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Chemical Analysis in Small Domains: Introduction

The creation of new capabilities in materials science and biological technologies requires new methods for chemical analysis on the scale of micrometers to nanometers. Advanced materials and biological systems have consequential heterogeneities, and techniques that can address heterogeneity will advance these technologies. The advent of scanning tunneling and atomic force microscopies more than a decade ago enabled extraordinarily valuable physical characterization on the nanometer scale. From a chemical viewpoint, these scanning-probe microscopies enabled detection and study of single atoms and molecules on surfaces, but they do not directly identify these species chemically. Understanding molecular-scale behavior will become increasingly important as new submicrometer devices are designed. The merging of materials science and biology to forge bioelectronic devices will continue to foster the need for new analytical methods that carry more chemical information. This thematic issue describes research areas of analytical chemistry where chemical information is sought in increasingly smaller dimensions.

Scanning force microscopy employs an atomic force microscope to measure intermolecular interactions between surface-bound functional groups, including Coulombic, repulsive, and adhesive interactions. Marc Porter and his group outline why scanning force microscopy is particularly applicable to surfaces in contact with liquids, and they describe research to study chemical interfaces and interactions of complementary biomolecules. Near-field scanning optical microscopy is another scanning-probe technique, where optical spectroscopy can be performed with spatial resolution typically an order of magnitude smaller than the one-half micrometer wavelength of light. This research area is detailed by Robert Dunn and his group, where they describe the technological hurdles, the ability to probe single molecules, and the applications in materials science and biology, where conventional optical microscopy does not provide adequate spatial resolution. Richard Keller and coworkers were the first to achieve single-molecule detection in fluids, where they used flow cytometry combined with fluorescence detection. They explain how the use of small volumes is essential to accomplishing single-molecule fluorescence spectroscopy, and they show that the scope of applications in single-molecule spectroscopy is burgeoning, especially with exciting opportunities for rapid genomic analysis. Raman spectroscopy provides more structural information than fluorescence spectroscopy; however, unlike fluorescence spectroscopy, the state of knowledge in Raman spectroscopy predicted the impossibility of single-molecule detection. Katrin Kneipp and co-workers write about the surprising discoveries in surface-enhanced Raman spectroscopy, where the colloids that give rise to surface enhancement are shown to be highly heterogeneous in morphology. This means that a small subset of particles gives most of the enhancement; hence, enhancement factors are many orders of magnitude higher than previously believed. They review experimental results on ultrasensitive and single-molecule detection by Raman spectroscopy.

Mass spectrometry is a powerful tool for structural analysis, and the methods of ionization are amenable to the micrometer and nanometer scales. Nick Winograd and his group detail the advances in imaging by mass spectrometry, where the microscopic heterogeneities in both materials and biological samples are studied to provide chemical maps of surfaces. Aerosols are inherently on the micrometer scale and smaller, and the chemical nature of these particles is important because they penetrate deep into the lungs. Kim Prather and her group describe the use of mass spectrometry to analyze the compositions of fine aerosol particles in environmental samples, as well as the basic research being performed to understand what controls aerosol composition. The control of the ionization process in mass spectrometry, using the small-scale methods of electrospray ionization and matrix-assisted laser-desorption and ionization, have heralded a new era of investigating protein structure. David Clemmer and his group describe the use of these new capabilities to investigate conformations of proteins in the gas phase and how these conformations relate to equilibrium structures in solution.

Chemical separations have been essential to chemical analyses, and the tremendous advances in the speed of chemical separations now enables real-time monitoring of chemical and biological phenomena. Robert Kennedy and his group outline the advances

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in miniaturization that have fueled this rapidly developing area, and they review the advances in capillary electrophoretic methods and lab-on-a-chip technology. High speed enables detection of short-lived species, such as unique conformations of proteins, and also allows multidimensional separations and on-line and in vivo chemical monitoring. NMR has been the most vital tool for structural elucidation of pure chemical components. Jonathan Sweedler and his group illustrate how miniaturization of NMR coils can be designed to provide a sufficient signal-to-noise ratio for small samples and show applications to small volumes that address problems in combinatorial chemistry, as well as detection in small-volume chemical separations.

The drive for advances in materials science, the biological sciences, and bioengineering, combined with continued advances in instrumentation, will hold this field of chemical analysis in small domains in the spotlight for years to come.

Mary J. Wirth
University of Delaware

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