implementing new procedures for EHS is a partnership between the Environmental Defense Fund, a leading non-profit organization, and DuPont that looks to develop a framework for the responsible development, production, use, and end-of-life disposal or recycling of engineered nanoscale materials (see sidebar above, "The Nano Risk Framework").

---

[10] See also the subsequent NSET document, *Strategy for Nanotechnology-Related Environmental, Health, and Safety Research* (NSET 2008).

7.5 SUMMARY

Environmental, health, and safety issues are of concern to all industries employing or considering the use of nanotechnology-based products. Applications in the biomedical and pharmaceutical industries are among the most significant concerns, given that many of the products from these industries are intended to have direct contact with the human body. Participants in many of the sessions of this workshop were interested in issues associated with the potential toxicity of nanoparticles or products incorporating them. As a result, much of the discussion addressed issues related to the need for sound metrology, instrumentation, and standards for characterizing potentially toxic nanoparticles.

7.6 REFERENCES

Bullock W.H., and J.S. Ignacio, eds. 2006. *A strategy for assessing and managing occupational exposures,* 3rd ed. Fairfax, VA: American Industrial Hygiene Association.

Chemical Industry Vision2020 Technology Partnership (Chemical Vision2020), in partnership with the Semiconductor Research Corporation. N.d. (~2005). *Joint NNI-ChI CBAN and SRC CWG5 Nanotechnology research needs recommendations*, Available online: http://www.chemicalvision2020.org/pdfs/chem-semi%20ESH%20recommendations.pdf.

International Labour Organization (ILO). 2005. *Safework: Chemical control banding*. Available online: http://www.ilo.org/public/english/protection/safework/ctrl_banding/index.htm.

———. 2008. *International chemical control toolkit draft guidelines.* Available online: http://www.ilo.org/public/english/protection/safework/ctrl_banding/toolkit/main_guide.pdf (accessed January 7, 2008).

Maynard, A.D. 2005. “Engineered nanomaterials and occupational health.” Presentation at the Society of Toxicology, National Area Chapter. November 2, 2005, Washington, DC. Available online: http://www.nanotechproject.org/file_download/22.

Maynard, A.D., and R.J. Aitken. 2007. Assessing exposure to airborne nanomaterials: Current abilities and future requirements. *Nanotoxicology* 1:26–41.

Nanoscale Science, Engineering, and Technology Subcommittee (NSET), Committee on Technology, National Science and Technology Council. 2006. *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*. Washington, DC: NSET. Available online: http://www.nano.gov/NNI_EHS_research_needs.pdf.

———. 2008. *Strategy for Nanotechnology-Related Environmental, Health, and Safety Research*. Washington, DC: NSET. Available online: http://www.nano.gov/NNI_EHS_Research_Strategy.pdf.

National Institute for Occupational Safety and Health (NIOSH). 2006. Approaches to safe nanotechnology: An information exchange with NIOSH (draft for public comment). Atlanta, GA: Centers for Disease Control and Prevention. Available online: http://www.cdc.gov/niosh/topics/nanotech/safenano/.

Schulte, P.A., C.L. Geraci, R.D. Zumwalde, M.D. Hoover, and E.D. Kuempel. 2008. Occupational risk management of nanoparticles. *Journal of Occupational and Environmental Hygiene* 5(4):239-249.

8. CONCLUSIONS

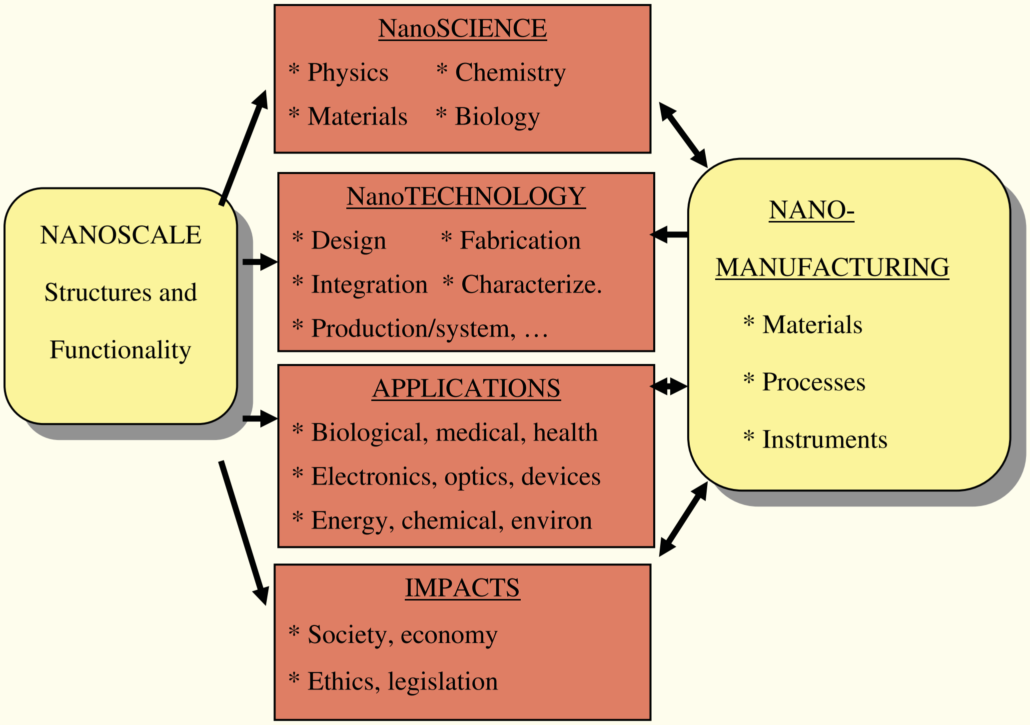
Nanotechnology contributions to end-of-road and beyond-CMOS will likely introduce new materials and modalities into information technology devices, including photonics; plasmonics; spintronics; printable, flexible, other inexpensive organic electronics; and MEMS/NEMS. The circuits will also incorporate more 3D structures. The introduction of these new modalities will require new nanometrologies. Information technology devices at the nanoscale will pose major challenges for reliability and manufacturability. As the density of ever smaller devices grows, it becomes ever more difficult to pattern and process those devices. It is likely that appropriate functional nanostructures will be grown and then incorporated into chip-scale architectures. This poses significant challenges for directed, hierarchical self-assembly.

Modeling of macroscopic properties of nanomaterials is crucial for enabling the design of high-performance applications in the chemicals, electronics, pharma/bio, and composites industries. In October 2006 representatives from NIST, DOE, NSF, NIH, and DOD met with approximately 60 stakeholders from industry, government research labs, government agencies, and academic institutions. Multiple industries identified the need for predictive models of nanomaterial synthesis, electronic properties, surface chemical reactivity, and mechanical and interface properties of nanostructured materials. Each of these would need fundamental algorithm development and experiments designed to validate the physics of the models. Industry should consider establishing a "pathfinder" or test case vehicle based on the current best-in-class modeling capabilities to guide the many possible avenues of exploration. The development of models of these predictive capabilities will be a long-term effort and may require different interaction models with each of the Federal agencies.

Realizing the societal and commercial potential of nanomanufacturing will require an effective platform for communication and information management, a system one may call a "nanomanufacturing-informatics network." The significant investment in nanotech R&D from Federal and private sources has resulted in an incredibly strong array of technical innovations, mostly at the proof-of-concept level, with more developing continually. At the same time, manufacturing advancements are needed to fuel the development of new products with compelling economic and societal impact. The use of current and emerging Web-based information and social networking technologies to match up the information and collaborative needs of academic, industry, and government stakeholders has the potential to greatly improve the efficiency of nanomanufacturing research and product development in the United States.

This need can be well served by a strong, open-access network and digital information clearinghouse that serves to support the needs of the nanomanufacturing community. The benefits of the open-access paradigm have been appreciated in the software and academic research communities for many years. Several companies have started to take full advantage of an open innovation paradigm for product development in which they no longer rely solely on expensive in-house R&D but rather use a relational network to find target solutions outside the company (Christensen, Olesen, and Kjær 2005). The "Connect and Develop" model used by Proctor & Gamble is one example (Huston and Sakkab 2006). The open innovation concept can be used to strengthen the nanomanufacturing R&D community in order to match technical innovations and product applications and also to efficiently advance nanomanufacturing research itself. An example of the latter might be the integration of a newly developed metrological sensing technique to provide better real-time, inline control of an emergent nanomanufacturing process.

National Science Foundation Supports Nanomanufacturing Through Nanoscale Science and Engineering Centers



(Figure is courtesy of NSF; see http://www.nsecnetworks.net/ for more information.)

The National Science Foundation (NSF) supports nine Nanoscale Science and Engineering Centers (NSECs) designed to bring together researchers with diverse expertise. The goal is the development of partnerships with industry, government laboratories, and partners from other sectors to address complex, interdisciplinary challenges in nanoscale science and engineering. The centers' efforts span the range from exploratory research to technology innovation, and incorporate a well-integrated research and education plan, and a strong effort in human resource development and societal impact. Four centers—Northeastern University; University of Illinois at Urbana Champaign; University of California, Los Angeles; and University of Massachusetts Amherst—are focused on manufacturing at the nanoscale. These centers emphasize fundamental research addressing advances in high-throughput, high-volume, and high-rate (scale-up) processes and integration of nanoscale elements and integration across the nano-micro-meso-macro size scales. Outreach and knowledge transfer are critical components in timely transition of center discoveries into the marketplace.

Nanomanufacturing research and product development frequently requires the collaboration of interdisciplinary workers and the integration of diverse technical topics. It is clear that a platform of communication and information management must provide effective nano-interoperability. Since distinct disciplines tend to develop their own research vocabularies, it is important either to encourage the use of a common nanomanufacturing vocabulary or to provide tools for the translation of terms between disciplines. Efforts on this issue must be made to be in sync with the national and international standards committees. The Cancer Biomedical Informatics Grid (caBIG) web portal (https://cabig.nci.nih.gov/) of the NIH National Cancer Institute provides an analogous example of research information management and technical vocabulary tools.

Although knowledge management database software exists to address some of the specific present-day EHS information management needs, a significant amount of middleware development will be needed in order to meet the evolving interoperability needs of the nanomanufacturing community. It is clear that utilizing present-day community-based, social networking web technologies (Web 2.0) can provide an efficient mechanism for facilitating interactions among members of this community. Looking to the future, efforts must be made to work closely with the Semantic Web informatics research community to employ emerging information networking and analysis techniques to further improve the efficiency of the developing "nanoinformatics" platform.

At the nanoscale, information technology devices will have the same dimensions as the molecules associated with physiology of living systems. This will open new possibilities for sense and response between the abiotic IT devices and those molecules. New technologies for diagnostics and therapeutics should follow from this facilitated interaction.

Finally, a major conclusion of the workshop is that there is a strong synergy between all of the working groups in regard to the concern for health-related lifecycle issues in manufacturing, especially those related to the measurement of nanoparticles. There is also a strong desire to develop a "consortium" of interested industries to pursue the needed research to push forward the concept of "materials by design," including the needed instrumentation, measurements, and modeling that are necessary to make this successful.

In addition, some of the research needs called out by each group are recapped below:

8.1 CHEMICALS

- Define a roadmap to develop standard reference materials for nanomanufacturing.
- Define standard operating procedures (SOPs) for the synthesis of nanomaterials and sample preparation procedures for measuring, handling, and storing these materials.
- Develop standard metadata formats for the capture, storage, and interpretation of raw data so that data pedigree and quality can be evaluated. Examples from other communities include the standard crystallography structure format or the minimum information about micro-array experiment (MIAME).
- Establish and populate a database of physical property data for nanomaterials. Examples of existing databases include the NIST Chemical WebBook.
- Provide funding and support for badly needed ("non-glamorous") systematic studies to measure the physical properties of nanomaterials.
- Support development of predictive multiscale models to discover new materials based on physical property data and reference materials, and for process development, control, and predicting product performance and lifecycle.
- Develop instrumentation for real-time process development, scale-up, and control; for quality control; and for EHS monitoring and control.
- Develop advanced, offline materials characterization tools that emphasize ways to increase the functionality of AFM, SEM, TEM, etc., making the tools multifunctional and capable of working with combinatorial methods.
- Organize a limited roadmapping activity on chemical nanomanufacturing, in which the highest-priority topics would probably include work on reference materials, nanoscale catalysts, and instrumentation for nanomanufacturing.

- Identify a few model systems (e.g., the next "fruit fly" or the gold nanoparticle reference material) that are of interest to multiple agencies and industries and would be of highest priority to explore in a coordinated program. Potential candidates include CNTs for purity and separation (an initial project is underway at NIST/NASA); ultrathin films of $Si0_2$ for dimensional metrology; GaN nanowires; ceramic-supported platinum; metal oxides (e.g., inert, catalytic, etc.); and standard reference nanocomposites.
- Develop tools for measurement that are capable of spanning multiple length and time scales simultaneously.
- Develop tools for understanding chemical reactivity at the interfaces.
- Develop tools for measuring and visualizing chemical dynamics; time-resolved chemistry.

8.2 ELECTRONICS, MAGNETICS, AND PHOTONICS

- Metrology that is capable of characterizing dynamic changes in local dipole alignment, spin orientation, stress, and plasmon properties to better enable the understanding of the coupling of the phenomena. Some of the possible capabilities include high-resolution photoelectron emission microscopy, x-ray phase sensitive reflection, near field microscopy with SiC superlenses, AFM/capacitance and impedance spectroscopy.
- Research that enables simultaneous characterization of nanostructure and multiple properties at the nanometer scale. Research should be pursued in sources, the physics of the source-probe-sample interaction, novel detectors, and especially models to enable decoupling the probe sample interactions and delineate the structure and properties, including novel probe techniques that can monitor the dynamic response of multiple properties to applied stimuli.
- Scanning probes with atomic control of the tip and shape.
- Novel probes that can detect spin, plasmons, molecular state, etc., with atomic resolution at surfaces and interfaces.
- Metrology that can characterize the control of self-assembled features and their alignment to previously fabricated structures.
- Miniaturized instruments for process monitoring and control.
- Reference structures for metrology, especially structures along the lines of the discovery platform model whereby a standard wafer is fabricated with a number of structures and functions on its surface on which researchers can deposit their own electronic layers, interconnects, and devices.
- Real-time tools for monitoring self-assembly processes, including 3D methods capable of probing through layer depths, e.g., primary inspection techniques such as ellipsometry or Raman, higher-resolution secondary techniques, registry tools to integrate bottom-up with top-down self-assembly processes.
- Centralized facilities with experts available for enabling the development and use of exotic and emerging techniques.
- Protection of intellectual property, e.g., SBIR funding support for small business use of public facilities for proprietary research.

8.3 PHARMACEUTICALS/BIOMED

- Real-time protein binding and control instrumentation.
- National characterization facility with expertise and means to conduct preclinical characterization of nanotechnology-enabled pharmaceutical products.
- New tools capable of imaging living biological structures at the nanometer scale without damaging or killing them.
- Instruments compatible with the environment required for living biological samples.
- Standard processes for creating uniform nanoparticles for test and characterization.
- Instrumentation for observing nanoparticle formation to support development of models for formation process.
- Tools for real-time monitoring of manufacturing processes.
- Development of synergy between nanobiotechnology and systems.
- Standard methodology to define size, shape, concentration, and other physical parameters.
- Investigation into the applicability/feasibility of microfluidics techniques for manufacturing processes and in addressing EHS concerns.
- A distributed repository of biological and physical characterization data for nanoparticles, especially toxicity; a network of databases linking size, shape, concentration, and other physical parameters to properties, functions, and toxicity.
- Ontologies/data dictionaries (e.g., similar to the program already in place in the cancer research community); XML-based applications and object-models.
- National facilities for preclinical characterization of nanoparticles.
- Coordinated development of prioritized list of standard reference materials.
- Coordinated development of standard test protocols for toxicity.

8.4 COMPOSITES

- Computational models for nanocomposites that provide predictive capability for correlating electrical, thermal, mechanical, and acoustic properties to the synthesis and manufacturing processes and quality-control metrics.
- New instruments or combinations of instruments to evaluate dispersion of nanoparticles during synthesis, throughout the manufacturing process, and into the final manufactured part.
- Framework to characterize changes in the matrix due to addition of nanoparticles (interphase) such as the creation of new crystal morphologies, distortions in polymer chain conformation, or mobility.
- New instrumentation to characterize the adhesion between the matrix and the nanoparticle, measurement methods for stress transfer, and kinetics.
- Framework to characterize the changes to composite properties upon addition of nanoparticles (rheology, strength, toughness, conductivity, permeability) with the size, interfacial chemistry, and intrinsic properties of the nanoparticles.
- Framework to characterize how the changes in matrix structure and composite properties affect the performance of the composite in applications (product stability, processability, spreadability, vapor-barrier properties, heat deflection, etc.).

- Framework to characterize nanoparticles that are introduced directly into a fibrous preform independently from the matrix via processes such as chemical vapor deposition, and to link these characteristics to resultant composite properties.
- Instrumentation that can ascertain the complex relationship between processing, rheology, and final properties (such as conductivity) in order to design cost-effective strategies for manufacturing materials using existing equipment in which sizable capital expenditures have already been made.
- Solution-based metrologies to disperse nanoparticles so that advanced characterization studies can be carried out.
- Nanostructured materials that will facilitate cross-laboratory comparisons and trade, and serve as the basis of testing for environmental, health, and safety effects.
- Development of standard characterization methods unique to each class of material: nanotubes, clays, fibers, and nanoparticles. Reliable metrics for measurement of dimensions, electronic and optical properties. There is a critical need to develop metrologies that will rapidly measure large numbers of particles (100s or 1000s) so that accurate statistics of particle distributions can be obtained.
- Three-dimensional visualization of structure at the nanoscale. Transport phenomena, such as electrical and thermal conduction, stress transfer, and viscous dissipation, are governed by particle-particle interactions as mediated by the matrix. The ability to observe the structure of the nanoparticles in its three-dimensional matrix would enable development of better models of the transport.
- Nanoscale nondestructive techniques to probe the buried interfaces; tools that can monitor, *in situ*, the fabrication and properties of nanocomposites.
- New or expanded NNI centers and/or user facilities that deal exclusively with metrologies for polymer nanocomposites, their processing, or their properties.

8.5 ENVIRONMENTAL, HEALTH, AND SAFETY ISSUES

During the workshop the subject of instrumentation, metrology, and standards for environmental, health, and safety (EHS) was identified as a cross-cutting issue applying to all of the potential industrial applications of nanotechnology. Research needs related to these issues are discussed in Chapter 7 of this report. Several recent National Nanotechnology Initiative documents also lay out nanotechnology-related EHS research needs, including in the instrumentation, metrology and standards arena (NSET 2006; NSET 2008).

8.6 REFERENCES

Christensen, J.F. M.H. Olesen, and J.S. Kjær. 2005. The industrial dynamics of open innovation: Evidence from the transformation of consumer electronics. *Research Policy* 34:1533.

Huston, L., and N. Sakkab. 2006. Connect and develop: Inside Procter & Gamble's new model for innovation. *Harvard Business Review* 84(3):58–66.

Nanoscale Science, Engineering, and Technology Subcommittee (NSET), Committee on Technology, National Science and Technology Council. 2006. *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*. Washington, DC: NSET. Available online: http://www.nano.gov/NNI_EHS_research_needs.pdf.

———. 2008. *Strategy for Nanotechnology-Related Environmental, Health, and Safety Research*. Washington, DC: NSET. Available online: http://www.nano.gov/NNI_EHS_Research_Strategy.pdf.

APPENDICES

APPENDIX A. AGENDA

Day 1 Tuesday October 17

7:30 Coffee (Provided by NanoMech, LLC)

8:20 Welcome. William Jeffrey, Director, NIST; Dale Hall, Interagency Working Group (IWG) on Manufacturing Research and Development (R&D), National Institute of Standards and Technology, Gaithersburg, MD

8:30 Introduction and Review of the Research Needs Identified in the 2004 Instrumentation and Metrology Workshop. Michael T. Postek, Assistant to the NIST Director for Nanotechnology, National Institute of Standards and Technology, Gaithersburg, MD

8:45 Introduction to the Toward Predictive NanoMaterial Design Session. Dan Herr, Material and Process Sciences Research, Semiconductor Research Corporation, Durham, NC

8:50 Nanometrologies Needed for the Monolithic Fabrication of Nanoscale Electronic Devices and Circuits. Skip Rung, President and Executive Director, Oregon Nanoscience and Microtechnologies Institute (ONAMI) Corvallis, OR

9:10 Nanometrology Challenges Facing the Chemical Industry. Donald B. Anthony, President and Executive Director, the Council for Chemical Research, Washington, DC.

9:30 Past, Present, and Future Challenges for Nanomaterials Manufacturing at DuPont. Gregory S. Blackman, Sr. Research Associate DuPont CR&D / Corporate Center for Analytical Sciences, Wilmington, DE.

9:50 Challenges and opportunities in nanotechnology for aerospace. Thomas Tsotsis, Technical Fellow, Boeing Phantom Works, Boeing Company Huntington Beach, CA.

10:10 Break (Provided by NanoMech, LLC)

10:30 Research Priorities for Analytical Methods for Characterization of Lignocellulosic Materials. Lori A. Perine, Executive Director, Policy Analysis & Research and Agenda 2020 Technology Alliance, American Forest & Paper Association, Washington DC.

10:50 Challenges and opportunities in nanotechnology for the automotive industry. Jean Dasch, Senior Staff Research Scientist, General Motors Research and Development, Detroit, MI

11:10 Measurement Challenges for Carbon Nanotube Material. Sivaram Arepalli, Staff Scientist, ERC Inc. and NASA Johnson Space Center, Materials and Manufacturing Division, Houston, TX

11:30 Metrology Challenges for Emerging Nanotechnology Manufacturing. Robert Geer, Assistant Vice President for Academic Affairs and Associate Professor of Nanoscience College of Nanoscale Science and Engineering, Albany NanoTech, NY.

11:45 Real Time Excursion Control for Nanomanufacturing Effectiveness. Erez Golan, Technology Project Manager, Applied Materials, Inc. and the College of Nanoscale Science and Engineering - NanoEconomic Program. Albany NanoTech, NY.

12:00 Lunch

01:30 Breakout Session Set 1

Electronics

Composites/Materials

Pharma/Biomedical

Chemical

03:00 Break (Provided by NanoMech, LLC)

03:15 Breakout Session (continued)

05:45 Bus or Drive to NIST Advanced Measurement Laboratory

06:00 Reception (Provided by Maryland Department of Economic and Business Development and FEI, Company) Food/Drink, Posters, Table Top exhibits, Laboratory Visits (7 PM)

08:00 Return via bus or car back to hotel

Day 2 Wednesday October 18

07:30 Coffee (Provided by Hitachi High Technologies America)

08:30 Process Check

08:45 Breakout Report-out 1a Electronics

09:00 Breakout Report-out 1b Composites/Materials

09:15 Breakout Report-out 1c Pharma/Biomedical

09:30 Breakout Report-out 1d Chemical

09:45 Group Discussion – Q and A

10:00 Break (Provided by Hitachi High Technologies America)

10:30 Metrology Challenges for Nanotechnology – A Semiconductor Manufacturer's Perspective. John Allgair, International SEMATECH Manufacturing Initiative, Austin TX.

10:50 Metrology and Instrumentation Challenges in Nanomanufacturing. John Randall, Chief Technical Officer, Zyvex Corporation, Dallas TX.

11:10 Making predictions...Measuring Progress. Michael N. Thompson, Business Development Manager – Nanotechnology, FEI Company, Hillsboro, OR

11:30 An Industry Perspective on the need for Measurement and Metrology Standards for Nanotechnology. Jonathan Tucker, Lead Marketing Engineer - Nanotechnology, Keithley Instruments, Cleveland OH.

11:50 Challenges and Opportunities in Nanotechnology in nanobiotechnology. Deb Newberry, President, Newberry Technologies, Inc. and Dakota County Community College, Rosemount, Minnesota

12:10 Lunch

01:30 Breakout Set 2

03:00 Break (Provided by Hitachi High Technologies America)

03:15 Breakout Set 2 (continued)

05:15 Dinner (on your own)

Day 3 Thursday, October 19

07:30 Coffee (Provided by Ben Franklin Technology Partners, MANA, and the Nanotechnology Institute)

08:30 Process Check

08:45 Breakout Report-out 2a Electronics

09:00 Breakout Report-out 2b Composites/Materials

09:15 Breakout Report-out 2c Pharma/Biomedical

09:30 Breakout Report-out 2d Chemical

09:45 Group Discussion – Q and A

10:00 Break (Provided by Ben Franklin Technology Partners, MANA and the Nanotechnology Institute)

10:30 Separate into writing groups develop assignments

12:00 Lunch

01:00 Toward Predictive NanoMaterial Design (Experimentation, Metrology, EHS, Modeling and Critical Algorithms) Michael Garner, INTEL, Santa Clara; Dan Herr, Semiconductor Research Corporation, Durham, NC; and Donald B. Anthony, Council for Chemical Research, Washington, DC; and others TBD (moderators)

3:00 Break (Provided by Ben Franklin Technology Partners, MANA, and the Nanotechnology Institute)

3:30 Resume Session

5:00 End of Workshop

APPENDIX B. LIST OF WORKSHOP PARTICIPANTS AND REPORT CONTRIBUTORS[†]

Hassan Ali
WTEC

John Allgair
ISMI / Freescale

Clare Allocca
NIST

Joseph Anderson
Camber Corporation

Donald Anthony
Council for Chemical Research

Sivaram Arepalli
ERC, Inc.
NASA Johnson Space Center

George Arnold
NIST

Amit Bagchi
National Institute of Standards and Technology

Ellyn Beary
NIST

Kathryn Beers
NIST

Ananthamurthy Bettadapur
Naval Surface Warfare Center

Gregory Blackman
DuPont

Susan Brainerd
NIST

Stanley Brown
Center for Devices and Radiological Health, FDA

Tom Campbell
ADA Technologies, Inc.

Altaf Carim
DOE

Alfred Carasso
NIST

Richard Cavanagh
NIST

John Carruthers
Portland State University

Anne Chaka
NIST

Shaochen Chen
The University of Texas

Guangjun Cheng
NIST/UMCP

Sun Cheng
SINAM, UC Berkeley

Inchan Choi
Naval Surface Warfare Center

Flora Chow
Environmental Protection Agency

Richard Colton
Naval Research Laboratory

Nicholas Dagalakis
NIST

Jean Dasch
General Motors R&D Center

Dwayne Davis
Consumer Product Safety Commission

Mark DeGrandpre
Ben Franklin Technology Partners

David DePaoli
Oak Ridge National Laboratory

Alain Diebold
SEMATECH

Frank DiMeo
SAIC

Richard Doyle
IEEE

Madan Dubey
U.S. Army Research Lab

Jeremiah Duncan
EPA

Franklin Dunmore
U.S. Consumer Product Safety Commission

Travis Earles
National Cancer Institute

Ivy Estabrooke
DOD

Sam Fain
University of Washington

Reginald Farrow
New Jersey Institute of Technology

Placidus Ferreira
University of Illinois

[†] Institutional affiliations as of October 2006

John Festa
American & Forest Paper Association

James Fitz-Gerald
University of Virginia

David Forman
Small Times

Aaron Forster
NIST

Chris Foster
Maryland Department of Business and Economic Development

Martin Fritts
SAIC-Frederick

Joseph Fu
NIST

Cedric Gagnon
Western Michigan University

Michael Gaitan
NIST

Michael Garner
Intel

Robert Geer
University at Albany, SUNY

Erez Golan
University at Albany, CNSE

Ms. Marilyn Gorsuch
SPIE

Stephen Gould
WTEC

Ed Griffith
FEI Company

Satyandra Gupta
University of Maryland, College Park

Dale Hall
NIST

Diane Hannemann
NIH

Takumi Hawa
NIST

Jennifer Hay
MTS Systems Corporation

George Hazelrigg
National Science Foundation

Daniel Herr
Semiconductor Research Corporation

Geoff Holdridge
NNCO

Stephanie Hooker
NIST

Mark Hoover
CDC-NIOSH

Roan Horning
WTEC

Louis Hornyak
University of Denver
NanoThread, Inc.

Steve Hudson
NIST

Karen Hunter
USDA/CSREES

William Jeffrey
NIST

Jeffrey Jordan
NanoDynamics

David Joy
University of Tennessee
ORNL

Yung Joon Jung
Northeastern University

Valliappa Kalyanasundaram
University of Arkansas

Alamgir Karim
NIST

Claire Kammer
Underwriters Laboratories, Inc.

Joon Won Kang
Honeywell

Goran Karapetrov
Argonne National Laboratory

Byungki Kim
University of Massachusetts

Beverly Klemme
Sandia National Laboratories

Annette Kolodzie
FEI Company

Arnaldo Laracuente
Naval Research Laboratory

David Larson
Imago Scientific Instruments Corp.

Thomas LeBrun
NIST

Virginia Lee
EPA

Stephen Lehrman
Office of Senator Pryor

James Liddle
NIST

Jeffrey Lindemuth
Lake Shore Cryotronics

Philip Lippel
NNCO

Kathy Lu
Virginia Polytechnic Institute

James Lynch
NIST

Kevin Lyons
NSF and NIST

Ted Maher
NIST

Roderick Mahoney
Sandia National Laboratories

Ajay Malshe
University of Arkansas
NanoMech LLC

Purabi Mazumdar
NIST

Page McAndrew
Arkema, Inc.

Christophe McCray
Office of Naval Research

Keith McIver
Boeing Phantom Works

Len McNally
Honeywell International, Inc.

Michael Meador
NASA Glenn Research Center

Alfredo Mendoza
Baxter Bioscience

M. Pinar Menguc
University of Kentucky

Emily Ann Meyer
National Academies of Science

Nancy Miller
NIH

Sonia Miller
S.E. Miller Law Firm

Linda Molnar
National Cancer Institute

Vladimir Murashov
NIOSH

James Murday
Naval Research Laboratory

Ghulam Mustafa
Crossing Automation

Emren Nalbant-Esenturk
NIST

Deb Newberry
Newberry Technologies
Dakota County Technical College

Tinh Nguyen
NIST

Mylene Ouimette
NIST

Rahmi Ozisik
Rensselaer Polytechnic Institute

Gerald Pate
Defense Threat Reduction Agency

Prahalad Parthangal
University of Maryland, College Park

Lori Perine
American Forest & Paper Association

Matt Perry
Maryland Department of Business and Economic Development

Dan Pierce
NIST

Anne Plant
NIST

Walter Polansky
DOE

James Poppiti
DOE

Michael Postek
NIST

Dianne Poster
NIST

Kambiz Pourrezaei
Drexel University

Dan Powell
NASA Goddard Space Flight Center

Jon Pratt
NIST

David Prigel
National Nuclear Security Administration

Michael Rabideau
ACH-LLC

John Randall
Zyvex Corporation

Joel Recht
Consumer Product Safety Commission

Mihail Roco
NSF

Robert D. Rung
Oregon Nanoscience and Microtechnologies Institute

Robab Safa-Bakhsh
The Boeing Company

Jay Satin
Maryland Department of Business and Economic Development

Nora Savage
EPA

Phil Sayre
EPA

John Henry Scott
NIST

David Seiler
NIST

Gordon Shaw
NIST

Jeffrey Simpson
NIST

Sharon Smith
Lockheed Martin Corporation

Santiago Solares
University of Maryland

Bob Sommewille
Ångstrom Scientific, Inc.

Edward Sosa
NASA

Scott Stanley
NIST

David Stieren
NIST

Stephan Stranick
NIST

Ulrich Strom
NSF

Li-Piin Sung
NIST

Treye Thomas
U.S. Consumer Product Safety Commission

Michael Thompson
FEI Company

Milos Toth
FEI Company

De-Hao Tsai
NIST

Thomas Tsotsis
The Boeing Company

Jonathan Tucker
Keithley Instruments, Inc.

Mark Tuominen
University of Massachusetts Amherst

Roger van Zee
NNCO/NIST

Ashok Vaseashta
Marshall University

Gary Ventry
Maryland Department of Business and Economic Development.

Theodore Vorburger
NIST

Craig Wall
Agilent Technologies

Chengqing Wang
NIST

Kang Wang
UCLA

James Watkins
University of Massachusetts Amherst

Robert Wiggins
U.S. Department of Labor

Claude Wilson*

Raymond Wittig
SAIC

John Wolfe
University of Houston

David Wollman
NIST

Tamae Wong
National Research Council of the National Academies

Zhenqi Zhu
Stevens Institute of Technology

APPENDIX C. NANOSCALE CHARACTERIZATION TOOLS AND CAPABILITIES

As discussed in previously in Chapter 6 of this report, a description is needed of the current state of the art for nanoscale measurements. Nanoscale measurements can be divided into two families: (1) nanoscale measurements that examine ensembles of nanoconstituents and (2) nanoscale measurements that examine nanoconstituents individually. The following tables, one for each family of measurements, describe many of the characterization techniques currently available and their respective capabilities and limitations. Although the focus of these tables is on application to nanocomposites, much of the same information applies to other application areas discussed in this report.

Table C.1
Nanoscale Measurements for Ensembles of Nanoconstituents

Characterization Tool	Nanocomposite measurement	Measured Properties	How It Works	Range
SANS (small angle neutron scattering)	Gross dispersion, and nanoconstituent ordering and orientation in the composite matrix	Structural information; the structural arrangement of atoms-planes, molecules, types of vibrations that occur in solids	A sample is placed in a collimated neutron beam. The samples scatters neutrons with $0.05^\circ \leq 2\theta \leq 3^\circ$	0.5nm to 500 nm
SAXS (small angle x-ray scattering)	Gross dispersion, and nanoconstituent ordering and orientation in the composite matrix	Structural arrangement of atoms	A sample is placed in an x-ray beam and the very low angle scattered electrons are analyzed	1nm to 300 nm
XRD (x-ray diffraction)	Interfacial information about the nanoconstituent and the matrix	Crystallographic information; crystal structure, interplaner differences, miller indices; SAXRD gives information about film thickness, interface roughness and surface topology	A sample is placed in an x-ray beam and the beam is diffracted by the periodic lattice of the crystalline material according to Bragg's law. The intensity in nanocomposite samples is very weak and usually requires a synchrotron source	In the vertical direction the resolution is <1 nm
Neutron Diffraction	Interfacial information about the nanoconstituent and the matrix	Atomic structure, magnetic properties at the surface	Similar to XRD, the sample instead is placed in a neutron beam and diffracted by the periodic lattice. Because neutrons are not charged particles they only interact with atomic nuclei	Nanometer scale
XAS (x-ray absorption spectroscopy) which includes XANES (X-ray absorption near edge structure) and EXAFS (extended x-ray absorption fine structure)	Interfacial information about the nanoconstituent and the matrix	Structural information, bonding and coordination number	A sample is placed in a monochromatic x-ray beam and when the beam passes though the material its intensity is reduced by several processes, scattering, absorption, diffraction, etc. This technique explores the variation in absorption coefficient with photon energy	Depth nm to µm

Characterization Tool	**Nanocomposite measurement**	**Measured Properties**	**How It Works**	**Range**
XPS (x-ray photoelectron spectroscopy) also known as ESCA (electron spectroscopy for chemical analysis)	Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Chemical elements at surfaces	X-rays impinge on the surface of a sample resulting in the ejection of electrons with varying energies. The electrons leaving the sample are detected by an electron spectrometer according to their respective kinetic energies	Depth 0.5 nm to 10 nm
AES (Auger electron spectroscopy)	Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Chemical analysis; the composition of the surface layers of a sample	Electrons impinge on the surface of a sample resulting in the ejection of electrons as electrons from upper levels make the transition to lower levels energy is released. The released energy is in the form of x-rays and Auger electrons. The energy of the Auger electrons are measured	Depth 0.3 nm to 3 nm
SIMS (secondary ion mass spectrometry)	Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Chemical compositions of the surface of a sample, surface impurity concentrations	The sample is bombarded with an ion beam which results in the sputtering of ions from the sample (secondary ions). The secondary ions from the sample are analyzed in a mass spectrometer according to their energies and mass-charge ratios	Depth 1 nm to 3 nm
FT-IR (Fourier transform infrared spectroscopy)	Interfacial information about the nanoconstituent and the matrix	Structural and chemical information	A sample is placed in an IR beam that has been sent through and interferometer. Frequencies which match the natural vibration frequencies of the molecules present are absorbed by the sample. The collected interferogram is converted into a spectrum by using the Fourier transform	Spatial resolution is typically micrometers
Raman Spectroscopy	Interfacial information about the nanoconstituent and the matrix	Structural and chemical information	A sample is placed in a laser path and photons which are inelastically scattered are detected. Inelastically scattered photons have a different wavelength from the incident radiation and result from a change in the motion of molecules	Spatial resolution is typically micrometers

Characterization Tool	Nanocomposite measurement	Measured Properties	How It Works	Range
NMR (nuclear magnetic resonance)	Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Compositional and structural information	NMR analyzes a magnetic nucleus by aligning it with a strong external magnetic field. The nuclei are perturbed by RF energy and their analyzing their relaxation is exploited by NMR spectroscopy	Spatial resolution is typically tens of micrometers
ICG (inverse chromatography	Molecular interactions and wetting characteristics between nanoparticles and matrix,	Surface free energy (nonpolar and acid-base components) of the nanoparticles and matrix, heat of adsorption and entropy of nanoparticles.	Inverse Gas Chromatography (IGC) is a gas phase technique for the characterization of powders, fibers, and thin films. Probing gases are injected into a sample-packed column, and the retention time is measured, which is inversely proportional to the gas/substrate interactions. By selecting the probe molecules, the nonpolar and polar (acid/base) thermodynamic parameters of the substrates are measured. The application of this technique for measuring the dispersion force and acid- base parameters of CNT and TiO_2 has been demonstrated.	Spatial resolution is typically tens of micrometers

Table C.2
Nanoscale Measurements for Individual Nanoconstituents

Characterization Tool	Nanocomposite measurement	Measured Properties	How It Works	Range
SPM (scanning probe microscopy)	Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct the dataset. Limited interphase information about the nanoconstituent and the matrix	Depending upon the mode of operation, three dimensional surface topography and morphology, in addition the following can be measured: elasticity, friction, magnetic and electrical properties (contact AFM, LFM, CSAFM, AC-AFM (tapping mode is a subset) EFM, MFM, force modulation, chemical force, scanning capacitance, scanning impedance, and force distance spectroscopy)	SPM uses a probe (cantilever) whose tip is slowly raster scanned across the sample surface. The interaction between the tip and the sample is recorded by a laser reflected off the back of the cantilever into a position sensitive photodetector	Spatial resolution: 0.5 nm to 5nm; depth: 0.014 nm
STM (scanning tunneling microscopy)	For conducting composites: Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct the dataset. Limited interphase information about the nanoconstituent and the matrix	Depending upon the mode of operation three dimensional surface topography and morphology, in addition the following can be measured current-voltage spectroscopy	STM uses a conductive tip which is brought very close to a conductive sample and when a voltage is applied tunneling occurs between the tip and sample. The tip is then slowly raster scanned across the surface	Spatial resolution 0.014 nm, depth 0.5 nm to 5 nm
NSOM (scanning near field optical microscopy)	Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct the dataset. Limited interphase information about the nanoconstituent and the matrix	Chemical and optical spectroscopic information	Similar to AFM, a probe (in this case an optical fiber fabricated to a nanoscopic point) which is slowly raster scanned across the sample surface.	20nm to 100 nm

Characterization Tool	Nanocomposite measurement	Measured Properties	How It Works	Range
TEM (transmission electron microscopy)	Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct. With incorporation of EELS or EDS-Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Sample morphology, crystallographic information, and elemental composition when coupled with EELS or EDS	A monochromatic electron beam is highly focused on a very thin sample (20nm to 100nm) the beam that passes thought the sample is collected on a phosphor or solid state imaging plate	0.01 nm to 20 nm
STEM (scanning transmission electron microscopy)	Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct. With incorporation of EELS or EDS-Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Sample morphology, crystallographic information, and elemental composition when coupled with EELS or EDS	Similar to TEM, a focused electron beam is used to interrogate the sample, however, with STEM the beam is raster scanned across the sample and the beam that passes though the sample is analyzed	2 nm to 20 nm
SEM (scanning electron microscopy)	Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct. With incorporation of EELS or EDS-Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Sample morphology, crystallographic information, and elemental composition when coupled with EDS or WDS	Similar to STEM, a focused electron beam is used to interrogate the sample, by raster scanning the beam across the sample. When the beam interacts with the sample the backscattered and secondary electrons are used to produce the image, the generated x-rays are analyzed to indicate elemental composition	1 nm to 20 nm
EDS & WDS (energy dispersive spectroscopy); (wavelength dispersive spectroscopy)	Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Quantitative elemental composition	When an energetic electron beam interacts with a sample, characteristic x-ray peaks are detected for each element present	0.1 µm for heavy elements and 1 µm for light elements

Characterization Tool	Nanocomposite measurement	Measured Properties	How It Works	Range
Electron Diffraction	Dispersion, and nanoconstituent ordering and orientation in the composite matrix but requires many serial sections to reconstruct the dataset.	Crystallographic information similar to XRD	Electron diffraction experiments are usually performed in conjunction with TEM or SEM. As the electron beam interacts with the sample diffraction is measured	Nanometer scale
Nanoprobe (multiprobe electrical measurements and sample manipulation)	Electrical characterization of the interfacial as well as limited interphase information about the nanoconstituent and the matrix	Electrical properties and nanomanipulation	Multipoint probes are brought into contact with the sample allowing a variety of electrical measurements including conductance/resistance, current-voltage spectroscopy, and dielectric properties	
EELS (electron energy loss spectroscopy)	Interfacial information as well as limited interphase information about the nanoconstituent and the matrix	Chemical composition of the sample, electronic structure and bonding in crystals and at interfaces	When electrons pass through a sample (for example during TEM) some lose energy along the way. The amount of energy is unique to the atomic species with which it has interacted. By examining the structure of the spectra it can be possible to determine the chemical state of the atoms	Depth 200 nm, Lateral resolution 1 nm to 100 nm

APPENDIX D. NANOTECHNOLOGY/NANOMANUFACTURING STAKEHOLDER MEETING

The following is material arising from a follow-on meeting between U.S. Government and industry leaders in the nanotechnology field that took place the afternoon after the main part of this workshop concluded.

Toward Predictive NanoMaterial Design - Experimentation, Metrology, EHS, Modeling and Critical Algorithms

Michael Garner, INTEL, Santa Clara; Dan Herr, Semiconductor Research Corporation, Durham, NC and Donald B. Anthony, Council for Chemical Research, Washington, DC.

Background: One of the most fundamental needs for nano-manufacturing to become viable is to understand and control the factors in nano-material synthesis that determine nanoscopic through macroscopic materials properties. The chemical and semiconductor industries have identified joint nanotechnology research needs that would enable the correlation and prediction of nanostructure and properties from synthetic conditions. Industrial sectors such as aerospace and automotive have also articulated similar needs. However, the development of such predictive models will require a great deal of experimentation, development of new metrology methodologies, instrumentation and the creation and enhancement of new algorithms. Models are needed that provide a framework for the systematic characterization of synthetic methods and material properties, which are sufficient to enable the retro-synthetic design of useful materials with a multiplicity of desired properties while keeping in mind the environmental, health and safety aspects of the manufacturing processes employed.

Many nanomaterial modeling and characterization efforts are under way at universities and national laboratories internationally. Unfortunately, these initiatives currently lack the coordination and levels of support that are required to develop these capabilities into an integrated resource with broad utility. No one agency or institution has the scope or resources to satisfy these predictive materials by design need. Many industries, including aerospace, energy, automotive, chemical, electronics, etc., would value the development of such a predictive modeling capability and nanotechnology design infrastructure that delivers high performance materials with superior properties. Additionally, this modeling infrastructure also would support and enhance the government's ability to achieve mission critical goals.

This meeting's goals are to identify:

1. Collaborative pathways and resources within and among different research institutions, which are currently developing and characterizing these models;
2. Perceived coordination and resource gaps that are barriers to achieving an interdependent and sufficient predictive modeling infrastructure;
3. Prioritize collaborative opportunities for multiple institutions and agencies to develop this materials modeling by design capability. Specifically, what is the best way to utilize the strengths of different research institutions to develop these enabling capabilities?

APPENDIX E. GLOSSARY OF ABBREVIATIONS AND ACRONYMS

AFM	Atomic force microscope/y
ASME	American Society of Mechanical Engineers
BAA	Broad agency announcement (DOD call for proposals)
BET	Brunauer-Emmett-Teller
BFTP	Ben Franklin Technology Partners
cAFM	Calibrated atomic force microscope
CARS	Coherent anti-Stokes Raman spectroscopy
CCD	Charge-coupled device
CD-AFM	Critical Dimension Atomic Force Microscopy
CDC	Centers for Disease Control and Prevention
CDRH	Center for Devices and Radiological Health (FDA)
CD-SAXS	Critical-dimension small-angle X-ray scattering microscope
CD-SEM	Critical Dimension Scanning Electron Microscopes
CFD	Computational fluid dynamics
ChI CBAN	Joint Chemical Industry Consultative Board for Advancing Nanotechnology
CMOS	Complementary metal-oxide semiconductor
CNSE	College of Nanoscale Science and Engineering (University at Albany)
CNT	Carbon nanotube
CoMoCAT®	Process for producing high-quality SWCNTs at very high selectivity and with a narrow distribution of tube diameters, developed at University of Oklahoma and commercialized by SouthWest Nanotechnologies. Inc.
COT	Committee on Technology (NSTC)
CPSC	Consumer Product Safety Commission
CRADA	Cooperative Research and Development Agreement Program (NIST)
CSREES	Cooperative State Research, Education, and Extension Service (USDA)
CWG5	NNI Consultative Working Group # 5 of the Semiconductor Research Council (SRC)

DARPA	Defense Advanced Research Projects Agency
DMA	Differential mobility analyzer
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOT	Department of Transportation
EHS	Environmental, health, and safety
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FET	Field-effect transistor
FRET	Fluorescence resonance energy transfer
HIM	Helium-ion microscopy
IIT	Instrumented indentation
ISO	International Organization for Standardization (and associated standards)
ITRN	International Technology Roadmap for Nanotechnology
ITRS	International Technology Roadmap for Semiconductors
IWG	Interagency Working Group (on Manufacturing R&D)
k	Dielectric constant (high-k/low-k)
MANA	Mid-Atlantic Nanotechnology Alliance
ManTech	Manufacturing Technology Program (DOD)
MEL	Manufacturing Engineering Laboratory (NIST)
MEMS	Microelectromechanical systems
MFM	Magnetic force microscope/y
MIAME	Minimum information about a microarray experiment
MRAM	Magnetic random access memory
MRFM	Magnetic resonance force microscope/y
MSDS	Material Safety Data Sheets
Nano-CEMMS	Center for Nanoscale Chemical-Electrical-Mechanical Manufacturing Systems (at the University of Illinois, Urbana-Champaign)

NASA	National Aeronautics and Space Administration
NCLT	Nanotechnology Center for Learning and Teaching (NSF)
NEMS	Nanoelectromechanical systems
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health (CDC)
NIST	National Institute of Standards and Technology
NNCO	National Nanotechnology Coordination Office
NNI	National Nanotechnology Initiative
NNN	National Nanomanufacturing Network (NSF)
NSEC	Nanoscale Science and Engineering Center (NSF)
NSET	Nanoscale Science, Engineering, and Technology Subcommittee of the National Science and Technology Council's Committee on Technology
NSF	National Science Foundation
NSOM	Near-field scanning optical microscopy
NSTC	National Science and Technology Council
NTRN	National Technology Roadmap for Nanotechnology
ORNL	Oak Ridge National Laboratory (DOE)
OSTP	Office of Science and Technology Policy, Executive Office of the President
PCA	Program Component Area (NNI)
QC	Quality control
R&D	Research and Development
RF	Radio frequency
RMS	Reference measurement system
SAIC	Science Applications International Corporation
SBIR	Small Business Innovation Research program (across several U.S. Government agencies)
SEM	Scanning electron microscope
SEMATECH	(SEmiconductor MAnufacturing TECHnology), a nonprofit U.S. research consortium for semiconductor manufacturing

SINAM	Center for Scalable and Integrated NAnoManufacturing at the University of California, Los Angeles
SOPs	Standard operating procedures
SPIE	An international society advancing an interdisciplinary approach to the science and application of light
SPM	Scanning probe microscope
SRM	Standard reference material
STED	Stimulated emission depletion (microscope)
STEM	Scanning transmission electron microscopy
SWCNT	Single-walled carbon nanotube (also SWNT)
TEAM	Transmission electron aberration-corrected microscope (DOE; see http://ncem.lbl.gov/team3.htm)
TEM	Transmission electron microscope
UMCP	University of Maryland College Park
USDA	U.S. Department of Agriculture
UV	Ultraviolet (light/wavelength)
WTEC	World Technology Evaluation Center
XML	Extensible Markup Language

APPENDIX F. INDEX

National Science and Technology Council

Committee on Technology

Interagency Working Group on Manufacturing Research and Development