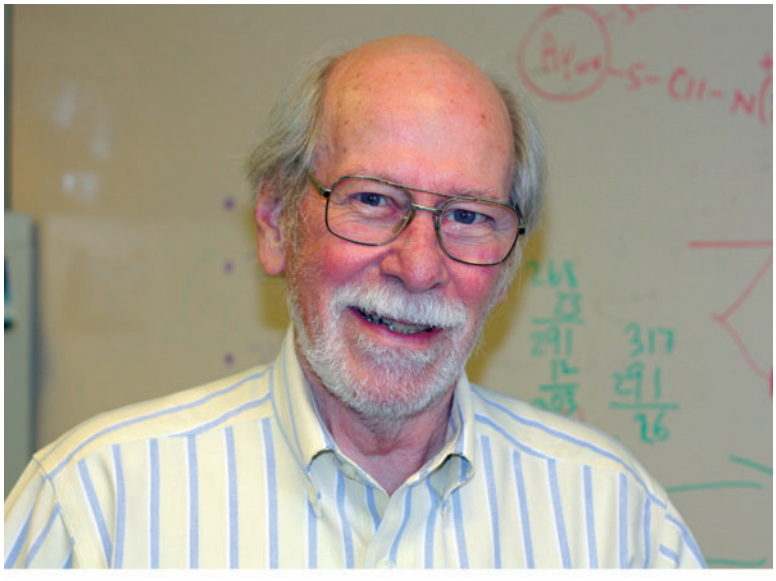

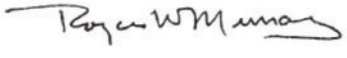

An Editor's View of Analytical Chemistry (the Discipline)

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Abstract

The author recounts progress observed in analytical chemistry (the discipline) from the vantage point of a 20-year editor of *Analytical Chemistry* (the journal). The recounting draws liberally from the journal's monthly editorials. A complete listing of the editorials can be found in **Supplemental Material** (follow the **Supplemental Material link** from the Annual Reviews home page at **http://www.annualreviews.org**).

1. AN EDITOR'S VIEW OF ANALYTICAL CHEMISTRY (THE DISCIPLINE)

Researchers can be prone to settling into a comfortable local pocket of scientific questions and not to wandering into other scientific spaces. I am not comfortable in narrow spaces, and I am happiest when my students and I are developing measurement tools and learning new ones in studies of original chemical materials that we ourselves synthesized. Having been trained as an electrochemist makes me necessarily fond of the chemistry of interfaces, which led me to the chemically modified electrode concept (1) and, presently, to the ligand-coated interfaces of very small nanoparticles (2). Nanoparticles whose properties depend on their size are, in purely scientific terms, fascinating. Large (>4 nm) metal ones have properties like those of bulk metals, whereas small ones exhibit molecule-like properties such as HOMO-LUMO gaps. In between, one finds quantized capacitors (3). An important lesson in the study of nanoparticles is that, in order to understand how and why properties change with size, you have to know much more than the traditionally accepted diameter. Measurement tools with a capacity to designate their exact compositions and chemical formulae, and ultimately their structures, are needed. A chemist should want to know the formula of a substance that has interesting properties. I refer to this as the analytical chemistry of nanoparticles and promote it as a broad and substantially undeveloped field of study (4). I thought hard about adopting that topic for this article.

Another choice I pondered adopts the vantage point of a 20-year editor-in-chief of *Analytical Chemistry*. That experience is like standing on a very high place with a far and wide view of a chemical discipline in its broadest contexts, witnessing its scientific advances and cultural changes. When I first became editor, I resolved to look—at least briefly—at every submitted manuscript, both as part of assigning it to an editor (or myself) for evaluation and to maintain a sense of what advances were being made and of what issues were arising for editorial decisions. That practice became a high place from which to view the discipline. Guiding the selection of manuscripts for publication, with the dedication and wisdom of my fellow journal editors and with the sage advice of the journal's advisory board and the legion of researchers who have served *Analytical Chemistry* as reviewers, gives one a sense of involvement in the discipline that has become as deep as my own research interests.

Yet another choice I pondered for this article was tracing the development of my professional life, but I did that when I was honored in 2001 by a Festschrift in the *Journal of Physical Chemistry* (5). And autobiographies can be like fishing stories—the tale grows larger with each retelling. Although the analytical chemistry of nanoparticles would have been fun to write about, the appeal of taking an editor's view of my (our) discipline became my choice. I liberally draw on the content of the monthly editorials that I (and guests) prepared for the journal. They are referenced in the article, and a complete listing of them can be found in **Supplemental Material** (follow the **Supplemental Material link** from the Annual Reviews home page at **http://www.annualreviews.org**).

Supplemental Material

What is the role of a journal editor, anyway? Central are guiding the selection of submitted manuscripts and maintaining a high standard for their scientific quality, originality, and impact on the discipline. Writing editorials gives the editor an additional role. Such editorials convey (indeed, demand!) thoughts about the character of the discipline, its research, the teaching of it, and its service to society. In editorials that I label frontier editorials, I act as a cheerleader for advances in measurement science and point to needs for further advances. Another editorial theme offers advice to prospective authors about improving the preparation of their manuscripts—any success there benefits the journal's readers. As a professor, I teach undergraduate and graduate students and postdoctorals; thoughts about students and the teaching profession and its contexts have informed numerous editorials. Some editorials reflect a personal outlook; some recount

a philosophy of how one should do science; others are discourses on journals, the publication business, and federal funding agency behavior; and yet others are about professional meetings. A handful represent inexpert attempts at satire. There are nearly 200 of them, so here I pick and choose among their themes.

An editor should not have illusions of leading a discipline. Being an editor is more like leading from behind: watching with pleasure as researchers plow ahead, and occasionally yelling "Turn left!" or trying to rescue an aberrant direction of effort, or pointedly declining manuscripts that are beating the proverbial dead horse (6). No individual editor should imagine he or she can lead the incredible range of independent intellectual endeavors aimed at measurements of chemicals, which take place in diverse settings and for a multitude of reasons and purposes.

I turn to a question central to the scope of the journal: What is analytical chemistry (the discipline), anyway? This was discussed in a 1991 editorial (7) that was subsequently reprinted with some editing (8). It is reproduced below.

Analytical Chemistry Is Still the Science of Chemical Measurements

The original version of this editorial was written in 1991, 3 months after I became Editor of *Analytical Chemistry*. The definition of what *is* the discipline of analytical chemistry, and thus what should be published in the field's leading journal, was then, to many, a topic of debate. Because I was concerned about that debate, I wanted to explicitly state that the journal would take a broad view of its scope, based on the criterion of measuring important chemical things. Attitudes and impressions can, however, be slow to change, and to this day we still receive questions from authors, "Is this measurement appropriate for the journal?" and comments from reviewers, "The authors did not measure a concentration, so it is not appropriate for the journal."

In this editorial, I wish to firmly reiterate that the journal's scope remains that of describing the fundamental and practical applications of how to measure important chemical things, which include concentrations, rate constants, lifetimes, and whatever—as long as what is measured is a chemically important parameter. I believe that this is a critically important viewpoint in modern chemistry as subdisciplines, and indeed disciplines, grow closer together in what researchers investigate as important subjects. I would like to see *Analytical Chemistry* report all original descriptions of what a *xxxxx* (name your area) chemist, *xxxxx* (again, name your area—biochemist, geochemist, atmospheric chemist, forensic chemist, art historian, etc.), would consider is an important measurement capability.

Here follows the (edited) 1991 editorial:

Analytical Chemistry (the discipline and the journal) prospers because it adapts to changes in chemical science. In the first half of the nineteenth century (roughly), analytical chemists investigated chemical reactivities that produced qualitative identifications and quantitative determinations of elements, functional groups, and molecules. Then, attention turned to chemical transducers—devices that emit electrical and optical signals, reflecting chemical composition—and to strategies for separating complex mixtures. This led to the science of designing instrument systems for control and measurement and to the U.S. adoption in the 1950s of an undergraduate course explicitly called "instrumental analysis." Education consequently indelibly labeled and nurtured this subject.

Instrumental analysis continues to evolve and yield capacities for chemical separations and measurement of chemical composition on breathtaking scales of complexity and sensitivity. These developments have opened many opportunities and doors to scientific progress, including those that support the broader chemical sciences enterprise and that of disciplines like biotechnology, materials

chemistry, environmental chemistry, chemical toxicology, and small-domain (nano) chemistry. These are historical facts in which analytical chemists can take justified pride.

A third, growing evolution in analytical chemistry is the explicit recognition of a broader scope of the discipline's intellectual turf; analytical chemists have become very good at devising ways to measure all sorts of things other than concentration. The users of analytical instruments are increasingly becoming chemical measurers of phenomena ranging across molecular and supramolecular structure in bulk and at surfaces, homogeneous and heterogeneous chemical reaction rates, excited-state lifetimes, transport rates in solids and membranes, molecular weight distributions, and receptor site specificity, to name just a few. Many workers in different subdisciplines contribute in depth to these activities, but collectively they can all be regarded as "measurers of chemical systems."

This editorial is to suggest that it is useful, and appropriate, to regard analytical chemistry in an expansive way; its evolution has made it today the science of inventing and applying the concepts, principles, and instrumental strategies for measuring the characteristics of chemical systems and species. Analytical chemistry needs to appreciate the breadth of its intellectual horizon, and how fertile are its pastures of exploration, to exploit its opportunities to play a full role in the advancement of scientific knowledge.

In the above, I am saying that the traditional boundaries of subdisciplines—analytical chemistry included—were in 1960 (for example) much more confining than their real boundaries are in 2009. Those boundaries now overlap extensively, leading to what I term permanently fading boundaries (9). It is useless for scientists to argue over intellectual turf when the boundaries of how research is conducted have become thoroughly indistinct.

Despite the overlapping of subdisciplines in research laboratories and journals, their identities are usefully maintained in the practice of teaching and in commerce. As I wrote in 1996, "[t]he organization of the teaching of chemistry is by subdiscipline, and there is in the commerce of chemistry great demand for workers in chemical subdisciplines, quality control and synthesis being significant examples" (9).

2. FRONTIERS IN ANALYTICAL CHEMISTRY

A frontier is a place on the edge of where you have not yet gone. Because frontiers in chemistry are not always easy to discern, it is helpful to ask what we do not know how to measure and what results we do not yet understand. As stated above, my frontier editorials have served as cheerleading for important advances and challenges. Crossing frontiers is a hallmark of a vibrant discipline; my summary of some of these editorials constitutes a major portion of this article's limited space. **Figure 1** is a simple illustration of the diversity of concepts in the journal—a luminescence measurement associated with a detailed protein structure and energy transfer.

2.1. Selectivity, Chemical Sensors, and Chemical Separations

"One of the most important themes in analytical chemistry is selectivity in detection and determination" (10). A chemical sensor can have many attractive attributes, such as ruggedness, fast response, low per-unit cost, remote operability, and self-calibration; but, most of all, a chemical sensor "exposed to a natural, unfiltered sample matrix require[s] excellent selectivity, or molecular recognition, for the chemical species whose detection and quantification is desired" (10). Research aiming at sensor platforms that can detect a successful recognition event using reaction properties of a chemical coating has given us sensors based on optical fibers and waveguides, surface acoustical wave devices, and ion-selective and chemically modified electrodes. However, more progress has been made in designing platforms than in solving selectivity issues.

Figure 1

Cover art from *Analytical Chemistry*. Reproduced with permission. Copyright 2009, American Chemical Society.

Fifteen years later, the above gloomy statement is still substantially accurate, not because progress has not been made but because the needs have grown even more rapidly. Improving chemical selectivity in the face of real-world complex matrices is an enormously difficult proposition, and chemists continuously enter into analysis in a wider range of matrices, from so-called smokers in deep oceans (11) to the interiors (12–14) of biological cells. The problem is worsened when we realize that the selective detection should be done at an enhanced sensitivity. Of course, much progress has been made, such as by exploiting the selectivity of products of evolution in biological chemistry, for example DNA hybridization and antibody-antigen binding, and by biological mimicry as in aptamers and in molecular templating of polymeric structures (15–17). Another research direction exploits mathematical approaches to "extract selectivity from the combined responses of arrays of imperfectly selective sensors," as in electronic noses (18). But our grasp of the expanding scope of this frontier's edge—in selectivities for increasing numbers of putative analytes and the concentrations, spatial locations, and dynamics thereof—has lagged.

The selectivity challenge has a friendly cousin in chemical separations (19), modern versions of which can separate complex mixtures of species differing only slightly in structure and composition. Unraveling the complex worlds of proteomics, metabolomics, and other -omics drives improvements in high-performance liquid chromatography (HPLC)—as in column packings (particle uniformity, monoliths) (20) and the design of two-dimensional separation schemes such as HPLC–capillary electrophoresis (CE).

If a chemical separation can be accomplished within a time comparable to the response time of a chemical sensor, or within the timescale desired for measurement of the chemical system or process, then such a separation tool is de facto a sensor (21). The analytical methodology for fast gas chromatography (GC) separations has evolved substantially, starting from a microcolumn etched into a Si wafer (22) in the 1970s to a significant volume of publications on fast GC applied to a wide variety of analytical situations at the present time (23–25). There are also commercial portable vapor and odor GC sensor instruments based on short columns and SAW device detectors that can complete separations and identification in less than 1 min (see **http://www.estcal.com/products/model4500_portable_znose.html**).

A much faster sensor timescale may be available in microchannel electrophoresis in the form of so-called lab-on-chip concepts (26–29), which "exploit modern microfabrication technology to fashion the part of the instrument that contains the analyte and reagent solutions into a monolithic block, disk, or plate. The geometry of the microcontainer depends on how the fluids are to be set in motion, manipulated and mixed, reacted in chambers, separated in tiny columns by chromatographic or electrophoretic or other principles, and detected" (26). High-efficiency separations have been demonstrated on the millisecond timescale (29).

Although the stage may seem to be set for a major erosion of analytical selectivity needs by use of fast separations, the appeal of instrumental simplicity in a chemical sensor is still perceived as a major advantage when compared to the sophistication required for fast separations (including making and translating the data record). Fast separations by GC or CE apparently require substantial further development in the simplicity direction. One recent innovation calls for making microfluidic devices from waxed paper (30, 31)!

2.2. Analytical Chemistry of Biological Materials

The analytical chemistry of biological materials has been an area of enormous growth in research activity. A strong propellant has been federal funding in the United States and abroad; political arguments for substantial investments in understanding, diagnosis, and treatment of disease are potent and socially accepted forces. "The Federal Rudder is the outlook of politicians and government policy makers that infusions of public funds into scientific research will produce knowledge that will aid in improving the lives of the nation's citizens and in providing for national security, and will ensure a future supply of scientific manpower. This philosophy is found in all developed nations" (32).

This emphasis led to the Human Genome Project, a visionary plan begun in 1990 to understand life's chemistry. Analytical chemists played key roles in the invention, development, multiplexing, and commercialization of CE as a powerful high-throughput measurement system (33). CE and its favorable separation characteristics were wedded to ideas of gel electrophoresis to create an enabler of DNA-sequencing science, which is now a major tool for workers in many genetic, diagnostic, and evolutionary research areas. Genomic sequencing is gaining a very large footprint, contributing to an understanding of disease vectors such as the RNA genome of the human immunodeficiency 1 virus (34). There is also considerable interest in disease prediction, which raises a number of bioethical issues. DNA-sequencing technology is still quite expensive, however,

and a search for analytical tactics to accomplish the needed separation and nucleotide identification at suitable sensitivity and throughput is driving a number of innovative new approaches, including, for example, the threading of DNA chains serially through nanopores with the dream of having nucleotide-specific detection capacities (2, 35).

Many scholars have moved on from this genomics-sequencing success to other ambitious -omics. Some are working in proteomics; others are tackling metabolomics. These are, respectively, the separation and identification (and ultimately the structure) of proteins in biological cells and plasma and of chemicals (e.g., proteins, medicines, caffeine, fish) degraded by life processes. Analytical chemistry today is helping to decipher the chemistry of life on a level of detail (e.g., systems biology) that will keep systems biologists and others wishing to understand biological behavior, organ function, etc., happy for a long time. (I say, modestly, "helping," but without the analytical chemistry discipline this topic would not make progress.) These bioanalytical areas are so important as to have spawned a number of specialized research journals chronicling their progress. I return to the proteomics arena of research in the section below on mass spectrometry, which is probably analytical chemistry's best helping hand in that area.

I predict that researchers currently involved in the above endeavors will look back on this era with awe at their fortunate timing of involvement and that they will be disappointed that all is not solved. That would be good, for when we understand the entire chemistry of biology, what is a comparably large and complex frontier? The global chemistry of nature?

In other growth areas of the bioanalytical arena, investigations (36, 37) of metal nanoparticles coated with single-stranded DNA chains as recognition elements of DNA targets—by the sequence-specific process of hybridization—have led to a proliferating array of ways to amplify the sensitivity of detecting when the recognition has occurred. This is an important tactic for diagnostic detection, and projection (by parallel tactics in immunoaffinity binding selectivity), into the equally important area of protein diagnostics through use of nanoparticles (37, 38). A goal in one community of researchers who have for the past several years used nanoparticles in this way has been to avoid use of polymerase chain reaction (PCR) amplification [or its modern cousin, isothermal MDA (multiple displacement amplification)] by amplified detection of DNA chains at a sufficiently low limit-of-detection (LOD) level. In some respects, the search for low LODs for target single-stranded DNA has grown into an arms race; an economist might say that this is a DNA "LOD bubble" without a defined exit strategy (i.e., defined scientific goals).

2.3. (Soft) Surface Analysis

All materials have surfaces. "The chemical behavior of surfaces is consequently an enormously important scientific and technological subject, which includes a host of analytical issues—what elements are present, what molecules are present, are there gradients of composition or solvation below the immediate surface, etc. A large portfolio of analytical surface measurements has emerged—the oldest and best developed (both conceptually and commercially) deal with analysis of hard, solid surfaces" (39).

"A new generation of analytical approaches is growing up that are applicable to 'softer' surfaces, e.g., molecular surfaces ranging from monolayers of molecules to molecular films to biological cells and gels" (39). An important example of such an approach is desorption electrospray ionization (DESI) mass spectrometry. Since 2004 (40–44), DESI has spawned a number of variants with generally confusing acronyms. "Basic DESI consists of aiming an electrospray emitter at the sample surface, where ionization and desorption droplet-projectiles splash into the soft surface, throwing out charged droplets containing analyte, some of which enter the MS [mass spectrometry] inlet capillary for droplet evaporation and mass analysis of produced analyte ions. This complex and as

yet incompletely dissected process is being actively investigated as to mechanism(s), geometrical parameters, quantitation, sensitivity, and selectivity. One aspect, however, seems quickly clear: applicability to a wide variety of soft surfaces, including lifting off of surfaces molecular components of pharmaceutical products, proteins, peptides, polymers, evaporated chromatographic eluents, and living cells [. . .]. Both fundamental and application studies seem destined to spread for a time, with the accompanying appearance of new equipment in the instrument marketplace" (39).

Another surface-sensitive tool, known for two decades (45–47) as scanning electrochemical microscopy (SECM), "has over the last few years surged in applications to soft, molecular interfaces" (39, 48). The surface studied may be conducting and function as an electrode, or instead may simply be a molecular surface. The SECM probe can variously detect, release, or recycle (feedback) chemicals that emanate from or react with the molecular surface. Because the probe-surface distances can be very small (nanometer scale), mass transport times are short. Accordingly, the timescales of detectable changes in the molecular surfaces are also short. The SECM experiment thus has some molecular specificity in terms of redox entities detected, surface dynamics sensitivity as to timescale, and, with rastering of the probe, a modestly good (circa micrometer) lateral imaging resolution. The probe can be coupled with an atomic force microscope tip function to concurrently provide molecular surface topology. Applications of these ideas include imaging of latent fingerprints (49); quantifying enzyme activity within single living cells (50); grafting polymers and fluorescent labels in surface patterns (51); titrating adsorbed molecules (52); and observing the dynamic thermal floppiness of tethered, terminally redox-labeled DNA strands (53). "The SECM probe capability for detect/release/recycle functions will continue to enable soft surface investigations, with a solid theory foundation for quantitation, and like DESI, profits from developments in the instrument marketplace" (39).

Although there are other soft surface tools in action, the above two examples illustrate the different kinds of information now accessible. This general area promises to facilitate numerous discoveries about the chemistry of soft surfaces over the coming decade.

2.4. Mass Spectrometry

By the 1970s, some researchers considered mass spectrometry, as used in an electron impact ionization mode, to have reached a state of maturity (i.e., it was no longer changing). Mass spectrometry then exploded back into significance with the introduction (54) of new ionization sources known as matrix-assisted desorption/ionization (MALDI) (55) and electrospray ionization (ESI) (56–58). Their particular importances are in so-called soft ionization (involving a minor amount of fragmentation) of fragile and nonvolatile samples—notably biological materials—and applicability to large molecules (more than approximately 10 kDa). With ESI, access to mass spectra of large molecules has chiefly been achieved through endowing them with large values of z in the electrospray process. MALDI's avenue to access large masses lies mainly in application of time-of-flight modes. Introduced earlier (59) and now at a breakthrough level of ultrahigh-mass resolution is mass analysis by Fourier transform ion cyclotron resonance (FT-ICR) (60–62). Coming into its own somewhat later is the simpler, versatile experiment known as ion mobility spectrometry (63, 64).

A central goal of the field known as proteomics is to achieve comprehensive identification and analysis of the proteins that become expressed in a biological cell or tissue; such analysis includes identifying the manner in which the proteins' expression changes with the state of cellular development and environment. This is a daunting task, given that the number of different proteins that can be expressed within a cell is estimated to be many thousands, with a dynamic range of population over five orders of magnitude (65). Substantially on the basis of ESI, MALDI, and FT-ICR developments, mass spectrometry has become a central force in proteomics progress.

Strategies for mass spectral protein identification include sequence-specific digestion (such as with the protease trypsin), which produces a mixture of peptides that are then separated and mass analyzed. The accurate mass results are then compared to databases of different protein sequences. The multitudinous complications of this process, and how to overcome them, constitute a list (65, 66) whose substantial length testifies to the improving insight and tool development capabilities gained by the mass spectrometry community over the ensuing period of study. A different strategy, known as top-down proteomics, aims at avoiding protein digestion by using the power of ultrahigh-mass resolution of FT-ICR to provide the protein formula (60). A recent significant entry into the high-resolution field is the ion cyclotron variant known as the orbitrap (60). Mass spectrometry lacks intrinsic chemical selectivity, except for formula-specific identification by sufficiently high mass resolution (63, 64), and differing drift velocities in ion mobility spectrometry. However, instruments in all of the areas named above have been interfaced to liquid chromatography, GC, and CE separations (67).

Mass spectrometry has been applied to a wide range of nonbiological materials, and useful reviews can be found in the February, 2001, thematic issue of *Chemical Reviews* (68). I take particular note of applications of mass spectrometry to the composition of airborne small particles (aerosols) (69, 70). An important tactic employed in such applications is to detect the introduction of individual particles and then intercept them with an ablating laser pulse, using a mass analyzer to detect the ions ablated from the particle surface. Study of individual particles is important because airborne particles usually have a mixture of origins and compositions (71). Another just-emerging application of mass spectrometry is to metal nanoparticles, where extensive fragmentation usually occurs, although in a few cases intact nanoparticles have been observed (72–74).

2.5. Electrochemistry

Analytical Chemistry has a long history of publishing substantial content on electrochemistry and electroanalytical chemistry. So when (electrochemist) Robert Osteryoung retired as associate editor and was replaced with (bioanalytical chemist) Norman Dovichi, I received some alarmed messages: "Is the journal deemphasizing electrochemistry?" I reminded our readers that the editor was also an electrochemist, and commented (75):

> So the primary message of this editorial is that, if anything, electrochemistry is to have an enhanced emphasis in this journal. Notice also that I said electrochemistry, which is a broader world than electroanalytical chemistry.
>
> Electrochemistry is a very broad topic indeed. It deals with measuring the thermodynamics and kinetics of motions of electronic and ionic charges (i.e., chemical potential and current). Its capacity for analysis of concentration is only one attribute; electrochemical measurements encompass electron transfer and mass transport kinetics, mass transport through pores and membranes, corrosion chemistry, interfaces of all kinds (solid/liquid and liquid/liquid in particular), and the generation of light from electrogenerated excited states. Electrochemical measurements are important tools for study of phenomena in small spaces and volumes—as can be done with microelectrodes both stationary and scanned, for study of small objects like metal and semiconductor nanoparticles (quantum dots), and for study of man-made molecular assemblies as in molecular electronics. Electrochemical phenomena are central to electrophoretic and electrospray mass spectrometric experiments, and indeed to life itself as for example membrane charge transport in living organisms. The range of chemical instrumentation employed in all these kinds of measurements is very substantial. Electron and ion motions are, to say the least, a ubiquitous part of chemistry, and the significance of new ways to measure them is unlikely

to vanish any time soon, if ever. If a chemist were ever so rash as to claim to be poised to "discover the secrets of the universe", I would wager that she or he is an electrochemist.

Like spectroscopy, the field of electrochemistry is difficult to separate into components by thinking of the traditional chemical subdisciplines: analytical, biochemical, physical, etc. I think of electrochemistry as a particular way to measure chemical things, and of *Analytical Chemistry* as a journal that publishes generally on ways to measure chemical things. As Editor I have and will continue to regard the scope of chemical measurements appropriate for the journal in an expansive light.

Significant trends in electrochemistry over the years include (*a*) a steady miniaturization of electrodes (now at the nanometer scale; 1, 76–78); (*b*) the use of small electrodes to selectively sample species in small spaces, such as the interiors of biological cells (12) and neurotransmitters (14, 79) emanating from cell surfaces; (*c*) the continuing development of sophistication in SECM uses (as noted above for soft surfaces); (*d*) the exploration of the electrochemistry of nanoparticles (2); and (*e*) inventions and explorations of mesoporous electrode materials (80), among others.

2.6. Spectroscopy

Enormous progress in optical spectroscopy has been made by exploiting the fast timescales of pulsed lasers. Although these results are welcome, few have made their way into *Analytical Chemistry*. A greater impact in our community has come through several experimental capacities for observing single molecules (81). Single-molecule spectroscopy (SMS) emerged in the 1980s (82–84):

> The importance of this subject—and indeed many, if not most, subsequent SM experiments—lies in the detection and study of the properties of individual molecules. Researchers began to recognize that the electronic absorbance and emission spectra of large groups of molecules (i.e., bulk samples) represent ensemble averages. The averaging conceals the diversity of actual molecular behavior that does exist and thereby denies the chemist a deeper understanding of molecular properties (81).

As of now,

> experimental SM tactics allow measurements at room temperature, in solutions, and on surfaces. The fluorescence emissions of isolated molecules resting on surfaces and of lone molecules in highly dilute and/or confined solution volumes have been widely reported. Fascinating molecular variances have emerged. For example, SM spectroelectrochemistry shows variations in the electrochemical oxidation potentials of individual, adsorbed, conducting polymer molecules. Individual enzymes in confined solution volumes exhibit variations in their reaction rates with substrates. Fluorescence microscopy has revealed a range of DNA bending and turning behavior during alternating-field gel electrophoresis. Surface-enhanced Raman emission of molecules at nanoparticle surfaces can sometimes be so highly enhanced as to illuminate SMs. Emitting molecules often exhibit photoblinking, meaning they alternate between highly emissive and nonemissive states, for a plethora of possible reasons (81).

The exquisite control of distance and force afforded by force microscopy (86) (the powerful piezo; see Reference 85) has

> produced other, nonphotonic avenues to SM investigation. In these experiments, the force(s) required to bend, stretch, or twist a molecule are measured by anchoring one end of it and measuring the force required to move the other end with some kind of probe tip or optical tweezers. This can even be done

while the captured molecule undergoes a chemical reaction. SM force measurements are mostly applied to biomolecules; they are large and more readily tethered and are typically folded in complex ways. Thus, SM force experiments open an important new window to understanding the energetics and dynamics of the internal bonding events that govern folding processes. This has evoked a high state of excitement in the biophysics and biochemistry communities. A recent issue of *Science* (May 25, 2007) has a special section on SM, including force measurements. Molecular mechanics has taken on a new meaning!

2.7. Environmental Analytical Chemistry

Writing about environmental aspects of analytical chemistry (another perpetual frontier; see Reference 87) could have consumed my entire dossier of editorials. My study leading to one such editorial (88) left me with a permanently positive impression about an often publicly maligned federal agency—the U.S. Food and Drug Administration (FDA). This underfunded organization faces a humongous task that demands high-throughput, zero-cost analysis and globally distributed sampling. "Once in awhile (daily?), we analytical chemists who read the news should note instances in which our subdiscipline has made a positive contribution to human society" (88). Also,

> [t]here are plenty of examples in the recent (U.S.A.) print news in which analytical chemistry is an underlying theme, including detecting residues of unapproved aquaculture antibiotics in imported seafood, detecting lead-containing paint on fashionable imported toys, detecting deadly adulterants in imported toothpastes, and detecting the sad examples of cheating in sports competition with body-enhancing drugs. In reading these news reports, I am chagrined that the public is usually given a very shallow picture of the underlying science, including the analytical input (88).

Although the public press paid especially nasty attention to certain nations about the incidents described above, reading the FDA Web site makes it clear that these ongoing problems are geographically widespread. Another problem in the U.S. public's perception of the FDA (and other protection agencies, such as the Environmental Protection Agency and the Department of Homeland Security) is that we have been schooled in the idea of zero risk—an unrealistic but emotively powerful thought. My editorial (89) on risk and the uncertainties of analytical measurements mirrors my concerns about a misled public.

2.8. Education in Analytical Chemistry

The long-term intellectual health of a chemistry discipline is enormously enhanced by attracting good students to its classes and research laboratories, and instructing them in its modern aspects (90):

> What is taught to our future analytical chemistry scholars and workers as they pass through their undergraduate chemistry experiences will also, and just as indelibly, serve to define future analytical chemistry. Education has to be considered as a perpetual frontier, else it stagnates and ultimately fails. Our educational apparatus determines the body of knowledge taught as "analytical chemistry", and thus future perceptions of its "boundaries" and indeed its identity as a subdiscipline of chemical sciences.

I and my immediate editor predecessors, Herb Laitinen and George Morrison, are all educators, and without ever discussing it with one another we saw the imperative of emphasizing teaching in our editorials. Additionally, what were then known as the journal's A-pages (now known as the news and features section, as the pages no longer have A-numbers), consistently included articles

with an educational bent. This attention to education is somewhat unique in the universe of top chemistry research journals.

"Analytical Chemistry Is What Analytical Chemists Do" (91), the title of a 1994 editorial, is a rather famous impertinence—easily taken as "I, not you, will define my science"—but that actually was the title of "remarks by Charles N. Reilley at the occasion of his Fisher Award address at the Detroit National American Chemical Society meeting in April, 1965." This timeless gem on the teaching of analytical chemistry (and any other subject) included an admonition for departure from tradition (91):

> Today, with the overwhelming growth of knowledge, there is simply no time for easily out-dated frills in our curriculum. As a result, it is essential that stress be given to core concepts—those principles that will remain as firm foundations for our thinking and action now and, hopefully, twenty years hence. In attempting to decide what subject matter should be included in today's curriculum, it is necessary to judge this, not from what has been the traditional content, but from the viewpoint of current research procedures and interests.

Thus, a course with the standard title Quantitative Chemical Analysis should present tomorrow's version of that topic, which our students need to know in order to contribute at its leading edge. For tomorrow's version to fit within the finite periods of allotted class and laboratory time in an academic schedule, some older topics must face eviction from prime time (92).

With this in mind, in many of my frontier editorials I have said (in effect) to teachers and textbook writers, "Pay attention; teach it!" I have also prepared editorials on specific issues: a presentation, to freshmen, on modern ideas of polymer chemistry (it's relevant!) and of materials science (93, 94); the value of teaching principles of modern instrument design (95); the content of an honors course (96); the meaning of the scientific method (97); and what controls are (98).

In my editorials I have commented on almost all aspects of the educational process. I have remarked on the influence of precollege math and science (99), on the usefulness to society of a wide variety of higher educational institutions (100), on the educational and research importance of a competent administrative structure (101), and on building modern science space (102). I have explained and defended the concept of tenure (103) and the importance of rigorous tenure evaluation (104), and have observed that universities should strive to manage rather than to avoid conflicts of interest (105), given that enterprising and creative faculty necessarily create conflicts and that, surely, such faculty should be valued.

But students are the currency of educational institutions, and over the years I wrote editorials offering encouragement to all levels of students (beyond preschool), including secondary (106), undergraduate (107–110), graduate (111–114), and postdoctoral (115, 116). I remarked on the crucial importance of the professor's role as a mentor in all things to the student (117). Lastly, with slight tongue in cheek, I presented some of "Michael Faraday's Advice to the Lecturer" (118), which—if you filter out the stiff English of a century ago—still offers some sage observations. The content of a lecture isn't everything—how it is delivered is also important.

Lastly, one of my favorite commentaries has been about how long it takes to do something. I wrote this editorial in 1995 as a reaction to news media's (and politicians') expectation that funding for science would lead to instant discovery and use (119). Not much has since changed, so I include some excerpts:

> How long does it take to. . .? This question is part of the daily fabric of our personal and professional lives. It asks what is the time constant for something to occur: water to boil, double layers to charge, tax refund to come, elution times, learn a foreign language, flight time of a molecular ion, children to

grow up, research to yield a product, build a journal's quality, change a curriculum, see a result of a new curriculum. Life would be so much less confusing and more predictable (maybe less interesting) if we always knew the answers to such questions. Time constants, and the dividends of knowing or of adjusting them, are so important that the Study of Time Constants should be a separate Science . . . . In analytical chemistry, time constants affect quality, accuracy, and usefulness of analytical measurements in numerous ways . . . . How to quantitatively model time constants in analytical measurements is generally understood, and in cases where it is not, the necessary tools for further investigation are identifiable.

Formal courses in analytical chemistry usually treat time constants in analytical measurements as a topic subservient to other issues. More typically, I think students learn by experience, being confronted by a dominating time constant in the real life of their analytical research or applications. Analytical chemistry students are not taught about the kinds of time constants that have human elements involved. These are much harder to quantify, but (119)

[they] have enormous pertinence to the professional lives of chemists. In the funding of higher education or of research activities, whether controlled or initiated in the political or in the industrial management arena, profoundly important but very poorly understood time constants connect investment-making and ultimate societal benefit (or detriment). Examples are the time constant between improving an educational system (such as modernizing a sophomore analytical chemistry laboratory) and the professional successes of the affected students, that between discovery of an analytically useful basic chemical phenomenon and the offering of an instrument based on that phenomenon for sale, and that between a decreasing investment in research activities (through closing or redirection of industrial research units or through ceasing financial support of students seeking higher degrees in chemistry) and an eventual degradation of national chemical science and technology. These are cause-and-effect time constants, and are immensely complicated by intrinsic human variability.

The point I want to make about cause-and-effect time constants is how poorly we understand their estimation (119):

[I]t is certain that each single question has no single, unique answer. Instead, these time constants cover a huge dynamic range and one must describe them in such terms. For example, consider the variability of the time constant between discovery of an analytically useful basic chemical phenomenon and the offering of an instrument for sale. The concepts of polymerase chain reactions (PCR) and of capillary electrophoresis quickly provoked (a few years) commercial products and instruments for use in pharmaceutical, forensic, and bio-analytical chemistry. On the other hand, the discovery of electrochemically-generated luminescence (ECL) preceded by two decades the instruments that now make possible its application in clinical analysis, and the discovery of twin electrode thin layer cells preceded by an even longer period their embodiment in automatic brightness-adjusting rear view mirrors in automobiles. There must be analogously wide variance in the consequences that the migrations of various instrumental analysis methods from the senior course into earlier undergraduate years have had on contemporary practices in industrial analytical chemistry.

I believe that elected officials and the public news media serve their public badly by insisting that cause-and-effect issues in research and education have simple, singular time constants. The reality of large (and uncertain) dynamic ranges is constantly ignored and oversimplified, as if the lay public were incapable of appreciating variability. I do not believe this need be so. Chemists may be defeated in their justification of the societal importance of education and research in analytical chemistry, by

an unwillingness to better address and articulate to politicians, managers, and public journalists, the dynamic nature of cause-and-effect time constants.

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LITERATURE CITED

1. Murray RW. 1980. Chemically modified electrodes. *Acc. Chem. Res.* 13:135–41
2. Murray RW. 2008. Nanoelectrochemistry: metal nanoparticles, nanoelectrodes and nanopores. *Chem. Rev.* 108:2688–720
3. Ingram RS, Hostetler MJ, Murray RW, Schaaff TG, Khoury J, et al. 1997. 28 kDa alkanethiolate-protected Au clusters give analogous solution electrochemistry and STM coulomb staircases. *J. Am. Chem. Soc.* 119:9279–80
4. Murray RW. 2009. Nanoparticles: an emerged and lasting frontier. *Anal. Chem.* 81:1723
5. Murray RW. 2001. Biography and reminiscences of a 40-plus year career as a chemistry faculty member. *J. Phys. Chem. B* 105:8642–47
6. Murray RW. 2004. "Cadmium horses" and glucose. *Anal. Chem.* 76:149a
7. Murray RW. 1991. Analytical chemistry: the science of chemical measurements. *Anal. Chem.* 63:271a. **http://pubs.acs.org/doi/pdf/10.1021/ac00005a600**
8. Murray RW. 2007. Analytical chemistry is still the science of chemical measurements. *Anal. Chem.* 79:1765
9. Murray RW. 1996. The permanency of fading boundaries. *Anal. Chem.* 68:457a. **http://pubs.acs.org/doi/abs/10.1021/ac961988b**
10. Murray RW. 1994. Chemical sensors and molecular selectivity. *Anal. Chem.* 66:505a. **http://pubs.acs.org/doi/pdf/10.1021/ac00081a600**
11. McCollom TM, Seewald JS. 2007. Abiotic synthesis of organic compounds in deep-sea hydrothermal environments. *Chem. Rev.* 107:382–91
12. Adams KL, Puchades ME, Ewing AG. 2008. In vitro electrochemistry of biological systems. *Annu. Rev. Anal. Chem.* 1:329–55
13. Borland LM, Kottegoda S, Phillips KS, Allbritton NL. 2008. Chemical analysis of single cells. *Annu. Rev. Anal. Chem.* 1:191–27
14. Wightman RM, Jankowski JA, Kennedy RT, Kawagoe KT, Schroeder TJ, et al. 1991. Temporally resolved catecholamine spikes correspond to single vesicle release from individual chromaffin cells. *Proc. Natl. Acad. Sci. USA* 88:10754–58
15. Murray RW. 1997. There is no analysis without sampling. *Anal. Chem.* 69:269a. **http://pubs.acs.org/doi/abs/10.1021/ac9715985**
16. Murray RW. 1997. Sampling of small spaces. *Anal. Chem.* 69:327a. **http://pubs.acs.org/doi/abs/10.1021/ac971635s**

17. Murray RW. 1999. Molecular recognition. *Anal. Chem.* 71:359a. **http://pubs.acs.org/doi/abs/10.1021/ac990020n**
18. Walt DR. 2005. Electronic noses: Wake up and smell the coffee. *Anal. Chem.* 77:45a
19. Murray RW. 1992. Ode to the separator. *Anal. Chem.* 64:661a. **http://pubs.acs.org/doi/pdf/10.1021/ac00037a601**
20. Murray RW. 2005. Enabling monoliths. *Anal. Chem.* 77:277a
21. Murray RW. 1994. Chemical sensors and molecular selectivity. *Anal. Chem.* 66:505a. **http://pubs.acs.org/doi/pdf/10.1021/ac00081a600**
22. Terry SC, Jerman JH, Angell JB. 1979. A gas chromatographic air analyzer fabricated on a silicon wafer. *IEEE Trans. Electron Devices* 26:1880–86
23. Murray RW. 2005. Enabling fast GC separations. *Anal. Chem.* 77:5a
24. White RL. 2008. Volatile mixture analysis by repetitive injection fast gas chromatography/mass spectrometry. *Anal. Chem.* 80:9812–16
25. Reidy S, George D, Agah M, Sacks R. 2007. Temperature-programmed GC using silicon microfabricated columns with integrated heaters and temperature sensors. *Anal. Chem.* 79:2911–17
26. Murray RW. 2003. Chips and more chips. *Anal. Chem.* 75:5a
27. Harrison DJ, Manz A, Fan Z, Luedi H, Widmer H. 1992. Capillary electrophoresis and sample injection systems integrated on a planar glass chip. *Anal. Chem.* 64:1926–32
28. Broyles BS, Jacobsen SC, Ramsey JM. 2003. Sample filtration, concentration, and separation integrated on microfluidic devices. *Anal. Chem.* 75:2761–67
29. Jacobson SC, Hergenröder R, Koutny LB, Ramsey JM. 1994. High-speed separations on a microchip. *Anal. Chem.* 66:1114–18
30. Carrilho E, Martinez AW, Whitesides GM. 2009. Micropatterning process for paper-based microfluidics. *Anal. Chem.* 81:7091–95
31. Martinez AW, Phillips ST, Whitesides GM. 2008. Three-dimensional microfluidic devices fabricated in layered paper and tape. *Proc. Natl. Acad. Sci. USA* 105:19606–11
32. Murray RW. 1996. The federal rudder. *Anal. Chem.* 68:649a. **http://pubs.acs.org/doi/abs/10.1021/ac9620977**
33. Zubritsky E. 2002. How analytical chemists saved the human genome project. *Anal. Chem.* 74:23–26
34. Watts JM, Dang KK, Gorelick RJ, Leonard CW, Bess JW Jr, et al. 2009. Architecture and secondary structure of an entire HIV-1 RNA genome. *Nature* 460:711–16
35. Deamer DW, Branton D. 2002. Characteristics of nucleic acids by nanopore analysis. *Acc. Chem. Res.* 35:817–25
36. Mirkin CA, Letsinger RL, Mucic RC, Storhoff JJ. 1996. A DNA based method for rationally assembling nanoparticles into macroscopic materials. *Nature* 382:607–9
37. Rosi NL, Mirkin CA. 2005. Nanostructures in biodiagnostics. *Chem. Rev.* 105:1547–62
38. Willner I, Willner B. 2002. Functional nanoparticle architectures for sensoric optoelectronic and bioelectronic applications. *Pure Appl. Chem.* 74:1773–83
39. Murray RW. 2009. Soft and molecular surfaces. *Anal. Chem.* 81:7127
40. Takats Z, Wiseman JM, Gologan B, Cooks RG. 2004. Mass spectrometry sampling under ambient conditions with desorption electrospray ionization. *Science* 306:471–73
41. Cooks RG, Ouyang Z, Takats Z, Wiseman JM. 2006. Ambient mass spectrometry. *Science* 311:1566–70
42. Venter A, Nefliu M, Cooks RG. 2008. Ambient desorption ionization mass spectrometry. *Trends Anal. Chem.* 27:284–90
43. Young S, Talaty N, Datsenko K, Wanner BL, Cooks RG. 2009. In vivo recognition of *Bacillus subtilis* by desorption electrospray ionization mass spectrometry (DESI-MS). *R. Soc. Chem.* 134:838–41
44. Costa AB, Cooks RG. 2008. Simulated splashes: elucidating the mechanism of desorption electrospray ionization mass spectrometry. *Chem. Phys. Lett.* 464:1–8
45. Bard AJ, Denuault G, Lee C, Mandler D, Wipf DO. 1990. Scanning electrochemical microscopy—a new technique for the characterization and modification of surfaces. *Acc. Chem. Res.* 23:357–63
46. Bard AJ, Fan F-RF, Kwak J, Lev O. 1989. Scanning electrochemical microscopy. Introductions and principles. *Anal. Chem.* 61:132–38

47. Bard AJ, Mirkin MV, eds. 2001. *Scanning Electrochemical Microscopy*. New York: Marcel Dekker
48. Amemiya S, Bard AJ, Fan F-RF, Mirkin MV, Unwin PR. 2008. Scanning electrochemical microscopy. *Annu. Rev. Anal. Chem.* 1:95–31
49. Zhang M, Girault HH. 2009. SECM for imaging and detection of latent fingerprints. *Analyst* 134:25–30
50. Gao N, Wang X, Li L, Zhang X, Jin W. 2007. Scanning electrochemical microscopy coupled with intracellular standard addition method for quantification of enzyme activity in single intact cells. *Analyst* 132:1139–46
51. Hauquier F, Matrab T, Kanoufi F, Combellas C. 2009. Local direct and indirect reduction of electrografted aryldiazonium/gold surfaces for polymer brushes patterning. *Electrochim. Acta* 54:5127–36
52. Rodriquez-Lopez J, Alpuche-Aviles MA, Bard AJ. 2008. Interrogation of surfaces for the quantification of adsorbed species on electrodes: oxygen on gold and platinum in neutral media. *J. Am. Chem. Soc.* 130:16985–95
53. Wang K, Goyer C, Anne A, Demaille C. 2007. Exploring the motional dynamics of end-grafted DNA oligonucleotides by in situ electrochemical atomic force microscopy. *J. Phys. Chem. B* 111:6051–58
54. Murray RW. 1993. The handsome 600 pound gorilla. *Anal. Chem.* 65:341a. **http://pubs.acs.org/doi/pdf/10.1021/ac00055a600**
55. Karas M, Hillenkamp F. 1988. Laser desorption ionization of proteins with molecular masses exceeding 10,000 daltons. *Anal. Chem.* 60:2299–301
56. Yamashita M, Fenn JB. 1984. Electrospray ion source. Another variation on the free-jet theme. *J. Phys. Chem.* 88:4451–59
57. Yamashita M, Fenn JB. 1984. Negative ion production with the electrospray ion source. *J. Phys. Chem.* 88:4761–75
58. Fenn JB, Mann M, Meng CK, Wong SF, Whitehouse CM. 1989. Electrospray ionization for mass spectrometry of large biomolecules. *Science* 246:64–71
59. Commisarow MB, Marshall AG. 1974. Fourier transform ion cyclotron resonance spectroscopy. *Chem. Phys. Lett.* 25:282–83
60. Marshall AG, Hendrickson CL. 2008. High-resolution mass spectrometers. *Annu. Rev. Anal. Chem.* 1:579–99
61. Kelleher NL. 2004. Top down proteomics. *Anal. Chem.* 76:196–203A
62. Bogdanov B, Smith RD. 2005. Proteomics by FT-ICR mass spectrometry: top down and bottom up. *Mass Spectrom. Rev.* 79:7984–91
63. Kanu AB, Dwivedi P, Tam M, Matz L, Hill HH Jr. 2008. Ion mobility–mass spectrometry. 43:1–22
64. Baumbach JI, Eiceman GA. 1999. Ion mobility spectrometry: arriving on site and moving beyond a low profile. *Appl. Spectrosc.* 53:338–55A
65. Aebersold R, Goodlet DR. 2001. Mass spectrometry in proteomics. *Chem. Rev.* 101:269–95
66. Lubec G, Afjehi-Sadat L. 2007. Limitations and pitfalls in protein identification by mass spectrometry. *Chem. Rev.* 107:3568–84
67. Tomer KB. 2001. Separations combined with mass spectrometry. *Chem. Rev.* 101:297–328
68. Bierbaum VB. 2001. Introduction: frontiers in mass spectrometry. *Chem. Rev.* 101:209–10
69. Noble CA, Prather KA. 2000. Real-time single particle mass spectrometry: a historical review of a quarter century of the chemical analysis of aerosols. *Mass Spectrom. Rev.* 19:248–74
70. Suess DT, Prather KA. 1999. Mass spectrometry of aerosols. *Chem. Rev.* 99:3007–35
71. Murray RW. 1996. Environmental analytical chemistry: basic and applied. *Anal. Chem.* 68:589a. **http://pubs.acs.org/doi/abs/10.1021/ac962063z**
72. Tracy JB, Kalyuzhny G, Crowe MC, Balasubramanian R, Choi J-P, et al. 2007. Poly(ethylene glycol) ligands for high-resolution nanoparticle mass spectrometry. *J. Am. Chem. Soc.* 129:6706–7
73. Schaaff TG, Knight G, Shafigullin MN, Borkman RF, Whetten RL. 1998. Isolation and selected properties of a 10.4 kDa gold:glutathione cluster compound. *J. Phys. Chem. B* 102:10643–46
74. Negishi Y, Chaki NK, Shichibu Y, Whetten RL, Tsukuda T. 2007. Origin of magic stability of thiolated gold clusters: a case study on $Au_{25}(SC_6H_{13})_{18}$. *J. Am. Chem. Soc.* 129:1322–23
75. Murray RW. 2003. An electrochemical evolution and invitation to the future. *Anal. Chem.* 75:325a
76. Arrigan DWM. 2004. Nanoelectrodes, nanoelectrode arrays and their applications. *Analyst* 129:1157–65

77. Watkins JJ, Chen J, White HS, Abruna HD, Maisonhaute E, et al. 2003. Zeptomole voltammetric detection and electron-transfer rate measurements using platinum electrodes of nanometer dimension. *Anal. Chem.* 75:3962–71
78. Morris RB, Franta DJ, White HS. 1987. Electrochemistry at platinum band electrodes of width approaching molecular dimensions: breakdown of transport equations at very small electrodes. *J. Phys. Chem.* 91:3559–64
79. Robinson DL, Hermans A, Seipel AT, Wightman RW. 2008. Monitoring rapid chemical communication in the brain. *Chem. Rev.* 108:2554–84
80. Long JW, Dunn B, Rolison DR, White HS. 2004. Three-dimensional battery architectures. *Chem. Rev.* 104:4463–92
81. Murray RW. 2007. Single-molecule chemistry. *Anal. Chem.* 79:4739
82. Moerner WE, Kador L. 1989. Optical detection and spectroscopy of single molecules in solids. *Phys. Rev. Lett.* 62:2535–38
83. Basché T, Moerner WE, Orrit M, Talon H. 1992. Photon antibunching in the fluorescence of a single dye molecule trapped in a solid. *Phys. Rev. Lett.* 69:1516–19
84. Lounis B, Moerner WE. 2000. Single photons on demand from a single molecule at room temperature. *Nature* 407:491–93
85. Murray RW. 2008. Technology foundations—the powerful piezo. *Anal. Chem.* 80:3939
86. Cui Y, Bustamante C. 2000. Pulling a single chromatin fiber reveals the forces that maintain its higher-order structure. *Proc. Natl. Acad. Sci. USA* 97:127–32
87. Murray RW. 1992. Environmental analytical chemistry: a continuing frontier. *Anal. Chem.* 64:1111a. **http://pubs.acs.org/doi/pdf/10.1021/ac00047a600**
88. Murray RW. 2007. Services offered by analytical chemists. *Anal. Chem.* 79:5495
89. Murray RW. 2008. Analytical chemistry and risk. *Anal. Chem.* 80:1
90. Murray RW. 1991. The education frontier. *Anal. Chem.* 63:671a. **http://pubs.acs.org/doi/pdf/10.1021/ac00013a600**
91. Murray RW. 1994. Analytical chemistry is what analytical chemists do. *Anal. Chem.* 66:682a. **http://pubs.acs.org/doi/pdf/10.1021/ac00085a600**
92. Murray RW. 2006. Educational budgets (i.e., time). *Anal. Chem.* 78:7353
93. Murray RW. 1993. A macromolecular proposal. *Anal. Chem.* 65:13a. **http://pubs.acs.org/doi/pdf/10.1021/ac00049a600**
94. Murray RW. 1991. The analytical side of materials science. *Anal. Chem.* 63:493a. **http://pubs.acs.org/doi/pdf/10.1021/ac00009a600**
95. Murray RW. 2006. Let's continue to talk about building instruments. *Anal. Chem.* 78:1372a
96. Murray RW. 2007. Honors course in introductory analytical chemistry. *Anal. Chem.* 79:8817
97. Murray RW. 1999. The scientific method. *Anal. Chem.* 71:153a. **http://pubs.acs.org/doi/abs/10.1021/ac990210y**
98. Murray RW. 2002. Controls and reliable conclusions. *Anal. Chem.* 74:109a
99. Murray RW. 2007. Influences of high school science and math. *Anal. Chem.* 79:7227
100. Murray RW. 1993. Diversity and quality in science education. *Anal. Chem.* 65:431a. **http://pubs.acs.org/doi/pdf/10.1021/ac00057a600**
101. Murray RW. 1994. Infrastructure. *Anal. Chem.* 66:17a. **http://pubs.acs.org/doi/pdf/10.1021/ac00073a600**
102. Murray RW. 2005. The chemical fertilizer called new space. *Anal. Chem.* 77:125a
103. Murray RW. 2002. Academic tenure equals freedom of inquiry. *Anal. Chem.* 74:229a
104. Murray RW. 2005. The responsibilities of tenure evaluators. *Anal. Chem.* 77:365a
105. Murray RW. 1999. University conflicts of interest: Manage rather than avoid. *Anal. Chem.* 71:713a. **http://pubs.acs.org/doi/abs/10.1021/ac9907538**
106. Murray RW. 2003. Science projects and (very) young analytical chemists. *Anal. Chem.* 75:445a
107. Murray RW. 2001. Undergraduate research secrets rediscovered. *Anal. Chem.* 72:237a
108. Murray RW. 2001. A primer for choosing a graduate school. *Anal. Chem.* 72:572
109. Murray RW. 2002. The graduate. *Anal. Chem.* 74:293a

110. Murray RW. 2005. Chapters of our lives. *Anal. Chem.* 77:156a
111. Murray RW. 1996. The teaching assistant. *Anal. Chem.* 68:709a. **http://pubs.acs.org/doi/abs/10.1021/ac9621332**
112. Murray RW. 1996. The season of the interview. *Anal. Chem.* 68:231a. **http://pubs.acs.org/doi/abs/10.1021/ac961866j**
113. Murray RW. 1996. Fewer PhDs? *Anal. Chem.* 68:161a. **http://pubs.acs.org/doi/abs/10.1021/ac961836g**
114. Murray RW. 1994. Employment and change. *Anal. Chem.* 66:395a. **http://pubs.acs.org/doi/pdf/10.1021/ac00079a600**
115. Murray RW. 2001. The post-doc: an opportunity for learning and more. *Anal. Chem.* 72:75a
116. Murray RW. 2009. A conversation with some postdoctorals. *Anal. Chem.* 81:857
117. Murray RW. 1999. Mentoring—one of the most important acts. *Anal. Chem.* 71:5a. **http://pubs.acs.org/doi/abs/10.1021/ac990077%2B**
118. Murray RW. 2007. Michael Faraday's advice to the lecturer. *Anal. Chem.* 79:6425
119. Murray RW. 1995. Time constants. *Anal. Chem.* 67:287a. **http://pubs.acs.org/doi/pdf/10.1021/ac00105a600**

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