

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)

CHEMICAL HERITAGE FOUNDATION
Oral History Program
FINAL RELEASE FORM

This document contains my understanding and agreement with the Chemical Heritage Foundation with respect to my participation in the audio- and/or video-recorded interview conducted by David C. Brock and Richard Ulrych on 2 March 2008. I have read the transcript supplied by the Chemical Heritage Foundation.

1. The recordings, transcripts, photographs, research materials, and memorabilia (collectively called the "Work") will be maintained by the Chemical Heritage Foundation and made available in accordance with general policies for research and other scholarly purposes.
2. I hereby grant, assign, and transfer to the Chemical Heritage Foundation all right, title, and interest in the Work, including the literary rights and the copyright, except that I shall retain the right to copy, use, and publish the Work in part or in full until my death.
3. The manuscript may be read and the recording(s) heard/viewed by scholars approved by the Chemical Heritage Foundation subject to the restrictions listed below. Regardless of the restrictions placed on the transcript of the interview, the Chemical Heritage Foundation retains the rights to all materials generated about my oral history interview, including the title page, abstract, table of contents, chronology, index, et cetera (collectively called the "Front Matter and Index"), all of which will be made available on the Chemical Heritage Foundation's website. Should the Chemical Heritage Foundation wish to post to the internet the content of the oral history interview, that is, direct quotations, audio clips, video clips, or other material from the oral history recordings or the transcription of the recordings, the Chemical Heritage Foundation will be bound by the restrictions for use placed on the Work as detailed below.
4. I wish to place the conditions that I have checked below upon the use of this interview. I understand that the Chemical Heritage Foundation will enforce my wishes until the time of my death, when any restrictions will be removed.

Please check one:

a. _____

No restrictions for access.

NOTE: Users citing this interview for purposes of publication are obliged under the terms of the Chemical Heritage Foundation Oral History Program to obtain permission from Chemical Heritage Foundation, Philadelphia, Pennsylvania.

b. _____

Semi-restricted access. (May view the Work. My permission required to quote, cite, or reproduce.)

c. _____

Restricted access. (My permission required to view the Work, quote, cite, or reproduce.)

This constitutes my entire and complete understanding.

(Signature) _____

Lloyd M. Smith

(Date) _____

March 8, 2011

This oral history is designated **Free Access**.

Please note: Users citing this interview for purposes of publication are obliged under the terms of the Chemical Heritage Foundation (CHF) Oral History Program to credit CHF using the format below:

Lloyd M. Smith, interview by David C. Brock and Richard Ulrych at New Orleans, Louisiana, 2 March 2008 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0407).



Chemical Heritage Foundation
Oral History Program
315 Chestnut Street
Philadelphia, Pennsylvania 19106



The Chemical Heritage Foundation (CHF) serves the community of the chemical and molecular sciences, and the wider public, by treasuring the past, educating the present, and inspiring the future. CHF maintains a world-class collection of materials that document the history and heritage of the chemical and molecular sciences, technologies, and industries; encourages research in CHF collections; and carries out a program of outreach and interpretation in order to advance an understanding of the role of the chemical and molecular sciences, technologies, and industries in shaping society.

LLOYD M. SMITH

1954 Born in Berkeley, California, on 3 October

Education

1976 B.A., Biochemistry, University of California, Berkeley
1981 Ph.D., Biophysics, under Harden M. McConnell, Stanford University

Professional Experience

Stanford University
1981 Postdoctoral Fellow, under Harden M. McConnell
1981-1982 Lecturer, Chemistry

California Institute of Technology
1982-1985 Postdoctoral Research Fellow
1985-1987 Senior Research Fellow, Division of Biology, under Leroy Hood

University of Wisconsin, Madison
1987-1992 Assistant Professor, Analytical Sciences Division, Department of Chemistry
1992-1995 Associate Professor, Analytical Sciences Division, Department of Chemistry
1995-present Professor, Analytical Sciences Division, Department of Chemistry
1999-2001 Chair, Analytical Sciences Division, Department of Chemistry
2001-present Director Genome Center
2003-2004 Chair, Analytical Sciences Division, Department of Chemistry
2006-2010 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.

TABLE OF CONTENTS

Early Years	1
<p>Grew up in Berkeley, California. One of four children. Father a physicist at Lawrence Berkeley National Laboratory. Mother professor of mathematics. Attended public schools.</p>	
College Years	7
<p>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.</p>	
Graduate School Years	13
<p>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.</p>	
Postdoctorate Years	18
<p>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. Finds own company, Third Wave Technologies (now Hologic). Paper leads to article in <i>Nature</i>. Patents on invention. European vacation.</p>	
Faculty at University of Wisconsin	31
<p>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.</p>	
Index	38

INDEX

- 4
454 Life Sciences, 29
- A**
- ABI. *See* Applied Biosystems
acrylamide, 15, 27, 28
Affymetrix, 31, 32, 33, 34, 35
Applied Biosystems, 16, 21, 22, 23, 25, 26,
27, 28, 31
array, 23, 29, 30, 31, 33, 34, 35
- B**
- Berkeley, California, 4
Biacore, 33
biochemistry, 1, 2
biology, 1, 2, 12, 14, 25, 36
biophysics, 6, 7, 11
Blattner, Frederick R., 34
- C**
- Cafiso, Dave, 11
California, 4, 13
California Institute of Technology, 12, 13,
16, 19, 20, 22, 23
California State University, Hayward, 4
Caltech. *See* California Institute of
Technology
Cartwright, Gene S., 9, 12
cell biology, 14
Cerrina, Franco, 34
Chait, Brian T., 28
Church, George M., 31
competition, 22, 25
Connell, Kip, 20, 23
Cornell University, 8
CuraGen Corporation, 29
- D**
- diffusion, 8, 9, 11, 12
digital light processing, 34
DNA, 4, 14, 15, 16, 17, 18, 19, 20, 25, 26,
27, 28, 29, 31, 33, 35, 36
cDNA, 16
Dodd, Chris, 20
- E**
- E.I. DuPont de Nemours and Company, 19,
25, 27
Edelman, Gerald M., 12
electron paramagnetic resonance, 2
electrophoresis, 27, 28
electrospray, 33
Eletr, Sam, 16
EPR. *See* electron paramagnetic resonance
Europe, 25
- F**
- Fisher, Douglas A., 14
fluorescence, 8, 9, 17, 20, 33
Fluorescence Recovery After Pattern
Photobleaching, 9
Fluorescence Recovery After
Photobleaching, 8
Foder, Stephen P.A., 31
France, 1
freeze fracture electron microscopy, 8
Fung, Steve, 19, 23
- G**
- Gann, Paul, 4
gas phase protein, 12, 16
Gibson, William, 37
Gilligan's Island, 12
- H**
- Hanawalt, Philip C., 6
Harvard University, 5, 6
Hewlett-Packard, 16, 23
Hillenkamp, Franz, 28
Hologic, 23

Hood, Leroy, 12, 13, 16, 17, 18, 19, 20, 22, 23, 26
Huang, Henry, 16
Hubbell, Wayne L., 2, 3, 5, 11, 13
Hughes, Peter, 20
Human Genome Project, 25, 26, 27, 36
Hunkapiller, Michael W., 13, 16, 19, 22, 24, 26
Hunkapiller, Tim, 16
HySeq, 31

I

Illumina, 31, 35
immunology, 12
instrumentation, 7, 9, 12, 13, 16, 19, 20, 21, 22, 23, 27, 33, 35, 36

J

Japan, 28
Jarvis, Howard, 4
JOE dye, 23

K

Kaiser, Robert J., 20, 26
Karas, Michael, 28
Keller, Dick, 30
Kent, Stephen B.H., 16, 20
Koshland, Daniel E., 2

L

laser, 9, 10, 11, 12, 21, 22, 25, 27, 36
Lawrence Berkeley National Laboratory, 1
Los Alamos National Laboratory, 30

M

Madison, Wisconsin, 34
major histocompatibility complex, 14
MALDI (matrix-assisted laser desorption/ionization), 28
Mars, 16
mass spectrometry, 28, 29, 33
McConnell, Harden M., 2, 6, 7, 8, 9, 13
membranes, 2, 6, 8, 9, 11, 12
Merrifield, R. Bruce, 16

molecular biology, 12, 14
Moore's Law, 35, 36

N

National Institutes of Health, 7, 32
NBD. *See* nitrobenzoxazole
NIH. *See* National Institutes of Health
nitrobenzoxazole, 21, 23
Nobel Prize, 28
nucleic acid, 29, 32, 33
Nucleic Acids Research, 19, 28

P

Palo Alto, California, 34
Parce, J. Wally, 9
patents, 22, 23, 24
physics, 1, 2, 5, 6, 11
Presidential Young Investigator Award, 28
Proposition 13, 4
proteomics, 33

R

Richards, John H., 18
RNA, 32
Roche NimbleGen, 33
Rockefeller University, 12, 13
Rothberg, Jonathan M., 30

S

Sanders, Jane Z., 20, 26
Schultz, Steve, 18
sequence/sequencing, 14, 16, 17, 19, 20, 25, 26, 27, 28, 29, 30, 31, 32, 36
pyrosequencing, 30, 31
Simon, Melvin I., 20
single nucleotide polymorphism, 32
Smith, Barton A., 9, 10
Smith, David A. (brother), 1, 12
Smith, Peter (brother), 1
Smith, Winnie (sister), 1
snip, 32, 34, 35
Solexa, 31
Stanford University, 3, 5
Stephenson, Neal, 37

Sussman, Michael R., 34
synthetic/synthesis, 2, 3, 4, 5, 8, 9, 11, 15,
16, 18, 19, 20, 22, 23, 30, 32, 35

T

Tanaka, Koichi, 28
T-cells, 14
Third Wave Technologies, 23

U

U.S. Department of Energy, 28
Uhlen, Mathias, 30
United States of America, 28
University of California, Berkeley, 1, 3, 5
University of Oregon, 5

University of Wisconsin, 7, 27, 34
UV (ultraviolet), 16, 17, 19

V

Vestal, Marvin, 28
Vestec, 28

W

Washington, D.C., 36
Webb, Watt W., 8
World War II, 36

Z

Zewail, Ahmed H., 12, 13