CHEMICAL HERITAGE FOUNDATION

LLOYD M. SMITH

Transcript of an Interview Conducted by

David C. Brock and Richard Ulrych

at

New Orleans, Louisiana

on

2 March 2008

(With Subsequent Corrections and Additions)

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LLOYD M. SMITH

Born in Berkeley, California, on 3 October		
Education		
B.A., Biochemistry, University of California, Berkeley Ph.D., Biophysics, under Harden M. McConnell, Stanford University		
Professional Experience		
Stanford University Postdoctoral Fellow, under Harden M. McConnell Lecturer, Chemistry		
California Institute of Technology		
Postdoctoral Research Fellow		
Senior Research Fellow, Division of Biology, under Leroy Hood		
University of Wisconsin, Madison		
Assistant Professor, Analytical Sciences Division, Department of Chemistry		
Associate Professor, Analytical Sciences Division, Department of Chemistry		
Professor, Analytical Sciences Division, Department of Chemistry		
Chair, Analytical Sciences Division, Department of Chemistry		
Director Genome Center		
Chair, Analytical Sciences Division, Department of Chemistry		
Chair, Analytical Sciences Division, Department of Chemistry		

Honors

1977-1981	NIH Pre-Doctoral Trainee
1982-1985	NIH Post-Doctoral Trainee
1985	Chosen as one of Science Digest's Top 100 Innovators
1989-1991	Eli Lilly Analytical Chemistry Award
1989-1994	NSF Presidential Young Investigator Award
1994	Kazusa DNA Research Institute, Japan, Inaugural Speaker
1994-1999	H. I. Romnes Faculty Fellowship, University of Wisconsin-Madison

1997	Association of Biomolecular Resource Facilities Award for Development of Automated DNA Sequencing
1999-2004	WARF Kellett Mid-Career Faculty Researcher Award, University of
	Wisconsin-Madison
2003-2008	John D. MacArthur Professorship, University of Wisconsin-Madison
2005	American Chemical Society Award in Chemical Instrumentation
2008-2010	Vilas Associate Award
2008	Jay Goodwin Lecturer, Auburn University
2009-present	Member, Faculty of 1000
2009	W. L. Hubbell Professor of Chemistry
2010	American Association for the Advancement of Science Fellow
2010	Pittsburgh Analytical Chemistry Award

ABSTRACT

Lloyd M. Smith grew up in Berkeley, California, one of four children. His father was a physicist at Lawrence Berkeley National Laboratory and his mother a professor of mathematics. Lloyd attended the Berkeley public schools, which he says were excellent. He developed no overwhelming interest in any of the sciences until he was a student at University of California, Berkeley. There he liked biology, chemistry and physics and chose to major in biochemistry. He worked in Wayne Hubbell's lab, studying membranes and synthetic chemistry. On Hubbell's advice he enrolled in graduate school at Stanford University, entering Harden McConnell's lab to work on diffusion in membranes, obtaining his PhD in biophysics and publishing nine papers. Now interested in instrumentation and in immunology, he accepted a postdoc with Leroy Hood at the California Institute of Technology. During months of sequencing he thought up the first fluorescence-based automated DNA sequencing instrument, thus combining his love of physics with his love of biology and chemistry.

Working with Michael Hunkapiller on commercialization of his technology, he became a consultant for Applied Biosystems (ABI), learning first-hand of the complications of relationships between academia and industry. With what became the seminal paper describing his work accepted for publication in the journal *Nature*, he spent several weeks in Europe.

Smith accepted an assistant professorship at the University of Wisconsin, eventually becoming Director of the Genome Center and Chair of the Analytical Sciences Division in the Department of Chemistry. There Smith developed another laser system for sequence analysis and began the use of matrix-assisted laser desorption/ionization (MALDI) on nucleic acids. He also founded his own company, Third Wave Technologies. He discusses such new methods as array technology; gene expression chips and Affymetrix; pyrosequencing; electrospray; and proteomics. He explains how parallelism has enhanced Moore's Law, and the roles of computers and lasers as drivers of all these innovations. He revels in the confluence of instrumentation, chemistry, and computation. Though he acknowledges that informatics is now required to make sense of the huge volumes of data enabled by technology, he emphasizes the continuing need for thinking

INTERVIEWERS

David C. Brock is a senior research fellow with the Center for Contemporary History and Policy at the Chemical Heritage Foundation. As a historian of science and technology, he specializes in the history of semiconductor science, technology, and industry; the history of instrumentation; and oral history. Brock has studied the philosophy, sociology, and history of science at Brown University, the University of Edinburgh, and Princeton University.

In the policy arena Brock recently published *Patterning the World: The Rise of Chemically Amplified Photoresists*, a white-paper case study for the Center's Studies in Materials Innovation. With Hyungsub Choi he is preparing an analysis of semiconductor technology roadmapping, having presented preliminary results at the 2009 meeting of the Industry Studies Association. **Richard Ulrych** is the director of institutional grants and strategic projects at the Chemical Heritage Foundation.

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Early Years Grew up in Berkeley, California. One of four children. Father a physicist at Lawrence Berkeley National Laboratory. Mother professor of mathematics. Attended public schools.

College Years

Attends University of California, Berkeley. Uncertain what to study. Takes sister's advice to study biology. Does well in chemistry. Declares major in biochemistry. Disappointed in biochemistry, tries physics. Loves physics. Undergraduate lab work in biophysical chemistry with Wayne Hubbell. Membranes. Synthetic chemistry. Nine months as technician in Hubbell's lab. Becomes very careful as technician.

Graduate School Years

Takes Hubbell's advice to study with Harden McConnell at Stanford University. Synthetic systems. Study of diffusion in membranes led to instrumentation thesis. Large number of papers as graduate student. Interest in immunology. PhD in biophysics.

Postdoctorate Years

Enters Leroy Hood's lab. Immunology and instrumentation. Huge lab. Months of sequencing. Fluorescence to label DNA. Works with Michael Hunkapiller at California Institute of Technology. Applied Biosystems (ABI). Chemistry of dyes. Becomes consultant to ABI. New understanding of relationship between academia and industry. Founds own company, Third Wave Technologies (now Hologic). Paper leads to article in *Nature*. Patents on invention. European vacation.

Faculty at University of Wisconsin

More and better sequencing. Competition from E.I. DuPont de Nemours and Company. Electrophoresis. Another laser system. Use of matrix-assisted laser desorption/ionization (MALDI) on nucleic acids. Array technology. Pyrosequencing. Affymetrix. Gene expression chips. Many genome projects led to diagnosis of problems with instrumentation, not chemistry. Electrospray; optical detection; proteomics. Surface invader arrays. Future of confluence of instrumentation, chemistry, and computation. All driven by computers and lasers. Parallelism. Informatics required to make sense of masses of data. Continuing importance of thinking.

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