

CHAPTER 2

ENABLING AND INVESTIGATIVE TOOLS: MEASURING METHODS, INSTRUMENTS, AND METROLOGY

Dawn A. Bonnell, Vinayak P. Dravid, Paul Weiss, David Ginger,
Keith Jackson, Don Eigler, Harold Craighead, Eric Isaacs¹⁵

2.1 VISION FOR THE NEXT DECADE

Changes in the Vision over the Past Ten Years

Advances in nanotechnology investigative tools have enabled fundamentally new approaches to the research carried out during the last decade. The crucial role of tools for manipulation and characterization of matter at the nanoscale was articulated by Nobel Laureate Horst Störmer in 1999 at the first U.S. Nanotechnology Research Directions workshop, as follows: “Nanotechnology has given us the tools... to play with the ultimate toy box of nature—atoms and molecules... [This scale] provides an impressive array of novel opportunities to mix-and-match hunks of chemistry and biology with artificially defined, person-made structures. The possibilities to create new things appear endless” (Roco, Williams, and Alivisatos 1999, p. viii). The workshop vision at that time was that the promises of nanotechnology could be realized only through “the development of new experimental tools to broaden the capability to measure and control nanostructured matter, including developing new standards of measurement.” A particular point was made to extend this recommendation to biomolecules (p. xvi).

The investments in the science of characterization tools in the last decade have resulted in exciting discoveries, enabling metrologies, and windows of opportunity for revolutionary changes in the future. It is now possible to detect the charge and spin of a single electron, image catalytic reactions in real time, track some dynamic processes with 100 femtosecond (fs)¹⁶ time resolution, map real and imaginary contributions to dielectric properties of molecules, and control chemo-mechanical interaction of individual essential biomolecules. Electron microscopy has achieved unprecedented spatial resolution with aberration correction, demonstrated 3D tomography, and developed *in situ* capacity, even for liquid-based systems. X-ray brilliance at beam lines has increased five orders of magnitude in the last ten years, enabling detailed observations of dynamic processes and 3D structure from x-ray scattering.

The consequence of the advances in instrumentation science of the last decade is that researchers can now envision a new generation of tools for the next decade that will:

- Revolutionize the fundamental concepts of solids and biomolecules

¹⁵For the institutional affiliations of authors, please see Appendix B, List of Participants and Contributors.

¹⁶ 10⁻¹⁵ of a second

- Allow new views of complex systems at small scales
- Probe dynamic processes and unexplored time scales

The Vision for the Next Ten Years

The next decade will see unanticipated new discoveries of nanoscale phenomena along with the implementation of early nanoscience into novel applications. New challenges will arise in direct measurement of dynamic processes in nanoscale systems, nanomanufacturing, integration of biosystems, and in higher levels of device and system complexity. At the dawn of this decade the scope of our ability to probe local phenomena is vastly increased. Researchers now envision capabilities that were unimaginable 10 years ago. Intriguing challenges on the horizon include:

- Atomic resolution of the three dimensional structure of a single protein with chemical specificity
- Mapping (so called) continuum properties of individual atoms in a solid
- Discovery of stable new compounds by the manipulation of atoms at room temperature
- Tracking electrons with sufficient speed to observe intermediate steps in chemical reactions
- Concurrent imaging of processes throughout and entire cell

While ambitious, achieving these goals is plausible and doing so would be the driver for the next generation of discovery and innovation.

2.2 ADVANCES IN THE LAST TEN YEARS AND CURRENT STATUS

The advances in and current status of experimental methods for characterization of structure, properties, and processes at the nanoscale are summarized here, with an emphasis on notable examples in scanning probe-based measurement approaches, electron beam-based microscopies, optical probes, scattering tools at beam lines, and nanolithography platforms.

In the last decade, new cheap and accessible methods of nanopatterning such as microcontact printing and imprint lithography allowed research and product development laboratories all over the world to easily fabricate specialized complex devices with which to explore new phenomena. The commercial availability of off-the-shelf nanoparticles in sizes ranging from one to hundreds of nanometers enabled rapid advances in the fundamental science and application of particles in products ranging from medical therapeutics to hybrid electronics. The new field of plasmonics evolved dramatically.

Instruments that access structure and properties at nanometer and atomic length scales have been, and continue to be, essential in advancing our understanding of the physics and chemistry of nanostructures. The ability to quantify nanoscale behavior is a limiting factor in understanding new physics and is a prerequisite to manufacturing. It is a basic tenet of science that, "If it can't be measured, it can't be understood." In manufacturing, if specifications can't be characterized, reliable manufacturing is not possible.

Scanning Probe-Based Approaches to Measure Structure, Properties, and Processes

At the beginning of the National Nanotechnology Initiative (NNI) in 2000, scanning tunneling microscopy and atomic force microscopy already had become routine tools for investigating surface structure and adsorption reactions. At low temperature, quantum phenomena were beginning to be explored. In addition, first-order properties such as surface potential and magnetic field variations were characterized regularly. The decade 2000 to 2010 witnessed a

geometric expansion of the variety of nanomaterial properties that can be measured locally, some aimed at advancing fundamental science and some developed in support of technology commercialization.

Observing Increased Complexity: From Chemical Identification to Mapping of Vector Properties

The wide range of phenomena that can now be accessed with high-spatial-resolution scanning-probe microscopy is illustrated in Figure 2.1. Davis and colleagues are among those researchers who image electronic properties with atomic resolution (Kohsaka et al. 2007); they have observed, for example, that in strongly correlated electron systems, the density of states may not be symmetric with respect to the Fermi energy. Figure 2.1a shows a conductance ratio map of a superconductor that maps such asymmetry.

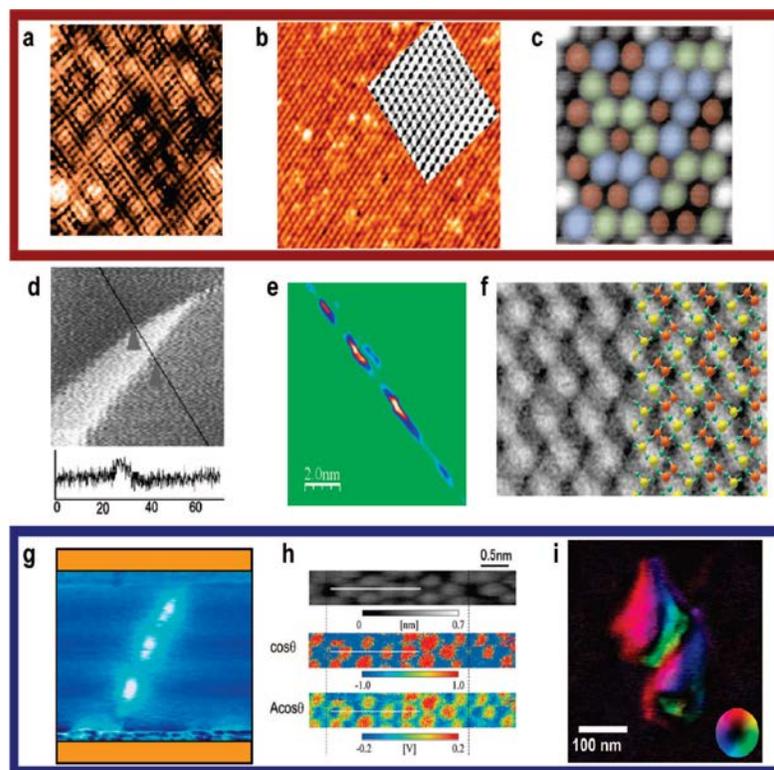


Figure 2.1. Spatially resolved properties of nanoscale materials and phenomena “mapped” and/or imaged using a variety of atomic-scale characterization tools: (a) Conductance asymmetry in a super-conductor, a variant of tunneling spectroscopy. (b) STM image of $K_{0.3}MoO_3$ containing the two periodicities of the atomic structure and charge density waves. (c) Non-contact atomic force microscopy image of Si(111) with atoms colored differently for chemical force in force spectroscopy. (d) Magnetic force microscope image of the magnetic domain structure of a thin film taken with a focused, ion beam-milled tip (e) Conductance map of a HfO thin film containing electronic defects that result in leakage current. (f) Electrostatic potential image of the Ge(105)-(1x2) surface superimposed with the atomic model. (g) Scanning impedance image of a single-wall carbon nanotube conducting current. (h) Scanning nonlinear dielectric spectroscopy of the Si(111)-(7x7) surface in which polarization of the adatoms is obtained from the second harmonic of capacitance. (i) Vector piezoelectric force microscope map of local electromechanical of protein microfibrils on human tooth enamel; color indicates the orientation of the electromechanical response vector (Bonnell 2008).

Charge density waves are another manifestation of electron interactions; the phase transitions responsible for charge density waves have recently been observed in real space on oxide surfaces (Brun et al. 2005; Nikiforov et al. 2007; Figure 2.1b). The last five years have seen particularly exciting advances in the understanding of atomic force microscopy (AFM) at atomic resolution (Giessibl et al. 2003; Giessibl and Bielefeldt 2000). Sugimoto et al. (2007) exploit local forces, taking this approach to the next level, using force differences between atomic sites for chemical identification (Figure 2.1c), thus enabling mapping of chemical properties at atomic resolution.

The nanometer-scale spatial resolution achieved recently in probing continuum properties such as resistance, capacitance, dielectric function, electromechanical coupling, etc., was unanticipated. Spatial resolution approaching 5 nm in magnetic fields is achieved by improving probe tip technology. Conductance and resistance are detected with sub-nanometer spatial resolution due to stress field focusing effects under the tip. Surface potential of Ge (105)-(1x2) (Eguchi et al. 2004; Figure 2.1f) and dielectric polarization of Si (111) (Cho and Hirose 2007; Figure 2.1h) have been imaged at atomic resolution. A significant advance of the last decade has been the increase in the complexity of properties able to be probed at local scales. The superposition of time-varying electric fields has led to new techniques such as scanning impedance spectroscopy and dielectric constant imaging. Figure 2.1g shows individual defects in a carbon nanotube through use of scanning impedance methodologies. And electromechanical coupling, a vector property, can now be mapped in liquids with ~ 3 nm resolution, as illustrated in the characterization of protein (Rodriguez et al. 2006; Figure 2.1i).

Advancing the Frontiers of Physics

Significant advances have been made in fundamental understanding of the physics of nanoscale material properties through investigations carried out at low temperature with scanning tunneling microscopy (STM). Magnetism at surfaces has been explored by spin-polarized STM. As illustrated in Figure 2.1a, local details of local electronic structure—elucidated by mapping derivatives, Mott gaps, and Fourier transforms of local density of states—provide information about the interactions of electrons in solids. A long sought-after goal of the probe community was realized when Ho and coworkers (2005) first demonstrated vibrational spectroscopy of organic molecules on surfaces with inelastic tunneling in a scanning tunneling microscope. Kawai and coworkers (2002), Pascual (2003), and others have shown the great promise of vibrational spectroscopy applied to chemical properties of adsorbed molecules. The technique is being extended to examine excitation and de-excitation channels of molecules in order to determine reaction pathways and coordinates (Hahn and Ho 2005).

In recent years, it has become possible to probe the low-energy spin excitation spectra of magnetic nanostructures at the atomic scale using inelastic spin excitation spectroscopy with a scanning tunneling microscope. Spin excitation spectroscopy engenders the ability to measure the energetics, dynamics, and spin configuration of single atoms and assemblies of atoms (Heinrich et al. 2004; Otte et al. 2009) and was used to show that magnetic coupling of a Kondo atom to another unscreened magnetic atom can split the Kondo resonance into two peaks.

Advancing the Frontiers of Chemistry and Catalysis

Scanning probe microscopy has been the primary method used to observe chemical interactions at surfaces. Improvement in video rate imaging has enabled real-space studies of atomic diffusion and surface reactions. New and further-developed scanning probe tools have

enabled greater control in self- and directed assembly, molecular devices, supramolecular assembly, and other areas (Han et al. 2009; Figure 2.2). As researchers came to understand that these systems exist at the nanoscale and can be maintained far from equilibrium (a direct result of SPM measurements), they learned how to control defect types and density and ultimately to exploit those defects (Saavedra et al. 2010). From there, they gained the ability to pattern all the way from the sub-nanometer scale to the wafer scale; the next accomplishment was to measure function of molecules and devices with scanning probes (Moore et al. 2006).

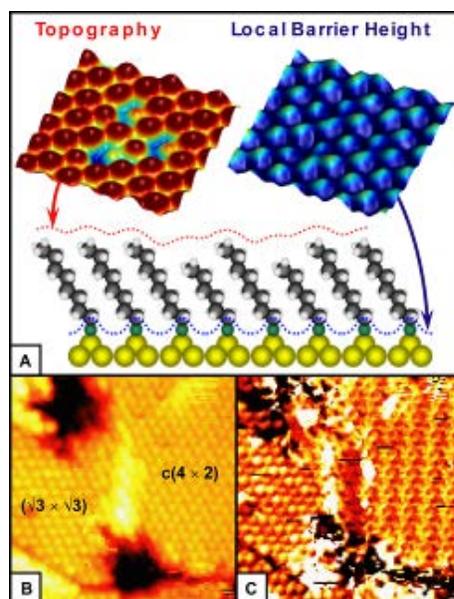


Figure 2.2. Simultaneous STM measurements yield absolute tilt angles of individual molecules in self-assembled monolayers (Han et al. 2009).

In situ Characterization of Devices

SPM-based tools can easily be configured for *in situ* characterization. Quantifying electrical properties of nanowire and nanotube devices, for example as illustrated in Figure 2.1g, has been essential to developing the present understanding of nanoelectronic and chemical sensor devices. Recent advances have extended the concept to more complex devices. Coffey and Ginger (2006) simultaneously imaged the topographic structure and photogeneration rate in organic solar cells, using STM, as shown in Figure 2.3.

Similarly, Bonnell and Kalinin (2001) have imaged topographic structure along with the magnitude and direction of current flowing through an operating varistor (Figure 2.3). The ability to examine variations in properties and processes under conditions relevant to device performance provides new information about the fundamental principles involved, as well as providing critical feedback that can facilitate product development. The photogeneration results in Figure 2.3 were shown to predict complete solar cell performance. Applications that will benefit from *in situ* device characterization at the nanoscale include photovoltaics, electrochemical/photochemical fuel generation, nanostructured batteries, thermoelectrics, supercapacitors, ferroelectric memory, and sensors, among others.

Electron Beam-Based Microscopies

Development of electron-beam instrumentation, techniques, and associated accessories has advanced at a breathtaking pace since 1999. The atomic-scale imaging (sub-0.2 nm nominal, so-called point-to-point Scherzer resolution) of beam-stable crystalline nanostructures is now readily and routinely possible given consistent and reproducible performance of both transmission electron microscopy (TEM) and scanning transmission electron microscopy (STEM) (Williams 2009).

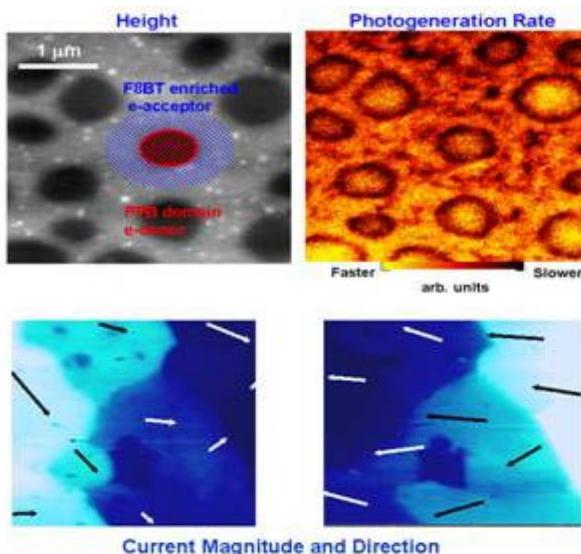


Figure 2.3. (Top) Simultaneous imaging of structure and photo current generation in an organic solar cell (Coffee and Ginger 2006), and (bottom) imaging of current magnitude (size of vector) and direction across an operating oxide device (Bonnell and Kalinin 2001).

Further, most modern S/TEM instruments are capable of achieving nominal point-to-point spatial resolution approaching 0.13 nm and an information limit approaching 0.1 nm (Rose 1994; Haider et al. 1998; Figure 2.4).

The vast improvement in performance has been made possible due to a combination of high-performance field-emission sources (Tonomura et al. 1979) for electrons (which extend the envelope function of the contrast transfer function of the important objective lens), improved aberration coefficients of lenses, overall stability of the microscope column, improvement in specimen stages, and adequate attention to control of the local environment at the sample. The practical realization of overall S/TEM performance has been greatly aided by innovative specimen preparation capabilities—including for biological/soft materials—coupled with image processing, simulation/modeling, and related computational developments.

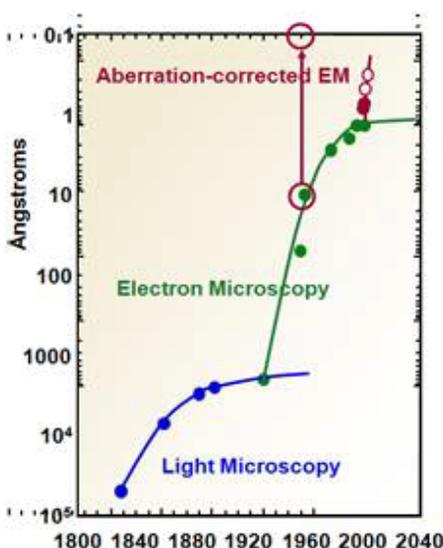


Figure 2.4. Schematic illustration of the evolution of the spatial resolution of microscopy, culminating in the advent of aberration-corrected electron microscopy (EM): (blue line) light microscopy; (green and red lines) electron microscopy.

Aberration Correction

Undoubtedly the most significant advance towards atomic-scale imaging (and many other attributes detailed later) has been the rapid emergence of aberration correctors (Rose 1994; Haider et al. 1998) for S/TEM (and for scanning electron microscopy, SEM). Until about a decade ago, the spatial resolution of modern S/TEM was limited by the ubiquitous presence of spherical aberration and chromatic aberration of the principal imaging lens (objective lens) of the electron optics column. The commercial development of aberration correctors (Rose 1994; Haider et al. 1998; Kabius and Rose 2008) that can be housed in commercial S/TEM columns has been the *transformative* development (Kabius and Rose 2008; Batson, Dellby, and Krivanek 2002; Kisielowski et al. 2008; Krivanek et al. 2008; Muller et al. 2008; Pennycook et al. 2006; Smith et al. 2008; Zhu et al. 2009; Prabhurashi et al. 2009) in the field of electron microscopy (Figure 2.5). It is interesting to note that the concept of using asymmetric lenses to improve lens performance was articulated by Richard Feynman (1959) in his famous speech at the California Institute of Technology, “There is plenty of room at the bottom,” which defined the concepts in modern nanotechnology.

Although modern aberration correctors employ the general concepts of quadrupole and octupole lenses to control aberrations in lenses, engineering realization of these concepts took decades to perfect and master. These remarkable new developments have also been incorporated into atomic-scale imaging with aberration-corrected SEM (Figure 2.6).

In a major ongoing initiative called the Transmission Electron Aberration-Corrected Microscopy (TEAM) project (Zhu et al. 2009), sub-1 Å spatial resolution was successful demonstrated in 2009 (Zhu et al. 2009; Erni et al. 2009; Kisielowski et al. 2001). Several TEAM microscopes are now being developed (Kabius et al. 2009). Many commercial manufacturers have rapidly translated aberration corrections into their newer models of S/TEMs.

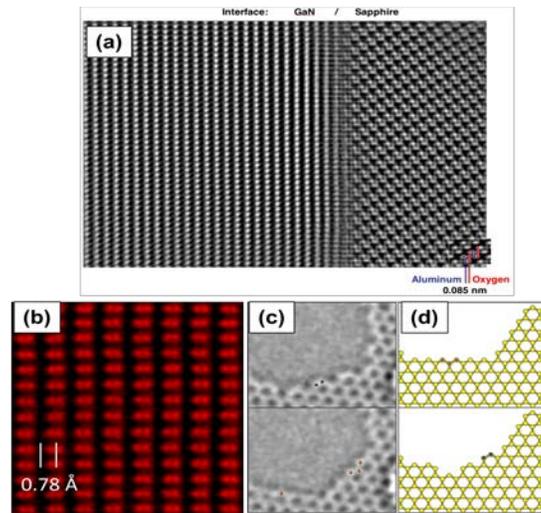


Figure 2.5. Montage of atomic-scale images and phenomena enabled by aberration-corrected S/TEM. (a) HREM image of an interface between GaN and sapphire (courtesy of Lawrence Berkeley National Lab.); (b) Silicon “dumbbells” at sub-Ångstrom resolution via HAADF/STEM (courtesy of O. Krivanek, NION Corp. and S. Pennycook, Oak Ridge National Lab.); (c) Dynamics of graphene with atom-by-atom motion in successive frames. Right side illustrations show schematics of the process. (courtesy of A. Zettl and C. Kisielowski, from C. Girit et al. 2009).

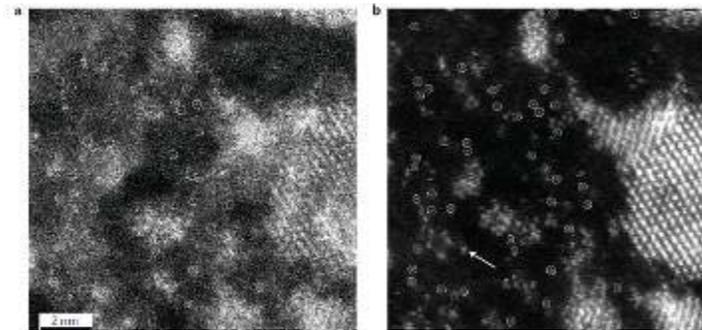


Figure 2.6. SEM image (left) and corresponding annular dark field image (right) with aberration-corrected STEM instrument, demonstrating atomic-scale resolution, even in scanning electron mode (Zhu et al. 2009).

More recently, atomic-scale imaging with low atomic number sensitivity has also been demonstrated (Krivanek et al. 2010). Concurrently, there has been remarkable progress in ancillary areas, ranging from specimen preparation tools and techniques to data analysis, processing, and mining. The combination of focused ion beam (FIB) and scanning electron microscopy is one example that has had a high impact in numerous fields, including routine commercial applications in defect metrology in microelectronics (Langford and Petford-Long 2001; Li et al. 2001; Mayer et al. 2007; Marko et al. 2007).

Beam Line-Based Nanocharacterization

The last decade has witnessed dramatic advances in the capabilities of beam line facilities. A comparison of improvements in x-ray brilliance with those in computer processing speed provides some insight. Computer processors have increased performance at a rate that is generally considered phenomenal, 12 orders of magnitude in 60 years; yet, x-ray brilliance

has improved 10 orders of magnitude in under 30 years (see Figure 2.7). The transition from 3rd-generation to 4th-generation capability in the last decade alone represents five orders of magnitude improvement. The current levels of beam intensity and coherence allow parallel signal acquisition and time resolution at unprecedented levels. Recent progress in high pressure and *in situ* capability lead toward analysis of materials in realistic environments. At the beginning of the last decade, femtosecond control had just been demonstrated on synchrotron radiation.

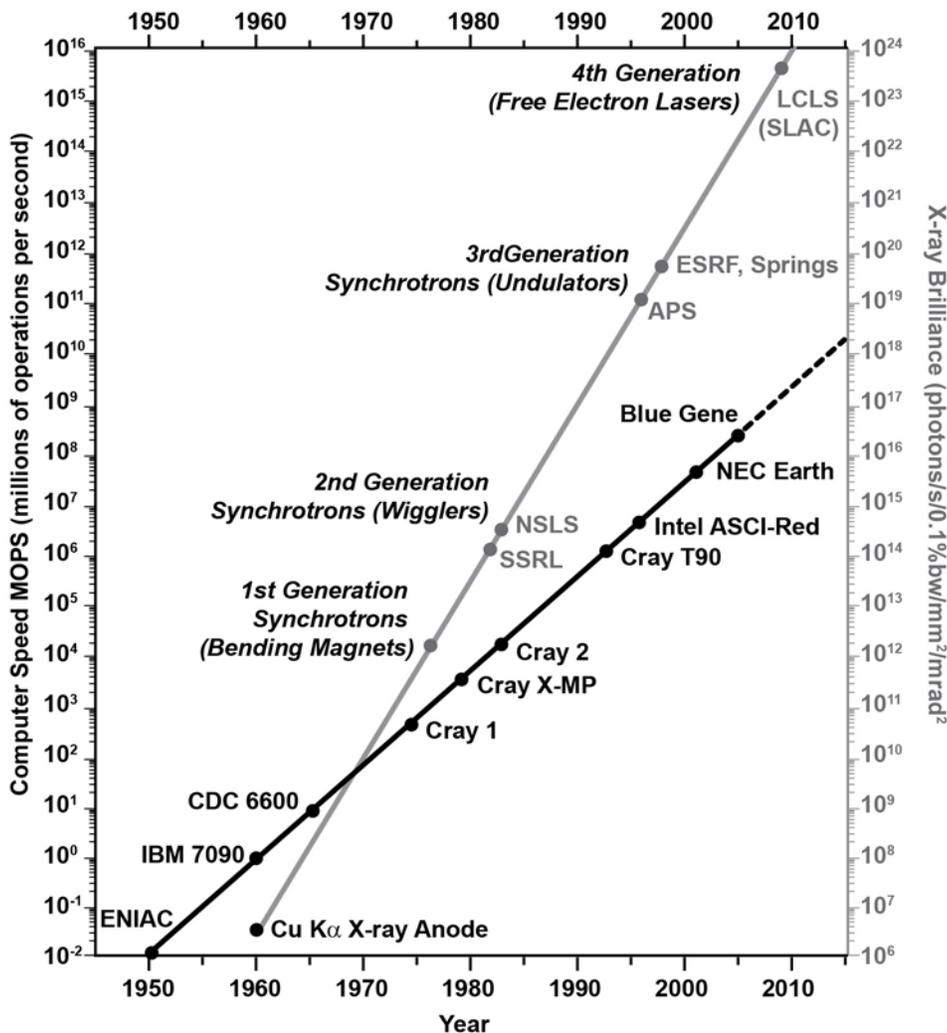


Figure 2.7. Comparison of increases in computer processor speed and x-ray brilliance over the last 50 years (adapted from information provided by Eric Isaacs).

The time evolution of structure is illustrated in the analysis of charge density waves on a Cr (111) surface (Shpyrko et al. 2007). Antiferromagnets carry no net external magnetic dipole moment, yet they have a periodic arrangement of the electron spins extending over macroscopic distances. The magnetic “noise” must be sampled at spatial wavelengths of the order of several interatomic spacings. Figure 2.8 shows a direct measurement of the fluctuations in the nanometer-scale superstructure of spin- and charge-density waves

associated with antiferromagnetism in elemental chromium. The technique used is x-ray photon correlation spectroscopy, where coherent x-ray diffraction produces a speckle pattern that serves as a “fingerprint” of a particular magnetic domain configuration.

Materials needed for next-generation device solutions are typically complex and difficult to fabricate. For example, novel thermoelectric material systems such as cobaltates for efficient exchange of heat and electrical energy could revolutionize waste heat power generation and refrigeration, but this goal requires synthesis of new materials with tailored nanostructures to create the desired separation and optimization of the phononic and electronic transport channels. The high brightness at penetrating x-ray energies allow unprecedented nanoscale imaging of materials as they are being synthesized in complex environments.

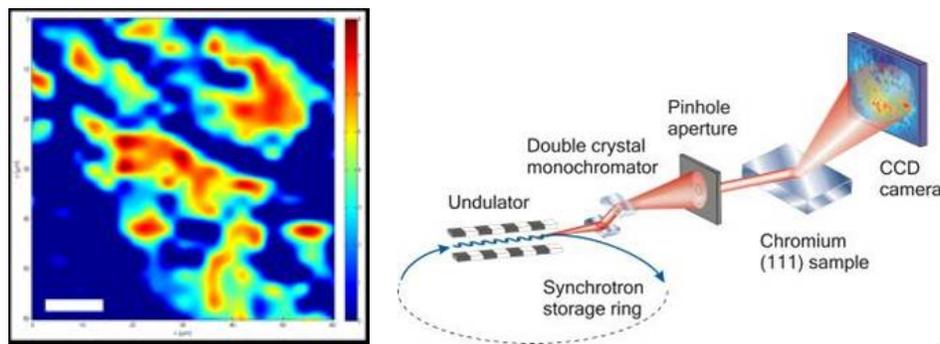


Figure 2.8. Diagram of the experimental set-up and charge-coupled device (CCD) image of the x-ray speckle observed for the [200] lattice Bragg reflection.

Researchers at next-generation synchrotron light sources and spallation neutron accelerators can watch self-assembly and directed self-assembly of nanomaterials, make tribological measurements on nanosystems, create nanomagnetic materials with novel properties, and fabricate superhard materials under pressure. Scientists are using x-rays and neutrons as nanoscale probes to:

- Solve the crystal structures of proteins
- Understand catalytic processes in toxicology measurements and atmospheric research
- Investigate plant genomics
- Image nanostructured materials, ceramics, and polymers
- Image cracks and atomic defects in structures with high resolution in real time

Instruments and Metrology in Support of Nanomanufacturing: Nanolithography

Many of the advances described above have been critical in providing the characterization necessary in the development of devices and products. Some scanning probe and electron beam-based tools have been developed for high-throughput analyses for quality control and, in some cases, for inline manufacturing. However, many of the challenges raised in earlier reports regarding standards, reference materials, and metrology tools for nanomanufacturing process control remain.

Fair progress has been made in the development of commercial nanofabrication tools that can be scaled for manufacturing (Figure 2.9). Nanoimprint lithography and Jet and Flash™ imprint lithography produce sub-30 nm resolution nanomaterials with <10 nm alignment over hundreds of millimeters.



Figure 2.9. Lithography tools for nanoscale manufacturing. (Left) Molecular Imprints, Inc. (left, Imprio® 300, <http://www.molecularimprints.com/products.php>). (Right) Nanonex Corp. (right, NX-2000, <http://www.nanonex.com/machines.htm>).

Probe based techniques for positioning atoms and molecules, inducing localized chemical reactions and patterning electric, ferroelectric and magnetic fields have made great strides towards enabling nanofabrication. One of the most dramatic results of the early days of STM was from the IBM group that positioned individual atoms into quantum corrals (Crommie et al. 1993). This beautiful physics that demonstrated the ability to build structure at the atomic level was achieved at 4K or lower and not very practical for manufacturing. In the last decade Morita and colleagues demonstrated atomic positioning of semiconductors at room temperature, a huge step towards the vision of building with atomic precision (Sugimoto et al. 2005). Lying and colleagues (1995) demonstrated tip based patterning and chemical reaction of hydrogen terminated silicon surfaces. This advance illustrated an atomic-scale lithography in the context of the computer chip industry and scale up is being explored by Zyvex. (<http://www.zyvex.com/>)

Innovative approaches to nanopatterning include exploiting tip induced fields and gradients. One obvious application of nanopatterning that has motivated much research is information storage. One concept developed at IBM Zurich is the “millipede” in which a tip heats a substrate locally to write and erase information bits. Arrays of tips geometrically expand the information density to 1 Terabyte/sq. inch (<http://www.zurich.ibm.com/st/storage/concept.html>). Ferroelectric materials offer possibly the highest density information storage due to the crystallographic nature of domain boundaries, e.g., bit boundaries. Local probes induce electric fields that switch ferroelectric domains into up and down (one and zero) bits. Significant progress has been made in understanding and controlling domain patterning and bit sizes as small as 2.8 nm have been demonstrated (Tanaka et al. 2008).

Probe-based patterning of ferroelectric domains has also been used to control nanoparticle deposition and local chemical reaction (Kalinin et al. 2002; Li et al. 2008). Patterned hybrid nanostructures consisting of proteins and plasmonic particles have been shown to increase efficiency in optoelectronic and energy harvesting devices (Banerjee et al. 2010). The ultimate spatial resolution of <5nm in patterning multi component nanostructures with device function opens a window of opportunity for future nanofabrication (Figure 2.10).

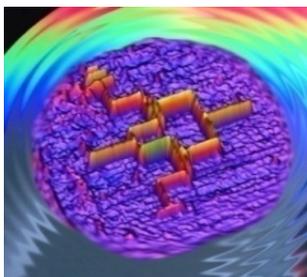


Figure 2.10. Surface potential image ferroelectric domains patterned on a lead zirconate titanate with an electric field from an SPM tip. The domains control chemical reactivity such that 5 nm metallic particles are deposited and peptides or optically active molecules selectively attached to produce a photo active switch (courtesy of the Bonnell group).

2.3 GOALS, BARRIERS, AND SOLUTIONS FOR THE NEXT 5–10 YEARS

The advances in scanning probe microscopy of the last decade have expanded our ability to relate structure and a wide range of properties/responses in real space at the nanoscale. The advances can be considered in the context of a pseudo-phase-space relating properties, length scale, and time scale (Figure 2.11). Early scanning probes were predominantly in the property/length scale plane and involved single-valued functions. Advances such as those described above have accessed higher complexity in property functions and extended somewhat into the time/frequency space. Now, the exciting potential exists to access regions in the center of this space by developing probes of structure and properties with high spatial resolution and time resolution. This would be a pathway to a vision articulated by Don Eigler (2010): 3D atomic resolution imaging of charge, spin, and vector properties at femtosecond time resolution. This vision is clearly in the center region of Figure 2.11.

The next decade will realize exciting advances in electron beam instrumentation as well as innovative accessories and specimen stages for creative and meaningful experiments to decipher atomic- and molecular-scale structural, chemical, and electronic phenomena at the heart of nanoscience and nanotechnology. These are being coupled with dynamic and *in situ* capabilities extending the temporal scale to unprecedented limits down to nano- and femtosecond scattering (Zewail 2010; Kim et al. 2008). Such advances will be essential to achieving fundamental understanding of and engineering developments in materials, structures, and systems for next-generation technologies related to energy (e.g., improved photovoltaics via understanding of interfacial dynamics, and 3D architecture of fuel cell electrodes); environmental monitoring/mediation (e.g., sensors and separation membrane structures); biomedicine (e.g., 3D reconstruction of protein complexes and bio-nano interfaces in implants/devices); and fuel production in extreme environments, among others.

The 1999 Nobel Prize in Chemistry (http://nobelprize.org/nobel_prizes/chemistry/laureates/1999/) recognized the importance of using ultrafast lasers to reveal how atoms move during reactions. The trajectory of advances in laser technology will enable experimental configurations with spatial control, opening new opportunities in monitoring of femtosecond processes—the time scale of many nanoscale phenomena. Synchrotron facilities now offer femtosecond optical spectroscopy combined with x-ray radiation.

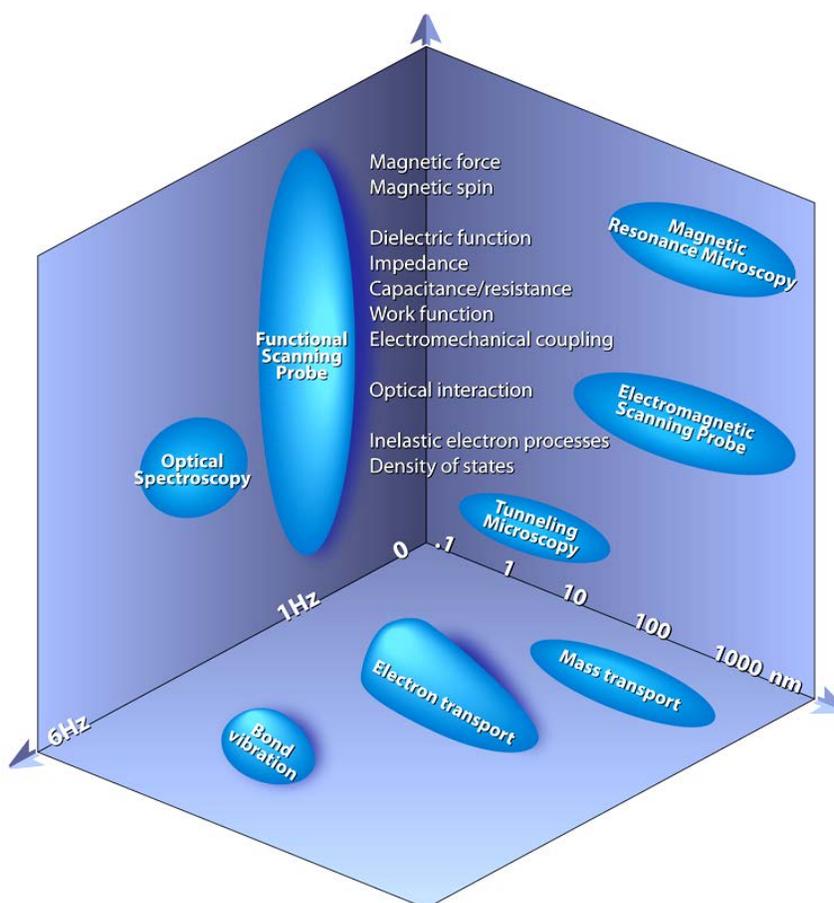


Figure 2.11. Relation of advances in scanning probes to space, time and complexity. The future is in extending these probes into the regions in the center where spatial resolution, time resolution, and complexity can be simultaneously probed (courtesy of D.A. Bonnell).

Probes of the Atomic Origin of Electromagnetic Phenomena

The physical interactions that yield function in solar cells, nanoelectronics, plasmonic sensors, etc., involve the interplay of multiple electromagnetic behaviors. Advancing energy systems, beyond-CMOS solutions in nanoelectronics, and optical devices require characterization of these interactions at increasing small, ultimately atomic scales. Simultaneous atomic resolution probes of photo conductance, resistance, work function, polarizability, and complex dielectric function are needed that operate over frequency ranges from static to GHz in order to access dynamic processes at the level of bond vibrations. Advances in integrating high frequency circuitry to scanning probe systems and combing multiple probes in one station is a path forward. This strategy would also result in new tools for *in situ* characterization of electronic and optical devices.

3D Atomic-Resolution Structure Determination with Chemical Specificity

Reports at the beginning of the NNI listed 3D atomic-resolution imaging as an important goal. It has required the tool advances of the last decade along several fronts to even begin to address this challenge. It is now possible to envision pathways toward this goal. Hybrid scattering near-field scanning optical microscopy (NSOM) has exhibited sub-100 nm

resolution in a 3D holographic mode. Higher spatial resolution and easier experimental realization is necessary. Electron holography has made impressive advances and in the context of aberration-corrected instruments could be combined with *in situ* spectroscopies and energy filtering to increase spatial resolution and chemical identification. 3D characterization by x-ray tomography is also a promising approach to 3D structure determination.

Characterization of Dynamic Processes with High Spatial and Temporal Resolution

While there exist atomic resolution structural characterization tools and spectroscopies that access processes in the femtosecond time regime, new opportunities to combine these have been enabled by advances in the last decade. The synergistic combination of aberration-corrected electron microscopy coupled with innovative *in situ* specimen stages should facilitate a wide range of in-process observation/analysis of important phenomena at high spatial resolution (atomic/molecular scale) and range of temporal resolution (seconds → femtoseconds). The high brightness, high coherence beam lines offer opportunities to access processes in this regime with scattering tools. Using new scattering techniques to directly measure dynamic processes on time scales of attoseconds¹⁷ will provide crucial information on the dynamic processes that drive replication, assembly, folding, and functioning in complex systems at the nanoscale. Combinations of scanning probes and laser spectroscopy or inelastic spectroscopies offer another approach.

Complexity in Biological and Soft Matter Systems

The potential of nanoscale probes for elucidating processes underlying protein function is considerable, but the experimental challenges are severe. Basic requirements are consistent video-rate (and above) imaging and analysis capability, simultaneous molecular resolution of many constituents, and control and manipulation of proteins in physiologically relevant environments. In addition to single-molecule/single-protein approaches, the behavior of wide networks of interacting biomolecules must be pursued. Combining near-field optical imaging, fluorescent microscopy, and scanning probes that image in liquid is one path forward. New tools such as ion conductance microscopy and higher spatial resolution patch clamp analysis would access cell processes. Increasing the spatial resolution and extending detection capability to higher complexity analysis by photo-activated localization microscopy (PALM) would access in-cell processes. Electron beam tools for soft matter should also be furthered. Continued developments are required on cryogenic preservation, encapsulated fluidic specimen cells, minimum-dose techniques, and detector technologies (e.g., phase plates).

***In situ* and Multifunctional Tools**

As outlined above, an enormous range of capability has emerged to characterize structure from different perspectives and to measure spatially resolved properties from bond vibrations to photoconductivity. Judicious combinations of *in situ* capabilities will be required to address the goals of the next decade. These considerations are compelling, for example, in “hybrid soft-hard” nanostructures, wherein hard-microscopy tools/techniques need to be merged with those in soft microscopy. A combination of SPM and SEM/FIB would allow researchers to create site-specific sections of important subsurface structure, patterns, or defects, which can be quantitatively measured by SPM techniques for local mechanical electronic properties. Similarly, given the remarkable range and innate quantitative nature of

¹⁷ 10⁻¹⁸ of a second

several x-ray scattering techniques, especially with synchrotron radiation, it should be possible to combine the best attributes of electron microscopy with (synchrotron) x-ray scattering, such that a given specimen or an experiment can be examined with diverse yet complementary techniques of x-ray scattering and electron microscopy/spectroscopy.

Tools for Nanomanufacturing

The next decade will see many of the early nanoscale science discoveries transition to manufacturing. The need for process metrology, quality control measurements, and associated standards is acute. These unmet requirements apply not only to manufacturing but also to the analysis of workplace safety, environmental impact, and life cycle calculations. In some areas, most notably the electronics industry, roadmapping exercises clearly articulate the needs. For example, additional R&D is required in next five to ten years, particularly in the area of actinic mask inspection (Ushida 2010; Hu et al. 2010; Brizuela et al. 2010). An effective actinic mask metrology tool that operates at a wavelength of 13.5 nm is required, as is actinic pattern inspection capability suitable for high-volume manufacturing to mitigate risks. In others, for example in the case of nanoparticles, nanotubes, etc., reliable fabrication and measurement technologies do not exist for all size regimes.

2.4 SCIENTIFIC AND TECHNOLOGICAL INFRASTRUCTURE NEEDS

As noted in a recent report by the National Academy of Sciences, a strategic plan and infrastructure for mid-sized instrumentation are missing and/or problematic. The electron microscopes, scanning probe systems, and advanced optical systems that push the limits in performance are high-cost (\$1-5 million) and require highly specialized staff to develop and maintain them. A new mechanism is required to support the human resource infrastructure. Universities are not able to subsidize these costs.

2.5 R&D INVESTMENT AND IMPLEMENTATION STRATEGIES

Success in pushing the frontiers in nanoscale measurement science requires effort sustained for appropriate time frames. Note that accomplishing the observation of single-electron charge and electron spin required over ten years. It can be argued that the United States is falling behind in some nanocharacterization fields, perhaps as a consequence of short support time lines. To realize the ultimate implementation of nanotechnology, support mechanisms should be developed that account for the realities of relevant (i.e., longer-term) time frames.

The various types of centers of excellence supported by the National Science Foundation, the National Institutes of Health, and the Department of Energy have soundly demonstrated the positive impact of collaborative programs, particularly for topics that intersect several traditional fields. Investments in such centers and synergistic networks of centers should continue. New longer-term funding mechanisms should not deplete resources for individual investigator efforts, where significant innovation occurs.

Incentives should be instituted that encourage government labs, industry, and universities to collaborate in the development of standards for nanometrology. These mechanisms should not simply subsidize industry research and development but should facilitate coordinated advancement toward common research goals.

2.6 CONCLUSIONS AND PRIORITIES

Advanced capabilities in investigative, fabrication, and metrology tools will be a primary factor that enables new scientific discovery and the translation of nanoscience to nanotechnology. In the absence of these critical instruments and tools, the full potential of nanotechnology cannot be realized. The previous decade produced concepts and approaches that provide a platform for a new generation of localized measurement tools. The priorities for the next decade are to develop:

- Probes of the atomic origin of electromagnetic phenomena
- 3D atomic resolution structure determination with chemical specificity
- Characterization of dynamic processes with high spatial and temporal resolution
- *In situ* and multifunctional tools for device characterization
- Translation of fabrication metrology tools to facilitate manufacturing
- New strategies that allow instrument access to relevant research and communities
- Support of academic infrastructures that train the workforce

2.7 BROADER IMPLICATIONS FOR SOCIETY

The implications of the research and development of experimental tools for the characterization and manipulation of nanoscale phenomena cannot be overstated. Discovery requires observation, so promoting the next generation of these measurement capabilities will produce the tools that produce new science. The manufacturing of nanodevices and systems cannot be accomplished without the development of new metrologies and standards. New horizons offered by biological systems will not be achieved without the extension of these characterization instruments into higher levels of complexity in broader environmental conditions. The concomitant development of a workforce trained in these metrologies will fuel national economic growth.

2.8 EXAMPLES OF ACHIEVEMENTS AND PARADIGM SHIFTS

Several examples here illustrate advances, in addition to those described above, that are transforming our ability to probe nanoscale phenomena.

2.8.1 Complex Dielectric Function of the Molecular Layer

Contact persons: Dawn Bonnell, University of Pennsylvania

Various techniques have been developed for high-spatial-resolution probes of light interactions with surfaces, including photon-assisted STM, surface-enhanced Raman spectroscopy, and NSOM. A scattering-type near-field scanning optical microscopy (s-NSOM) offers the best opportunity for high spatial resolution. A sharp probe tip is positioned near a surface and illuminated with optical radiation. The field is enhanced at the tip, which acts as an optical antenna, (Eguchi et al. 2004; Cho and Hirose 2007; Kim, Komeda, and Kawai 2003; Pascual 2003; Hahn and Ho 2005), modulating the tip-sample distance in the enhanced field, detecting the reradiated light to distinguish variations in materials properties. Dielectric functions are an inherent component of the response of a tip-surface junction in this configuration. Figure 2.12 illustrates that it is possible to determine the real and imaginary coefficient of the dielectric function for a single molecular layer (Nikiforov et al. 2009). Harmonics up to the fourth order and polarization-dependence of incident light enabling probes of dielectric properties monolayers of organic molecules on atomically smooth

substrates. An analytical treatment of light/sample interaction using the NSOM tip was developed in order to quantify the dielectric properties. To date, the third harmonic provides the best lateral resolution and dielectric constant contrast, and the strength of s-NSOM contrast for s-polarized light is one hundred times higher than that of p-polarized light for this configuration.

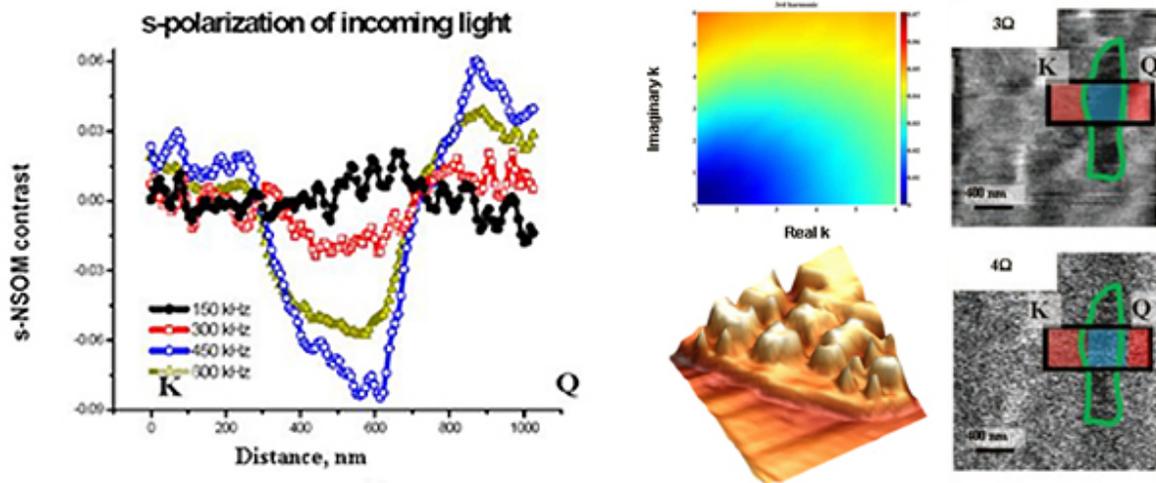


Figure 2.12. The scattered NSOM signal profiles (left) and images (right) are compared to a model of the complex dielectric function of a molecular layer (top, right) and the topographic structure (bottom, right) (Nikiforov et al. 2009).

2.8.2 Single-Electron Spin Detection

Contact person: Dan Rugar, IBM

The continued development of magnetic resonance force microscopy (MRFM) by Rugar and colleagues (Figure 2.13) has demonstrated unprecedented coherent control of individual electron spins, and has extended the sensitivity and spatial resolution of nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR) spectrometry by many orders of magnitude.

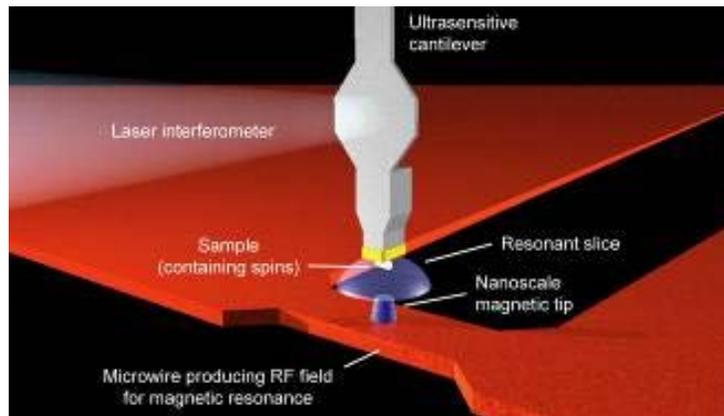


Figure 2.13. Schematic diagram of magnetic resonance force microscopy (from Degen, Poggio, Mamin, et al. 2009).

2.8.3 Attosecond Processes with X-Ray Scattering

Contact persons: *Peter Abbamonte, University of Illinois Urbana-Champaign; Dawn Bonnell, University of Pennsylvania*

Current x-ray probes are capable of determining the electronic and structural dynamics of individual nanostructures, whereas neutrons measure the dynamic response of assemblies of nanostructures—with the additional capability of separating a single particle from collective dynamics. Abbamonte et al. (2004) show that the momentum flexibility of inelastic x-ray scattering may be exploited to invert its loss function, allowing real-time imaging of density disturbances in a medium (Figure 2.14). They show the disturbance arising from a point source in liquid water, with a resolution of 41.3 attoseconds (4.13×10^{-17} s) and 1.27 Å (1.27×10^{-8} cm). This result is used to determine the structure of the electron cloud around a photoexcited chromophore in solution, as well as the wake generated in water by a 9 MeV gold ion.

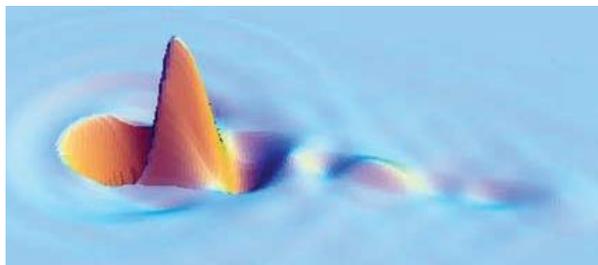


Figure 2.14. Attosecond snapshots of electronic disturbances in water calculated to be produced by a diffusing gold ion based on inelastic x-ray scattering measurements.

2.8.4 Electron Optics

Contact person: *Vinayak Dravid, Northwestern University*

Collectively, basic and aberration-corrected S/TEMs (and SEMs) coupled with accessories have taken the field of electron microscopy to new heights. These techniques have been applied to reveal atomic and molecular scale architecture, chemical partitioning, and varied aspects of electronic structures in materials and systems of great significance to modern society.¹⁸ They range from understanding interface limitations in modern microelectronics devices to emerging opportunities beyond classical silicon technologies, as in multifunctional oxides. Though advanced and cutting-edge improvements in the graphical user interfaces (GUI), new ease of operation and diversity of applications have made electron microscopy tools, techniques, and associated accessories essential to understanding broad issues and limiting factors in energy/environment technologies, information technology devices, biomedical materials and interactions, and food-package interactions, to name a few broad applications.

¹⁸ For more information on these structures and their significance, resources include Muller et al. 2008; Pennycook et al. 2006; Smith 2008; Zhu et al. 2009; Prabhumirashi et al. 2005; Dahmen et al. 2009; Kisielowski et al. 2001; Castell, Muller, and Voyles 2003; Girit et al. 2009; Jia, Lentzen, and Urban 2003; Meyer et al. 2008; Midgley and Durkan 2008; Nellist et al. 2004; Oshima et al. 2010; Hawkes and Spence 2007; Rossell et al. 2009; Suenaga et al. 2009; Thomas 2009; Varela et al. 2004; and Voyles, Grazul, and Muller 2003.

Analysis of Soft Matter

Since 1999, the community of vendors/manufacturers and scientists has risen to the challenge and contributed to a portfolio of electron microscopy-based tools and instrumentation essential for imaging and analysis of soft matter.

Field-emission-gun SEM/S/TEM instruments capable of operating at ultralow voltages with minimally required beam current, coupled with innovative specimen stages (liquid-cell stage, cryo stage, and environmental stage), have greatly advanced the ability to image/analyze the surfaces and sub-surface phenomena of soft matter (Bartesaghi et al. 2008; Costello 2006; de Jonge et al. 2010; Koning and Koster 2009). Vendors/manufacturers have identified critical applications to soft matter and configured modern S/TEMs to include variable energy (60–300 keV), cryopreservation of biological and soft matter, thin sectioning methods, cryospecimen stages for S/TEM, and 3D tomographic reconstruction (Figure 2.15; Xiao et al. 2009) via automated specimen tilting coupled with high-throughput image collection and analysis, among other related developments (Costello 2006; Koning and Koster 2009; Al-Amoudi et al. 2004; Beck et al. 2004; Cyrklaff et al. 2007; Grunewald et al. 2003; Nickell et al. 2007; Sartori et al. 2007).

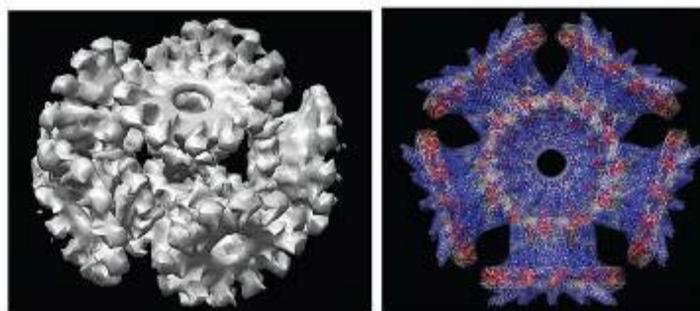


Figure 2.15. Image reconstruction of biological ellipsoid nanoparticle of bacteriophage DNA packaging motor complex (Xiao et al 2009).

STEM imaging techniques, especially annular dark field (ADF) and high-angle annular dark field (HAADF) techniques, have been successfully developed and applied for quantitative imaging/analysis of soft matter (Costello 2006; Al-Amoudi et al. 2004; Hohmann-Marriott et al. 2009; Aoyama et al. 2008). Specialized instruments have been conceived, designed, and developed for specific soft matter scientific issues, including cryo-bio nanoscale chemical analysis and mapping with high sensitivity and overall stability. The key issues in microscopy of soft matter continue to revolve around consistent, reproducible, and viable specimen preparation means and methods, increasing automation, and computer-aided microscopy/analysis.

Moving forward in the next decade, the analysis of soft matter will greatly benefit from aberration-corrected S/TEM, coupled with back-end innovative developments in specimen preparation techniques, novel multispecimen stages and specimen holders, as well as continued incorporation of automation, computer/software interfaces, and pattern recognition and processing. Novel detectors and their configuration (e.g., phase plate) coupled with fast detection (Zewail 2010; Kim et al. 2008) are being pursued; these promise significant improvements in ubiquitous contrast problems in soft matter with minimal dosage to reduce beam damage. Correlative microscopy (Sartori et al. 2007), i.e., coupling and correlation of data and analysis from different microscopy (and spectroscopy) approaches, will provide unique opportunities for understanding the form-function relationship, which is

the cornerstone of modern biology and nano-bio medicine. These advances in soft microscopy are critical for detailed understanding of complex biological structures and phenomena—especially at the interface with physical science and engineering. These developments will prove invaluable for improving health, environment, and sustainability in the context of nanomaterial life cycles.

3D Structure Determination

The decade 2000–2010 has seen innovative developments in electron microscopy tools and instrumentation and associated accessories (specimen holders) and techniques for 3D reconstruction and visualization of nanostructures (Midgley and Durkan 2008; Batenburg et al. 2009; Gonzalez et al. 2009; Midgley and Dunin-Borkowski 2009; Ziese et al. 2002). Three-dimensional tomographic reconstruction in biology has advanced significantly to allow for sub-nanometer-scale spatial resolution for 3D structure of biomolecular complexes ranging from protein clusters to biological tissues and hybrid organic-inorganic nanostructures (Bartesaghi et al. 2008; Costello 2006; de Jonge et al. 2010; Koning and Koster 2009; Aoyama et al. 2008).

Specialized low-dosage exposure, high- and low-kV imaging with TEM and STEM imaging modalities, coupled with advances in specimen stages (high-tilt), specimen holders (axial full-tilt, cryo), and specimen support (hydrophilic surface treatment, SiN_x window grids, graphene substrate, etc.) have all contributed to significant achievements in 3D rendering of nanostructures. Image processing algorithms, computational and processing power, and wide spectrum visualization tools and techniques have enabled improved appreciation of 3D rendering of nanostructures (Figure 2.16), defects, and substructure.

The 3D tomography and analysis approaches are rapidly becoming mainstream, thanks to improved microscope stability, innovative specimen stage and holder designs, and much more integrated hardware (microscope, detectors, and holders) and software (auto-image capture, auto-focus, rapid archiving, etc.). Nanometer-scale resolution in most cases and sub-nanometer-scale resolution in emerging approaches is readily possible in modern commercial S/TEMs.

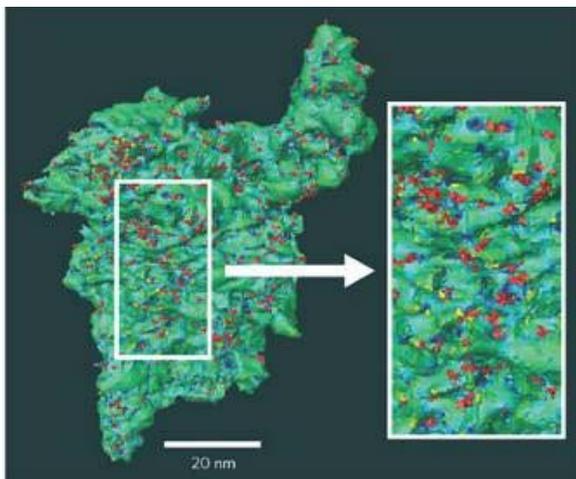


Figure 2.16. 3D tomographic reconstruction of a heterogeneous catalyst based on disordered mesoporous silica supporting bimetallic ruthenium–platinum nanoparticles (Midgley and Dunin-Borkowski 2009).

Here, too, the emergence of aberration-corrected S/TEM would prove indispensable in pushing the spatial (and depth) resolution in 3D reconstruction towards the molecular and atomic scales. The ability to open up pole-piece gaps in aberration-corrected S/TEM would allow researchers to develop innovative specimen stages, holders, and *in situ* experiments geared towards understanding biological processes under physiologically viable fluidic environment and external stimuli to probe complex dynamics of bio-nano interfaces. Such studies are vital not only for fundamental understanding of biological structures and processes but also for their tailoring and control for development of technologies for human health, environmental monitoring/remediation, and energy production, transfer, and storage using biological principles, among other developments that depend on 3D atomic and molecular structures and their dynamics.

Subsurface Metrology and Imaging Buried Structures/Phenomena

The remarkable advances in focused ion beam (FIB, including dual-beam SEM+FIB) instrumentation have enabled sectioning and fabrication for revealing buried and embedded structures and features (Mayer et al. 2007; Stokes et al. 2007). This has greatly advanced microelectronic metrology and defect analysis to the extent that significant improvement in yield and quality of final products has become possible in manufacturing. So-called dual-beam FIBs have proved to be a major boon to semiconductor/microelectronics manufacturing industries in their need for sub-surface metrology and defect analysis (Langford and Petford-Long 2001; Fu and Bryan 2004).

The FIB-SEM combination is continuing to improve in not just performance figures (i.e., of beam size and current) but also in innovative *in situ* capabilities such as lift-off, micro/nano-manipulation, gas-injection/deposition, and related *in situ* material manipulation capabilities (Figure 2.17).

These capabilities are rapidly advancing to enable multiple experiments and are being coupled with other instrumentations for synthesis, characterization, and measurements.

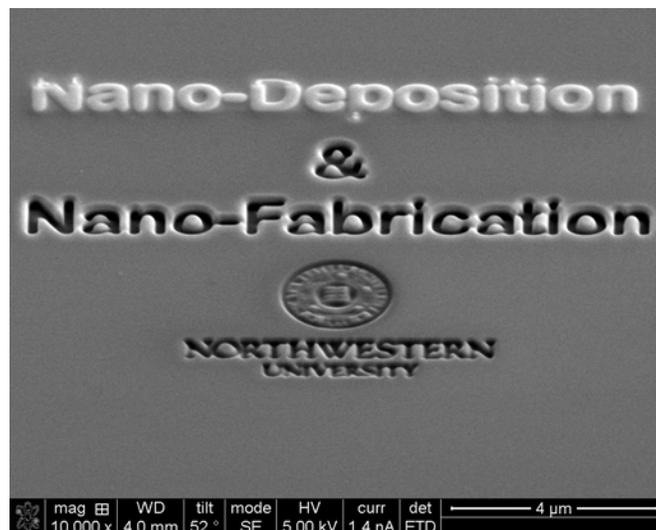


Figure 2.17. The complementary nanoscale fabrication capabilities of modern FIB are depicted in this image, showing both deposition and fabrication of materials (courtesy of B. Myers and V.P. Dravid).

2.9. INTERNATIONAL PERSPECTIVES FROM SITE VISITS ABROAD

The following are summaries from the International WTEC Nano2 workshops held in Germany, Japan, and Singapore, with a focus on international convergence in governance.

2.9.1 United States-European Union Workshop (Hamburg, Germany)

Panel members/discussants:

Liam Blunt (co-chair), University of Huddersfield, UK

Dawn Bonnell (co-chair), University of Pennsylvania, United States

Richard Leach, National Physical Laboratory, UK

Clivia M. Sotomayor Torres, Centre d'Investigació en Nanociència i Nanotecnologia, Spain

Malcolm Penn, Future Horizons, Ltd., UK

This group of scientists from the UK, Spain, and the United States met for several days at the Hamburg “Nano2” Workshop to assess the impact of tools that access nanoscale phenomena on scientific discovery and technology innovation. Vigorous discussion informed by the participants’ expertise and knowledge of various European road-mapping and strategic planning exercises resulted in the following summary of opportunities for the next decade of nanotechnology. The discussions emphasized metrology needs for commercialization.

The last decade has seen a realignment of the perception of nanotechnology according to the Gartner Hype Cycle (Fenn 1995) moving from the early over-hyped “technology trigger phase” through the “trough of disillusionment phase,” where the technology failed to meet early wild speculation. Finally we are now reaching the “slope of enlightenment phase” where realistic yet exciting possibilities in nanotechnology are becoming clear.

In the next decade, the design and production of nanostructures and materials will be of enormous importance in order to create materials with new and novel combinations of properties and functions. This will necessitate the convergence of the key enabling disciplines of chemistry, physics, and biology

New disciplines have emerged from interdisciplinary mixes such as plasmonics. We are now at the point where relatively inexpensive and accessible methods of nano-patterning (micro-contact printing, nanoimprint lithography, thin layer deposition, etc.) allow research and product development in laboratories all over the world, facilitating fabrication of specialized complex devices that allow exploration of new phenomena.

The commercial availability of off-the-shelf nanoparticles and nanoporous materials in sizes ranging from 1 nm to hundreds on nanometers has enabled rapid advances in the fundamental science and application of particles ranging from medical therapeutics to hybrid nanoelectronics. Patterning processes by electron or ion beam as well as x-rays, offer the chance to control and modify the relevant materials parameters at the nanoscale in a research environment. These examples of patterning and available nanoparticles are key drivers towards up-scaling nanotechnology from the research field into the world of real industrial production. Key to developing nanoscale production are quality systems; at the heart of these systems is metrology.

Key needs for nanometrology in the future will be:

- Full 3-D metrology using reliable instrumentation
- Mastering the challenge of handling large volumes of metrology data in a production-like environment
- Multiscale measurement technology (resolution and range, nm to m)

- Hybrid measurements for materials (dimensional/properties)
- Hybrid measurements for nanostructures (dimensional/functional)
- Globally accepted standards for measurement
- Standard reference materials for nanoscale measurement
- Routine online measurements suitable for a production environment
- Metrology across the process chain
- Metrology for nano-bio processes
- Metrology for dynamic processes

Instruments that access structure and properties at the nanoscale and atomic length scales were, and continue to be, essential in the understanding of physics and chemistry of nanostructures and nanosystems. The ability to quantify nanoscale behavior is a limiting factor in understanding new physics and is a prerequisite to manufacturing. If it cannot be measured, it cannot be made or even understood in any quantifiable manner. If specifications cannot be characterized, reliable and reproducible manufacturing is not possible. Critical processes for up-scaling nanotechnologies into production are infrastructure development and cooperation with R&D organizations during the development phase, and of particular importance, transfer of knowledge to SMEs in the nanotechnology field.

The consequence of the advances in instrumentation science of the last decade is that we are now poised for a new generation of tools that will:

- Revolutionize the fundamental concepts of solids and biomolecules
- Allow new views of complex systems at small scales
- Probe dynamic processes and unexplored time scales

Novel concepts emanating from the understanding of the properties and interactions in the nanometer scale may provide new metrology methods. To enable nanoscale metrology requires instrumentation that is easy to use and fit for purpose in an industrial setting. However, the investment needed in research at this second stage is far greater than at the basic research stage. Unless this is recognized, nanometrology research will fail to expand to meet the future needs. Metrological standardization will require the development of routes for communication between standards bodies and industrial users at the global level.

2.9.2 United States-Japan-Korea-Taiwan Workshop (Tokyo/Tsukuba, Japan)

Panel members/discussants:

Dae Won Moon (co-chair), Korea Research Institute of Standards and Science (KRISS)

Dawn Bonnell (co-chair), University of Pennsylvania, United States

Seizo Morita, Osaka University, Japan

Masakazu Aono, National Institute for Materials Science (NIMS), Japan

Mike B.C. Yao, Industrial Technology Research Institute (ITRI), Taiwan

Kunio Takayanagi, Tokyo Institute of Technology, Japan

A team of scientists from Korea, Japan, and the United States met for several days at the Tsukuba Nano2 Workshop to assess the impact of tools that access nanoscale phenomena on scientific discovery and technology innovation. Based on the expertise of the participants, discussion emphasized scientific achievements that offer opportunities for future technological breakthroughs.

Ten years ago, nanotechnology was an area of academic research exploring noble science and new applications in various disciplines. At present, nanotechnology demonstrates a strong potential to overcome critical challenges in many areas of electronics, energy, and medicine. This potential arises in a large part due to the advances in tools for measurement and atomic manipulation.

For example, in the last decade, scanning tunneling microscopy manipulation at low temperature for atom-by-atom assembly made several dramatic demonstrations, and its main application was in physical science. Recently, atomic force microscopy was used to interchange atoms with an AFM tip apex atom at room temperature. The ability for room-temperature atomic manipulation leads to practical strategies for the construction of new compounds by design. Multiple-tip scanning probe systems have been developed that quantify local transport properties in atomic and nanodevices, which was not possible previously.

Sub-Ångstrom resolution in TEM with aberration correction demonstrated in the last decade. An illustrative example of the potential of TEM is given by sub-70 pm spatial resolution imaging of Li atoms; a most stringent test of detectability and critical in energy applications. In addition, the capabilities of beamline-based characterization tools have evolved, with a 10 orders of magnitude increase in brightness over the last ten years. The 4th-generation beamlines promise advances in atomic dynamics and biomolecule analysis.

A shift from nanotechnology to “nanoarchitectonics” (from nanofunctionality to “nanosystem functionality”) is a clear change moving forward. No full-fledged application of nanotechnology can be expected without this paradigm shift; conversely, if this paradigm shift is realized, it will bring invaluable advancement in a wide variety of technological fields. Control of self-assembly and -organization of atoms, molecules, and nanostructures (with the use of local external fields and advanced nanochemical control) with single-molecule-level ultra-high sensitivity and novel methods to measure electrical, optical, and magnetic properties at the nanoscale (including multi-probe SPMs) enable this vision.

Success in realizing any of the future advances in nanotechnology depends on the capability to manipulate matter at nanometer length scales and measure the relevant and often complex properties at the same scale. The ultimate goal of atomic/molecular imaging is the spatial, temporal, 3D, single-molecule identification on surfaces and in complex environment such as cells *in vivo* and *in vitro* for nanoscale biology and medical diagnosis. Successful approaches may involve combinations of scanning probe, electron, and optical microscopy/spectroscopies. Realizing this goal will simultaneously provide several instrumentation innovations required for similar advances in devices.

A prerequisite for transitioning from fundamental physics to applications is the ability to routinely manipulate matter at room temperature in order to fabricate new compounds/nanostructures by design. AFM- and STM-based approaches have been demonstrated, but this must become routine.

To realize the exciting potential in science, engineering, and applications, the requirements for scientific and technological infrastructure are:2.

- Mechanisms to maintain infrastructure for 5 years, which is a typical length of time for nanotechnology programs in many countries. The lack of continuity has particularly impact in the physical infrastructure required for characterization at the nanoscale.
- In order for nanomanufacturing to be realized at a large scale, new infrastructure will be required, and global partnerships will be critical.

- New educational systems are necessary to train an innovative workforce with the appropriate skill sets.

2. 9.3 United States-Australia-China-India-Saudi Arabia-Singapore Workshop (Singapore)

Panel members/discussants:

John Miles (co-chair) National Measurement Institute of Australia

Dawn Bonnell (co-chair), University of Pennsylvania, United States

Li-jun Wan, Institute of Chemistry, Chinese Academy of Sciences (CAS)

Yong Lim Foo, Institute of Materials Research & Engineering (IMRE), Singapore

Huey Hoon Hng, Nanyang Technological University (NTU), Singapore

Scientists and research agency directors from Australia, China, Singapore, and India met to determine the global impact of experimental tools that enable scientific advance and commercialization of nanotechnology. The outcome summarized here emphasizes developing global consensus in developing tools and metrology standards and places these needs in the context of opportunities for the next decade of nanotechnology.

The vision of nanotechnology has changed in the last ten years to a quieter, more subdued one, with an understanding that the potential risks need to be addressed as much as the benefits. This has led to less funding from government and industry. Nanotechnology has penetrated into almost every research area and discipline in science and engineering, although the word “nanotechnology” has changed from a stand-alone term to one used now used in conjunction with specific applications, such as energy, water, medicine, etc. R&D has moved from individual nanostructures to nanosystems. A large number of commercial products have been developed.

The vision for the next ten years is that most R&D will be motivated by the requirements of society (e.g., energy, water, health care). There will be an increasing need for the development of instruments capable of measuring nanomaterials *in situ* in matrices such as soil, water, food, and living organisms. The manipulation and manufacture of nanomaterials at the atomic level at room temperature and the simultaneous imaging of multiple complex processes in living systems are considered to be important, desirable, and bold objectives.

Generally, the main metrological advancements in the last ten years are the significant increases in the use and capability (e.g., uncertainty, resolution, range, accuracy) of microscopy, analytical instruments, and spectroscopic and related techniques. These include the development of aberration correction for TEMs, the development of metrological AFMs, the measurement of single-charge, single-spin, inelastic vibrations, advances in energy-dispersive x-ray (EDX) detector technology and Si-drift detectors that can cope with higher count rates, allowing faster and more accurate mapping and more accurate chemical analyses, electron holography and magnetic induction maps, and multiprobe SPMs. The development of methods for creating reference standards for nanoparticles and for 2-dimensional and 3-dimensional nanoscale measurements is also an important advance.

The main goal for the next five years for general nanotechnology is to achieve large-scale applications of nanotechnology, with barriers being the scaling-up of processing/synthesis processes and safety issues of nanoparticles/nanomaterials. The main goals for the measurement and standards sector are

- Increased engagement and understanding between national measurement institutes, documentary standards developers, and the R&D community

- Further development of the linkages between national and international nanometrological systems
- Lower operating voltages (<35kV) for TEM; 3D imaging with atomic resolution
- Publication of a large number of documentary standards for use by the nano community
- Bond-level, femtosecond-time frame measurement capability
- Development of new portable and cheap nanoscale instruments capable of operating in an industrial environment
- Development of instruments capable of measuring nanomaterials in matrices such as water, soil, food and living tissue, etc.

The scientific and technological infrastructure considered to be required includes the rather bold need for an international funding agency to pay for work in activities such as documentary standards development, toxicological testing, international regulatory reform, etc. These activities often rely on goodwill and are too important to be left to volunteers. More realistic is a strong need for the continued development of the international metrological infrastructure to support the development of nanotechnology. This includes the establishment of physical standards by national measurement institutes that provide measurements traceable to the SI (international system of units), reference materials, standardized methods, international comparisons, uncertainty analyses, and appropriate quality systems. The need for documentary standards for nanotechnology is still urgent and growing.

Instrumentation and sensing is seen as the core of the emerging topics and priorities for future nanoscale science and engineering research, particularly in the biomedical and energy sectors.

2.10 REFERENCES

- Abbamonte, P., K.D. Finkelstein, M.D. Collins, and S.M. Gruner, 2004. Imaging density disturbances in water with a 41.3-attosecond time resolution. *Phys. Rev. Lett.* 92:237401, doi:10.1103/PhysRevLett.92.237401.
- Al-Amoudi, A., J.-J. Chang, A. Leforestier, A. McDowall, L.M. Salamin, L.P.O. Norlén, K. Richter, N. Sartori Blanc, D. Studer, and J. Dubochet. 2004. Cryo-electron microscopy of vitreous sections. *EMBO J.* 23(18):3583–3588.
- Aoyama, K., T. Takagia, A. Hirasec, and A. Miyazawa. 2008. STEM tomography for thick biological specimens. *Ultramicroscopy* 109(1):70–80.
- Banerjee, P., P. Conklin, D. Nanayakkara, T.-H. Park, M.J. Therien, and D.A. Bonnell. 2010. Plasmon-induced electrical conduction in molecular devices. *ACS Nano* 4(2):1019–1025.
- Bartesaghi, A., P. Sprechmann, J. Liu, G. Randall, G. Sapiro, and S. Subramaniam. 2008. Classification and 3D averaging with missing wedge correction in biological electron tomography. *J. Struct. Biol.* 162(3):436–450.
- Batenburg, K.J., S. Bals, J. Sijbers, C. Kübel, P.A. Midgley, J.C. Hernandez, U. Kaiser, E.R. Encina, E.A. Coronado, and G. Van Tendeloo. 2009. 3D imaging of nanomaterials by discrete tomography. *Ultramicroscopy* 109(6):730–740.
- Batson, P.E., N. Dellby, and O.L. Krivanek, 2002. Sub-angstrom resolution using aberration corrected electron optics. *Nature* 418(6898):617–620.
- Beck, M., F. Förster, M. Ecke, J.M. Plitzko, F. Melchior, G. Gerisch, W. Baumeister, and O. Medalia. 2004. Nuclear pore complex structure and dynamics revealed by cryoelectron tomography. *Science* 306(5700):1387–1390.
- Bonnell, D.A. 2008. Pushing resolution limits of functional imaging to probe atomic scale properties. *ACS Nano* 2:1753–1759, doi:10.1021/nn8005575.
- Bonnell, D.A., and S. Kalinin. 2001. Local potential at atomically abrupt oxide grain boundaries by scanning probe microscopy. In *Solid state phenomena*, eds., O. Bonnaud, T. Mohammed-Brahim, H.P. Strulnk, and J.H. Werner, 33–47. Uettikon am See, Switzerland: SciTech Publishing.
- Brizuela, F., S. Carbajo, A.E. Sakdinawat, Y. Wang, D. Alessi, B.M. Luther, W. Chao, Y. Liu, K.A. Goldberg, P.P. Naulleau, E.H. Anderson, D.T. Attwood, Jr., M.C. Marconi, J.J. Rocca, and C. S. Menoni. 2010. Improved performance of a table-top actinic full-field microscope with EUV laser illumination. *Proceedings of SPIE* 7636.

- Brun, C., J.C. Girard, Z.Z. Wang, J. Dumas, J. Marcus, and C. Schlenker. 2005. Charge-density waves in rubidium blue bronze $\text{Rb}_{0.3}\text{MoO}_3$ observed by scanning tunneling microscopy. *Phys. Rev. B* 72:235119–235126, doi:10.1103/PhysRevB.72.235119.
- Castell, M.R., D.A. Muller, and P.M. Voyles. 2003. Dopant mapping for the nanotechnology age. *Nature Materials* 2(3):129–131, doi:10.1038/nmat840.
- Cho, Y., and R. Hirose. 2007. Atomic dipole moment distribution of Si Atoms on a Si(111)-(7x7) surface studied using noncontact scanning nonlinear dielectric microscopy. *Phys. Rev. Lett.* 99:186101–186105, doi:10.1103/PhysRevLett.99.186101.
- Coffey, D.C., and D.S. Ginger. 2006. Time-resolved electrostatic force microscopy of polymer solar cells. *Nat. Mat.* 5:735–740, doi:10.1038/nmat1712.
- Costello, M.J. 2006. Cryo-electron microscopy of biological samples. *Ultrastruct. Pathol.* 30(5):361–371, doi:10.1080/01913120600932735.
- Crommie, M.F., C.P. Lutz, and D.M. Eigler. 1993. Confinement of electrons to quantum corrals on a metal surface. *Science* 262:218–220.
- Cyrklaff, M., A. Linaroudis, M. Boicu, P. Chlanda, W. Baumeister, G. Griffiths, and J. Krijnse-Locker. 2007. Whole cell cryo-electron tomography reveals distinct disassembly intermediates of *Vaccinia* virus. *PLoS One* 2(5):e420, doi:10.1371/journal.pone.0000420.
- Dahmen, U., R. Erni, V. Radmilovic, C. Ksielowski, M.-D. Rossell, and P. Denes, 2009. Background, status and future of the transmission electron aberration-corrected microscope project. *Philos. Transact. A Math. Phys. Eng. Sci.* 367(1903):3795–3808.
- Degen, C.L., M. Poggio, H.J. Mamin et al. 2009. Nanoscale magnetic resonance imaging. *Proc. Natl. Acad. Sci. U. S. A.* 106(5):1313–1317.
- de Jonge, N., R. Sougrat, B.M. Northan, and S.J. Pennycook. 2010. Three-dimensional scanning transmission electron microscopy of biological specimens. *Microsc. Microanal.* 16(1):54–63, doi:10.1017/S1431927609991280.
- Eguchi, T., Y. Fujikawa, K. Akiyama, T. An, M. Ono, Y. Hashimoto, Y. Morikawa, K. Terakura, T. Sakurai, M.G. Lagally, and Y. Hasegawa. 2004. Imaging of all dangling bonds and their potential on the Ge/Si(105) surface by noncontact atomic force microscopy. *Phys. Rev. Lett.* 93:266102, doi:10.1103/PhysRevLett.93.266102.
- Eigler, D. 2010. New tools for nanoscale science and engineering. Paper read at the Workshop, International Study of the Long-term Impacts and Future Opportunities for Nanoscale Science and Engineering, 9–10 March, Evanston, Ill.
- Erni, R., M.-D. Rossell, C. Kisielowski, and U. Dahmen. 2009. Atomic-resolution imaging with a sub-50-pm electron probe. *Phys. Rev. Lett.* 102(9):096101, doi: 10.1103/PhysRevLett.102.096101.
- Fenn, J. 1995. *The Microsoft system software hype cycle strikes again*. Stamford, Conn.: Gartner Group.
- Feynman, R.P. 1959. There's plenty of room at the bottom. Talk given at the annual meeting of the American Physical Society at the California Institute of Technology, December. Available online: <http://www.its.caltech.edu/~feynman/plenty.html>.
- Fu, Y., and N.K.A. Bryan. 2004. Fabrication of three-dimensional microstructures by two-dimensional slice by slice approaching via focused ion beam milling. *J. Vac. Sci. Technol. B* 22(4):1672–1678.
- Giessibl, F.J. 2003. Advances in atomic force microscopy. *Rev. Mod. Phys.* 75:949–983.
- Giessibl, F.J., and H. Bielefeldt. 2000. Physical interpretation of frequency-modulation atomic force microscopy. *Phys. Rev. B* 61:9968–9971, doi:10.1103/PhysRevB.61.9968.
- Girit, C.O., J.C. Meyer, R. Erni, M.D. Rossell, C. Kisielowski, Li Yang, C.-H. Park, M.F. Crommie, M.L. Cohen, S.G. Louie, and A. Zettl. 2009. Graphene at the edge: Stability and dynamics. *Science* 323(5922):1705–1708.
- Gonzalez, J.C., J.C. Hernández, M. López-Haro, E. del Río, J.J. Delgado, A.B. Hungría, S. Trasobares, S. Bernal, P.A. Midgley, and J.J. Calvino. 2009. 3D characterization of gold nanoparticles supported on heavy metal oxide catalysts by HAADF-STEM electron tomography. *Angew. Chem. Int. Ed. Engl.* 48(29):5313–5315.
- Grunewald, K., P. Desai, D.C. Winkler, J.B. Heymann, D.M. Belnap, W. Baumeister, and A.C. Steven. 2003. Three-dimensional structure of herpes simplex virus from cryo-electron tomography. *Science* 302(5649):1396–1398.
- Hahn, J.R., and W. Ho. 2005. Orbital specific chemistry: Controlling the pathway in single-molecule dissociation *J. Chem. Phys.* 122:244.

- Haider, M., S. Uhlemann, E. Schwan, H. Rose, B. Kabius, and K. Urban. 1998. Electron microscopy image enhanced. *Nature* 392(6678):768–769, doi:10.1038/33823.
- Han, P., A.R. Kurland, A.N. Giordano, S.U. Nanayakkara, M.M. Blake, C.M. Pochas, and P.S. Weiss, 2009. Heads and tails: Simultaneous exposed and buried interface imaging of monolayers. *ACS Nano* 3:3115–3121, doi:10.1021/nn901030x.
- Hawkes, P.W., and J.C.H. Spence, eds. 2007. *Science of microscopy*. New York: Springer.
- Heinrich, A.J., J.A. Gupta, C.P. Lutz, and D.M. Eigler, 2004. Single-atom spin-flip spectroscopy. *Science* 306:466–469, doi: 10.1126/science.1101077.
- Hohmann-Marriott, M.F., A.A. Sousa, A.A. Azari, S. Glushakova, G. Zhang, J. Zimmerberg, and R.D. Leapman. 2009. Nanoscale 3D cellular imaging by axial scanning transmission electron tomography. *Nat. Methods* 6(10):729–732.
- Huh, S., L. Ren, D. Chan, S. Wurm, K. Goldberg, I. Mochi, T. Nakajima, M. Kishimoto, B. Ahn, I. Kang, J. Park, K. Cho, S.-I. Han, and T. Laursen, 2010. A study of defects on EUV masks using blank inspection, patterned mask inspection, and wafer inspection. In *Extreme ultraviolet (EUV) lithography*, ed. B.M. La Fontaine. *Proceedings of SPIE* 7636.
- Jia, C.L., M. Lentzen, and K. Urban, 2003. Atomic-resolution imaging of oxygen in perovskite ceramics. *Science* 299(5608):870–873.
- Kabius, B., and H. Rose, 2008. Novel aberration correction concepts. *Advances in imaging and electron physics*, Vol. 153:261–281. San Diego, Calif.: Elsevier Academic Press.
- Kabius, B., P. Hartel, M. Haider, H. Müller, S. Uhlemann, U. Loebau, J. Zach, and H. Rose. 2009. First application of C_c -corrected imaging for high-resolution and energy-filtered TEM. *J. Electron. Microsc.* 58(3):147–155.
- Kalinin, S., D. Bonnell, T. Alvarez, X. Lei, Z. Hu, J. Ferris, Q. Zhang, and S. Dunn. 2002. Atomic polarization and local reactivity on ferroelectric surfaces: A new route toward complex nanostructures. *Nano Lett.* 2:589–594.
- Kim, J.S., T. LaGrange, B.W. Reed, M.L. Taheri, M.R. Armstrong, W.E. King, N.D. Browning, G.H. Campbell. 2008. Imaging of transient structures using nanosecond *in situ* TEM. *Science* 321(5895):1472–1475, doi:10.1126/science.1161517.
- Kim, Y., T. Komeda, and M. Kawai, 2002, Single-molecule reaction and characterization by vibrational excitation. *Phys. Rev. Lett.* 89:126104–126108, doi:10.1103/PhysRevLett.89.126104.
- Kisielowski, C., B. Freitag, M. Bischoff, H. van Lin, S. Lazar, G. Knippels, P. Tiemeijer, M. van der Stam, S. von Harrach, M. Stekelenburg, M. Haider, S. Uhlemann, H. Müller, P. Hartel, B. Kabius, D. Miller, I. Petrov, E.A. Olson, T. Donchev, E.A. Kenik, A.R. Lupini, J. Bentley, S.J. Pennycook, I.M. Anderson, A.M. Minor, A.K. Schmid, T. Duden, V. Radmilovic, Q.M. Ramasse, M. Watanabe, R. Erni, E.A. Stach, P. Denes, and U. Dahmen. 2008. Detection of single atoms and buried defects in three dimensions by aberration-corrected electron microscope with 0.5-Ångstrom information limit. *Microsc. Microanal.* 14(5):469–477.
- Kisielowski, C., C.J.D. Hetherington, Y.C. Wang, R. Kilaas, M.A. O’Keefe, and A. Thust. 2001. Imaging columns of the light elements carbon, nitrogen and oxygen with sub Ångstrom resolution. *Ultramicroscopy* 89(4):243–263.
- Kohsaka, T., C. Taylor, K. Fujita, A. Schmidt, C. Lupien, T. Hanaguri, M. Azuma, M. Takano, H. Eisaki, H. Takagi, S. Uchida, and J.C. Davis. 2007. An intrinsic bond-centered electronic glass with unidirectional domains in underdoped cuprates. *Science* 315:1380–1385, doi:10.1126/science.1138584.
- Koning, R.I., and A.J. Koster, 2009. Cryo-electron tomography in biology and medicine. *Ann. Anat.* 191(5):427–445, doi:10.1016/j.aanat.2009.04.003.
- Krivanek, O.L., M.F. Chisholm, V. Nicolosi, T.J. Pennycook, G.J. Corbin, N. Dellby, M.F. Murfitt, C.S. Own, Z.S. Szilagy, M.P. Oxley, S.T. Pantelides, and S.J. Pennycook. 2010. Atom-by-atom structural and chemical analysis by annular dark-field electron microscopy. *Nature* 464(7288):571–574.
- Krivanek, O.L., G.J. Corbin, N. Dellby, B.F. Elston, R.J. Keyse, M.F. Murfitt, C.S. Own, Z.S. Szilagy, and J.W. Woodruff. 2008. An electron microscope for the aberration-corrected era. *Ultramicroscopy* 108(3):179–195.
- Langford, R.M., and A.K. Petford-Long. 2001. Broad ion beam milling of focused ion beam prepared transmission electron microscopy cross sections for high-resolution electron microscopy. *J. Vac. Sci. Technol. A* 19(3):982–985.
- Li, D.B., M.H. Zhao, J. Garra, A.M. Kolpak, A.M. Rappe, D.A. Bonnell, and J.M. Vohs. 2008. Direct *in situ* determination of the polarization dependence of physisorption on ferroelectric surfaces *Nat. Mater.* 7(2008):473–477.
- Li, J., D. Stein, C. McMullan, D. Branton, M.J. Aziz, and J.A. Golovchenko. 2001. Ion-beam sculpting at nanometre length scales. *Nature* 412(6843):166–169, doi:10.1038/35084037.

- Lyding, J.W. Shen, T.C. Hubacek, J.S. Tucker, and J.R. Abein. 1994. Nanoscale patterning and oxidation of H-passivated Si(100)- 2×1 surfaces with an ultrahigh vacuum scanning tunneling microscope. *Appl. Phys. Lett.* 64(15):2010–2012, doi:10.1063/1.111722.
- Marko, M., C. Hsieh, R. Schalek, J. Frank, and C. Mannella. 2007. Focused-ion-beam thinning of frozen-hydrated biological specimens for cryo-electron microscopy. *Nat. Methods* 4(3):215–217, doi:10.1038/nmeth1014.
- Mayer, J., L.A. Giannuzzi, T. Kamino, and J. Michael. 2007. TEM sample preparation and FIB-induced damage. *MRS Bull.* 32(5):400–407.
- Meyer, J.C., C.O. Girit, M.F. Crommie, and A. Zettl. 2008. Imaging and dynamics of light atoms and molecules on graphene. *Nature* 454(7202):319–322.
- Midgley, P.A., and C. Durkan, 2009. The frontiers of microscopy. *Materials Today* 11:8–11.
- Midgley, P.A., and R.E. Dunin-Borkowski. 2009. Electron tomography and holography in materials science. *Nat. Mater.* 8(4):271–280.
- Moore, A.M., A.A. Dameron, B.A. Mantooth, R.K. Smith, D.J. Fuchs, J.W. Cizek, F. Maya, Y. Yao, J.M. Tour, and P.S. Weiss, 2006. Molecular engineering and measurements to test hypothesized mechanisms in single-molecule conductance switching. *J. Am. Chem. Soc.* 128:1959–1967, doi: 10.1021/ja055761m.
- Muller, D.A., L. Fitting Kourkoutis, M. Murfitt, J.H. Song, H.Y. Hwang, J. Silcox, N. Dellby, and O.L. Krivanek. 2008. Atomic-scale chemical imaging of composition and bonding by aberration-corrected microscopy. *Science* 319(5866):1073–1076, doi: 10.1126/science.1148820.
- Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the Committee on Technology of the National Science and Technology Council. 2008. *X-rays and neutrons: Essential tools for nanoscience research*. Report of NNI Workshop 16–18 June 2005. Washington, D.C.: NSET. Available online: http://neutrons.ornl.gov/workshops/nni_05/.
- Nellist, P.D., M.F. Chisholm, N. Dellby, O.L. Krivanek, M.F. Murfitt, Z.S. Szilagy, A.R. Lupini, A. Borisevich, W.H. Sides, Jr., and S.J. Pennycook. 2004. Direct sub-Ångstrom imaging of a crystal lattice. *Science* 305(5691):1741–1741.
- Nickell, S., F. Beck, A. Korinek, O. Mihalache, W. Baumeister, and J. Plitzko, 2007. Automated cryoelectron microscopy of “single particles” applied to the 26S proteasome. *FEBS Letters* 581(15):2751–2756.
- Nikiforov, M.P., S. Schneider, T-H Park, P. Milde, U. Zerweck, C. Loppacher, L. Eng, M.J. Therien, N. Engheta, and D. Bonnell. 2009. Probing polarization and dielectric function of molecules with higher order harmonics in scattering-near-field scanning optical microscopy. *J. Appl. Phys.* 106:114307, doi:10.1063/1.3245392.
- Nikiforov, M.P., A.F. Isakovic, and D.A. Bonnell. 2007. Atomic structure and charge-density waves of blue bronze $K_{0.3}MoO_3(201)$ by variable-temperature scanning tunneling microscopy. *Phys. Rev. B* 76:033104.
- Oshima, Y., Y. Hashimoto, Y. Tanishiro, K. Takayanagi, H. Sawada, T. Kaneyama, Y. Kondo, N. Hashikawa, and K. Asayama. 2010. Detection of arsenic dopant atoms in a silicon crystal using a spherical aberration corrected scanning transmission electron microscope. *Phys. Rev. B* 81(3): 035317– 035322, doi:10.1103/PhysRevB.81.035317.
- Otte, A.F., M. Ternes, S. Loth, C.P. Lutz, C.F. Hirjibehedin, and A.J. Heinrich. 2009. Spin excitations of a Kondo-screened atom coupled to a second magnetic atom. *Phys. Rev. Lett.* 103:107203–107207, doi:10.1103/PhysRevLett.103.107203.
- Pascual, J.I., N. Lorente, Z. Song, H. Conrad, and H.-P. Rust. 2003. Selectivity in vibrationally mediated single-molecule chemistry. *Nature* 423:525–528.
- Pennycook, S.J., M. Varela, C.J.D. Hetherington, and A.I. Kirkland. 2006. Materials advances through aberration-corrected electron microscopy. *MRS Bull.* 31(1):36–43.
- Prabhumirashi, P., V.P. Dravid, A.R. Lupini, M.F. Chisholm, and S.J. Pennycook. 2005. Atomic-scale manipulation of potential barriers at SrTiO₃ grain boundaries. *Appl. Phys. Lett.* 87(12):121917–121920.
- Roco, M.C., R.S. Williams, and P. Alivisatos, eds. 1999. *Nanotechnology research directions: IWGN [NSTC] workshop report: Vision for nanotechnology R&D in the next decade*. Baltimore, Md.: International Technology Research Institute at Loyola College. Available online: <http://www.nano.gov/html/res/pubs.html>.
- Rodriguez, B.J., S. Jesse, A.P. Baddorf, and S.V. Kalinin. 2006. High-resolution electromechanical imaging of ferroelectric materials in a liquid environment by piezoresponse force microscopy. *Phys. Rev. Lett.* 96:237602.
- Rose, H. 1994. Correction of aberrations. A promising means for improving the spatial and energy resolution of energy-filtering electron-microscopes. *Ultramicroscopy* 56(1–3):11–25.
- Rossell, M.D., R. Erni, M. Asta, V. Radmilovic, and U. Dahmen. 2009. Atomic-resolution imaging of lithium in Al₃Li precipitates. *Phys. Rev. B* 80(2): 024110, doi:10.1103/PhysRevB.80.024110.

- Saavedra, H.M., T.J. Mullen, P.P. Zhang, D.C. Dewey, S.A. Claridge, and P.S. Weiss. 2010. Hybrid strategies in nanolithography. *Rep. Prog. Phys.* 73:036501, doi:10.1088/0034-4885/73/3/036501.
- Sartori, A., R. Gatz, F. Beck, A. Rigort, W. Baumeister, and J. Plitzko. 2007. Correlative microscopy: Bridging the gap between fluorescence light microscopy and cryo-electron tomography. *J. Struct. Biol.* 160(2):135–145.
- Shpyrko, O.G., E.D. Isaacs, J.M. Logan, Y. Feng, G. Aeppli, R. Jaramillo, H.C. Kim, T.F. Rosenbaum, P. Zschack, M. Sprung, S. Narayanan, and A.R. Sandy. 2007. Direct measurement of antiferromagnetic domain fluctuations. *Nature* 447:68–71.
- Smith, D.J. 2008. Development of aberration-corrected electron microscopy. *Microsc. Microanal.* 14(1):2–15.
- Stokes, D.J., L. Roussel, O. Wilhelmi, L.A. Giannuzzi, and D.H.W. Hubert. 2007. Recent advances in FIB technology for nano-prototyping and nano-characterisation. In *Ion-beam-based nanofabrication*, MRS Proceedings Vol. 1020, eds., D. Ila, J. Baglin, N. Kishimoto, and P.K. Chu. Paper No. 1020-GG01-05. Warrendale, Pa.: Materials Research Society.
- Suenaga, K., Y. Sato, Z. Liu, H. Kataura, T. Okazaki, K. Kimoto, H. Sawada, T. Sasaki, K. Omoto, T. Tomita, T. Kaneyama, and Y. Kondo. 2009. Visualizing and identifying single atoms using electron energy-loss spectroscopy with low accelerating voltage. *Nat. Chem.* 1(5):415–418, doi:10.1038/nchem.282.
- Sugimoto, Y., M. Abe, S. Hirayama, N. Oyabu, Ó. Custance, and S. Morita. 2005. Atom inlays performed at room temperature using atomic force microscopy. *Nat. Mater.* 4(2):156–159, doi: 10.1038/nmat1297.
- Sugimoto, Y., P. Pou, M. Abe, P. Jelinek, R. Perez, S. Morito, and O. Custance. 2007. Chemical identification of individual surface atoms by atomic force microscopy. *Nature* 446:64–67, doi:10.1038/nature05530.
- Tanaka, K., Y. Kurihashi, T. Uda, Y. Daimon, N. Odagawa, R. Hirose, Y. Hiranaga, and Y. Cho. 2008. Scanning nonlinear dielectric microscopy nano-science and technology for next generation high density ferroelectric data storage. *Jpn. J. Appl. Phys.* 47(5):3311–3325.
- Thomas, S.J.M. 2009. The renaissance and promise of electron energy-loss spectroscopy. *Angew. Chem. Int. Ed. Engl.* 48(47):8824–8826.
- Tonomura, A., T. Matsuda, J. Endo, H. Todokoro, and T. Komoda. 1979. Development of a field emission electron microscope. *J. Electron Microsc.* (Tokyo) 28(1):1–11.
- Ushida, K. The future of optical lithography. Plenary talk, SPIE Advanced Lithography conference, 22 February 2010, Santa Clara, Calif.
- Varela, M., S.D. Findlay, A.R. Lupini, H.M. Christen, A.Y. Borisevich, N. Dellby, O.L. Krivanek, P.D. Nellist, M.P. Oxley, L.J. Allen, and S.J. Pennycook. 2004. Spectroscopic imaging of single atoms within a bulk solid. *Phys. Rev. Lett.* 92(9), doi:10.1103/PhysRevLett.92.095502.
- Voyles, P.M., J.L. Grazul, and D.A. Muller. 2003. Imaging individual atoms inside crystals with ADF-STEM. *Ultramicroscopy* 96(3-4):251–273.
- Williams, D.B., and D.B. Carter. 2009. *Transmission electron microscopy* (2nd ed.). New York: Springer.
- Xiao, F., Y. Cai, J. C.-Y. Wang, D. Green, R.H. Cheng, B. Demeler, and P. Guo. 2009. Adjustable ellipsoid nanoparticles assembled from reengineered connectors of the bacteriophage Phi29 DNA packaging motor. *ACS Nano* 3(8):2163–2170, doi:10.1021/nn900187k.
- Zewail, A.H. 2010. Four-dimensional electron microscopy. *Science* 328(5975):187–193, doi:10.1126/science.1166135.
- Zhu, Y., H. Inada, K. Nakamura, and J. Wall. 2009. Imaging single atoms using secondary electrons with an aberration-corrected electron microscope. *Nat. Mater.* 8(10):808–812, doi:10.1038/nmat2532.
- Ziese, U., C. Kübel, A. Verkleij, and A.J. Koster. 2002. Three-dimensional localization of ultrasmall immuno-gold labels by HAADF-STEM tomography. *J. Struct. Biol.* 138(1–2):58–62.