Chemical & Engineering News

Cover Story

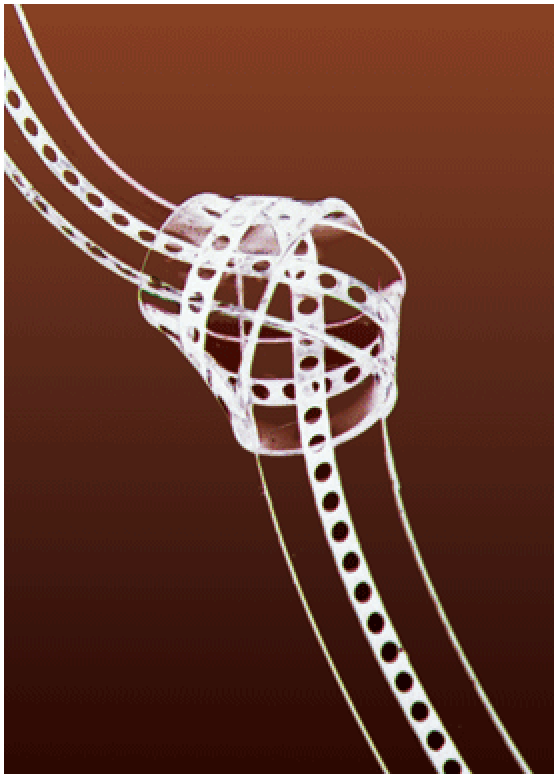
March 26, 2007
Volume 85, Number 13
pp. 12-17

Revolutions In Chemistry

Priestley Medalist George M. Whitesides' address

LET ME BEGIN with two opinions.

First, I have never known a time when chemistry had better opportunities or more important research to work on. Chemistry is n the natural home of many of the most engaging problems in fundamental science and of the problems in applied science about which society cares the most. The Priestley Medal is a lifetime achievement award. Our present moment has become so interesting, however, that I wish my lifetime were unachieved and that I were starting over.



Adam Siegel/Whitesides Group

Tiny Pathways By injecting molten solder into a microfluidic channel and then cooling, it's possible to make metallic microstructures flexible enough to tie in a knot.

Second, the past is not a good predictor of the future. What we know now, and how we work now, will not provide sufficient mea to solve these new problems. Chemistry has had a wonderful 50 years, but new types of problems require new approaches: It is unlikely that the disciplines that were the favorites of the past—the ones with which I grew up—will remain the most important in the future. I believe that we will see major changes—in fact, revolutions—in what chemistry does, and in our view of what chemistry is, as we move on to these new problems.

WHY AM I HERE? In the second week after I arrived at Massachusetts Institute of Technology in 1963, I was stopped in the hal by a small man, a complete stranger, with burning eyes. He grabbed me by my shirt, shook me, and said, "You are working on i aren't you?" Confused, I said, "What is 'it'? And forgive me, but who are you?" He sputtered back: "It? It's the only problem wort working on in chemistry. It's the norbornyl cation problem!" He never did tell me his name. (He was Gardner Swain, one of the founders of physical organic chemistry.)

At that time, I barely knew what "it" was, and I certainly wasn't working on it. (And in fact, I never did.) So how, if I missed the on important problem of the time, did I get here? How did I redeem myself? Some of you may be wondering, and it's only fair for me to try to answer the question. I will be brief in answering.

Many scientists and I share the weakness that we neglect history. For me, "science past" (specifically, my own past) is history, and much less interesting than "science future" (the future belonging to those of you who are young), and particularly so in a tim of change. But before elaborating, let me emphasize that it is not only "I" who am here receiving this honor; it is "we"-the researc group. I'm the poster child for our group.

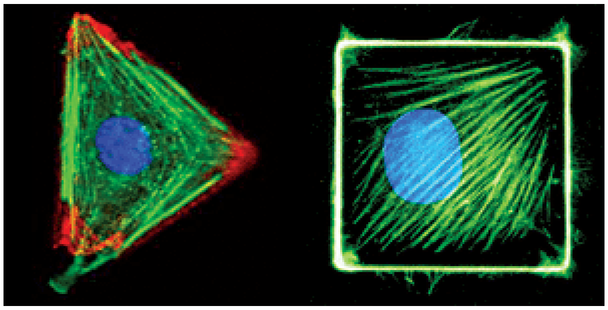
We—the group and I—have, I hope, contributed to chemistry in two ways: one scientific and one social. First, scientifically, we have tried to start things, particularly in areas of science that were not familiar parts of chemistry at the time that we (and others) worked on them. Some caught on; others did not. Some babies are more winning than others.

Among the more winning ones were dynamic nuclear magnetic resonance (NMR) spectroscopy, the organometallic chemistry of copper(I) and platinum(II), enzymes as catalysts in organic synthesis, self-assembly, surface chemistry and self-assembled monolayers, "materials-by-design" in the guise of wettable surfaces, soft lithography, microfluidics, microtools for cell biology, an polyvalency in drug design.

We also worked on other areas that either did not catch on or, more optimistically, have not yet caught on. Among these are thiolate-disulfide interchange in biochemistry, heterogeneous reaction mechanisms of formation of Grignard reagents and of surface organometallic compounds, protein charge ladders, protein-ligand binding, complexity and emergence, and using first-world science for problems in the developing world. It has been great fun. We have, fundamentally, studied mechanisms and made tools.

The second area in which we have experimented is social—the organization of the group. As a matter of necessity in working on problems that require a wide range of skills, especially in their earliest stages, when we are trying to figure out which way is up, have evolved a structure for our group that is unusual for chemistry, but it works.

We are a large group, usually about 45 graduate students and postdoctoral fellows, drawn from a wide variety of disciplinary backgrounds, including many that are not considered to be "chemistry." All the work in the group is done collaboratively; no one works in isolation, which is neither much fun nor very productive.


Whitesides Group

Cell Blocks On a gold surface painted with tiny geometric patterns of self-assembling alkanethiols, cow cells can adhere and gro into decidedly nonbiological shapes.

I do not "manage" the group in any usual sense of the word. The group is too big for that, and the people in it are too smart and too independent to take direction gracefully. I'm certainly a part of the enterprise, but it is more accurate to say that I work for the group, rather than that the group works for me.

And how do we choose problems, and how do we recruit members of the group? We choose problems for many reasons: for curiosity, because they might be important, because there is money available to work on them, because we think collaborating with someone to work on them might be fun.

I'll give one example in the "curiosity" category. In winter, when I lean down to kiss my wife, she instinctively avoids me, giggling The reason she does so is that the spark that comes from tribocharging in New England winters hurts when it goes from lip to lip Chapped lips, combined with 30 kV/cm, catches the attention, especially when often repeated.

This kind of spark is interesting. It also connects to other questions: Where does lightning come from? How about the spark between the fingertip and the doorknob after you have walked across the rug? How does a Van de Graaff generator work? A Xerox machine? What causes your hair to stand on end when you comb it? (Not that I would know.) The observation of a curiou process that is ubiquitous and—it turns out—not at all understood, provides the basis for an interesting research problem: conta electrification.

And the people in our group? They just come. We have a reputation for welcoming many different types, and as a result, we get applications from many different types, including—for this problem of contact electrification—people who understand Maxwell's equations, polymers, and physical organic chemistry. It seems to work out without too much planning.

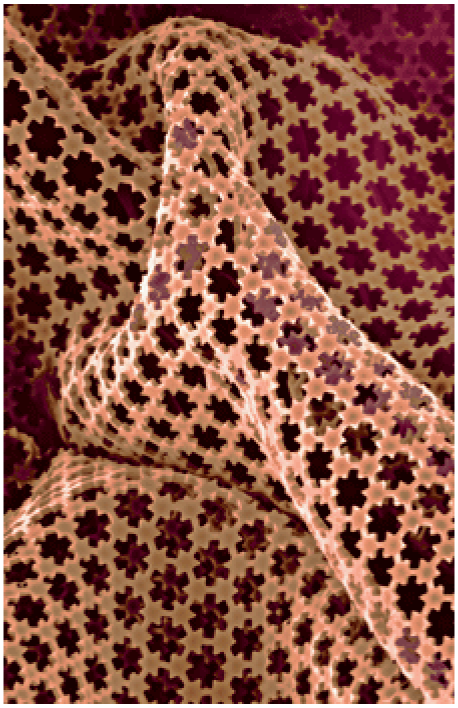
THE STRUCTURE OF SCIENTIFIC REVOLUTIONS. I have said that I believe and hope that chemistry is on the verge of a revolution. I subscribe to two theories of revolution. The first, supported by Freeman Dyson, Peter Gallison, and others, emphasizes the role of new experimental techniques in enabling scientific revolutions. In short, this theory holds that new keys open new doors. The role of scanning tunneling microscopy in nucleating nanoscience is a current example; so are the contribution of the polymerase chain reaction (PCR) to molecular genetics, the contribution of organic synthesis to drug development, and of NMR spectroscopy to organic synthesis. Computers are all-purpose tools that have changed everything.

The second theory of scientific revolutions that I find compelling was famously articulated by Thomas Kuhn. It argues (to simplify complex story) that scientific revolutions occur only when there is no way out; that is, when a field concedes, usually reluctantly, that its current theories are simply incompatible with its own experimental evidence. The development of quantum mechanics in the early 1900s was an example; so was the discovery of oxygen about 200 years ago by Joseph Priestley.

"The Structure of Scientific Revolutions" is the title of Thomas Kuhn's most famous book, and it has many lessons for chemistry. Kuhn suggests that activity in science has two principal forms: so-called normal science, which develops an existing and accept idea or scientific paradigm, and discovery, which is the basis of a fundamental change in thinking; that is, a revolution.

Normal science is focused on the solution of what Kuhn calls puzzles. These are classes of problems in which (again to simplify the answer is already known before the work starts, in which the answer is not important, and in which the interest lies entirely o largely in the elegance of the solution. Sudoku puzzles provide a familiar example; chiral europium shift reagents (to take an example from the shadows of my childhood) is another.

By contrast, discovery or revolution is focused on much larger scale questions in which the answer does matter, in which the strategy to a solution is not known, and in which it is not even known that there is a solution. The "nature of sentience" might be such a question; so is "best strategies for global stewardship."



Courtesy of Felice Frankel

Template Writ Small A square centimeter of this light-cured, molded microfabric of plastic hosts 3 million bridgelike connections between features as thin as 1 µm.

The scientific community tends to think that discovery is a more exalted activity than normal science. Kuhn makes the point—I think quite correctly—that both are essential and that normal science is required to select, albeit idiosyncratically, specific scienti puzzles for the intense cultivation that makes clear the fundamental limitations of science and that occasionally leads to a fundamental reconsideration of its tenets, that is, to scientific revolution.

OPPORTUNITIES. So, why do I think that chemistry might now be teetering on the threshold of a revolution? There are four reasons: First, as a field, we now have—in my view and, interestingly, in the view of many outside of chemistry—the intellectual responsibility for solving some of the most interesting problems in science and technology.

Second, we now have, after an exceptionally productive period of development, tools that should make possible at least some o the types of research needed to address these problems.

Third, for this big work, chemistry offers a fine balance of skills. We have a unique and useful synthetic approach to science: When we are faced with a problem, we make something—a new molecule or material or system—to solve it. We can also assimilate and disentangle complex systems quantitatively, and we are accustomed to problems with many moving parts.

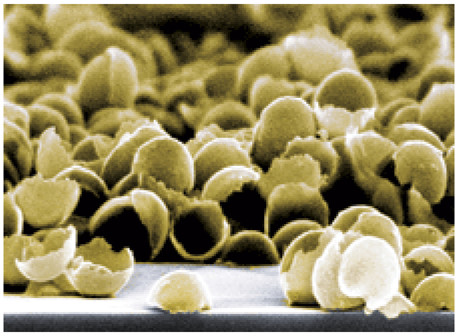
Fourth, we are reasonably certain that we cannot solve these problems knowing only what we now know. Among the disciplines chemistry is perhaps most suited to take on many of the problems that need to be solved because we do better at digesting deta than does physics, and we are better at quantitative analysis than is biology.

Let me give you examples of the problems for which chemistry seems so promising for supplying solutions. The list is, of course personal, but it makes a point in which I believe strongly: Nowhere is it written that chemists must work only on molecules and materials; we can also take on ambitious problems, in Kuhn's sense of the word.

The Cell and the Nature of Life. I believe that understanding the cell is ultimately a question of chemistry and that chemists are in principle, best qualified to solve it. The cell is a bag—a bag containing smaller bags and helpfully organizing spaghetti—filled with a Jell-O of reacting chemicals and somehow able to replicate itself. Yes, it is important to know the individual reactions that make the cell what it is, but the bigger problem is understanding why life—the cell—is dynamically stable as a strongly interconnected network of reactions, organized in space and time in ways we do not grasp.

Although we presently have no theory to explain this kind of system, understanding the kinetics of systems of coupled reactions the kind of thing that chemists and chemical engineers are—in principle—uniquely qualified to do.

Energy, the Environment, and Global Stewardship. The web of reactions that we must understand, if we are to begin to understand the idea of sustainability—from oil field or coal mine to refinery to automobile to atmosphere to ocean to mineral—is, remarkably, a problem similar to that of understanding life: It requires predicting the behavior of a web of interacting chemical processes when you tug it at different points.



J. Christopher Love/Whitesides Group

Nuovo Egg-Making Place silica nanospheres on glass, puff palladium onto them, liberate the coated beads from the glass, dissolve the silica. The result: submicrometer-diameter metallic half-shells.

Here, again, there are many questions of great but local interest. How does photosynthesis work, and how can it be improved? What is the best way to sequester CO_2? What is the most cost-effective solar cell?

But the larger question is that of understanding how it all connects. It is in understanding the network, the complex system, wher we need revolutionary ideas. If one changes one part of the system—say, if the U.S. and China burn much more coal—then wha happens to other parts, for example, the temperature in Greenland, the global rates of photosynthesis, and rainfall in Niger? At t moment, we do not know how to find out, and we do not know how long we have to learn.

The Origin of Life. This problem is one of the big ones in science. It begins to place life, and us, in the universe. Most chemists believe, as do I, that life emerged spontaneously from mixtures of molecules in the prebiotic Earth.

Courtesy of Felice Frankel

Red Cross Network Floating on liquid are macroscopic plastic pieces, chemically treated so that the liquid wets their bottoms an edges and elicits a rapid, regimenting restructuring.

How? I have no idea. Perhaps it was by the spontaneous emergence of "simple" autocatalytic cycles and then by their combination. On the basis of all the chemistry that I know, it seems to me astonishingly improbable. The idea of an RNA world is good hint, but it is so far removed in its complexity from dilute solutions of mixtures of simple molecules in a hot, reducing ocean under a high pressure of CO_2 that I don't know how to connect the two.

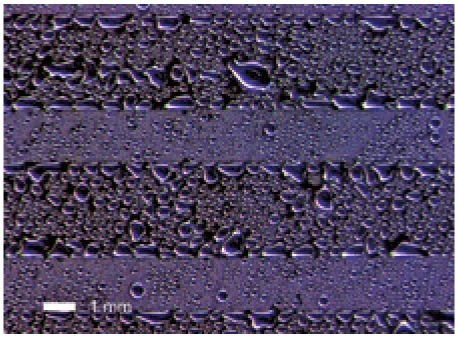
We need a really good new idea. That idea would, of course, start us down the path toward systems that evolve autonomously— revolution indeed.

Molecular Recognition in Water and the Design of Drugs. One of the most important contributions of chemistry to society ha been through medicine, through the design and synthesis of drugs. The binding of a small molecule—a drug, ligand, substrate, transition state—to a protein is arguably the most fundamental molecular process in biology.

When I first entered chemistry, the idea of rational design of drugs, or more modestly and realistically, of ligands, was an objecti we all understood. It still is, and we have made mostly a kind of negative progress over the intervening years. We do understan better now than we did then what we don't understand and why the problem remains so difficult, but we still cannot design ligan

Our frustrations in this arena highlight areas in which there are great opportunities for increasing our fundamental understanding How do reactants in any process, especially those in molecular recognition, interact with solvent and especially with water? How should we think about entropy? Why is water so extraordinary?

Catalysis. Almost everything in chemistry is catalyzed. Refining petrochemicals, most of complex synthesis, metabolism, hydration of CO_2 in rock, photosynthesis, and uptake of neurotransmitters—these are just a few examples among an endless lis of chemical processes for which catalysts are central. I am astonished at how little we still understand about the fundamentals o catalysis and how difficult it is for us to design new catalysts. This is another wonderful area that will require something dramatically new!



Adam Siegel/Whitesides Group

Wet Designs Largish water drops adhere to black, hydrophilic stripes on a gold surface exposed to a vapor, while small ones for on the purple, more hydrophobic stripes.

The Molecular Basis of Sentience. Memory, thought, and perception ultimately have molecular foundations. It is certain that molecules and ions are only a part of the story, just as transistors and electrical currents are only a part of the World Wide Web. But to understand sentience, we ultimately must try to connect thought to the simplest components of the brain—to such things acetylcholine, potassium ions, proteins, and water—and tell a story that extends from them to "The Well-Tempered Clavier." It is hard to find a problem that has more to do with being human; it is also difficult, with our current way of doing business, to understand where we should begin to take on this problem.

WHY SO SLOW? Over the course of my career, chemistry has been happy to assemble an ever-more-useful toolbox—better analytical devices, better synthetic methods, better fibers—and has been spectacularly good at doing so. But we tend to build th wrench, not the car. The developments of new organic reactions and of the tactics of complex organic synthesis, for example, a beautiful to us, but they're important to society for what they make possible, namely, the synthesis of drugs and other molecules that solve problems.

Mass spectroscopy is important, not because it generates a tsunami of data, but because it gives the isotope ratios that write a historical record of the global temperature. Electrochemistry is not just ions and electrons and molecules; it is the basis for batteries and fuel cells.

We now have at least some of the tools needed to take on these bigger, more ambitious problems, among the nature of life and understanding climate and the environment. But so far, chemistry has only slowly begun to sidle up to them. Why are we so slo Kuhn has a number of comments on this subject. I quote only one, and I find it quite comforting because it suggests that we are not so different from other fields.

Kuhn says: "No part of the aim of normal science is to call forth new sorts of phenomena; indeed, those that will not fit the box a often not seen at all. Nor do scientists normally aim to invent new theories, and they are often intolerant of those invented by others."

I suggest that chemistry now has five issues to deal with if it is to move to the exploration of fundamentally new territories.

What We Know and What We Don't. We don't know as much as we believe we do. As we begin to think about ambitious problems, we find that our current theories—of complex, tightly coupled kinetic networks; of protein-ligand binding; of catalysis; dissipative, out-of-equilibrium systems; of liquids and solutions; of noncovalent interactions; of entropy; and so on—simply do n work. In some cases, we have ideas why our theories fall short; in others, we don't.

Peer Review. The peer review system, especially in a time of financial drought, is between conservative and Luddite. It filters o all the bad ideas, most of the new good ones, and all of the really unusual ones. There is, of course, an alternative to this "intolerance" for new ideas, to use Kuhn's term: If chemistry wishes to welcome new ideas, the peer review system can express that wish.

Capitalism. The current pressures on publicly traded companies to maximize financial return to stockholders in the short term a now so intense that it is difficult for these companies—some of them historically great centers of innovation and fundamental research and, not incidentally, of jobs in chemistry—to do more than product development.

David Gracias/Whitesides Group

Make Thyself On this penny sits a dozen wire- and LED- riddled truncated octahedrons, which self-assembled, making conducti connections that let current reach the lights.

There is again, perhaps, a solution to this problem, and one that has worked spectacularly well in biomedicine to transfer fundamental academic research into successful commercial technology: to use start-ups. If a large company is not interested in your new idea, start your own baby company! Chemistry can learn to do so as well as biology; it could also help students who want to be entrepreneurs by teaching them something about how to go about it.

Teaching and Textbooks. What we teach is often based more on the convenience of what is available in textbooks than on consideration of what students should learn. What's more, textbooks are designed to maximize sales, not to prepare students fo research in new and undefined fields. Again, it is for us to choose what we teach. We are free to ignore the textbooks and to introduce material that prepares students for new problems. We can also use the Web to trade good ideas for free.

The Academic Social System. We ought to become more welcoming to new faces. Chemistry needs smart young people, eve if—especially if!—they come from less familiar backgrounds than ours and bring unexpected points of view.

We might also consider our undergraduates, whom we tend to treat as little colleagues and encourage them to create their own curricula. They do so, but with a sensible eye to minimizing the workload and seldom by volunteering to take the most demandi subjects. They might benefit-as might chemistry and society-if we asked them to do more. It is not a criticism of students to say that they may have to be coerced into working; after all, we write proposals because we have to, not because we want to.

Finally, we might wonder at our inconsistency in thinking of graduate students, who are certainly more advanced than undergraduates, as inexperienced beginners who can learn best by working on our ideas. We might instead consider that they a younger, smarter, less bureaucratically encumbered, and more energetic versions of ourselves, and best able to learn by workin on questions that turn them on, even if we might not be able to answer them or even understand them!

CODA. We are at a wonderful time for chemistry. It is, I believe, in the position of physics in the 1910s, just before quantum mechanics made the world impossibly strange, or biology in the 1950s, just before the double helix obliterated the old biology.

Of course, chance and opportunity favor the prepared mind. And there is a tempo to revolutions. Miss the timing, and it is you w are up against the wall. Science and society will take on these big questions and others. Chemists are the natural leaders for much of the research that needs to be done. But physicists can learn molecular detail, and biologists can learn differential equations. If we do not wish to work on these problems, others certainly do. If it is not our revolution, it will be someone else's.

My colleagues and I are deeply honored by this award.

Cover Story

- Revolutions in Chemistry Introduction
- Revolutions in Chemistry
- Priestley Medalist George M. Whitesides' address.
- Always On The Move
- George M. Whitesides, this year's Priestley Medalist, has influenced academia, government, and industry

[Top of Page]