

ALANNA SCHEPARTZ

# A ROLLER COASTER RIDE OF THRILLS

Chemical biology issues involve basic questions of life and death—an irresistible challenge

**I**N HIS BOOK “ADVICE TO A YOUNG SCIENTIST,” the British anatomist Peter Medawar notes, “It is not enough that a problem should be ‘interesting’—almost any problem is interesting if it is studied in enough depth. A problem must be such that it matters what the answer is—whether to science generally or to mankind.”

I cannot imagine a better quote to represent the future of my field, chemical biology. Today’s practitioners of chemical biology have an opportunity to apply their distinct set of skills to study problems that are both interesting and important. In this essay, I want to share my enthusiasm for chemical biology and describe how this field provides a powerful way to identify and study essential problems.

Although it is impossible to predict the accomplishments of the next 125 years (and unwise to try), the excitement about the future of chemical biology is palpable. Much of this energy is related, either directly or indirectly, to the sequencing of the human genome. The human genome sequence sets forth the grand challenge to understand, quantify, and control the exquisitely coordinated actions of all human genes (even if there are only 26,000). Chemical biology reaps postsequencing benefits because life and death are deter-

mined by the activities and interactions of the proteins and enzymes that the DNA sequence encodes and of the oligosaccharides, lipids, and natural products that these proteins and enzymes act upon. Our charge is to characterize, monitor, and manipulate these interactions at the molecular level. Who can imagine a time when a problem that matters to humanity has been defined so well?

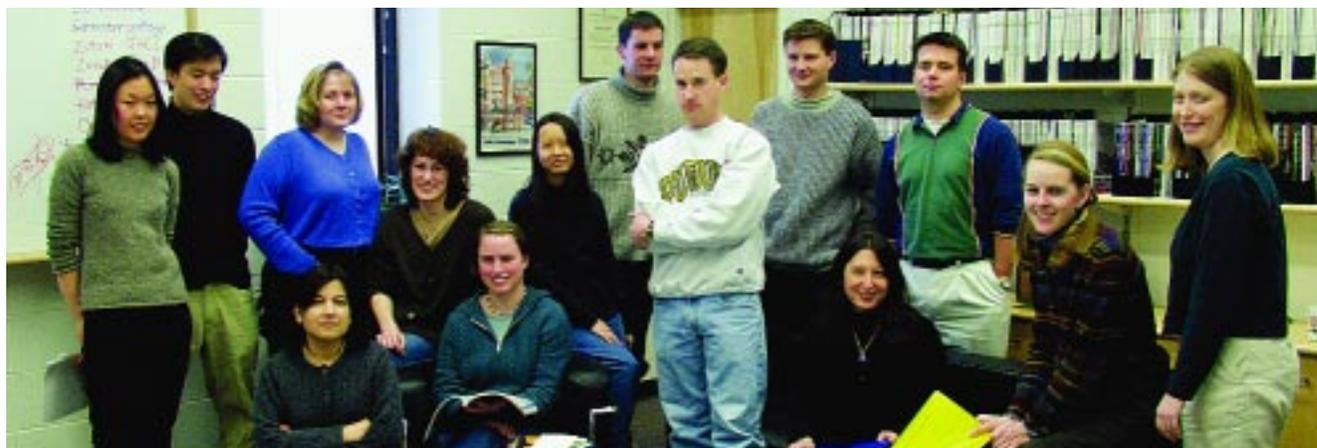
Although much of the enthusiasm for the sequencing effort is driven by the universally recognized need for better, cheaper health care, the bounties of this information extend far beyond new drugs and drug targets. It is almost certain that studies of newly identified proteins, RNAs, and DNAs will reveal or require fundamentally new chemistry and stimulate the creativity of chemists for decades. Focusing on the macromolecules themselves, one can imagine discovering proteins and nucleic acids that perform unprecedented chemical reactions and use unanticipated strategies for optimizing the rate, strength, or selectivities of macromolecular associations. Such discoveries could, in turn, foster the design of new catalysts, materials, and assays for molecular recognition. Novel reactions and synthetic strategies will be required to discover ligands for newly identified macromolecules. Because many of these ligands

will interact with receptor surfaces and not with the deep active sites found in enzymes, their design will require original approaches to achieve the desired goals of affinity and selectivity. The possibility for new technology, fundamental understanding, and true changes in the human condition cannot be overestimated.

The extraordinary potential of chemical biology highlights the overarching challenge facing the chemistry profession today: The only way to realize the promises of expanding scientific horizons is to ensure that postgraduate training provides value to talented young men and women. We know that the pursuit of knowledge through creative and rigorous research—the work that we actually do—is intellectually satisfying and unbelievably fun. Careers in academics and industry are dominated by the joy of interacting with bright, enthusiastic people who share common goals and interests, and the satisfaction of solving problems that matter.

However, the technical, analytical, and managerial skills acquired during the four or five years of graduate school toil (no more!) also can be parlayed effectively into stunning success in the fields of communication, consulting, law, and finance. Because a scientist can answer questions that matter in any occupation, we would all benefit if we encouraged our students to aspire to leadership positions in these fields as well.

**Alanna Schepartz** is Milton Harris ’29 Ph.D. Professor of Chemistry at Yale University. She received a B.S. in chemistry from the State University of New York, Albany, in 1982 and a Ph.D. from Columbia University in 1987. She completed a two-year postdoctoral fellowship at California Institute of Technology.



**EXPANDING HORIZONS** Schepartz (fourth from right, seated) is shown with some of the bright, enthusiastic people from her research group at Yale.