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About the Nanoscale Science, Engineering, and Technology Subcommittee

The Nanoscale Science, Engineering, and Technology (NSET) Subcommittee is the interagency body responsible for coordinating, planning, implementing, and reviewing the National Nanotechnology Initiative (NNI). It is a subcommittee of the Committee on Technology of the National Science and Technology Council (NSTC), which is one of the principal means by which the President coordinates science and technology policies across the Federal Government. The National Nanotechnology Coordination Office (NNCO) provides technical and administrative support to the NSET Subcommittee in the preparation of multiagency planning, budget, and assessment documents, including this report. More information about the NNI can be found at http://www.nano.gov.

About the National Nanotechnology Initiative

The National Nanotechnology Initiative is the Federal nanotechnology R&D program established in 2000 to coordinate Federal nanotechnology research, development, and deployment. The NNI consists of the individual and cooperative nanotechnology-related activities of 25 Federal agencies that have a range of research and regulatory roles and responsibilities. The goals of the NNI are fourfold: (1) to advance a world-class nanotechnology research and development program; (2) to foster the transfer of new technologies into products for commercial and public benefit; (3) to develop and sustain educational resources, a skilled workforce, and the supporting infrastructure and tools to advance nanotechnology; and (4) to support responsible development of nanotechnology. The NNI’s member agencies are committed to involving the full spectrum of stakeholders in development of responsible and forward-looking U.S. R&D and regulatory programs with respect to nanotechnology advancement.

About this Report

This document is the report of a workshop held in May 2009. It was part of a series of topical workshops sponsored by the NSET Subcommittee to inform long-range planning efforts for the NNI. Any ideas, findings, conclusions, and recommendations presented in this report are those of the workshop participants.

About the Report Design

The report cover design is by N.R. Fuller, Sayo-Art LLC. Central image: Scanning electron micrograph image of a nanoscale piezoresistive force sensor. Patterned from single-crystal silicon epi-layer membranes using micro- and nanomachining processes, the device is 130 nm thick, of which the topmost 30 nm comprise the doped p+ transduction element. The central gold-coated silicon “line” running longitudinally along the center of the devices enables biological sensing applications (image used with permission from Nano Letters 6, 1000 [2006]. ©American Chemical Society, provided by J. L. Arlett and M. L. Roukes, California Institute of Technology). Background image: An artistic rendition of a scanning tunneling microscopy image of a flat silver surface covered with C_{60} molecules. The book design is by Lapedra P. Tolson of the National Nanotechnology Coordination Office.

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Nanotechnology-Enabled Sensing
Report of the National Nanotechnology Initiative Workshop

Arlington, Virginia
May 5–7, 2009

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Subcommittee on Nanoscale Science, Engineering, and Technology
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The Nanotechnology-Enabled Sensing Workshop was one of several NNI workshops held in 2009 to further the vital work of responsibly and publicly addressing the science of nanotechnology and how best it should be harnessed and monitored for the national good. Many enthusiastic and committed individuals, noted below, dedicated their time and expertise to making this workshop a reality. Their efforts have been invaluable.

The workshop organizing committee was responsible for all the essential groundwork for the event:

- Chagaan Baatar, Office of Naval Research
- Hongda Chen, Department of Agriculture
- James Glownia, Department of Energy
- Laverne Hess, National Science Foundation
- Gary Hunter, National Aeronautics and Space Administration
- Eric Houser, Department of Homeland Security
- Igor Linkov, Army Engineer Research and Development Center
- Philip Lippel, National Nanotechnology Coordination Office
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- Larry Nagahara, National Institutes of Health
- Pehr Pehrsson, Naval Research Laboratory
- Gernot Pomrenke, Air Force Office of Scientific Research
- Nora Savage, Environmental Protection Agency
- Roger van Zee, National Institute of Standards & Technology
- Lloyd Whitman, National Institute of Standards & Technology
- Dwight Woolard, Army Research Office

The substance of the workshop depended on the thoughtful engagement of the speakers, moderators, and participants. Their presentations and discussions are captured in this report for future reference in the ongoing planning activities of the NNI agencies.

The staff of the National Nanotechnology Coordination Office assisted the organizing committee with all workshop logistics. In particular, Philip Lippel coordinated the Organizing Committee, Heather Evans and Halyna Paikoush handled planning matters, and Patricia Johnson and Patricia Poland, both of WTEC, provided technical and other assistance at the workshop.

A critical group of workshop participants drafted the various components of this workshop report: Harry Atwater, Igal Brener, Michael Carpenter, Bill Carter, Peter Hesketh, Gary Hunter, Saif Islam, Jing Li, Gary Maki, Ashok Mulchandani, Jim Murday, Doug Natelson, Yoshio Nishi, Suranjan Panigrahi, Pehr Pehrsson, Jeremy Pietron, Gernot Pomrenke, Mike Roukes, Omowunmi Sadik, Mike Sailor, Steve Semancik, Selim Shahriar, Ranganathan Shashidhar, Richard Silberglied, Joseph Stetter, Duncan Stewart, Mark Stiles, Thomas Thundat, Mark Tondra, Selim Unlu, Randy Vander Wal, Roger van Zee, and Lloyd Whitman (for affiliations, see Appendix B).

Crystal Havey was responsible for integrating and rewriting the various first draft report materials, and Pat Johnson assisted in proofreading and refining the final draft. Nicolle Rager Fuller designed the report cover, and Lapedra Tolson was responsible for the report’s layout. Heather Evans served as report editor.

Finally, financial support for the workshop and for this report was provided by the member agencies of the Nanoscale Science, Engineering, and Technology Subcommittee through their support of the National Nanotechnology Coordination Office, with additional support from the Air Force Office of Scientific Research.
Preface

Advancing a world-class research and development program is one of four overarching goals of the National Nanotechnology Initiative (NNI). Fostering such a program requires identifying challenges, recognizing opportunities, and stimulating new ideas. One means for mapping the leading edge of R&D trends is to develop a snapshot of the state of the art and use this to forecast research directions. Towards this end, the December 2007 NNI Strategic Plan called for a series of topical workshops in science and technology areas where nanotechnology holds the potential for transformative impact.

The demand is large and growing for highly selective, highly sensitive smart sensor systems capable of simultaneously detecting multiple species. Nanotechnology holds the potential to enable a new generation of high-density, multianalyte sensors to fill this rising demand. Because of this convergence in need and potential nanotechnology-enabled capabilities, participating in a workshop on nanotechnology’s potential contribution to future sensor systems was of interest to a wide range of NNI agencies. In response to their interest, the National Nanotechnology Coordination Office (NNCO) coordinated the May 2009 “Nanotechnology-Enabled Sensing Workshop,” sponsored by the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council’s Committee on Technology.

Recognizing the numerous potential topics that could have been included in the workshop, the organizers chose to focus on nanotechnology-enabled signal transducers and the insertion of these sensing elements into sensor systems. The organizers also recognized that in comparison to sensors that are used to measure system state variables such as temperature and pressure, one of the major demands of current and future sensor platforms is specificity of sensing: the unambiguous detection, identification, and quantification of chemical and biological species. Those applications constituted the major thrust of the workshop.

The workshop assembled a group of science and technology leaders from academia, government, and industry. Each day of the two-day public workshop began with a series of overview presentations in which subject matter experts discussed the status of specific sensor-related technologies and potential impacts of nanotechnology-related discovery. These presentations gave the group a common vocabulary and sense of priorities. The hard work of the workshop occurred during the breakout sessions. In these sessions, participants considered application opportunities for nanotechnology in sensing technology; evaluated the state of the art for several nanotechnology-enabled sensing modalities; identified obstacles to integrating nanoscale transducers into sensing systems; and proposed research directions, needs, and priorities.

This report summarizes and distills the plenary presentations and breakout group discussions. The ideas, conclusions, and recommendations presented here are those of the workshop participants. The report is intended to provide input to the NSET Subcommittee as it coordinates the various nanotechnology activities and programs across the Federal Government. Additionally, the details of this report should prove useful for program managers and laboratory administrators, as well as for active researchers involved with managing sensors-related and nanotechnology programs.

On behalf of the NSET Subcommittee, we thank the workshop co-chairs and the other members of the Organizing Committee for planning this workshop and leading the preparation of this report. Our sincere thanks also go to all the speakers, moderators, and participants for their manifold contributions to the workshop and to this report.

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About the Workshop and this Report

The Nanoscale Science, Engineering, and Technology Subcommittee of the National Science and Technology Council’s Committee on Technology, working through the National Nanotechnology Coordination Office, convened the Nanotechnology-Enabled Sensing Workshop to identify high-impact opportunities for the application of nanotechnology to sensing systems and to identify worthwhile research directions for nanotechnologies that are key to new sensing applications. The workshop was held May 5–7, 2009, at the Sheraton National Hotel in Arlington, Virginia.

The agenda (see Appendix A) encompassed a mixture of talks, breakout sessions, and writing group meetings. The two days of the public workshop (May 5–6) began with plenary presentations on sensors and areas where nanotechnology can impact sensing systems. These broad overviews were followed by short, focused presentations on specific types of nanotechnology-enabled transducers and the challenges associated with fabricating, integrating, and networking these transducers into sensor systems. The afternoons were spent in breakout sessions in which the participants examined the relevant topics in detail. Additionally, on the evening of the first day, each interested participant was offered a ninety-second time slot to provide a succinct overview of his or her recent research findings or perspectives on the field. Participating in the event were some eighty science and technology experts from academia, government, and industry (see Appendix B).

The breakout sessions were where the hard work of the workshop was conducted. Two May 5 breakout sessions focused on the state of the art and future research directions for various sensor transduction mechanisms, specifically, (1) electro/chemical and optical, and (2) mechanical and magnetic mechanisms. One May 6 breakout session addressed the practical barriers to harnessing the capabilities that nanotechnology-enabled sensors offer (fabrication, integration, and networking issues), and a second May 6 session identified transformative applications for these sensors.

Participants in the breakout sessions examining sensor transduction mechanisms and practical barriers to using nanotechnology-enabled sensors were asked to:

■ Provide a succinct statement of the state of the art
■ Identify and rank the challenges, opportunities, and technical hurdles involved
■ Identify three to five research targets and measures of progress towards those targets
■ Recommend strategies and mechanisms to address the issues identified above

Participants in the breakout session on application opportunities were asked to address:

■ Where (and how) can nanotechnology play a role in sensing technology?
■ What transformational sensing applications can nanotechnology uniquely enable?
■ What are the cross-cutting issues limiting nanotechnology in sensing?

On May 6, workshop participants were given an opportunity to voice their opinions and concerns as citizens on the potential social impact of nanotechnology, and to discuss potential ethical, legal, and societal implications of nanotechnology-enabled sensing.

Invited participants (speakers and moderators) and Organizing Committee members were asked to stay through May 7 to capture the key findings and recommendations of workshop participants; their resulting written materials formed the core of this final report. The report forecasts natural insertion points for nanotechnology into research and development (R&D) of future sensor systems. It is organized as follows: Chapter 1 broadly examines the state of the art in sensor R&D and discusses challenges and potential nanotechnology-enabled approaches to meet the challenges. Chapter 2 takes a detailed look at five classes of nanoscale transducers that recognize analytes by electro/chemical, electromagnetic, spectroscopic, magnetic, and mechanical means. Chapter 3 discusses challenges associated with manufacturing, integrating, and networking sensor systems.
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A sensor is a device that responds to a physical, chemical, or biological parameter and converts its response into a signal or output. The market drivers and scientific and engineering vectors of sensor R&D point toward accelerating development of sensor systems built from components for sampling, preconcentration, transduction, and signal analysis that are interoperable, extensible, and integrated. Future sensor systems will incorporate transducers that use complementary physical, chemical, and biological phenomena to measure orthogonal characteristics of chemical or biological species (analytes) of interest. A single system will be able to identify and quantify many analytes, in a wide range of backgrounds, with great sensitivity.

Nanotechnology will play an enabling role in realization of these future sensing systems. There are many high-impact opportunities for nanotechnology in sensing, which are categorized generally into eight application areas:

- Medicine, health, and wellness
- Workplace safety
- Environmental monitoring
- Agriculture and food industries
- Energy
- Manufacturing and industrial processes
- Transportation
- National security and emergency response

The insertion points for nanotechnology in sensing applications are many. Among these are materials for analyte preconcentration, separation, and transduction; energy harvesting and storage components; powerful computing systems to analyze transducer response; and optoelectronic systems for communications. The most transformative opportunity for nanotechnology lies in the discovery and application of transducers based on unique material properties and unusual phenomena that emerge at the nanoscale.

Substantial progress has been made. One-dimensional nanoscale materials, such as nanowires, have been functionalized to recognize specific analytes and have shown single-molecule sensitivity. Label-free optical methods for sensing biological molecules have been demonstrated using nanoscale colloidal gold. Highly sensitive, fast-response microwave resonant sensors for monitoring toxic industrial chemicals have been built from carbon nanotubes. Detector response enhancements have been demonstrated using surface nanoscale patterning. Nanoscale mechanical inertial balances capable of detecting as few as fifty atoms have been demonstrated. In short, the field is on a sound footing based on these and other advances in nanotechnology; still, many important fundamental discoveries lie ahead.

Five categories of nanotechnology-enabled transducers are explored in this report: (1) electro/chemical, (2) electromagnetic, (3) spectroscopic, (4) magnetic, and (5) mechanical. Each transducer and class of transducers has a unique set of scientific questions to be addressed and technical hurdles to be overcome. Nevertheless, certain broad, key challenges and needs in nanotechnology-enabled sensing naturally arise in the areas of fundamental research, practical technical issues, and device and system integration. Societal dimensions such as workforce development and dialog with the public are also vital to realizing the great potential of nanotechnology-enabled sensing. These common challenges are summarized below.

**Fundamental Research**

Further insights into the physical, chemical, and biological interactions between the transducers and analytes are required; better understanding is needed of the processes that generate observable signals and how to optimize them. While significant insights into the signal transduction process have been obtained, these phenomena are not adequately understood. Models to predict a transducer’s performance do not exist, and this greatly slows the discovery and development process.
Executive Summary

Significant effort should be invested in understanding the processes that underpin sensing.

**Technical Challenges**

Getting the analyte to the sensor presents many challenges; in particular, methods are needed for preconcentrating dilute analytes and separating complex analytes. When presented with the same analyte, two identical transducers, in many cases, give different responses. The origins of this irreproducibility are not established, although factors such as uneven doping, crystalline heterogeneity, and inconsistent processing are believed to play a role and must be studied. Most demonstrations of transducer function have been conducted in the laboratory; development is needed to enable performance in the complex environments where sensors will be deployed. Nanoscale transducers often produce low-level signals that must be amplified. Electronic noise can often mask or degrade the fidelity of the signals; noise-reduction strategies must be explored.

**Integration**

Sensing systems will incorporate many materials. Strategies for integrating organic materials, inorganic materials, and biological species into devices need to be developed. Wider access of researchers and designers to foundries capable of handling diverse materials would accelerate the sensor development process.

**Societal Dimensions**

A nanotechnology-savvy workforce with a multidisciplinary background is needed to execute the intensive and wide-ranging R&D programs implicit in the realization of nanotechnology-enabled sensing.

The sensing systems described here stand to increase the quality of life for many citizens. As such, these systems will be ubiquitous. Deploying these new technologies and understanding both the potential benefits and risks of nanotechnology will require developers and educators to engage citizens in proactive and ongoing conversations.
A sensor is a device that responds to a physical, chemical, or biological parameter and converts its response into an output or signal. The process may be as common as the chiming of a door bell in response to a person pressing a button or as subtle as the minute resistance change across a functionalized nanowire when a single protein attaches to it. Figure 1.1 shows an example of the sensing process from recognition event to sensor output. This description of a sensor and the sensing process are the working definitions used in this report. “Sensors/sensing” as used here are distinct from sensors that measure system state variables such as temperature and pressure.

**SENSING SYSTEMS**

A principal need in sensor development is the recognition, identification, and quantification of specific chemical and biological substances, which are referred to as “analytes” in this report. Furthermore, these types of sensors are forecast to benefit substantially from advances in nanotechnology.

The application drivers and the scientific and engineering vectors behind sensor technology point toward future sensing systems being built from components (concentrators, separators, transducers, signal processors, power supplies, etc.) that are integrated onto a single platform and that are interoperable and thus extensible, as shown in Figure 1.2. Future sensors will incorporate sensing arrays containing thousands of functionalized transducers based upon multiple sensing phenomena and capable of detecting multiple analytes. The transducer elements will be extremely selective (to particular chemical or biological species) and highly sensitive (to ultra-low concentrations). Users will demand that these sensing systems function reliably in a wide range of backgrounds and environments, ranging from hospitals to landfills to factories, with the ability to communicate results to the users through wireless means. Ultimately, such sensing systems will become ubiquitous and an integral part of buildings, cars, textiles, and point-of-care medical devices.

Nanotechnology has the potential to enable this vision of future sensor technology and sensing systems. The high surface-to-volume ratio of nanowires improves a transducer’s sensitivity. Other nanostructured materials hold the promise of being used as highly efficient sample concentrators or in separation technologies for complex mixtures. Nanofabrication processes are making it possible to build high-density arrays of transducers, and nanoelectronics will process and analyze the signals coming from these arrays. Figure 1.3 shows an example of a prototype sensor array.
Chapter 1: Sensing Systems and Nanotechnology

DIRectionS iN SENSoR RESEARCh

Targeted Transducers

Most environments are complex, containing a vast variety of chemical and biological species in each cubic centimeter. A core objective of sensor R&D is to build sensor systems that quantitatively measure targeted species over a range of concentration levels in a multicomponent environment. Target-specific transducer design is becoming possible because of very recent advances in modeling, simulation, and combinatorial materials synthesis and characterization. Harnessing these tools in a focused effort will enable directed materials discovery to flow more naturally through to scale-up for a given application, and will also allow critical questions about environmental health and safety for the technology to be answered up front.

First-principles modeling tools, combined with multiobjective optimization and parallel computation, can permit rapid exploration of nanoscale phenomena and their potential applicability for a given sensor modality. Where theories are not robust or modeling has not achieved the desired level of complexity, high-throughput screening (e.g., fluidic approaches to combinatorial synthesis combined with fast spectroscopic interrogation) can simultaneously facilitate accelerated materials discovery, early tests of sensor assembly processes, and rapid assessment of the potential for scale-up. Nanotechnology has the potential to enable a new generation of sensor materials that selectively target and detect specific species.

Multiplexing

In addition to being able to target specific analytes, future sensor systems should be capable of detecting multiple analytes; for example, chemical sensors should be capable of simultaneously detecting several airborne toxic industrial chemicals. The promise of nanotechnology-enabled sensors lies in their ability to achieve a high density of spatial packing of sensor arrays in a small area, in the increase in active surface area per sensor, and in the potential for new functionality. Multiplexing can be approached in many ways. A sensor could contain multiple nanoparticle species, each able to target a specific molecule; alternatively, new sensing modes could probe parameters such as optical properties or mass. Challenges include ensuring reliable sensing in the presence of large backgrounds when the signal is small, and the use of binding chemistries that are compatible with sensor elements at the nanoscale.

Multiparameter, Orthogonal Transducers

Most existing sensors rely on a single parameter to identify a target analyte, but single-parameter measurements often do not provide a response that can unambiguously identify a single analyte. Nanotechnology and nanoscale materials promise a next generation of transducers and devices able to take multiple, simultaneous measurements of a target analyte within the same system. Measurement for a given analyte of several different physical, chemical, or biological properties—such as mass, chemical potential, and optical adsorption—provides improved discrimination of that target analyte.

The information provided by the various transducers should be orthogonal, that is, each should provide a different, independent piece of information about the analyte. This approach will give broad coverage of multiple measurement parameters, allowing cross-correlation between measurements in order to improve reliability of both the sensor data and the system-level information. The different measurements can be combined to give significantly enhanced information about the environment and to improve the ability of the user to respond appropriately to changing environmental conditions.
Ongoing Challenges

Drift and Fouling

A transducer interacts with the environment in order to make the desired measurement. Ideally, this interaction should be reversible, and the sensor should always respond in the same way to a given concentration of a target chemical species. However, it is often the case that the sensing materials age with time, react with analytes, or are fouled by contaminants in the environment. In biology, sensing systems have natural antifouling mechanisms; for example, mucous flow in a nose continuously restores the nose’s sensing capabilities. Such restorative systems are not typically built into man-made sensors, although in some sensor systems, approaches such as temporary heating of transducer elements are used to cleanse the sensors. In general, however, a man-made sensor system’s response characteristics drift over time, and the data delivered by that system becomes less accurate. A significant technical challenge is to make transducers that self-clean and do not drift significantly. Nanotechnology may contribute to this goal through the discovery of self-correcting materials, internal regeneration mechanisms, integrated intelligence, or the ability of the sensor system to internally correct calibration drift.

Preconcentration, Sampling, and Separation

When an analyte is present at very low concentrations, large sample volumes are often required to collect sufficient amounts of the material to detect the species of interest, thus necessitating preconcentration of a large sample volume. The use of cascading preconcentration technologies that allow sample volumes of cubic meters to be reduced to liter volumes and subsequently to microliter analysis volumes is required to realize the future of sensing. Several large-volume preconcentration technologies currently are available commercially for air sampling; these perhaps could be adapted to interface with nanotechnology-enabled sensing systems. More likely, unique properties of new materials structured at the nanoscale will be developed and adapted for this purpose.

After preconcentration, a sample can be presented to a transducer for analysis; however, the high density and small size of nanofabricated transducers present unique challenges. If the analyte is vapor or liquid, microfluidic methods might be adapted to provide an interface with the transducer array. If the analyte is solid, a robotic or an automated sampling method might prove more appropriate. In both cases, systematic research is needed to develop appropriate sampling methods for different types of analytes. Because the goal is field deployment under various conditions, a universal platform for sampling different types of analytes should be a primary objective.

Separation techniques are critical for the full functionality of sensor systems. Samples extracted from the environment are sufficiently complex to make clear identification of any specific analyte very difficult. Separation is already necessary for the analysis of materials by full-scale laboratory chemical analytical equipment, and miniaturizing those analytical capabilities is likely to introduce new complications. The nanoscale can provide large surface-to-volume ratios for separations based on adsorption/desorption mechanisms, molecularly imprinted membranes for specific recognition sites, artificial gels that can be tailored for specific separation needs, and fluidics with channel-constrained flows to separate longer-chain molecules such as DNA.

Detection Levels

A considerable advantage of nanotechnology-based systems is the potential for highly sensitive systems, that is, systems that can detect very small amounts of an analyte. In effect, the surface-to-volume ratio of structured nanoscale materials is much larger than that of macroscopic-sized materials, which results in nanoscale transducers having the potential for much higher surface reactivity and greatly increased sensitivity. One of the technical challenges of realizing

Key Words Defined

- **Analyte** - A substance (chemical, protein, etc.) that is being sensed.
- **Transducer** - A material or device that converts a recognition event into a measurable physical phenomenon, such as a change in electrical resistance.
- **Sensing System** - An assemblage of multiple components that combine tasks important to sensing, such as sampling, preconcentration, transduction, and signal conditioning, along with analysis, information storage, and communication.
this potential is understanding and controlling the transducer structure and its relationship to sensing. This implies having a good understanding of transducer material properties and processing constraints as well as issues related to the fabrication of the surrounding sensor structure. However, the possibility also exists of saturating the sensor with too large an exposure to the target chemical species. A balance will be required in sensor design between enabling high transducer element sensitivity and avoiding saturation during operation in a range of environments, so as to optimize detection levels. Detection levels are also linked to the sampling and preconcentration issues discussed above.

Reliability and Robustness in Signal Processing

Sensor systems must be reliable and rugged. False alarms are one of the major barriers to the use of sensor systems; incorrect information can be just as problematic as no information at all. Users must be able to rely on the data reported by these systems and trust their ability to respond correctly to changing situations. Developing strategies to improve robustness at the beginning of sensor development, rather than at the end, can speed the insertion and acceptance of the technology at the application level. The multiparameter orthogonal transducers approach outlined above is likely to be an important element of the ultimate solution to this challenge.

Integration and Material Processing

Integration of various components into sensor systems will be a significant technical challenge. A system-level approach is needed that addresses issues such as sample preparation and handling, power storage and scavenging, communication, environmental compatibility, and packaging. These issues are important because, in the end, no matter how good the transducer, if one cannot power it, communicate with it, or properly provide it with a sample, then the system will not perform.

Practical methods for integrating dissimilar materials and devices on a substrate need to be developed. In principle, monolithically integrated nanoscale semiconducting materials with diverse bandgap and electrical and optical properties could offer the optimal range of opportunities. Capability for inexpensively integrating these materials onto a single substrate would offer an enormous economic opportunity for applications.

At the systems level, many other factors will impact the acceptance of a given sensor configuration beyond the effectiveness of the sensor itself. Of critical importance is having robust interfaces between the nanoscale sensor components, microscale platform, macroscopic platform, and, ultimately, the end-user. Early in the R&D cycle, it may be necessary to understand and prepare for power, energy management (possibly including harvesting as well as storing energy), networking, and communication requirements.

Modeling

Multiscale modeling will be needed to better understand the performance of transducers and sensor systems. This need extends to the fundamental level in order to design new materials tailored to have specific physical, chemical, or biological properties. The capability of modeling multiple physical phenomena in transducer and array interactions would allow an engineering system design to optimize sensor dynamic performance. Currently available software and modeling tools run under various (often incompatible) systems and use various, almost always ad hoc, assumptions, models, and parameters. The computer-aided design tools for nanodevice integration with standard microelectronics require validation of their accuracy at the nanoscale. In addition, improved predictions based upon models of reliability, drift, and aging of sensors would be of benefit as the field matures.

What is Nanotechnology?

Nanotechnology is the understanding and control of matter at dimensions between approximately 1 nanometer (nm) and 100 nm, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering, and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale.

A nanometer is one-billionth of a meter. A sheet of paper is about 100,000 nm thick; a single gold atom is about a third of a nanometer in diameter. Dimensions between approximately 1 nm and 100 nm are known as the nanoscale. Unusual physical, chemical, and biological properties can emerge in materials at the nanoscale. These properties may differ in important ways from the properties of bulk materials and single atoms or molecules.

- National Nanotechnology Initiative Strategic Plan
  December 2007 (available at http://www.nano.gov/)
Chapter 1: Sensing Systems and Nanotechnology

NANOTECHNOLOGY-ENABLED SOLUTIONS

The new materials, powerful computing and analysis capabilities, and unique physical, chemical, and biological phenomena of the nanoscale will impact future sensor systems at multiple levels. Figure 1.4 shows schematically how nanotechnology solutions can meet existing sensing application needs. These capabilities and insertion points are reviewed below.

The use of nanoscale materials in sensing applications is growing quickly, with encouraging early results. Carbon nanotubes, nanostructured metal oxides, polymers, and many other materials are being functionalized with chemical and biological species to selectively identify specific analytes. These technologies are leading to smaller, more capable environmental monitors for sensing ammonia, nitrogen oxides, hydrogen peroxide, hydrocarbons, volatile organic compounds, and other potentially hazardous gases. Early commercial examples include sensors that use carbon nanotubes to detect ozone in water and air, and hotplate transducer arrays coated with nanostructured tin oxide that are used for automotive cabin climate control. Metal and dielectric films patterned at the nanoscale, able to control and amplify electromagnetic signals, are another example of nanotechnology-enabled sensing capability. The following sections discuss four broad categories where nanotechnology stands to enhance sensor performance.

Enhancement of Specificity

Nanostructured materials and nanoscale fabrication methods and techniques naturally lend themselves to biological sensing applications, in part because the scales are well-matched to many naturally occurring biological recognition processes. This unique interface of nanoscale materials with chemical and biological processes at the molecular level can be the basis of sensing, monitoring, and understanding of associated processes. Of primary benefit is the high degree of specificity that can be achieved. This provides enhanced signal-to-noise ratios for sensing a particular material under investigation. Single-molecule statistics for a given process and reaction rates at any given instant, or for a given period of time, can also be determined. Recognition events can be accompanied by changes in physical properties, such as a change in optical signature, an adhesion event, adjustments in local charge state, or a change in conformation. The desire is to capture and transduce this functionality by incorporating additional functionalities such as optics, microfluidics, or electronics into the sensing system.

Enhancement of Sensitivity

When reduced to nanoscale dimensions, many materials reveal novel properties that can be desirable for a variety of sensing applications. These attractive characteristics can stem from the high surface-to-volume ratios at the nanoscale or from changes in optical properties (reflectivity, absorption, and luminescence), volumetric or surface diffusivity, thermal conductivity, heat capacity, mechanical strength, and magnetic behavior. Many of these effects can be harnessed to develop new, highly sensitive detection techniques. Examples include utilizing the inherent ultrahigh specific surface areas of materials structured (or porous) at the nanoscale to enhance the reaction rate or overall reactivity with a desired analyte. New chemical pathways could be accessed at the nanoscale in numerous ways only now being explored. They include changing the conformation of adsorbed or bonded functional species or enzymes, or changing surface curvature to give rise to unique surface structures. Materials such as nanoporous gold (see Figure 1.5) could be designed and fabricated for separation or filtration of analytes, or for concentration of vapor or liquid analytes prior to sensing. Porous nanoscale materials could also be used as nanoscale bioreactors, wherein single or multiple precursor reactions (i.e., physical, chemical, or biological) occur that generate specific compounds or byproducts to be sensed.

Figure 1.4. Nanotechnology-enabled sensors are driven by application requirements and realized through nanotechnology. (Image credit: N.R. Fuller, Sayo-Art LLC.)
Enhanced diffusion characteristics of selected nanoscale materials can be harnessed for sample preparation of analytes to be sensed.

**Nanophotonics-Enabled Enhancements**

The past decade has seen a great deal of activity in nanophotonics, the area broadly encompassing nanoscale plasmonics, photonic crystals, and metamaterials. The physical effects in nanophotonics lead to different modes of interaction between light and matter at the nanoscale, and they open up new possibilities for multiplexed-array sensing and monitoring applications. Two broad categories of sensing can be distinguished that take advantage of these effects: detection of chemical or biological species, and light detection utilizing nanophotonics. For example, plasmonic phenomena have been used in surface-enhanced Raman spectroscopy (SERS) and surface-enhanced infrared absorption (SEIRA) to enable a number of sensing applications.

Additional systematic investigations aimed at understanding and applying nanophotonics for developing robust, smart, and next-generation sensor systems can be helpful. Two- and three-dimensional photonic crystals can enable new sensing systems based on fluorescent molecules and/or quantum dots and plasmonic effects.

Metamaterial structures, typically associated with negative optical refractive index but more generally including tailored permittivity and permeability, also hold great promise as sensor structures. To be effective at optical or infrared wavelengths, metamaterials require nanoscale structuring. The resulting tailored properties can be highly sensitive to the local dielectric or magnetic environment. For detection of light, these effects can be equally powerful.

Plasmon-based light sensing involves the use of metal nanostructures as effective optical antennas. This can allow simultaneous expansion in signal-to-noise ratios using plasmonic enhancement and reductions in the required volume of detector material. Photonic crystal materials can also act as absorbers or scatterers that enhance optical sensors. Harnessing these effects could ultimately lead to compact hyperspectral chip-scale detectors for a variety of applications.

**Nanoelectronics-Enabled Enhancements**

System-level integration of nanotechnology-enabled sensors represents both an opportunity and a challenge. Existing semiconductor electronics components are at or near the nanoscale, and new components with unprecedented capabilities are exploiting nanoscale phenomena. Taking advantage of this similarity in scale and the new processing capabilities presents a natural opportunity to join nanoelectronics with nanotechnology-enabled transduction and sensing mechanisms. Key to this process will be adopting or adapting the existing semiconductor manufacturing framework as the platform for nanotechnology-enabled sensors. This can be done by developing chip-level integration techniques to incorporate nanotechnology-enabled sensors. Leveraging the existing knowledge and capabilities from the field of electronics also presents a path toward high-volume manufacturing of nanotechnology-enabled sensors so that they are inexpensive and widely available.

**Figure 1.5.** Nanoporous gold leaf electrodes (left: cross-section view; scale bar is 300 nm) can be used to immobilize functional biological species, in this case, a species called photosystem I. (Reprinted with permission from ACS Nano 2, 2465, © 2008 American Chemical Society.)
HIGH-IMPACT OPPORTUNITIES FOR NANOSECOND TECHNOLOGY IN SENSING

There are many general applications and technology thrust areas that would benefit from the multitude of unique properties that are characteristic of nanotechnology-enabled sensors. Broadly speaking, these can be grouped into the eight overarching categories described below.

Medicine, Health, and Wellness

Sensor systems capable of rapidly assessing wellness indicators and disease markers would be a significant new healthcare tool. Such systems are likely to be massive sensor arrays; ideally, these systems would also be disposable, point-of-care devices. Diagnostic applications such as mobile sensors for vascular transport and imaging could be part of integrated nanomedicine applications that include targeted drug delivery. Wellness areas include sensors for hormones, proteins, and glucose. A tremendous market will be realized in this area and will require devices with a very low cost that will have to coincide, in many cases, with high capabilities. The ability to detect disease markers and hormones at orders of magnitude below the concentration of the local biological (corporal) environment will be a challenge. The ideal sensing system would work with a small amount of sample, have rapid response time, and would not require highly trained operators or expensive reagents.

Workplace Safety

Environmental health and safety encompasses worker exposure to chemicals, materials, and biological agents. Nanotechnology-enabled sensors could exist in the form of personal health monitors, as badges, or even as active devices to indicate exposure limits in a work environment. Other sensors, networks, and systems could provide workplace monitoring throughout the manufacturing process. Sensing systems are not only important in industrial workplaces but also could play a role in environmental monitoring in office buildings where long-term exposures to various substances might cause illness.

Typical industrial safety sensors need to monitor a range of species from specific gases to pathogens. Gas detection systems for safety (including those able to sense oxygen, carbon monoxide, hydrogen sulfide, and sulfur dioxide) can currently cost thousands of dollars per installation. If inherently safe, low-power, nanotechnology-enabled sensors could replace the many millions to tens of millions of monitors in use today, the immediate capital installation cost would be reduced significantly in this single market area.

Environmental Monitoring

Air, land, and water sensors for pollution monitoring are an ever-growing need. Secondary organic aerosols (that is, organic-laden particulates formed from vapors and particles emitted directly into the atmosphere) are now recognized as an important consequence of combustion emissions. Detection and monitoring are key steps towards remediation of water and soil affected by organic chemicals ranging from dyes and cleaning fluids to fuels. Sensor networks are needed to detect and track emissions or events. Also, measuring buildup of organics in confined environments such as planes, trains, buildings, and cars is an ever-present need. Nanotechnology can clearly play a role in developing sensors that can actively detect analytes, with high specificity, at costs allowing for market realization.

Agriculture and Food Industries

Agriculture has a range of specific needs for sensors, including feedstock process monitoring and environmental characterization (of air, water, and soil) for efficient fertilization and irrigation. Improved farming practices and cost-effective agriculture would benefit from sensors able to monitor fertilizer levels and crop chemistry while in the field. The food industry has a great need for efficient, timely detection of food-borne pathogens by novel sensors and sensing systems enabled through a variety of molecular recognition methods or label-free transduction techniques. Illness caused by food-borne pathogens is a serious concern for public health. Development and integration of nanotechnology-enabled sensors at different critical points in the food supply chain are needed to monitor for the presence or absence of pathogens or other contaminants in different food products during processing, harvesting, storage, and just prior to use by consumers. It is essential to alert consumers to potential dangers before they consume contaminated food products. Similarly, nanotechnology-enabled sensors could aid in the rapid diagnosis of animal and plant diseases in field conditions.
Chapter 1: Sensing Systems and Nanotechnology

Energy
Petroleum-based and renewable energy technologies will benefit from gains offered by improved sensor systems. For example, sensors are needed to monitor product chemistry and purity at each stage of petroleum production, including in-field measurements, transportation, refining, distribution, and marketing. Biodiesel production would benefit from monitoring both main-reaction and side-reaction products, since fuel properties can sometimes change, to the detriment of the engine. Combustion processes and increasing regulations on combustion emissions from both stationary and mobile sources will require monitoring from more sources, on larger scales, and for more species.

After routine measures of insulating structures and managing heat absorption/reflection from windows, the next phase of energy conservation for existing buildings will likely rely on distributed and wireless sensor networks and interpretative algorithms. Smart power usage will be inherent to all desktop office units. New buildings have the opportunity to gain from multifunction sensors that not only sense the power draw or heat gain but actively and collectively function to reduce the power load. A simple example is electrochromic windows that can turn opaque in intense sunlight.

Manufacturing and Industrial Processes
In manufacturing, in-line process control for any chemical-based industry and a range of other industries would benefit from real-time sensors specifically tailored to monitor the quality of a given product, and corresponding supply chain management through use of sensors would likely enable better reliability and security within an industry sector. For example, radio-frequency identification sensing is now commonly used by a number of shipping industries to track packages. Further functionality added to these devices to monitor environmental changes (e.g., temperature, pressure, relative humidity, and vibration) optically and non-intrusively would be useful. Other applications include devices that could track tampering of materials, chemical spills, and spoilage. These devices would be enabled by the high sensitivity and selectivity of sensor arrays. Optimized sensor systems would allow for manufacturing industries to ensure that their products are not only produced to the highest expected specifications, but that those specifications are still valid and viable at the time they are used.

Transportation
Applications in the transportation industry are broad in spectrum and can include mass transit, infrastructure (for example, self-healing materials and stress sensors for bridges or other stressed structures), roadways, roadway safety measures, and automobiles. Although oxygen sensors presently exist in commercial autos, sensor durability and power requirements are issues, and measurement and control of other species is not presently available for a range of applications. With this large number of subdisciplines and the very large market for these sectors, transportation-related sensing is a technology area that could realize a large societal impact. In many of these areas, a common theme should include “smart systems,” which not only enable devices to perform a series of measurements but also enable the system to respond.

National Security and Emergency Response
Emergency responders and national security providers require chemical, biological, and nuclear sensors with multiple functionalities in a range of environmental conditions. Nanotechnology-based approaches could benefit future systems by providing improved chemical sensitivity and specificity for toxic, hazardous, and flammable chemicals and for biological species such as proteins, viruses, and bacteria. The overall ability to provide situational awareness is limited in present sensor systems. A multifunctional, multiparameter system based on nanotechnology can provide information on biohazards and contaminants, toxic agents and gases, the presence of hazardous conditions such as fires, and even the health of individuals. The combined set of information could be wirelessly transmitted from a web of distributed sensor systems, allowing a comprehensive understanding of the environment. This would alert security officials of critical events, enable defense personnel to better understand field conditions, and allow first responders to be aware of conditions at an accident or fire and monitor the environment in the case of a chemical spill. In the end, the response to a hazardous condition or event is often based on incomplete information. This could be corrected by easily implemented and fast-responding sensor systems.
SYNOPSIS OF THE PUBLIC COMMENT SESSION

Societal Dimensions of Nanotechnology-Enabled Sensing

The 21st Century Nanotechnology Research and Development Act calls for ethical, legal, environmental, and other appropriate societal concerns to be considered during the development of nanotechnology, and it also calls for providing for public input to be integrated into the technology development programs. As part of the NNI’s commitment to supporting the responsible development of nanotechnology, this workshop included a comment period during which workshop participants offered comments and posed questions relating to nanotechnology-enabled sensing or nanotechnology in general. Statements from individuals reflected their perspectives as public members and not as representatives of their occupational or employment status.

The following are the general sentiments and questions shared by workshop participants:

- **Personal information security**: What are the risks to individuals of nanotechnology-enabled, point-of-use sensors that can store large amounts of personal information and transmit that information to the government?

- **Federal investments**: There is a need for more coordinated Federal investments in nanotechnology to prevent unnecessary duplication within and between agencies.

- **Innovation**: Are existing programs such as the Small Business Innovation Research Program being used to full capacity? What other mechanisms exist to transition basic research to commercialization?

- **Learning from the past**: What lessons can be learned (e.g., from the development of other technologies) that could inform appropriate guidance of emerging technologies such as nanotechnology?

- **Safety**: It is important to consider and mitigate, when possible, the “unintended consequences” of new nanotechnologies. Scientists will need to contribute to policy discussions that inform legislation and regulation.

- **Education**: The NNI should more actively motivate specific public discussions about the potential benefits and risks of nanotechnology overall, as well as nanotechnology-enabled sensing and the likelihood of these sensors’ ubiquitous use.
2. Nanotechnology-Enabled Transducers for Sensing

Existing Capabilities, Emerging Directions, and Research Needs

INTRODUCTION

Future sensors will be systems that have multiple features, including sample collection, preconcentration, and separation capabilities; transducers able to sense multiple analytes; sophisticated analysis electronics; and wireless communication systems. Each of these components is critical to the system, and nanotechnology offers new solutions for the technical challenges associated with realizing each of these components. However, at the very heart of any sensor is the transducer, the material or device that converts a recognition event into a measurable signal. Nanotechnology offers many new sensing modes and capabilities. This chapter describes five classes of nanotechnology-based transduction in detail: electro/chemical, electromagnetic, spectroscopic, magnetic, and mechanical (Figure 2.1). The following sections on each of these broad transducer classes summarize existing capabilities, discuss emerging directions in terms of both in-progress and desired developments, and identify research needed to move the field in these directions.

ELECTRO/CHEMICAL TRANSDUCTION

Existing Capabilities

One-Dimensional Nanostructure-Based Sensors

One-dimensional (1D) nanoscale materials such as nanowires and nanotubes are extremely attractive as building blocks for sensors, because they can function both as the transducers—i.e., key elements in the initial sensing event—and as wires that carry the signal. When used as sensors, these nanoscale materials offer significant advantages over bulk or thin-film planar devices. First, since their sizes are small and sometimes comparable to those of the analytes being sensed, binding of an analyte to the surface of a nanowire or nanotube can cause large resistance/conductance changes. This is due to either enhanced impact of scattering in these 1D structures, or to the depletion or accumulation of carriers in the core of the nanowire; in comparison, in planar structures, these changes occur primarily at the surface region (see Figure 2.2). Another advantage of 1D nanoscale materials for sensing is that they can lead to massive multiplexing in small devices. This stems from the combination of tunable physical and chemical properties of 1D nanoscale materials.

Figure 2.1. Future sensor systems will incorporate nanoscale transducers that use multiple physical phenomena to sense a broad range of analytes. Illustrated here are (left to right): optical transducers, which measure light; electro/chemical transducers, which measure electrical properties; magnetic transducers, which measure changes to the local magnetic field; and mechanical transducers, which detect changes in motion. (Image credit: N.R. Fuller, Sayo-Art LLC.)
materials, and the direct conversion of chemical information into an electronic signal that can readily couple to existing electronic technologies. Finally, the size of these nanoscale materials makes it possible to develop high-density arrays of individually addressable units for simultaneous analysis of a range of different species. The ability to develop high-density arrays in a controlled manner also allows for massive replication in order to improve the accuracy of the measurements and increase the signal-to-noise ratio.

**Liquid and Gas Sensor Arrays**

Semiconducting single-walled carbon nanotubes (CNTs), conducting polymers, and metal oxide nanowires can be used as the channels of field-effect transistors that are able to sense gases such as ammonia, nitrogen dioxide, and carbon monoxide, and volatile organic compounds such as methanol, hexane, chloroform, benzene, toluene, and the nerve gas stimulant dimethyl methyl phosphonate. Significant improvement in sensitivity and some improvement in selectivity have been achieved through functionalization of CNTs with metal nanoparticles such as palladium, platinum, gold, and tin, and with polymers such as polyaniline, polypyrrole, and polyethylene imine. Similarly, functionalization of conducting polymer nanowires with metal nanoparticles significantly improves their sensitivity. For example, polyaniline nanowires functionalized with gold nanoparticles have a marked improvement in sensitivity and selectivity for hydrogen sulfide gas. However, the extension to practical environmental and variable conditions (real air samples and real water samples) has not been made and requires additional research.

**Label-Free Biological Sensor Arrays**

The majority of the monitoring methods for biomolecular reactions require the application of a reporter or label to biological or chemical species in order to detect molecular recognition events. Most label-dependent platforms are based on the measurement of fluorescence or radioactivity. The multistep reaction and washing processes for subsequent analyses renders this approach tedious and time-consuming and necessitates use of elaborate hardware that does not lend itself easily to miniaturization and portability. These drawbacks have motivated the search for label-free assays.

Advantages of label-free and multiplexed detection include a simple assay format and greatly reduced time for assay development, combined with the extremely small size of the nanostructures. Recent advances in electronic detection based on nanowires and nanotubes have revolutionized the ability to provide label-free and real-time yet highly sensitive and selective detection of a wide range of biological species. For example, CNTs, conducting polymers, and semiconductor nanowires have been functionalized with antibodies, DNA, binding proteins, aptamers, and peptide nucleic acid. These new nanomaterials can be used to detect a wide range of biological molecules, including antibodies, viruses, nucleic acids, and disease protein biomarkers.

**Emerging Directions**

Looking to the future of electro/chemical transduction, there are several new and developing trends that point toward the future of this research area:

- Fundamental studies of interfacial chemistry are emerging to provide the knowledge to achieve stable, reproducible, and renewable interfaces.
- New nanoscale materials are becoming available that provide unique sensing properties and improved selectivity for target analytes.
- Already in development are several room-temperature-operable devices that provide low-power, selective sensors that are insensitive to fouling and are able to carry out self-calibration and self-cleaning to renew the interface.

**Research Needs**

Single-molecule sensing has been achieved for very few compounds and remains a challenge for several important
compounds. Sample handling for both air and liquid samples is inefficient and time-consuming. Also, sensors can give false-positive responses for these samples. Because transducers do not adequately identify analytes in a complex mixture, separation technology is required. Label-free detection has been achieved under laboratory conditions, but it needs to be extended to real-world conditions.

**Carbon Nanotubes**

Some of the potential drawbacks of using CNTs as sensing elements are the lack of specificity to different gaseous analytes and the low sensitivity towards analytes that have no affinity to CNTs. These shortcomings can, at least in part, be circumvented by functionalizing the CNTs with analyte-specific entities. Functionalization also sometimes affects the sensor dynamics. There are two main approaches for the surface functionalization of CNTs, covalent and noncovalent, depending on the types of linkages of the functional entities onto the nanotubes. Currently, most covalently functionalized CNTs are based on esterification or amidation of carboxylic acid groups that are introduced on defect sites of the CNTs during acid treatment. In addition to chemical polymerization, electrochemical polymerization can be used to functionalize CNTs, an approach that offers site-specific functionalization of CNTs with a high degree of success and using standard lab equipment. In general, functionalization of CNTs is still a technical challenge, and using this platform to sense a single chemical or biological species in complex mixtures will require significant discovery and development.

**Conducting Polymers**

Conducting polymers are particularly appealing because they exhibit electronic and optical properties of metals or semiconductors while retaining the attractive mechanical properties and processing advantages of polymers. Their conductivity can be reversibly modulated by controlling the dopant level, and they have been used, in thin-film form, in a variety of sensing applications. Among the conducting polymers, polyaniline and polypyrrole are most frequently used and studied, owing to their very good sensitivity at room temperature, stability in a range of environments, and relative ease of processing.

**Metal Oxides and Ceramic Materials**

Metal oxides (e.g., tin oxide or zirconia) and ceramic materials (e.g., silicon carbide or boron nitride) are useful for ambient- and high-temperature sensing applications, but the surface properties must be controlled. New functional chemistries ought to be explored to enhance response for this class of materials. Crystal uniformity is important to understand, and comparative studies of single-crystal and polycrystalline materials are necessary to resolve any interparticle junction effects and depletion effects. If post-synthesis processing is used, changes to material characteristics must be explored and understood. In particular, tests should be performed to ensure that no other unexpected changes occur, such as in the surface chemistry. Further improvements are needed to increase the response times, detection limits, sensitivity, and selectivity, through the tailored design of both the metal oxide material and its associated catalytically active coating or doping material. Mixed approaches, such as those that couple catalytic metal oxide sensing materials with the plasmonic properties of embedded gold nanoparticles, could prove transformational.

**Surface Chemistry**

The surface chemistry of nanoscale materials may differ from that of the bulk material. The degree of uniformity (i.e., purity of chemistry, homogeneity of size, and consistency of crystal structure and morphology) needs to be studied. Moreover, different morphologies are unlikely to have identical degrees of uniformity. A suite of characterization tools will be required to document heterogeneities in material chemistry, crystallinity, size, and morphology in order to understand variation in transducer response. While mainstay techniques such as x-ray photoelectron spectroscopy are adequate for ensemble measurements, advanced electrical and optical surface probe microscopies are required for single-nanowire devices. New orthogonal techniques involving both optical and electron microscopy techniques must be employed and compared in order to understand the effects of dopants and defects. As exposure to the analyte occurs at its surface, exploring and understanding these surface chemistry effects is central to understanding nanoscale transducers. Ultimately, such data can direct material design.

**Device Contacts and Material Integration**

Controlled integration of nanoscale materials that will be used in sensors and creating contacts to these materials for measurement and device integration is a
significant challenge. Integration of nanoscale materials such as nanowires into devices would benefit from a significantly increased level of understanding and control. Characterization of the electrical contacts of nanoscale structures is important in order to verify device integrity, to identify a suitable operating regime, and to correctly interpret device parameters beyond analyte responsivity. Effects of boundary layers, interfaces, and cross-doping between nanowires and electrode metals must be identified and understood. Sophisticated techniques such as electron-beam lithography are excellent for single nanowire studies but are ill-suited for scale-up and are not generally available to most researchers or companies. Some processes such as dielectrophoresis have been demonstrated for CNTs but are relatively untested for oxide materials. Exploration is needed of coupled-force methods of assembly and integration, for example, such approaches as hydrodynamic flow during dielectrophoresis.

**Fabrication**

While engineered nanoscale materials such as transducers show significant promise, their fabrication methods have some limitations. Successfully harnessing the utility of these materials requires new nanoscale fabrication capabilities and proper attention to the interconnection challenge. For example, existing techniques involving the manipulation of individual CNTs or a random dispersion of suspended CNTs, while adequate for proof-of-principle experiments, have low throughput and/or limited controllability, and they are unattractive for scaling up. Often, surface modifications are required to incorporate biological receptors and have to be performed post-synthesis and post-assembly, adding additional complexity to the manufacturing process. Attempts have been reported to improve fabrication controllability by applying an electric field to align nanowires and carbon nanotubes, by growing metal nanowire arrays on etched templates, and by aligning nanowires in flow; these methods merit further study.

**Standard Methods and Materials**

Standard and reproducible synthesis methods and materials are needed for meaningful comparison and evaluation of transducer performance. For example, although nanowires have been synthesized by many techniques (e.g., hydrothermal, electrodeposition, self-assembly, and plasma), most are still synthesized by hot-wall chemical vapor deposition (CVD) using tube furnaces. Such units are prone to variability in flow recirculation during a run, and signals are affected by drifts in temperature. Physical and chemical properties of deposited/collection materials change over time. The fact that most metal oxides are not inherent semiconductors, but rather rely upon defects in the form of oxygen vacancies (or purposely added dopants) to achieve semiconducting status, clearly demands consistency of synthesis conditions within and between laboratories. Reference standards to trace the full path of material processing and integration are vital to adequately compare sensor characteristics.

**ELECTROMAGNETIC TRANSDUCTION**

**Existing Capabilities**

**Nanoplasmics**

Plasmonics is concerned primarily with the manipulation of light at the nanoscale, based on the properties of propagating and localized surface plasmons. Optical waves can couple to these electron oscillations in the form of propagating surface waves or localized excitations, depending on geometry. Although all conductive materials support plasmons, the coinage metals (copper, silver, and gold) have been most closely associated with the field of plasmonics. These metals have plasmon resonances that lie closer to the visible region of the spectrum, allowing plasmon excitation by standard optical sources and methods. The field of plasmonics is based on exploiting plasmons for a variety of tasks; designing and manipulating the geometry of metallic structures consequently tunes their plasmon-resonant properties.

A cavity-free, broadband approach has been demonstrated for engineering photon–emitter interactions via subwavelength confinement of optical fields near metallic nanostructures, as shown in Figure 2.3. When a single cadmium selenide quantum dot is optically excited in close proximity to a silver nanowire, emission from the quantum dot couples directly to guided surface plasmons in the nanowire, causing the wire’s ends to light up. Nonclassical photon correlations between the emission from the quantum dot and the ends of the nanowire demonstrate that this light stems from the generation of single, quantized plasmons. Results from a large number of devices show that efficient coupling is accompanied...
Chapter 2: Nanotechnology-Enabled Transducers

by more than a two-fold enhancement of the quantum dot spontaneous emission, in good agreement with theoretical predictions.

Chemical sensing based on surface plasmon resonances (SPRs) can be accomplished in a variety of ways. SPR sensing was first performed using propagating surface plasmons on continuous metal films that had been chemically functionalized. Modifications in the chemical environment due to the binding of molecules to a functionalized film were monitored as a change in the incidence angle required for surface plasmon excitation in an evanescent coupling geometry. Similarly, metallic nanoparticles that support the excitation of a localized SPR are also highly sensitive to the environment, because the resonance frequency depends on the dielectric constant of the local medium. In nanoparticle-based SPR sensing, changes in the dielectric constant of the medium surrounding the metallic nanostructure are detected by measuring the shift of the SPR absorbance maximum. This enables the detection of molecules with different dielectric properties at the nanoparticle surface. Although the SPR response is not chemically specific, this disadvantage has been overcome by detection techniques using metal particles conjugated to, for example, antibodies or DNA, allowing for selectivity of target-receptor molecules through binding specificities.

When an electromagnetic wave interacts with a roughened metallic surface or a nanoparticle, the electromagnetic fields near the surface are greatly enhanced relative to the incident electromagnetic field. This phenomenon is due to two processes. The first is the “lightning rod” effect, conventionally described as the crowding of the electric field lines at a sharp metallic tip. The second process is the excitation of localized surface plasmons at the metal surface and is responsible for the amplification of fluorescence and second-harmonic generation from thin metal films. For metal nanoparticles, often both processes are involved in creating the localized enhanced near field. Although this electromagnetic enhancement effect has been exploited in several spectroscopy techniques, it is mainly the amplification of the otherwise very weak Raman signal that has triggered the greatest amount of interest. Surface-enhanced Raman spectroscopy (SERS) (Figure 2.4) is a very attractive spectroscopic method because the Raman signal contains detailed information derived from molecular structure, which may be useful in chemical identification.

Controlled Electromagnetic Properties

Highly tunable nanowire arrays with optimized diameters, volume fractions, and alignment form one of the strongest optically scattering materials discovered to date. Using a new broadband technique, the scattering strength of the nanowires is explored by systematically varying the diameter and alignment on the substrate. Strong internal resonances of the nanowires have been identified by this method. These resonances can be tuned over the entire visible spectrum, as shown in Figure 2.5. This tunability of nanowire materials opens up exciting new prospects for fundamental and applied research exploiting the extreme scattering strength, internal resonances, and preferential alignment of the nanowires for applications ranging from random lasers to solar cells.

Figure 2.3. A coupled quantum dot can either spontaneously emit into free space, with rate $\Gamma_{\text{rad}}$, or emit into the guided surface plasmons of the nanowire, with rate $\Gamma_{\text{pl}}$. (Reprinted by permission from Macmillan Publishers Ltd: Nature 450, 402, © 2007.)

Figure 2.4. Surface-enhanced Raman spectroscopy. (a) Schematic sample geometry for nanoparticle-based SERS. (b) Raman spectrum of p-mercaptoaniline collected with no nanoshells (blue) and SERS spectra with nanoshells (red). (Reprinted by permission from Macmillan Publishers Ltd: Nature Photonics 1, 641, © 2007.)
Antireflective coatings are commonly used in planar optical devices to suppress reflection that generally contributes to lower quantum efficiency. Unlike the flat surfaces that are illuminated in a regular optoelectronic device such as a photodetector, nanowire-based devices offer the potential for trapping the incident photons through subwavelength diffractive effects between nanowires and through multiple reflections in the dense network of nanowires, until the photons are completely absorbed in the active absorption layer. This reduced reflectance has been found to enhance the efficiency in solar cells and the short-circuit photocurrent. The phenomenon of significant light trapping offers enormous opportunity for designing novel nanophotonic devices with simpler physical structures and better performance. Figure 2.6 shows a dramatically reduced reflectance for a nanowire-coated surface over the spectral range from 400 nm to 1150 nm, even without using any anti-reflective coating. More work is needed to correlate nanowire parameters such as length, diameter, periodicity, absorption coefficient, surface condition, orientation, and shape with the reflections and absorption properties of a tile and a mosaic.

**Controlled Propagation of Light**

Slow-light generation can be used for a variety of applications based on wavelength agility, allowable pulse durations, conceptual simplicity, ease of use, and maximum total and/or relative delay. Slow light includes optical buffers, continuously variable optical delays, low-power optical switching, and quantum memory. Slow-light generation using a Raman fiber amplifier has demonstrated the advantage of being able to accommodate the bandwidth and to adjust delay pulses less than a picosecond in duration. This presents the first step in the application of Raman amplifiers in optical devices and as controllable delay lines for ultrafast sensor systems.

Electromagnetically induced transparency (EIT) for the controllable generation, transmission, and storage of single photons with tunable frequency, timing, and bandwidth is also a new technology. Specifically, EIT has been used to study the interaction of single photons produced in a “source” ensemble of rubidium atoms at room temperature with another “target” ensemble. This allows simultaneous probing of the spectral and quantum statistical properties of narrow-bandwidth, single-photon pulses, revealing that their quantum nature...

**Figure 2.5.** Gallium phosphide nanowires: (a–c) scanning electron micrographs of nanowires with increasing diameter; (d–f) white-light–enhanced backscattering spectra of the same series. The significant variations in the spectra of nanowires with different sizes demonstrate how nanoscale materials can be tailored to have specific properties. (Reprinted with permission from *Nano Letters* 9, 930, © 2009 American Chemical Society.)
is preserved under EIT propagation and storage. The time delay associated with the reduced group velocity of the single-photon pulses can be measured, and storage and retrieval of these pulses can be observed. These results demonstrate that EIT represents a very effective technique for generation and controlled propagation of narrow-bandwidth, single-photon light pulses in optically dense atomic ensembles. Applications of quantum-optical processes involving simultaneous control over temporal, spectral, and quantum statistical properties of single photons are possible. The ability to understand and control single photons and their interactions in the environment could significantly impact nanotechnology-enabled sensing.

Emerging Directions

Progress in electromagnetic transduction, and its integration into sensor systems, leverages the ongoing decrease in feature sizes that can be created in semiconductor manufacturing facilities. Some key emerging directions are in the areas of communications (single-photon sensing for on-chip/intra-chip communication), wide-spectral detectors/sensors, plasmonics-assisted sensors, and plasmon-based electrical-optical conversion. Further, new nano-optical sensors will be able to detect a single molecule or a few molecules of gases, chemicals, toxic materials, and disease markers.

Research in electromagnetic transduction will empower a number of new systems capabilities, including:

- The capacity for real-time decision making, with time-sensitive events detected by sensors in a prompt manner, will be highly valuable for point-of-care diagnostics and in instances of medical emergencies and exposures of soldiers in the field to various chemical and biological threats.
- Ultrasensitive chip-scale integrated imaging focal plane arrays (FPAs) are being developed that will have broad spectral operation and facilitate real-time decision making in all environments. Such decision making would be facilitated by low-cost, terabit-level optical data pipes inside future computers.
- The eventual coupling of silicon electronics with III-V photonics (e.g., indium phosphide, gallium arsenide, gallium phosphide) will enable new revolutionary devices with high bandwidth, faster response time, lower energy consumption, and compact architecture.

Research Needs

The current state-of-the-art technologies are limited by several features. There is a lack of mass-fabrication processes for nanophotonic materials/structures such as photonic crystals and substrates for SERS. Relatively narrow-band and nontunable, most of the readout circuits are discrete electronics with noise and limited pixel-pitch resolution. Focal plane array-based sensors are very expensive because the read-out circuitry and the sensors are fabricated on separate substrates. Many sensors must be operated at low temperatures to overcome the noise generated at room temperature.
Multifunctional Materials

Monolithic integration of multifunctional material sensor tiles containing numerous pixels in proximity to each other, constructed with different bandgap and material properties, are needed for sensing a wide spectral range of electromagnetic wavelengths within a single aperture. This integration not only allows for portable, low-energy, and lower-cost sensors, but it simultaneously facilitates high-speed communication and faster decision making.

Impedance Matching

It has been well established that plasmonic modes on noble metal nanostructures offer strong subwavelength confinement and hence facilitate the realization of nanometer-scale integrated optical circuitry. An optical impedance matching network consists of (1) optical antennas as receivers of far-field radiation, (2) a small footprint network of optical transmission lines to distribute and manipulate plasmonic excitations, and (3) another set of optical antennas for converting guided modes into propagating photons or amplifiers.

Figure 2.7 offers an illustration of such a network. The receiving antenna is excited by a linearly polarized Gaussian source and launches guided modes that propagate along the nanoscale two-wire optical transmission line. The emitting antenna (right) converts the guided modes into propagating photons. The corresponding equivalent circuit would consist of a generator, a transmission line, and a load. These systems of interconnected nano-optical elements can be optimized by applying concepts of impedance matching that may also be applied to understand and control the coupling between emitters, receivers, and metallic nanostructures.

Thermal Control

Arrays of large two-dimensional photodetectors are currently made from a variety of materials, such as cadmium telluride, mercury cadmium telluride, indium antimonide, gallium antimonide, and indium gallium arsenide, whereas the readout integrated circuit is typically made of silicon. The two components must be bonded, and the bonding process has two key functions: to provide electrical interconnection, and to provide mechanical connection. However, because the multilayer sandwich of different substrates is cooled from room temperature to cryogenic operating temperatures, the devices often experience stress and reliability issues from the thermal mismatch due to the differences in the coefficients of thermal expansion of the two materials. The drastic differences in these values are obvious, and the thermal stress may be further amplified by the choice of the interlayer bonding, with or without epoxy or polymer underfill. Hence, good thermal control is essential for higher device yield and reliability.

Fabrication Issues and Challenges

Smooth metal films. For most plasmonic applications, use of noble metals with smooth surfaces is vital to ensure that the optical losses are kept to a minimum. Most deposition techniques utilize methods such as thermal evaporation, ion-beam-assisted deposition, and sputtering, which consistently reveal a rough surface morphology with larger grains than the size suitable for desired nanoscale building blocks and electrical interfaces. Recently, a method to obtain smooth silver films has been demonstrated using a very thin germanium nucleation layer. This method is very promising for large-scale applications such as molecular anchors, optical metamaterials, plasmonic devices, and several areas of nanophotonics sensors and communications. Similar techniques will be crucial for other metals such as gold and platinum.

Controlled nanoscale gaps and nanofabrication. The next generation of nano-optical integrated circuits will benefit from the use of plasmonic waveguides. In this regard, the drive to obtain the lowest signal loss with high curvatures for compact circuit size has been focused on silver nanowires. An exciting development in this area has shown that when arrays of parallel metallic nanowires
are fabricated within a nanometer of each other with a precise gap, they can provide a tunable, robust, and versatile platform for plasmon interconnects (Figure 2.8). The proposed guiding mechanism relies on gap plasmons existing in the region between adjacent nanowire pairs and multiwire arrays. The development of this mechanism is still in its nascent stage, and physical realization depends very much on how researchers can best fabricate and control the gap throughout the transmitting and receiving ports. Furthermore, more tools will be needed for designing plasmon-based interconnects and achieving a high degree of integration with minimum cross-talk between adjacent plasmon guides, which are all relevant components of future multiplexed biosensors.

**Heteroepitaxy.** The recent trend in semiconductor R&D has focused to a considerable extent on monolithic integration of multiple materials for applications that include integrated optoelectronics, on/off-chip communications, and devices with ultrawide spectral responses for imaging and sensing. However, formidable technological challenges in metamorphic/heteroepitaxial material synthesis and device fabrications lead to an unfeasible cost-to-performance ratio. In this regard, many of the same severe limitations of the long-investigated epitaxial lift-off and wafer bonding technologies still exist: (1) an inability to develop mass-manufacturable techniques to grow and integrate a variety of materials and devices on a host of surfaces; (2) incompatibility with standard microelectronics due to extreme physical growth conditions such as high temperature; (3) loss of a complete starting substrate, contributing to substantial cost that greatly exceeds the benefit; and (4) the interface defects, vacancies, and traps in heteroepitaxy of mismatched materials and the resulting unpredictable performance degradations.

**Nanowires.** The vapor-liquid-solid (VLS) technique allows the synthesis of nanowires via chemical vapor deposition (Figure 2.9). The VLS technique forms nanowires with small dimensions (with diameters in the range of a few to hundreds of nanometers) without using fine-scale lithography. For example, in the case of a silicon nanowire, a small metal nanoparticle accelerates the decomposition of a silicon-containing gas (typically silane), and the silicon atoms precipitate between the nanoparticle and the substrate, forming a column of single-crystal silicon (i.e., a silicon nanowire or nanopillar) with the desired high surface-to-volume ratio. However, even if mass-manufacturable fabrication methods can be developed for nanowire-based electrical and optical sensors, there are still formidable device issues due to the inherent characteristics of nanowires. These include high-energy surface states, persistent traps, impurities induced by catalysts, randomness in the orientation, and uncontrollable nanowire-bulk interface properties.

Although it is extremely challenging to achieve high-quality epitaxial (monocrystalline) growth of planar layers of compound semiconductors on silicon substrates, nanowires offer an opportunity to grow continuous thin films on highly mismatched materials. As an example, germanium nanowires can be grown on a silicon substrate by precise positioning of catalysts using an oxide mask. After removing the metal catalysts, lattice-matched gallium arsenide can be grown as a thin film on the surfaces of germanium nanowires via molecular beam epitaxy or metal-organic chemical vapor deposition. A planarization technique and a thermal annealing process can be used to address interfacial issues. Important challenges include dislocations, defect density and surface roughness, polar/non-polar mismatch, and antiphase boundaries.

**Band-gap tailoring.** Photonic crystals are unique artificial electromagnetic materials with periodic dielectric structures that forbid propagation of electromagnetic waves in a certain frequency range. Such photonic crystals can be designed by band-gap tuning and arranging lattice defects to open up a variety of possible applications in lasers, antennas, and millimeter wave devices.

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**Figure 2.8.** Gap plasmon modes of two parallel silver nanowires in silica. (Left) Schematic of nanowire array. (Center) The local density of states is distributed as shown for parallel nanowires (left), where brighter regions correspond to higher density of states and local density of states. (Right) The photonic density of states is a function of energy (y-axis) and momentum (x-axis) parallel to the wires. (Reprinted with permission from *Nano Letters* 9, 1285, © 2009 American Chemical Society.)
SPECTROSCOPIC TRANSDUCTION

Existing Capabilities

Spectroscopic methods, such as infrared or Raman spectroscopy, involve probing a sample with a beam of light. The reflected or absorbed light provides signatures characteristic of the species in the sample. These methods do not require contact with the sample. Just as a radar station can locate and identify airplanes at a distance, many spectroscopic methods can be employed from a safe distance. For example, a toxic chemical cloud could be interrogated without exposing the equipment or the operator to the chemical. Nanotechnology-enabled methods are needed to improve existing spectroscopy capabilities or to develop altogether new spectroscopies with greater sensitivity, specificity, and ability to operate from long-standoff ranges. One example of a nanotechnology-enabled spectroscopy is SERS. The use of nanoscopic gold particles in this technique increases the sensitivity of laser-based Raman spectroscopy by six orders of magnitude (Figure 2.10). Figure 2.11 gives an application of SERS to identification of a chemical agent.

Single-modality optical sensing is highly developed, with a wide variety of dedicated optically enabled chemical and biological sensing techniques, each of which has its own associated sensitivities and footprints. A breakdown of the state of the art of several spectroscopic methods follows.

Figure 2.9. 1D nanowires grown by bottom-up fabrication methods. (a) Schematic of nanowire growth in mismatched condition; (b) lateral silicon (Si) nanowires grown between two vertical Si surfaces; (c) indium phosphide (InP) nanowires on Si surface; (d) gallium arsenide (GaAs) nanowires on GaAs; (e) InP II-V nanowires on an InP surface; (f) Si nanopillars grown via VLS method. (Images: [a] and [b] courtesy of S. Islam; [c] reprinted with permission from Appl. Phys. Lett. 89, 133121, © 2006 American Institute of Physics; [d] reprinted with permission from Appl. Phys. Lett. 86, 213102, © 2006 American Institute of Physics; [e] reprinted with permission from Physica E 25, 313, © 2004 Elsevier; [f] reprinted with permission from Appl. Phys. Lett. 91, 103110, © 2006 American Institute of Physics.)

Figure 2.10. This figure shows SERS detection in which a rough metal surface acts like an optical antenna to enhance the scattering of light by a molecule. (Reprinted with permission from Phys. Chem. Chem. Phys. 10, 6079 [2008].)
Chapter 2: Nanotechnology-Enabled Transducers

Fluorescence

Fluorescence microscopy with single-molecule or single-fluorophore sensitivity has been demonstrated and applied extensively in biological and biochemical assays. Single-molecule fluorescence detection requires a dedicated optical system, including an excitation light source, highly sensitive photodetection, and often time-resolved spectroscopic capabilities. Fluorescence resonant energy transfer (FRET) is a proximity assay based on fluorescence quenching due to direct resonant interactions between a fluorophore and a metal nanoparticle. Due to its direct nature, conventional FRET is limited by the spatial extent of the quenching interaction to the few-nanometer range. Furthermore, the utility of FRET is determined by the ability to conjugate fluorophores to desired analytes through selective chemistry. The hardware requirements for FRET are similar to those of ordinary fluorescence detection.

Raman Spectroscopy

Raman spectroscopy is a standard, label-free chemical characterization technique based on inelastic light scattering, in which energy is exchanged between the radiation and the molecule-specific Raman-active vibrational modes. The sensitivity of Raman spectroscopy may be greatly enhanced through coupling to the evanescent electromagnetic fields from plasmon excitations in metal structures. The SERS signal is proportional to the product of the near-field intensity enhancements at the incident and scattered wavelengths. SERS enhancement factors exceeding $10^{12}$ have been reported, and single-molecule Raman sensitivity has been demonstrated. SERS sensing with lower sensitivity is available commercially for trace chemical detection. Raman is a more demanding technique than fluorescence, generally requiring a laser source, a grating spectrometer, and a photodetector.

Other Methods

Many other techniques for optical detection exist. These include infrared absorption and colorimetric assays. The latter can be based on chemical reactions or take advantage of analyte modification of dielectric response to produce color changes through iridescence. Optical phase-based sensing can also be used as a transduction mechanism. One example is a surface plasmon interferometric sensor array, which distinguishes an analyte layer by modifying the phase and amplitude modifications of surface plasmon polariton waves. An extension of this is the plasmonic modulator shown in Figure 2.12.

Emerging Directions

The future of spectroscopic transduction will be linked with achievements in some critical emerging directions:

- Efforts are underway to develop the next generation of fluorescent nanoparticles. These will be small nontoxic nanoparticles that are photostable at any wavelength (ultraviolet to mid-infrared), have a high quantum efficiency, are compatible with all useful surface conjugation schemes, and have switchable optical properties in response to analytes or environmental changes.

- Stable, manufacturable, single-molecule–sensitive SERS and SEIRA substrates readily integrated with other sensing modalities will greatly improve the capabilities of Raman spectroscopy as a sensing method.

- SPR-type sensing will demand multiplexed high spatial density structures that are readily interfaced with readout mechanisms.

- Leveraging the existing knowledge of FRET, new proximity assays are being developed with by-design length sensitivity and improved control of probe location with respect to the quencher.

Research Needs

Current technical problems and challenges that exist for spectroscopic transducers include unstable dyes, broad spectral emission, instability of nanoparticle systems, difficulty in integrating chemically synthesized nanoparticles and top-down nanofabricated structures.
multiscale modeling, and materials limitations for plasmonics in certain frequency bands (mid- and far-infrared, blue, and ultraviolet). Several nanotechnology insertion points are described below:

- Optical antennas/plasmonic focusing/metamaterials: Metal nanostructures can act as optical antennas and waveguides, producing regions of enhanced optical intensity where enhanced spectroscopies can take place. Likewise, novel resonators can be local (nanoscale) probes that are ultrasensitive to tiny changes in environment.

- Plasmonic/metamaterials having ultracompact mode confinement: This allows optical energy to be transferred and manipulated on deep subwavelength scales. This drastically reduces background signals and allows for extremely local probes.

- Metamaterials, plasmonic structures, and photonic crystals that allow dispersion engineering: This includes the capacity to slow light and thus increase interaction times with fluorophores and absorbers.

- Engineered energy transfer via plasmons: FRET interactions are limited to the dipole-dipole length (~6 nm). Plasmonic structures allow this coupling to be engineered over much longer distance scales (tens of nanometers or more).

- Optical coupling from the nanoscale to the macro-scale: Photonic crystals, plasmonic structures, and metamaterials perform impedance matching and transform evanescent fields into far-field propagating modes. This is very useful for in- and out-coupling of electromagnetic radiation for sensing based on optical spectroscopy and local dielectric properties.

**MAGNETIC TRANSDUCTION**

**Existing Capabilities**

There is a growing collection of integrated solid state nanotechnologies for detecting and measuring magnetic fields. These devices, as a group, are called magnetoelectronic devices. Spintronics is another name sometimes given to this class of devices and to novel and exotic devices that seek to expand upon and go beyond this class. Roughly, in order of technological sophistication, magnetoelectronic techniques include the Hall effect, anisotropic magnetoresistance, superconducting quantum interference device (SQUID) magnetometry, giant magnetoresistance, and tunneling magnetoresistance.

In all of these nanotechnologies, the magnetic field is transduced to an electronic signature by measuring a change in resistance of the device as a function of an externally applied magnetic field. These are all planar technologies that are commonly built on top of or integrated into silicon wafers. As such, they are extremely valuable for their ease of integration into a wide variety of circuit and data-handling applications.

Magnetoelectronic devices are, themselves, a very advanced nanotechnology because they depend on atomic-scale control of multilayer conductive structures with layer thicknesses on the order of 0.2 nm to 100 nm. High-performance devices must have extremely clean interfaces between magnetic and nonmagnetic layers, and very low surface roughness.

Industrial applications of nanomagnetic sensor technologies include motion detection in automated systems, vehicle detection and identification, and wheel speed measurement. Biomedical applications include magnetic switches in pacemakers and other implantable devices. One example of a device enabled by nanomagnetic technology is a hearing aid that contains a sensor able to detect the magnet in a cell phone and automatically adjust the gain to prevent feedback.

**Absolute Magnetic Field Sensitivity**

Many additional applications in miniaturized magnetic field sensing will be possible if the noise floor of magnetic
sensors can be lowered sufficiently. A combination device with vibrational/inertial sensors may also be needed to account for motion within the earth’s magnetic field. A distributed array of room-temperature magnetoresistive sensors measuring simultaneously could be used for magnetic medical imaging, e.g., nanomagnetic particles for detecting cancer.

**Magnetic Nanoparticles**

Magnetic nanoparticles provide magnetic field signatures that are detected by magnetoresistive nanosensors. Typically these nanoparticles are coated with a biospecific material that facilitates the binding of the nanoparticle to a biochemical species of interest (i.e., DNA, proteins, antibodies, cells, and bacteria). These nanoparticles are routinely used in clinical chemistry as sample sorting, capture, and concentration tools. However, this nanotechnology has yet to make an impact in point-of-care, home, or remote settings.

In using magnetic nanoparticles as biolabels for nanomagnetic detection, two sets of biospecific binding can be used to capture a specimen of interest between a nanomagnetic particle and a nanomagnetic sensing chip surface. This is commonly called a “sandwich assay.” Research results have shown that these assays can be very sensitive with only modest complexity of sample preparation (see Figure 2.13). However, none of these arrays have yet reached the marketplace. The current array size is about a hundred sensors on a chip. These magnetic biosensor arrays will find their best applications in distributed miniaturized systems. Nanomagnetic detection is enabling for low-cost, distributed applications such as home use because it does not require optics or photonics. This drastically simplifies the materials choices for microfluidic sample handling and sensor interface structures (for example, plastic is fine; glass is unnecessary).

**Emerging Directions**

Looking forward, developments in some key areas will help realize the future of nanomagnetic sensing:

- Several “flavors” of magnetic nanoparticles with unique magnetic field signatures can be created, having different shapes, sizes, and magnetic structures. Nanoparticles are used as sample capture and sorting tools in a fieldable, continuous-flow microfluidic sorting device using a combination of magnetophoretic and electrophoretic on-chip forces. By using multiple sorting force mechanisms, a mixed sample of cells, bacteria, etc., could be divided into multiple outlets for detection or processing. This could enable life-saving therapies, such as bone marrow treatments, to be provided at much lower costs and at a greater number of facilities.

- A system for quantification of flowing nanomagnetic objects in an affordable device would enable rapid identification of bacteria in food, pollutants in ground water, and any other species of interest that could be labeled with a magnetic nanoparticle.

- A biocompatible magnetic nanosensor can be designed for introduction into the body to perform important tasks such as measuring analytes of interest or finding nanomagnetic markers for cancer cells. A radio frequency link would enable real-time transmission of analysis data to a receiving system outside of the body.

- High-count, low-cost arrays of low-noise sensors will open a new field of portable biomedical imaging capabilities in medicine. For example, these could be used to measure the magnetic susceptibility of blood (directly related to the oxygenation of hemoglobin).

**Research Needs**

**Noise Reduction**

The single most important area of research for nanoscale magnetic sensing relates to noise reduction. There is noise in the detection systems at several levels. The source of this noise includes background signals (magnetic fields, vibrations, biomolecular, nonspecific binding) and time variance of the nanoparticle properties. Other noise is caused by device defects or non-uniform sensing.

![Figure 2.13. Photograph of a spintronic magnetic sensor chip capped with a photodefined polymer microfluidic channel. The sensor is designed to detect the presence and concentration of magnetic nanoparticles that pass through or stick to the sensor surface. (Image courtesy of Z. Peng et al. [2004], LSU–CAMD; NVE Corp.; and M. Tondra, Diagnostic Biosensors, LLC.)](image)
properties. In many cases, atomic-level fabrication control is needed. A greater understanding of these potential noise sources is also highly desirable. However, better modeling and characterization of magnetic nanoparticles and nanomagnetic sensors will help to overcome this difficulty. Investigations of the physical causes of low-frequency and other noise in nanomagnetic sensors are ongoing and will contribute to advancements in this field.

MECHANICAL TRANSDUCTION

Nanomechanical sensors have made considerable progress recently, and many promising approaches using nanomechanical sensor platforms have been demonstrated. Nanomechanical sensing involves measuring extremely small displacements or mechanical oscillations of mechanical structures in response to physical, chemical, or biological stimuli. Physical stimuli include extremely small changes in temperature, pressure, flow rate, viscosity, density, electrical fields, magnetic fields, or radiation that result in resonance and bending responses of miniature structures such as the cantilever beam illustrated on the cover of this report. Resonance responses include changes in resonance amplitude, frequency, and phase of oscillation. Chemical and biological stimuli include molecular adsorption/absorption and changes in surface charge due to changes in pH, ionic concentration, and chemical reactions.

Emerging Directions

The purpose of a nanomechanical sensor is to detect a chemical, biological, or electromagnetic signal, most frequently via small mechanical changes in cantilever platforms. This sensing should occur with high selectivity, reversibility, and reproducibility without using any receptors or extrinsic labels. In this regard, receptors are defined as biological molecules or chemically specific interfaces. Detection within the sensing system will involve integrating nanotechnology-based sample collection with in situ processing.

- Orthogonal signal generation has the potential to be achieved by simultaneously measuring the responses of a mechanical sensor (for example, resonance frequency, magnitude, and direction of surface stress-induced bending, oscillation phase, and Q-factor of resonance) and mass measurement using resonance frequency and molecular adsorption-induced surface stress (adsorption energy).

- Photothermal deflection of a bimaterial cantilever when exposed to different wavelengths of light can provide a unique orthogonal signal. In photothermal deflection spectroscopy, deflection of a mechanical bimaterial cantilever is monitored as a function of optical illumination wavelength. When adsorbed target molecules absorb light, nonradiative decay causes the cantilever to bend in proportion to light absorption by the target molecules. This technique, which does not utilize any chemical interfaces for achieving selectivity, is ideal for nanomechanical sensors.

- Because nanomechanical sensors have very low thermal mass, they can be controllably heated to high temperatures in milliseconds using very little power. The thermal flexibility of nanomechanical sensors allows catalytic reactions to be carried out at high temperature. This capacity for high temperatures allows thermal regeneration of sensors when detecting target molecules with chemical interfaces that are irreversible at room temperature. In addition, thermal gravimetric measurement of very small quantities of adsorbed target molecules can provide another, independent indication of the presence of an analyte.

- Nanomechanical sensors can be used to measure the magnetic and electrical properties of target molecules or target molecules coupled to nanomagnets.

Research Needs

Research goals for nanomechanical sensors that have yet to be reached include fabrication of sensors with electronic readout that provide reliable performance characteristics, integration of multimodal operation on a single chip, and synthesis of chemical interfaces that are highly specific. Coupling nanomechanics with optical spectroscopy and thermodynamics are still in the early stages, while coupling with nanomagnetism remains to be studied. Incorporating all of these multimodal effects into a single chip with an array of nanomechanical sensors is yet to be done. In addition, the process of optimizing and perfecting orthogonal modes is still in its infancy.

Another area in need of development is theoretical and computational understanding of nanomechanical phenomena and the relation of nanomechanical science to other nanoscale sciences. Focused efforts are needed to understand fundamental nanomechanical phenomena and their relation to other nanoscale effects such as
spectroscopic, magnetic, electrical, electrochemical, or thermogravimetric effects.

Without bringing analytes to nanosensors, no sensor signal can be generated. Methods and strategies need to be investigated for fast sample collection using nanoscale effects. The very small surface areas associated with nanomechanical sensors, often much smaller than the diffusion length of the adsorbed molecules, raise concerns regarding the relationship between the concentration of target molecules in the bulk (air or solution) and their concentration on the sensor surface. Generally these two concentrations are orders of magnitude different from each other, and in the case of nanosensors, this difference may be even greater. Therefore development of efficient and creative ways by which molecules can be collected and transported to the sensor surface need to be emphasized. These preconcentration steps should be fast and readily integrated into a sensor platform without increasing the size, power requirement, or detection time.
3. Putting It All Together

Fabrication, Integration, and Manufacturing

INTRODUCTION

Application of nanotechnology to sensing systems has demonstrated potential for a great deal of novel functionality. Though many of the exciting developments are only recent and many important discoveries lie ahead, the basic concepts associated with nanotechnology-enabled sensing have now been widely debated and reasonably clarified, and the fundamentals have been laid out. Furthermore, experiments have proven the feasibility of the enterprise. In short, the field is on a sound footing, and it is appropriate to consider the challenges associated with integrating individual components into sensor systems, and ultimately, the difficulties of mass-producing these systems. The next stages in the R&D process will be critical to developing viable products; a focused, application-driven approach may prove helpful. Questions of scalability, manufacturability, control, and integration with existing systems should—and can—be addressed near the beginning of a research program. Society should proactively understand health and safety implications and direct the policies and standards that may govern the manufacture, use, and disposal of new sensing systems.

The stages associated with fabrication, integration, and manufacture of sensor systems that incorporate nanotechnology are illustrated in Figure 3.1. At the base of the pyramid are the materials from which nanoscale structures are fabricated. These individual components or structures, often made from dissimilar materials with diverse physical and chemical properties, must ultimately be integrated into devices and sensing systems. As seen in Figure 3.1, the development of these new devices builds on the knowledge and creation of structures bridging nanoscale and macroscopic length scales, as well as the use of sound methods for modeling, characterizing, and integrating components into operational devices and systems. An appreciation of these various levels of challenges can be gained from following the operation of a sensor from a recognition event to signal output. As illustrated in Figures 1.1 and 1.2 (Chapter 1), the recognition event is an early and pivotal step in the sensing process. A transducer converts this event into a measurable signal. This signal must be read, analyzed, and generated into an output to the user. Each of these components—and those not mentioned such as sample collection, concentration, and separation modules—must be brought together. Integration of the sensor elements onto semiconductor electronics platforms, an engineering requirement for large-scale production, injects certain restrictions in terms of processes and materials. However, this integration offers the decided advantages of scalability, high quality and yield, and low cost. These advantages help capture more of the value chain for a given product type.

There are, as discussed in Chapter 2, many transducer types, made from a plethora of different materials and functional layers. This leads to the need for new and economical manufacturing processes with features such as inclusion of electronic elements and scalable batch processing. New processes could include advanced lithographic techniques or laser micromachining that are compatible with systems having special requirements, such as low-volume chemical and biological sensors, as well as use of a greater diversity of materials. The
availability of new approaches to the different stages in sensing development (as shown in Figure 3.1) will create additional quality, space, yield, and packaging issues that must be addressed in order to produce successful sensing systems.

Several general needs in the areas of fabrication, integration, and manufacturing are recognized. These include the needs for improved processing methods for handling the new and different sensor materials, and for improved understanding of the specific activity of the materials used for sensing. Better understanding of the relationships between desired sensor performance and nanoscale materials, processing, specific structures, and operating methods is needed at the time integration begins. Sensor response includes sensitivity, selectivity, response time, stability, detection limit, and dynamic range. The operating methods depend on the device design (of, for example, a transistor, diode, chemiresistor, photo-junction/conductor, or capacitor) and on the way in which the sensor signal is obtained (for example, at constant current, voltage, temperature, or other constant or variable conditions). Such understanding is necessary to generate the best integration support tools and enable effective integration activities for sensor work.

**BROADLY ENABLING CAPABILITIES**

**Design & Modeling**

There is a critical need for modeling programs that can predict the output of nanoscale detector elements and their interaction with other sensor system components, much like the Simulation Program with Integrated Circuit Emphasis (SPICE) used in the semiconductor electronics industry. The goal should be to provide a comparable level of design support for the creators of nanotechnology-enabled sensors as currently exists for the modern electronics analog/digital designers. The current methodology is one of trial and error in the worst way: it is a cyclical process of design and fabrication followed by testing, which is a complex and expensive approach. With good modeling tools, designers would be able to accurately predict performance and material interactions for nanoscale sensing systems. Design could then move forward rapidly, expanding research opportunities and commercial product development.

The simulator model must predict electrical behavior for several important factors. The first factor is variation—in foundry capabilities, materials used for the detector element, and fabrication constraints (e.g., dose, semiconductor material, semiconductor dimensions, and fabrication specifications). In addition, the model must address variation in arbitrary structures such as metal pads, surface layers, wafer material, and layouts. The presence of charged particles acting through relevant structures attached to the detector element surface also has an impact on the system, and a good modeling program should include these effects. Examination of the requirements of existing sensors will provide input/output guidance in the model for the range and types of input/output signals needed for sensors and sensor platforms. New sensor systems will, of course, have new requirements; however, availability of modeling tools will go a long way toward reducing costly integration efforts.

Existing semiconductor design and process software is a good place to start in designing sensor simulation tools, because it is available and because nanotechnology-enabled sensor systems will rely on many of the processes and tools used in the microelectronics industry. For these same reasons, it would be desirable for the sensor modeling software to produce an output similar to that of the existing SPICE simulator.

The sensor model will require a great deal of reference data. The understanding of the surface chemistry of most of the emerging nanoscale materials is still rudimentary, and chemists working on new materials are far from achieving profound understanding of the underlying developments in highly integrated systems such as lab-on-a-chip. An in-depth understanding would be very important for integration and reproducible fabrication of sensing devices, and for models that aim to predict the behavior of new materials and sensing systems. Because nanotechnology-enabled sensor systems will involve a wide variety of materials, surfaces, and surface modification, this will be a significant undertaking. Modeling the interaction of charged particles through a biomolecular structure and surface structures will be another challenge.

**Foundries**

Access to advanced foundries is critical to the development of nanoscale sensor systems. Some NNI facilities, such as the National Science Foundation’s National Nanotechnology Infrastructure Network, the Department of Energy Nanoscale Science Research Centers, and...
the National Institute of Standards and Technology Center for Nanoscale Science & Technology’s Nanofab, provide user access to high-end facilities. However, new leading-edge equipment is a continuous need, and affordable access is an ongoing challenge; policies regarding user fees and costs for travel vary considerably. Moreover, in most cases, these facilities are strict in their requirements for compatibility with standard semiconductor materials, which limits the number and types of materials that can be used. In addition, not all foundries are equipped for the monolithic integration of multiplexed sensor systems. Besides the technical requirements, access to nanofabrication facilities is a growing need for all researchers who are working in the area of nanotechnology-enabled sensors, regardless of their affiliation. These facilities may prove critical in the realization of the transfer of technologies into the marketplace. Challenges in pricing structure, access to outside users, and instrument reliability all must be met in order to address the needs of academia as well as those of large and small companies.

Shared Platforms
The infrastructure funded under NNI auspices could make an enormous contribution by developing standard sensor platforms. One example is a digital signal-processing module. At present, most sensor systems use electronics and signal wires that are subject to numerous interferences such as resistance, capacitance, and other noise sources, and these interferences often dominate the signal. In addition to the converter module, there is a need for standard digital signal processor circuitry that can analyze signal data. The design of a digital signal processor can be straightforward if the number of tasks is well defined. The important contribution that is needed from the nanotechnology research community is to determine the specifications of such an interface structure. The input signal levels and expected wave forms need to be established. The output signals are likely to be designed more easily, but they need to be specified. Design of a digital unit that reads the response from numerous sensors simultaneously is also needed. Such a controller is best contained in a hybrid package or two-chip package associated with the sensor. An embedded digital controller can perform tasks such as identification of faulty sensor devices, determination of the baseline electrical parameters of the detection devices prior to exposure, determination of electrical parameters of the detection devices after exposure, and simple analysis or averaging of data values for output signals. With current microelectronic processing capabilities, performing these tasks at microsecond processing time is feasible. However, the issue of noise injected into the detectors from the microelectronics is an important consideration.

Standardization
Manufacturing scale-up of sensor systems designed in the lab will inevitably involve standardization of measurement techniques, communication protocols, and metrics for manufacturing and performance. This includes the development of standard characterization metrics for nanotechnology-enabled sensor systems. In particular, fast and low-cost methods for characterizing nanoscale materials and assembled devices will be needed. To date, most research has focused on transducer demonstrations, largely depending on expensive or highly specific techniques for device characterization. Fast and high-throughput methods will be needed to bolster large-scale manufacturing in order to reduce costs to competitive levels. Standard reference materials will be needed for comparison of sensor performance. Since the sensors rely on different transduction mechanisms (i.e., optical, electrical, electronic, magnetic, and mechanical), performance standards need to be established for the different types of sensors.

Packaging & Integration
Embedding nanoscale materials, especially those with organic or biological components, on silicon platforms presents problems associated with high process temperatures. New research is needed to produce either low-temperature semiconductor materials or altogether new materials that can prevent embedded electronics from being exposed to high temperatures. Another option is to develop a new type of packaging technology. Many integration challenges also need to be addressed, since nanotechnology-enabled sensors will have a large number of elements that need to be connected to standard electronics. These challenges include the following: transducer connections, in situ characterization, design for manufacturing, axiomatic design, compatibility, backend processing, sharing common tools, and physical conditions (e.g., pressure and temperature).
Several other aspects of packaging and integration need to be considered, such as backend process, stress, and passivation mechanisms. Since the goal is to have multiple orthogonal sensors on the same chip, issues concerning the multiple sensor and circuit interface (monolithic versus hybrid) have to be considered. The processing conditions need to be environmentally friendly and biologically compatible. Since the read-out lines and interconnects must be very closely spaced, the electrostatic and charging effects can pose major challenges.

**Workforce**

A solid educational foundation and a skilled workforce are essential to the successful design, development, and deployment of nanotechnology-enabled sensing systems. The workforce must include nanotechnology researchers, technicians, manufacturing engineers, and production workers. Nanotechnology-specific educational programs and partnerships among universities, Federally funded R&D centers, and industry would best foster the development of a workforce capable of realizing the broad vision and specific goals discussed in this report.

**Roadmap**

The issues surrounding fabrication, integration, and manufacturing of nanotechnology-enabled sensors, ranging from materials to facilities and from applications to staffing, are complex and interrelated. A roadmap, jointly written by academic, industrial, and government leaders, could speed this effort. For example, the complexity of surface modifications and interfacial control in a multipart material and highly variable target analyte space makes modeling difficult, if not impossible. Key quantities still need to be measured. The most important of these quantities could be systematically identified in a roadmap. In a similar spirit, a roadmap could provide guidance on near-term issues such as measurements and standards for comparing transducers. The metrics by which to judge sensor component and system performance are needed and would be a natural part of any roadmapping activity.

**FABRICATION APPROACHES**

Despite significant progress in several novel single-sensing devices, large-volume sensor fabrication has been stalled by an inability to controllably incorporate devices and nanomaterials within integrated circuits. Following a decade of research-based approaches to sequential interfacing of individual nanosensors for device physics studies, it is now vital for the research community to develop a massively parallel and manufacturable interfacing technique for reproducible fabrication of dense, low-cost sensor arrays. The two dominant fabrication approaches, top-down and bottom-up, are described below.

**Top-Down Methods of Fabrication**

**Lithographic Fabrication Methods**

Top-down methods of fabricating nanoscale sensors are largely, but not exclusively, built upon technology developed for and by the semiconductor electronics industry. Such methods have the advantage of being well understood and well automated. They are primarily comprised of methods such as deep ultraviolet, x-ray, and electron-beam lithographies. Further modification of fabricated structures is enabled by ion-implantation capabilities, allowing well-controlled doping of semiconductor structures. Because semiconductor logic and memory devices are based on transistor-transistor logic, the transducers most readily amenable to lithographic fabrication are based on the field-effect transistor (FET; see three examples in Figure 3.2). In FETs, source, gate, and drain electrodes, as well as interconnects, are lithographically fabricated by well-established methods. The gate electrode is then modified in some way to enable it to interact specifically with some analyte. The source-drain-gate combination acts as the transducer element, where modification of the gate electrode or gating mechanism yields the recognition element with the sensors. Recognition elements may include chemical or biochemical monolayers—especially

---

**Key Words Defined**

- **Top-down & bottom-up** – Descriptive terms for the fabrication methods used in making advanced devices.
- **Top-down** refers to making a system from a larger component, typically by adding or removing materials and patterning using conventional microfabrication techniques.
- **Bottom-up** refers to assembling a system from multiple, smaller components.
- **Foundry** – Facility capable of fabricating micro- and nanoscale electronic components and devices.
antibodies and nucleic acids—that bind to specific target molecules. Upon binding of target analytes, the local electric field at the gate changes, changing the resistance and thus the current flow between the source and the drain. The connection between the source and the drain may be a lithographically defined metal film (as is often the case with monolayer-based transducing layers), or inherently nanoscale materials such as CNTs, metal and semiconductor nanorods, or nanoparticles.

Challenges Inherent in Lithographic Methods

Top-down methods have also been used to create layered structures (Figure 3.3) and patterned surfaces with nanoscale features (Figure 3.4). All top-down fabrication approaches are mature, with good control of doping, surface, impurity, and crystal quality. Most facilities have processing capability for nanoelectronics, photonics, and nano- and microelectromechanical processing systems. A nanofabrication facility typically can fabricate device features down to 30 nm using electron beam writing; however, the equipment is extremely expensive and not easily accessible. One subtle issue specific to sensor research is the fact that silicon oxide, which is by far the most common passivating layer in silicon-based nanostructures, is not stable in water for long periods of time. Such limitations may necessitate special coating and passivation methods.

Another challenge for lithographic sensor fabrication is interfacing sample preparation and sample introduction with lithographically fabricated arrays, especially when samples are liquid-phase solutions and mixtures. Existing lab-on-a-chip microfluidic technologies are an obvious, if somewhat partial, solution to the problem. Separation columns enabling on-chip liquid chromatography, gas chromatography, and electrophoresis allow separation of small-volume samples in columns generally between 2 µm and 50 µm in diameter, although a “fluidic impedance mismatch” may still result when stepping-down the dimensions from such separation channels to the nanometer-scale channels that feed transducer arrays.

Still another challenge to lithographically fabricated nanoscale sensor integration is on-sensor or on-chip signal processing. The most obvious solutions are based on conversion of response directly to an electrical signal, as in the chemical FET designs outlined above. Good sample preparation and interfacial design at the modified electrode (comprising the FET gate) allow interconnects to carry output from the source-drain electrodes directly to interfaced microprocessors. If optical signals are

Figure 3.2. Sensors made by top-down methods: (a) nanotube sensor, (b) etched nanowires, and (c) organic transistor. (Images: [a] reprinted with permission from Nano Letters 3, 459, © 2003 American Chemical Society; [b] reprinted by permission from Macmillan Publishers Ltd: Nature Materials 6, 379, © 2007; [c] reprinted with permission from Langmuir 18, 5299, © 2002 American Chemical Society.)

Figure 3.3. Cross-sectional view of a porous silicon double-layer structure. (Reprinted by permission from Macmillan Publishers Ltd.: Nature Nanotechnology 4, 255, © 2009.)
Chapter 3: Putting it All Together

to be processed, charge-coupled device (CCD) camera interfacing provides a readily integrated approach. However, challenges remain in integrating light sources and directing them to analysis zones.

Electrochemical Fabrication Methods

A vastly different class of top-down method for sensor fabrication is electrochemical etching. While providing imperfect control of feature structure and location, it is a laboratory-scale technique that can readily produce electrodes with features of many different geometries and aspect ratios (see Figure 3.3). These electrodes can be left in place on the electrode structure or detached as nanoparticles, nanorods, or other nanoscale shapes. The electrodes themselves can be modified for electrochemical sensing in various ways, or used as optical elements if the features are regular enough to render the structures photonic. The technologies derived from electrochemical etching methods are different from those derived from lithographic top-down methods. Generally, devices made using electrochemical etching feature ensembles of nanostructures, where the nanoscale structures themselves enable sensing but are not individually addressed. In this sense, devices derived from electrochemical etching are similar in class to those derived from bottom-up techniques. These devices are then interfaced with a macroscopic platform to achieve the final device structure.

Bottom-Up Methods of Fabrication

Bottom-up methods of fabricating nanoscale sensors are extremely varied (for three examples, see Figure 3.5). With a few notable exceptions, they generally do not provide the level of spatial control and individual device addressability as do lithography-based methods, unless they are done in conjunction with preliminary lithography-based patterning. In the case of many of the bottom-up sensing elements and materials, the nanotechnology aspect enables the signal transduction in some way, but the overall device is on a larger scale.

Examples of Bottom-Up Methods

Bottom-up methods include chemical vapor deposition (CVD), thermal evaporation, sonochemical processes, electrodeposition (including those through porous and track-etched membranes), sol-gel deposition, self-assembly, and dip-pen lithography. The general advantages of these methods are that they are usually inexpensive and often offer flexibility in production of objects of well-controlled size—often achieved by preforming the nanoscale objects chemically, electrochemically, or by some other sort of templating methods. Chemical and biological functionalities that can be introduced by bottom-up methods are highly varied.

Dip-pen lithography is a method that has received considerable attention. This method entails using an atomic force microscope (AFM) tip coated with some chemical agent that can be written from the tip onto a separate substrate upon which the chemical agent can self-assemble, as shown in Figure 3.6, where lipid molecules are placed on a surface. The agents can be themselves of interest, for example proteins or other

![Figure 3.4](image1.png)

Figure 3.4. Two-dimensional arrays of high-refractive-index structures of different shapes fabricated using electron-beam lithography. (Reproduced with permission from *Advanced Materials* 15, 49, © Wiley-VCH Verlag GmbH & Co. KGaA.)

![Figure 3.5](image2.png)

Figure 3.5. Sensors fabricated with bottom-up methods: (a) scanning electron microscope image of vertical silicon nanobridges formed between two horizontal silicon surfaces; (b) a bridged silicon nanowire between two vertical silicon electrodes (source and drain); (c) gallium oxide nanowires with ultrasharp tips for field-ionization-based sensing. (Images: [a] and [c] courtesy of S. Islam; [b] reprinted with permission from *Nano Letters* 7, 1536, © 2007 American Chemical Society.)
functional molecules; on the other hand, they may be used either to mask or nucleate deposition of metals, nanoparticles, or other molecules. Features down to about 20 nm can be achieved reproducibly and with good spatial control. Drawbacks to this method include the slow time to produce single patterns and incompatibility with prototyping, although efforts are underway to achieve large-scale parallelization of tips to enable large-scale production.

Integration Dependence on Platform

When integrating bottom-up devices with the outside world (sample introduction, preparation, and signal output and processing), the available methods will depend on the platform. If the nanotechnology aspect is strictly responsible for enabling signal transduction, many existing microscale and macroscale chemical and physical sensing platforms can be exploited. Some notable examples include micrometer-scale chemiresistor hardware typically used for conducting polymers, metal oxide powders and other conducting or semiconducting materials, different potentiometric sensing hardware, and a myriad of different spectroscopic interfaces. If the bottom-up–derived nanoscale material is to be integrated into dense device platforms, the same interfacing challenges of lithographically derived top-down devices apply, in addition to the challenges of assembling the nanoscale materials in a controlled fashion on the device platform.

Challenges Inherent in Bottom-Up Sensor Fabrication

Critical challenges facing bottom-up techniques include poor control of doping and impurity distribution (in deposited semiconductor materials), of final surface characteristics, of orientation, and of material quality. Obstacles to mass manufacturing include developing wafer-scale approaches for functionalizing surfaces and process tools for device integration. There is a critical need to develop new ways of addressing individual elements, especially those derived using bottom-up fabrication methods. It is possible that adequate electron-beam writing and skillful placement of bottom-up materials on electron-beam-derived circuits will continue to solve many of these problems. However, if substrates are desired that are not amenable to standard semiconductor fabrication technology, such as flexible plastic materials, new interconnect methods will be necessary. One possibility may be to use dip-pen nanolithography to write lines of metal precursors, metal nanoparticles, or conducting polymers between elements. The feasibility and scalability of such an approach is only speculative. Furthermore, if attempts are successful to genuinely render sensor nanostructures either in layered structures or in aperiodic sol-gel and colloidal structures, methods of wiring and addressing elements in the third dimension will be necessary. Such self-directed wiring is still difficult to control but is directed by the surface chemistry of the solid upon which deposition occurs. Control of surface chemistry may enable finer control of wiring and interrogation of functional devices and reaction centers within three-dimensional nanoscale architectures.

GENERAL FABRICATION CHALLENGES

Regardless of whether top-down or bottom-up approaches are used, several general fabrication, integration, and manufacturing challenges exist. These can be grouped into either technical or broad, framework issues.

From a technical perspective, there is a serious need for improved individual electrical connections and integration of useful contact metals, as well as more uniform and reproducibly manufactured nanoscale materials. Fundamental knowledge of the surface, doping, and distribution of doping in these materials is needed, as is an improved understanding of functionalization processes. The challenge of matching the physical conditions implicit in manufacturing (i.e., high temperature and pressure) with the inherent properties of some nanoscale materials remains significant.
Broader issues include the necessity for standards development in the areas of measurement, sensitivity, and materials. Improved, and possibly new, in situ characterization methods are critical to the successful development of robust manufacturable devices. The evolving understanding of the safety, health, and environmental implications of nanoscale materials must also be taken into account as these technologies move forward. It is absolutely essential to build and provide access to hybrid processing and fabrication facilities.

In conclusion, nanotechnology holds the potential to enable a new generation of high-density, multianalyte sensors and devices. The discovery and application of transducers and devices will be based on unique material properties and unusual phenomena that emerge at the nanoscale. There is a tremendous opportunity to realize revolutionary advances in application areas ranging from medicine and health to national security. A sustained and tactical investment in the research areas outlined in this report will help to realize this promise.
## Appendix A. Workshop Agenda

### Tuesday, May 5

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>8:15 am</td>
<td>Welcome (T. Earles)</td>
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<tr>
<td>8:30 am</td>
<td>Plenary Session: Application Opportunities (T. Earles, Moderator)</td>
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<tr>
<td></td>
<td>“Toward biological large-scale integration” (M. Roukes)</td>
</tr>
<tr>
<td>9:45 am</td>
<td>Break</td>
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<tr>
<td>10:15 am</td>
<td>Session: Nano-optical Sensors (L. Whitman, Moderator)</td>
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<tr>
<td></td>
<td>“Plasmon-based sensing, including single-molecule surface-enhanced Raman detection” (D. Natelson)</td>
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<td></td>
<td>“Plasmonic sensors” (H. Atwater)</td>
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<tr>
<td>11:30 am</td>
<td>Session: Nanomechanical Sensors (L. Whitman, Moderator)</td>
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<tr>
<td></td>
<td>“Nanomechanical sensors: Challenges and opportunities” (T. Thundat)</td>
</tr>
<tr>
<td>12:00 pm</td>
<td>Lunch</td>
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<tr>
<td>1:00 pm</td>
<td>Session: Nanomagnetic Sensors (K. Bussmann, Moderator)</td>
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<td></td>
<td>“Nanomagnetic sensors” (M. Tondra)</td>
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<tr>
<td>1:45 pm</td>
<td>Session: Nanoscale Electro/Chemical Sensing (G. Hunter, Moderator)</td>
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<td></td>
<td>“Metal-oxide nanomaterial-based chemical sensors” (M. Carpenter)</td>
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<tr>
<td></td>
<td>“Nanoscale electro/chemical sensing” (M. Sailor)</td>
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<tr>
<td>3:00 pm</td>
<td>Charge to Breakout Session (R. van Zee)</td>
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<tr>
<td>3:15 pm</td>
<td>Breakout Sessions Begin</td>
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<td></td>
<td>Session 1: Nano-Optical and -Electro/Chemical Sensing (M. Sailor &amp; P. Hesketh, Facilitators)</td>
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<td></td>
<td>Session 2: Nano-Magnetic and-Mechanical Sensing (M. Tondra, Facilitator)</td>
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<tr>
<td>5:30 pm</td>
<td>Adjourn</td>
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<tr>
<td>6:30 pm</td>
<td>Working Dinner (R. van Zee, Moderator)</td>
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### Wednesday, May 6

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<tr>
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<td>Welcome and Announcements (G. Pomrenke)</td>
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<td>“Connecting nanotechnology to the future” (J. Stetter)</td>
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<td>9:30 am</td>
<td>Session: Putting it Together (H. Chen, Moderator)</td>
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<td>“Fabrication: Making it work” (Y. Nishi)</td>
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<td>10:05 am</td>
<td>Break</td>
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<tr>
<td>10:30 am</td>
<td>“Integration: Electronic biomolecular sensors” (G. Maki)</td>
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<td>“Networking: Microsensor networks and bio/nano/info research” (S. Kumar)</td>
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<tr>
<td>11:45 am</td>
<td>Public Comment Period (R. van Zee &amp; V. Ota Wang, Facilitators)</td>
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<tr>
<td>12:00 pm</td>
<td>Lunch</td>
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<tr>
<td>1:00 pm</td>
<td>Charge to Breakout Groups (R. van Zee)</td>
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<tr>
<td>1:15 pm</td>
<td>Breakout Sessions Begin</td>
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<td></td>
<td>Session 4: Application Opportunities (D. Stewart, Facilitator)</td>
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<tr>
<td>3:15 pm</td>
<td>Breakout Group Summaries (R. van Zee, Moderator)</td>
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<td></td>
<td>Fabrication/Integration/Networking (S. Islam)</td>
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<td></td>
<td>Application Opportunities (D. Stewart)</td>
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<td>3:30 pm</td>
<td>Writing Group Convenes</td>
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### Thursday, May 7

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<td>Writing Group Convenes</td>
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<tr>
<td>3:00 pm</td>
<td>Writing Group Concludes</td>
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## Appendix B. Workshop Participants*

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christopher Anton</td>
<td>Army Research Laboratory</td>
</tr>
<tr>
<td>Harry Atwater*◊</td>
<td>California Institute of Technology</td>
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<tr>
<td>Chagaan Baatar</td>
<td>Office of Naval Research</td>
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<tr>
<td>Igal Brener*,§,◊</td>
<td>Sandia National Laboratories</td>
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<tr>
<td>Todd Brethauer‡</td>
<td>Combating Terrorism Technical Support Office</td>
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<tr>
<td>Konrad Bussmann‡</td>
<td>Naval Research Laboratory</td>
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<tr>
<td>Michael Carpenter*,§,◊</td>
<td>University at Albany – SUNY</td>
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<td>William Carter§,◊</td>
<td>HRL Laboratories</td>
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<td>German Cavelier</td>
<td>National Institutes of Health</td>
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<td>Samar Chatterjee</td>
<td>Environmental Protection Agency</td>
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<td>Hongda Chen*</td>
<td>United States Department of Agriculture</td>
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<td>Zhong Yang Cheng‡</td>
<td>Auburn University</td>
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<td>Jeffrey DePriest</td>
<td>Defense Threat Reduction Agency</td>
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<td>White House Office of Science &amp; Technology Policy</td>
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<td>Marlowe Epstein</td>
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<td>Matthew Ervin</td>
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<td>Heather Evans</td>
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<tr>
<td>Patricia Poland</td>
<td>World Technology Evaluation Center</td>
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<tr>
<td>Richard Gaster†</td>
<td>Stanford University</td>
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<tr>
<td>Bonnie Gersten</td>
<td>Department of Energy Office of Basic Energy Sciences</td>
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<td>Crystal Havey◊</td>
<td>World Technology Evaluation Center</td>
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<td>Peter Hesketh*,†,◊</td>
<td>Georgia Institute of Technology</td>
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<td>King-Fu Hiu‡</td>
<td>The George Washington University</td>
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<td>Geoff Holdridge</td>
<td>National Nanotechnology Coordination Office</td>
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<tr>
<td>David Hopkinson</td>
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</tr>
<tr>
<td>Gary Hunter*,†,◊</td>
<td>NASA Glenn Research Center</td>
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<td>Saif Islam*,†,◊</td>
<td>University of California Davis</td>
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<tr>
<td>Pat Johnson</td>
<td>World Technology Evaluation Center</td>
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<tr>
<td>Keith Karasek‡</td>
<td>NanoBusiness Alliance</td>
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<tr>
<td>David Kuehn</td>
<td>Federal Highway Administration</td>
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<tr>
<td>Srikanta Kumar</td>
<td>BAE Systems Inc.</td>
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<tr>
<td>Robert Latiff</td>
<td>Science Applications International Corp.</td>
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<tr>
<td>Jing Li*,§,◊</td>
<td>NASA Ames Research Center</td>
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<td>Xiulan Li*</td>
<td>Polestar Technologies</td>
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<td>Tao Liu*</td>
<td>Florida State University</td>
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<tr>
<td>Dan Luo*</td>
<td>Cornell University</td>
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<tr>
<td>Gary Maki†,◊</td>
<td>University of Idaho</td>
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<tr>
<td>Emily Morehouse*</td>
<td>United States Department of Agriculture</td>
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<tr>
<td>Ashok Mulchandani*,†,◊</td>
<td>University of California Riverside</td>
</tr>
<tr>
<td>Vladimir Murashov</td>
<td>National Institute for Occupational Safety and Health</td>
</tr>
<tr>
<td>James Murday*,§,◊</td>
<td>University of Southern California</td>
</tr>
</tbody>
</table>

* See end of participants’ list for key to symbols. Affiliations of participants are as of the date of the workshop.
Appendix B. Workshop Participants

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National Institutes of Health

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Dianne Poster
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Barbara Ransom
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Kitt Reinhardt
Air Force Office of Scientific Research

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Booz Allen Hamilton

Andrew Schwartz
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Randy Vander Wal§,◊
The Pennsylvania State University

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Department of Energy

Michael Weinrich
National Institutes of Health

Lloyd Whitman*,◊
National Institute of Standards & Technology

Dwight Woolard*
Army Research Laboratory

Key to Symbols in List of Workshop Participants

* Participated in Nano-optical and Electro/chemical Sensing breakout session
‡ Participated in Nano-Magnetic and Mechanical Sensing breakout session
† Participated in Fabrication/Integration/Networking breakout session
§ Participated in Application Opportunities breakout session
◊ Contributed to the preparation of this report
Appendix C. Resources and Further Reading*


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* Publications are listed in descending order by publication year.
Appendix D. Figure Credits


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### Appendix E. Glossary

<table>
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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>AFM</td>
<td>atomic force microscope</td>
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<tr>
<td>CCD</td>
<td>charge-coupled device</td>
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<td>CNTs</td>
<td>carbon nanotubes</td>
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<td>CVD</td>
<td>chemical vapor deposition</td>
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<td>R&amp;D</td>
<td>research and development</td>
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<td>EEG</td>
<td>electroencephalograph(y)</td>
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<td>EIT</td>
<td>electromagnetically induced transparency</td>
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<td>EKG</td>
<td>electrocardiogram</td>
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<td>FET</td>
<td>field-effect transistor</td>
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<td>FPA</td>
<td>focal plane array</td>
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<td>FRET</td>
<td>fluorescence resonant energy transfer</td>
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<td>MEMS</td>
<td>microelectromechanical systems</td>
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<td>nanoelectromechanical systems</td>
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<td>NNI</td>
<td>National Nanotechnology Initiative</td>
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<td>SEIRA</td>
<td>surface-enhanced infrared absorption</td>
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<tr>
<td>SERS</td>
<td>surface-enhanced Raman spectroscopy</td>
</tr>
<tr>
<td>SPICE</td>
<td>simulation program with integrated circuit emphasis</td>
</tr>
<tr>
<td>SPR</td>
<td>surface plasmon resonance</td>
</tr>
<tr>
<td>SQUID</td>
<td>superconducting quantum interference device</td>
</tr>
<tr>
<td>STM</td>
<td>scanning tunneling microscope</td>
</tr>
<tr>
<td>VLS</td>
<td>vapor-liquid-solid</td>
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