CHEMICAL HERITAGE FOUNDATION

LUBERT STRYER

The Pew Scholars Program in the Biomedical Sciences

Transcript of Interviews Conducted by

David J. Caruso

at

Stanford University Stanford, California

on

3 and 4 December 2008

(With Subsequent Corrections and Additions)



Lubert Stryer

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LUBERT STRYER

1938	Born in Tientsin, China on 2 March
	Education
1957 1961	B.S., University of Chicago, Physiology M.D., Harvard University
	Professional Experience
1961-1962	Harvard University Research Fellow, Physics
1962-1963	MRC Laboratory of Molecular Biology, Cambridge, England Visiting Investigator
1963-1969	School of Medicine, Stanford University Assistant and Associate Professor, Biochemistry
1969-1976	Yale University Professor, Molecular Biophysics and Biochemistry
1989-1990	Affymax Research Institute President and Scientific Director
1993-Present	Affymetrix, Inc. Chairman, Scientific Advisory Board
1996-2001 2001-2008	Senomyx, Inc. Chairman and Chief Scientific Officer Chairman, Scientific Advisory Board
1976-1979 1976-2004 2004-present	School of Medicine, Stanford University Chair, Department of Structural Biology Winzer Professor of Cell Biology Winzer Professor of Cell Biology, Emeritus

<u>Honors</u>

1961-1964	Helen Hay Whitney Post-doctoral Fellowship	
1970	American Chemical Society Award in Biological Chemistry (Eli Lilly Award)	
1975	Fellow of the American Academy of Arts and Sciences	
1984	Member of the National Academy of Sciences	
1987	National Lecturer for the Biophysical Society	
1992	American Association for the Advancement of Science Newcomb Cleveland Prize	
1992	Honorary Doctor of Science degree, University of Chicago	
1993	Distinguished Inventors Award, Intellectual Property Owners' Association	
2002	Molecular Bioanalytics Award, German Society for Biochemistry and Molecular Biology	
2006	European Inventor of the Year Award	
2006	Member of the American Philosophical Society	
2006	National Medal of Science	
	Leadership Positions	
1982-1990	Jane Coffin Childs Memorial Fund Scientific Advisory Board Member	
1991-1996	Pew Scholars Program in the Biomedical Sciences Advisory Committee Member	
1992-1998	Ruth and Milton Steinbach Fund Program on Macular Degeneration Scientific Advisory Board Member	
1996-2001	Helen Hay Whitney Foundation Board of Trustees	
1998-2007	McKnight Endowment for the Neurosciences Board of Directors	
2005-2008	Howard Hughes Medical Institute Medical Advisory Board Member	

ABSTRACT

Lubert Stryer was born in Tientsin (now Tianjin), China. He and his family lived in Shanghai until he was about ten. Lubert's father had come to China from Germany, his mother from Russia, in order to escape the turmoil in Europe, but the Japanese invaded and interned Shanghai's British, Canadian, and American citizens. Somehow the Stryers escaped notice and, after the war, obtained visas for the United States, moving to Forest Hills, New York. Lubert had always loved school, and he found his high school to be of excellent quality. As a youngster he loved baseball and chemistry; he founded his own newspaper, *The Daily Bugle*, and he became interested in photography.

Stryer was fascinated by history when he was in high school, and he planned to become a lawyer, but the head of the science department asked him to do some research on bioluminescent bacteria, and Lubert was "hooked." He applied to Harvard University and the University of Chicago for college, knowing that he would need a good scholarship; he accepted the offer from Chicago, matriculating at sixteen. With medical school as his goal and majoring in physiology, he worked at Argonne National Laboratories in the summers, becoming interested in photodynamic action. Here began his lifelong passion, "light and life." The intellectual experience in college was intense, and friendships abounded. It was also an exciting time of exploding knowledge in science, with DNA being discovered, oscilloscopes replacing smoke drums. Always eager for the next experience or challenge, Lubert finished college in three years, accepted an offer from Harvard, and entered medical school at the age of nineteen.

At Harvard Lubert again found himself among the brightest scientific minds of his generation; he called upon his friendships to establish a relationship with Elkan Blout, who remained his mentor throughout his school years. Blout directed Lubert to Children's Cancer Research Foundation, where he worked on polypeptides conformation and learned spectroscopy. When he was in his last year of medical school, Stryer knew that he did not want to practice medicine and forwent internship for an immediate postdoctoral fellowship. In Carolyn Cohen's laboratory, he learned x-ray diffraction, drank much coffee, and engaged in many wide-ranging discussions with labmates. During this year he also was tutored in physics and mathematics by Edward Purcell and began learning computing; having married his Chicagoan fiancée, Andrea, when he was twenty, for which he needed his parents' consent, he also fathered his first child. At that point Blout arranged for Stryer to study with Sir John Kendrew at the Medical Research Council in Cambridge, England. Again he worked among and with Nobel Prize-winning scientists: Kendrew, Crick, Watson, Perutz, Sanger.

After about a year Arthur Kornberg asked Kendrew for recommendations, and Stryer's next stop was Stanford. Teaching protein structure and function, he found wonderful science and scientists at Stanford too. Stryer believes that he flourished during the "golden age" of science, which began to change after the Vietnam War.

After a few years at Stanford Lubert, now an associate professor, wanted to change his research area to visual excitation, so when Yale offered him a full professorship and all the lab space he wanted, he and his wife and now two sons moved east. Using the notes he developed for his class in biochemistry Stryer wrote his now-canonical textbook. He feels that although he did not publish so much while at Yale his work there set the stage for his later discoveries in amplification in vision.

Stanford offered him chairmanship of the new department of structural biology, and back they all went to California. There Stryer wrote the next edition of his textbook. He gave up his chairmanship after a couple of years because he found it "not fun." This relinquishment allowed him to become more proficient on (very early) computers, even writing his own programs. Most importantly, he enjoyed a "magic moment" when he discovered that a single photon can lead to the activation of five-hundred molecules of transducin.

As Stryer has gradually disentangled himself from his university work his position in the scientific community has evolved. He sees himself creating new ways to do interesting things outside of the lab. He became an advisor for the Pew Scholars Program in the Biomedical Sciences, helping to promote new young scientists. He has been involved in several companies in private industry, a result of his interest in olfaction and vision; he has established and led BIO2010 to study the future of undergraduate biology education, and helped implement those ideas at Stanford; he remains interested in human evolution, continuing several projects, studying just for the sake of learning.

Lubert Stryer's list of honors, culminating in the National Medal of Science, is extensive and impressive. His own description of his science, "light and life," best describes Stryer himself.

INTERVIEWER

David J. Caruso earned a B.A. in the History of Science, Medicine, and Technology from the Johns Hopkins University in 2001 and a Ph.D. in Science and Technology Studies from Cornell University in 2008. His graduate work focused on the interaction of American military and medical personnel from the Spanish-American War through World War I and the institutional transformations that resulted in the development of American military medicine as a unique form of knowledge and practice. David is currently the Program Manager for Oral History at the CHF. His current research interest focuses on the discipline formation of biomedical science in 20th-century America and the organizational structures that have contributed to such formation.

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INTERVIEWER:	David J. Caruso
LOCATION:	Stanford University
DATE:	3 December 2008

CARUSO: Thank you very much for taking the time to meet with me. We're here at Dr. Stryer's office at Stanford University. And what I'd like to do is really start from beginning. I know you were born in 1938 in—I hope I pronounce this correctly—Tientsin, China.

STRYER: That's right. It's now called [...] Tianjin; Tientsin was the [old name used by] Europeans.

CARUSO: Okay. And were you raised there? Or were you just born there and your family left?

STRYER: The story here is that my dad, who was born in Germany, started doing business in China in the 1920s and spent a good deal of time in the Far East generally. My mother was born in Russia and left Russia around 1915. Her family wanted to pursue better economic opportunities, to get away from the pogroms, and her family settled in Harbin. My parents met in 1937, in [Harbin] and got married within a few weeks.

It turned out that China was a very good haven from [Adolph] Hitler and [Joseph] Stalin during World War II, and we were fortunate not to be bothered by the Japanese. There was the Japanese occupation, but we slipped between the cracks, and we managed to get along reasonably well during World War II, during the Japanese occupation, and came to the United States in 1948. I recall during World War II, as the U.S. B29s were bombing Shanghai, my dad would point to them and point to a U.S. flag and say, "That's going to be your country." It was his expectation that the war would end and that everything would work out well. And it did.

CARUSO: What business was your father in?

STRYER: Hog hair; bristles for brushes.

CARUSO: Brushes, okay.

STRYER: In the days before nylon.

CARUSO: And did your mother have an occupation, or was she more of a stay-at-home?

STRYER: She was more of a stay-at-home [mother]. It was very unusual in those days, especially in the Orient, for women to work, to have careers.

CARUSO: [...] What sort of family life did you have growing up? Were you near other children? I don't know the state of the city that you were in...I don't know if it's large or small, rural...

STRYER: Well, let's start with Shanghai. After Pearl Harbor Day [7 December 1941] the Japanese occupied the city, and sometime after [that...] U.S. citizens—including my aunt and uncle—and Canadians and the British were taken to detention camps and kept there during the war. A large part of the [foreign] community vanished from Shanghai. It was a very solitary existence during the war.

I went to a school run by two Danish ladies in their apartment. It was a one-room, oneapartment schoolhouse with about fifteen kids in it, most of whom had slipped between the cracks as my family did [...]. We taught each other. Once I learned subtraction, I would teach addition—which I had learned before—to the younger student, and I would learn multiplication from the older student. There was very much a spirit of learning by teaching, and I think that's where I developed my love for teaching and my capacity to use teaching as a way of continuing my learning and exploring new areas. It was a wonderful school.

After World War II, after V-J Day [15 August 1945], starting in the fall of 1945, the Shanghai American School opened again [...]. I had a lot of friends there. It was a very good time [in Shanghai, from 1945 to] 1948. We had planned to come to the United States. We received an immigration visa, came here, and it was fortunate...the timing was fortunate because it was just then that Mao [Zedong] was coming down from north China and, in not too long, Shanghai—like much of China—fell into Communist hands. And so, it was a very good time to leave the country.

[I] moved to Forest Hills, New York and there met a wonderful group of youngsters. Many of them were immigrants. They were all eager to learn. [I went to] a fabulous school there, and that's where I got interested in science. And so, I would say that my childhood had different periods: a period of relative solitude and staying out of the way and not being very visible during World War II, and then very lively years in Forest Hills before I went to college. **CARUSO:** Just to focus a little more on your time in China, the one-apartment school that you were attending with just a few number of students, were they just teaching you basic language skills, basic reading schools, or did you have a relatively diverse curriculum that they were trying to give you at the time?

STRYER: I don't really remember. [...] I left that school when I was seven years old, and so I was there probably at ages five, six, seven. What I do remember was the basic skills of reading and arithmetic. I also remember that it was a very interesting place; [...] I really wanted to go there every day.

CARUSO: And when you transitioned into the more formal school setting, were you introduced to regular subjects at that point?

STRYER: Yes. Yes. And actually, there's a funny story on that. So, I was seven years old. My dad registered me at the Shanghai American School, which got rolling very soon after V-J Day. [...] 14 August was when the war ended, and the school opened soon after, and the reason was that the principal and all the teachers had been interned by the Japanese, and they were ready to go. They had a lot of time while in detention to plan the next school year, whenever that would come. When my dad registered me, they said, "Well, seven years old. We'll put him in the second grade." My dad took me to school the first day and led me to a classroom. The teacher started by saying, "Welcome, third graders." I said, "Oh my god. I'm in the wrong class," but I just kept quiet. And she said, "I want to make sure that all of you will be happy here, so I'm going to give you a little test to see what your skills are and make sure that this is the right classroom for you." And so she did that. I took this little test, and after about an hour or so, she said, "Lubert, would you please come up here and talk to me?" And I said, "Ah, she found me out. I'll be sent to second grade." And she said, "You know, I just looked at your test, and I don't think you'd be happy in this classroom. I think you need more [of a] challenge, and we're going to put you in the fourth grade." So, within two hours, I skipped two grades. [I] came home, and I just could not break the news to my parents that way. I said I was promoted to third grade, and the next day I came home and I told my parents I was promoted to fourth grade. And years later, when I told them this story, they just would not believe me. So, that accounted for my getting a very early start in science.

CARUSO: So, just basic science classes, the introduction to everything?

STRYER: Right. The Shanghai American School was very much run the way an elementary school here in the United States in a suburb would be run. It was a very colonial environment. There was no teaching of the Chinese language, to my great regret. I forgot Chinese while I was

in China, and that's something that really saddens me to this day [...]. It was a good school, a lot of fun.

And then in New York, I went to a junior high school in Forest Hills, and it was a hard transition for me going from the school [in Shanghai] that had large playing fields, kind of like what Stanford has in some of its athletic areas—very open, very cloistered, protected from the world. [I was dismayed to] go to a junior high school that was right on the street .I wouldn't quite call it an urban jungle, but it did not have a campus feel.

But then Forest Hills High School had more of that feeling that I had first experienced in China, of a real campus and a very aesthetic environment. And there, the classes were really terrific, [especially] in science. I remember each of my teachers, and I remember many of the things that they taught. For example, Mr. McSheehy, who was my physics teacher, gave me a ruler and asked me to measure something, and I measured it from the tip of the ruler, where the zero point is, to 4.3 inches or whatever, and he said, "No, that's not the best way to do it, because," he said, "the end of the ruler might be eroded. You want to start it at the one, where it's in good shape." [These lessons] I remember to this day. I also had incredibly good teachers in history and English: I was introduced to *The New Yorker* magazine, which I continue to enjoy. I had a first-class high school education.

CARUSO: What actually prompted the move to the United States? Why did your family want to come to the U.S.?

STRYER: It was very much a feeling that this was going to be the future for me. My dad had visited the United States in the 1930s and thought that this was just a great country. My mother...most of my mother's family was from Russia, the ones who had gone to the Far East, many of them came to New York. The older generation was in the fur trade. The next generation, many of them went into academic life. It was a family that valued learning and culture [...]. My dad loved the commerce of the Far East, but he recognized very early that this was the country for me, and so it was very much in the plans [...]. I admired [his attitude]: "This war will be over. The Japanese will be out of here, and we'll be heading to the United States."

CARUSO: Do you remember what the travel was like? How did you actually get from where you were to the United States? How long did it take?

STRYER: Very pleasantly. It was on a Pan Am[erican World Airways] plane. It had sleeper seats, [...which were] very comfortable. It would be the equivalent of first class today. And the path was interesting [...]. We left on 6 December 1948, and the first stop was Tokyo, which was under [General] Douglas MacArthur in the U.S. occupation. In retrospect, fortunately, there was a mechanical problem with the plane, and so we had to spend another day in Tokyo.

We got a very good tour of the city. Saw Mount Fuji resplendent—a very clear day. I haven't seen Mount Fuji that clear from Tokyo since.

CARUSO: Had Tokyo recovered, pretty much, from the fire bombings?

STRYER: No. No. It was still recovering. The hotels weren't really functioning or there were very few of them. We were put up in railway Pullman cars.

The next stop was Wake Island. We had a military base there, and it was really something coming from cold Tokyo to tropical Wake Island. I remember the beach [of] Wake Island, you could see shrapnel. The war had ended only about three years earlier.

The next stop was Midway Island, and it was very interesting seeing the Gooney birds [albatrosses]. It was the middle of the day.

And then we landed in Honolulu Territory, Hawaii, our formal entrance into the United States. It took only a few minutes to go through immigration. I marvel at that when I look at the long lines today. And I vividly remember my dad pulling out one hundred and fifty dollars. Fifty dollars per person was the immigration fee—a lot of money, well spent—and we were on U.S. soil. We then flew to San Francisco [California], where my aunt and uncle greeted us. We spent a couple weeks here and then went to New York by train, and a few weeks later got settled in Forest Hills.

CARUSO: And was New York because of it being a commerce center? Was it because your mother's family had been moving in that direction?

STRYER: It was both. For my dad, it was the center of commerce. [...But] within a very short period, business was tough because Mao took over China. Trade with China stopped. So, first he loses a business to Hitler, then he loses a business to Mao, and it took him quite a few years to really get going again. So, economically, they were tough years after a rather comfortable time in China.

CARUSO: And did he stay in the same business, or did he...

STRYER: Bristles were gone, for two reasons. One was the supply of bristles [was gone]— trade with China stopped—and, [second], nylon came in. Probably even without Mao, my guess is that my dad would have had to change his [business] area, an example of [technological displacement].

CARUSO: What did he move into then?

STRYER: Went into scissors with Italy. He was a born trader.

CARUSO: You mentioned that ultimately, once you got settled into Forest Hills, especially when you got to high school, it was a nice community to be in, but how was the transition for you? You came over starting in December. You took a little while to get settled in. You probably didn't go to school until the following fall?

STRYER: No. [I] went to school in Forest Hills within a day of getting our apartment there—mid-January.

CARUSO: Okay. And how was it starting up...I mean, this was...

STRYER: It was very uncomfortable because it felt like—this is a slight exaggeration—it felt like an inner-city school. Here I had these gorgeous playing fields...The Shanghai American School, kind of, had colonial architecture. It looked like [The College of] William and Mary or something like that. And I went back years later...a few years ago I was in Shanghai and I went back there and saw the outside, and [the front of the school] still looks lovely today.

And so suddenly from a class size of maybe eighteen to a class size of maybe more than thirty. It was a shock, coupled with the fact that it was a difficult time for my dad. For my mother, not having servants was hard. She was very used to that over the course of her life. It was tough until I got to Forest Hills High School, where I really found an incredible community of kids, and that changed everything.

CARUSO: When you went into the school system, since you were, I guess in some ways, two years ahead when you were in China, did you keep that same pattern when you enrolled in school in the United States? Were you younger than all your classmates?

STRYER: Yes, I kept the same pattern, but it [...got] exacerbated. When I was at the University of Chicago, my adviser there said to me in my sophomore year, "You know, Lubert, you've got enough placing out advanced credit that you really could graduate here in three years." And so, I had a three-year undergraduate education. I got three years ahead of the game.

CARUSO: Okay. Oh, wow. So, you graduated in '57, so you were 19. That's three years ahead of the game. When you came to the United States and you were starting up schooling here, did you find that the classes...I'm assuming you started in junior high school?

STRYER: Correct.

CARUSO: [...] Like the tail end of seventh grade?

STRYER: [Yes, exactly].

CARUSO: So, the tail end of seventh grade. You at least had some time with...

STRYER: Yes. And then...and junior high included eighth and ninth, and I went into Forest Hills High School in the tenth grade.

CARUSO: Tenth grade, okay. And how did the students respond to you? I don't know if you came in...you probably had a different background from many of the students.

STRYER: Yes, and it was awkward. Now, at one level, it was easy getting adjusted. In China, I was a [New York] Yankee fan; on the Armed Forces Radio, I would hear about Joe DiMaggio. [...] Baseball was no surprise to me. I played baseball in China. But there was something that felt just very different, and it was hard. It was a different culture. But then, as I said, once I hit high school, there was a group of students who loved learning and were very sharp. They were fun, they were funny, and we had a great time.

CARUSO: How did your family treat your education? Clearly, you were advanced. Clearly, you were a smart child. Were they ever really involved in your education: when you came home, they made sure you sat down and did your homework, or they reviewed things once you've ...?

STRYER: Never. They never asked me when my homework was due. They never asked me what my homework was. That was my world. That was my responsibility, and they never gave advice on which subjects to take or not take. And they, very early, very much respected my decisions, for which I am very grateful.

CARUSO: Did you have any responsibilities, outside of being a student, in the home? Did you have chores to do? On the weekends you were expected to mow the lawn or anything along those lines? Or was it pretty much that your job was being a student?

STRYER: I think, like many immigrant kids, I was, kind of, an interface to the broader society. I can't give you an example but I would occasionally run interference because I was treated as someone who was on the in with this new [society]. My parents spoke English. It was the common language of my parents. My dad's native language was German. My mother's was Russian. English was their second language, and they spoke English all their life together. Russian and German were forbidden languages. These were the languages of oppression, and they didn't want me to learn [them]. They wanted me to speak only English. And so, while they had a good command of English, there were still certain things that were [difficult for them to express]...I was getting information for them or handling something at a rather early age.

CARUSO: In some ways, acting more like, maybe, a cultural broker since you were involved in the high school.

STRYER: Yes. Yes, that's a good way to put it.

CARUSO: Did you have hobbies as a child? Did you like to take nature walks? Did you read tons? Did you like playing sports? I know you mentioned you listened to baseball and...

STRYER: I love baseball. Apart from baseball, I was not good at athletics. First, I'm short, and then being two years ahead really makes you the smallest kid on the block. I enjoyed writing. After World War II, I would put out, from time to time, a little newspaper called *The Daily Bugle*, where I reported on events and banged it out on a typewriter with carbon paper. And my aunt and uncle fortunately kept some copies of it, and it's kind of amusing. So, streaks of the future writer were already evident. I very much enjoyed photography, and I remember when I was in the eighth or ninth grade that I saved up enough money—I remember the exact amount, it was fifty dollars—and I got a Voigtlander Vito camera and joined the camera club at the high school in later years. I did a lot of processing of film and printing, and I got an enlarger. One of my other friends liked photography, so I was really into photography. I enjoyed doing chemical experiments, to the consternation of my parents. So, I was into…yeah, very much into chemistry…and sandlot baseball.

CARUSO: Okay. Was there any specific type of photography that you enjoyed more, were you...snapshots of the world around you? Was it scenic shots? Was it just going out with a camera?

STRYER: It was very eclectic. It was going out with the camera, and sometimes it would be people. Sometimes it would be a flower. Sometimes it would be a zoo scene, a street scene.

CARUSO: Let's talk a little bit about your high school, since it sounds like that's where a lot of your interests wound up developing even more, and you mentioned that you had a number of good teachers and good friends. What classes were you...you had high school for three years. What classes were you taking in high school? Was it standard English, math, bio, chem?

STRYER: The classes were English, French, social studies, and a science course and they were all very positive experiences. I started out high school, and for a year or a year-and-a-half, I was very much interested in Law. I had a very good grasp of American history, of the U.S. Constitution. I won a contest that was run by [United States Military Academy at] West Point on American history. I won it in my high school. In my high school, the graduating class was about 900 students; it was a good size school.

I was just fascinated by history, [...] history looking towards law. And my guidance counselor one day pulled me aside and said, "Lubert, that's fine, but you should really be thinking about engineering. You're not going to make any money in law, and you have a good mind, and you should be really thinking about engineering." [...] It did not particularly inspire me but it was heartfelt advice.

Then one day the chairman of the science department, Paul [F.] Brandwein, asked to see me, and he said, "I see you've been doing well in science courses. I would like you to do some research. I think you might enjoy it." So I said, "Well, that's a good idea." He didn't try to dissuade me from social studies at all. The first project involved bioluminescent bacteria. And I was, right away, hooked [...]. The idea that you can explore new terrain was very exciting. But there were some nasty looking colonies on the plate, and so Dr. Brandwein said, "This is a good project, but we really don't have the facilities here for you to carry it out safely. Here are a bunch of papers. You read them, and maybe you'll get an idea about some other project. And so, I read them, and there was a project on aging. Albert [I.] Lansing, who was a scientist in Michigan, was studying aging in rotifers, and rotifers seemed pretty harmless. And so, that was, in fact, my high school project, the effect of maternal age on the lifespan of the offspring rotifers. Paul Brandwein made sure that everyone in the research course, which was an elective, would compete for the Westinghouse Science Talent Search, which today is the Intel [Science Talent Search] or whatever it's become.

CARUSO: Yeah, it's a new name.

STRYER: But it's the same type...

CARUSO: Same program.

STRYER: ...Our high school had quite a record. Along with Bronx High [School] of Science, it was one of the leading producers of winners of that talent search. And so, as part of that, you read *Science* magazine for a year or two, and you really studied, intensively, quite a few things in science. We had a group of people really preparing for it, and it was wonderful because you acquired a lot of scientific vocabulary. Then you [wrote] a research report, sort of, a mini thesis on what you've done. I ended up with an honorable mention, but it was a fabulous introduction to science. Social sciences and law just receded, and I knew that I wanted to become a scientist.

CARUSO: So, how did this course actually run? Were you given your own lab space? How many students were doing this research component?

STRYER: There were about fifteen students, and if we had a free hour during the school day, we would come there, and then we'd come after school, and there was always a science teacher there to help, but it was pretty much [that] you had to ask for help. You weren't told what to do. You had to ask for help, and then you would get some help. At one point—maybe that's when I was still working on bacteria—I wrote Selman [A.] Waksman, who had just won the [1952] Nobel Prize [in Physiology or Medicine] and was at Rutgers [The State University of New Jersey]. I was just amazed, he answered the next day, and that was just wonderful, being in contact with a fabulous scientist.

[I recall that] the school library and even the Queens Borough Public Library did not have [the scientific articles] I needed. I remember going to the Columbia University library, where somehow access had been arranged, and I was looking at scientific journals. That was very, very inspiring.

CARUSO: You mentioned that you had some great teachers while you were in high school. Teachers beyond Mr. McSheehy and Brandwein?

STRYER: Yes, indeed. As I said, an English teacher introduced me to *The New Yorker*. I remember reading [Alfred, Lord] Tennyson and the line "The war of Time against the soul of man," and that still sticks with me from high school days.¹ I remember my social studies teacher and going over American History, transition periods between isolationism of the United States and internationalism. And we had a social sciences club and we would invite speakers from different consulates [...]. [Forest Hills High] was a very lively place.

¹ Alfred, Lord Tennyson, <u>Gareth and Lynette</u> (London: Macmillan, 1902).

CARUSO: So, very broad-based education...

STRYER: Very broad-based education.

CARUSO: ...that allowed you to also go into more depth. It sounds like you had these outside clubs that...

STRYER: Yes, I had the outside clubs. We would have a mini mock-U.N. session, like at Hunter College [of the City University of New York]. There were a lot of things going on. And best of all was that we had a cohort of students...so, out of the nine hundred students, there was probably a group of about fifty or sixty who were very intellectual, very motivated. They all succeeded superbly. In fact, one year I went to a Gordon Research Conference, and in the evening we sat around, had beer, and at a table...of the ten people at the table, eight had gone to my high school.

CARUSO: Really?

STRYER: Yes. Amazing.

CARUSO: Just randomly assigned.

STRYER: Randomly. And here's a meeting that had maybe one hundred and twenty people at the meeting, and my gosh. And so you hear about these kids from Forest Hills High. The chairman of our psychology dependent [at Stanford], Brian [A.] Wandell, is a Forest Hills graduate, and so they keep coming up all over the place.

CARUSO: Outside of this research class, what were your science classes like in high school? Was it just pure lecture/memorization? Did you have a chance to do experimentation in those classes?

STRYER: We always did experiments. Lab was a very important part, and as I recall, it was pretty decently equipped, and very much in the spirit of inquiry, and the teachers had a very good command of science. [...Our] teachers grew up and started looking for jobs in the Depression Era, and so the New York City School System was fortunate to have attracted these people. Had they grown up in the 1990s, [...] they'd be in start-up companies, or they'd be in

major corporate labs, but the New York City School System managed to get these people because they could offer them a secure job and a good environment...a very talented group of people.

CARUSO: Clearly you were interested in science. Was it just always assumed that you'd be going to college? Did you just know that's what you were going to do? Did your family just...?

STRYER: Oh, yeah, that was...

CARUSO: That was just given.

STRYER: That was a given, right. It was also clear to me that, because of my parents' financial situation, I would need to get a scholarship. It was very clear that that was absolutely essential.

CARUSO: So, your father's financial situation didn't pick up after...

STRYER: It took quite a while, after I was in college.

CARUSO: So, that had to be a factor for you, the financial...was it pretty much that you were going to be on your own?

STRYER: Clearly.

CARUSO: Clearly, okay. When you started to think about college, you have this financial thing in the back of your mind; what were you thinking, in terms of where you wanted to go? And you mentioned science, was there one specific area of science that you wanted to be in? Or was it just, "I'll go to college and figure out..."

STRYER: I was thinking of medicine, basically of medical research. And so, in terms of where you apply, well, it was pretty obvious. You apply to Harvard [University], to Yale [University], to Columbia. I also applied to Cornell [University] because, as a New York resident, that was a place where tuition was...

CARUSO: Right, in-state.

STRYER: And also, they had some scholarships. And then my guidance counselor said, "Those are wonderful places, but you should also apply to the University of Chicago. You'd get an outstanding education there, and you might be able to get a very good scholarship there." So, I applied there and to Columbia. I applied to five places...For Columbia, I was too young. They chucked out my application because I was just too young. I could apply a year later, but...

CARUSO: You were sixteen?

STRYER: I was [first] admitted to Cornell, [...and then] to Harvard and Yale, but with financial aid packages that were not ideal, whereas the University of Chicago gave me a full scholarship, essentially covering nearly [everything]...tuition, housing, essentially everything except for incidental expenses and travel. [...That was a] very appealing offer. I would not have to go into debt, and so I went to the University of Chicago.

CARUSO: How did your family feel about you moving to the Midwest? Were they encouraging of it? Was it not...?

STRYER: Well, they were certainly encouraging because of the financial aspect—they thought it was just wonderful that I had this full support. And then, as they started talking to people who knew something about universities, they found out that the University of Chicago was a very good place.

CARUSO: How was it as a sixteen year old moving from New York out to Chicago [Illinois]?

STRYER: Well, it was glorious, actually. I remember getting there, and the idea that you did not have to be in a room from 8:30 in the morning to 3:30 in the afternoon—that you actually had time for yourself, you had time to do things, you had time to think—it was just a great liberation. And the idea that you were working on your own...so, I loved it from the very first moment. And the dorm was kind of fun. The first year I lived in a dorm, and then I joined a fraternity. And I had a really terrific time. And once again, I had superb teachers, and I was able to pursue research in the summers.

And so, let's see, one summer I worked at the Chicago Lying-in Hospital, and it wasn't original research, but I was in a cytology laboratory that was essentially doing papanicolaou smears diagnostically, but the person who was doing that really had a very good grasp of cell biology and would teach me a lot of cell biology. He would have me looking at [tissues and

cells] under the microscope and [gave me an appreciation of] what cancer was all about. And so, that was a terrific experience.

And then the subsequent summers, I had research projects. A wonderful one was the year that I was at Argonne National Lab, in the summer, with Douglas [E.] Smith, who was very interested in the area of photodynamic action—that is dyes that sensitize chemical reactions that have destructive consequences. That really got me into the area of what I call light and life, which my research has been centered on. [It] got me interested in excited states of molecules, got me interested in spectroscopy, and launched me on a truly lifelong interest.

CARUSO: When you came into college, did you have...was there a pre-med major at Chicago? Or was there....?

STRYER: No, you majored in a discipline. I mean, you would take the courses that were necessary for medical school, but that was just a normal part of taking a very strong science program. I took chemistry, and my chemistry professor was Harold [C.] Urey. But it wasn't just Harold Urey lecturing [...in the chemistry course]. I remember inviting Harold Urey to the dorm [during my freshman year] to speak about the origin of life because he had a student, Stanley [L.] Miller, who had just done [pioneering] electric arc experiments where, from simple molecules they generated [...] amino acids. I thought this was fascinating. [After Urey gave] this wonderful talk, I walked him back to what is now the James Franck Institute and the Fermi Institute], and he started talking about what interested him beyond the origin of life. He was interested in the abundance of the different atoms. And we're out there on this bitter and cold night, [...] right next to Stagg Field [Stadium] west stands, [the site of the first nuclear] chain reaction, when suddenly he said to me, "Why don't you come in my office? We shouldn't be standing out here." And for the next two hours he continued with his seminar on the origin and abundance of elements. So, I give that as an example of the kind of things that I was exposed to, and there were many others. I had a first-class scientific and...well, much more than a scientific education. The courses in the humanities that I took and social sciences were also really terrific.

CARUSO: And so, when did you start focusing in on one specific discipline to be your overall major at the university? Was that in your freshman year?

STRYER: Yes, in my freshman year I knew that I would major in the biological sciences. I got my bachelor's degree in physiology [and focused on what was] then called general physiology. We call that molecular physiology today [...]—the interplay of molecules to give rise to physiologic processes, in contrast to a study of the molecules alone. So, it was always in the context of some biological process. That's where I really developed what has been a very long-term interest.

CARUSO: For the science classes that you were taking, again, did they have lab components associated with them?

STRYER: Yes, very much so. For some of them, they were demonstration labs, but demonstrating really important things. For example, in our introductory biology course, we had a lab on the Hill reaction in photosynthesis, where we showed using redox-sensitive dyes...that when you illuminate the chloroplast, a reduction occurs, and that a primary event in photosynthesis is the generation of reducing power. A very fundamental experiment, a very beautiful experiment, and very exciting to carry out. Rather like the [exhilaration years] earlier, of generating hydrogen and oxygen and hearing the pop when [...] I lit the mixture. There were many of these. Oh, I remember in physics doing the Millikan Oil-Drop Experiment and carrying it out on the same floor that Millikan did it—that's very moving—and to actually measure the charge on an electron. That's pretty good stuff. And so, there were a lot of these very fundamental experiments that were really interesting to carry out.

CARUSO: Was there anything similar to what you had encountered in high school, in terms of not just doing the experiments that had been done, but to take on your own research program? I know you had the summertime programs, but during the...

STRYER: Yes, very much so. I spent [one of the summers] with Daniel [L.] Harris, who was in the physiology department at the University of Chicago. I was studying glycolysis in intact cells. I had the opportunity of really doing research and being near people who would be working essentially day and night, and what I enjoyed was this community of people. We would go out for a late bite, like, at 11:00 at night, and the camaraderie was very, very good.

CARUSO: [...] What were you doing outside of your classes during college? Did you still do your...were you publishing any of your own papers again?

STRYER: [laughter] No, the *Daily Bugle* stopped. They were very intense years intellectually. I belonged to a fraternity, Psi U[psilon], which had the jocks on campus. I think they wanted to raise their grade point average, so they picked up two people. They chose Don [Donald S.] Burnett, who became professor of geology at Caltech [California Institute of Technology], and they acquired me, and we always suspected that it was because of our grade point averages, but we had a good time there and expected to participate [actively in athletics]. I remember going out for intramural track, but it was very dispiriting when I was lapped by one of the leading runners [...] it was not my thing. I would say that the years at the University of Chicago were very intense intellectually, with relatively little in the way of non-science, non-academic activities.

CARUSO: Okay. How did the lab positions—the summer lab positions—come about? Was this something that was suggested to you by advisors? Did you go out and search for these labs?

STRYER: Both. And I...so, when I took the physiology class, the instructor, Daniel Harris, said, "Well, Lubert, why don't you think about spending the summer here?" And so that was very straightforward. The Argonne job, I applied for. I was probably told about it by one of the instructors. And so, the answer is both.

CARUSO: You mentioned that there was a camaraderie, especially with the Harris lab. What was the general lab life like for you during that summer? Was it 8:00 a.m. to 8:00 p.m. you were in the lab? Were there many other people in the lab with you? What was the culture of the lab like?

STRYER: Well, it was a later start, and it was like 10:00 in the morning to midnight, and you'd take time off for coffee or tea. And there'd be a lot of discussion. So, this was about the year that [James D.] Watson and [Francis H.C.] Crick published their paper.² I remember having discussions about that, and it was immediately recognized what that was all about and how crucial it was. That was very, very exciting. And oscilloscopes were coming in, replacing smoke drums, and I remember using an oscilloscope and measuring the neuron's potential.

The lab was not an isolating experience. We were part of a community, and everyone was...there were frustrations, but everyone basically enjoyed what they were doing. They were there because they really loved it. And some were trying to finish their thesis; others were further along. It gave me a sense of what it means to be a scientist, and it was very positive.

CARUSO: There were graduate students? Were there post-docs?

STRYER: Yes, there were people all along the academic progression.

CARUSO: And did you work much directly with Dr. Harris? Or were you, pretty much, more on your own or under the guidance of a post-doc?

² J.D. Watson and F.H. Crick, "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid," *Nature* 171 (1953): 737-738.

STRYER: Actually, both. More of the hands on with the equipment was with a post-doc, Henry Tedeschi. Daniel Harris would look the data over, and then we would talk about its broader implications. He was educating me about science in general. I remember getting together in groups of three and four to talk about something [...].

CARUSO: [...] Were you working on multiple projects in that lab, or just one?

STRYER: Pretty much one, one project.

CARUSO: One. And was that of your own designing, or was that handed down to you?

STRYER: It was very much suggested by him. That was the year before Argonne. I was beginning to get a sense of how you formulate a proposal, what it takes to pick a good one. I was very much in the learning stage of how you go about designing experiments and picking something that's interesting.

CARUSO: And were you exposed at all to what it meant to be an academic scientist, the politics that might go into running a lab, or having to become a manager of so many different people? Was that something that you were thinking about or that you were actively told about while you were in this position?

STRYER: That's an interesting question. Let's see. First, in those days being a professor was tantamount to taking a vow of poverty. And it was very clear that the choice, if one were to go into research, one was choosing a distinctly lower economic lifestyle than if one went into medicine. And I remember thinking about this a lot. "How can I do research," which I really enjoy doing, "but how can I get an M.D.'s salary?" That was in my mind. It was not yet in my mind what it takes to run a lab, because the lab I was in was relatively small, very personal, and it did not seem very complex as an operation, and one grant funded it. A few years later, I began to see what bigger science was like. That was at Harvard Medical School. And then I began to really see that side. But yes, I was becoming aware of politics and so on. But it struck me it was, sort of, part of the human condition, and that you would have it in any field. What also struck me was that science was a pretty open structure, and that it was something where an immigrant kid could succeed.

CARUSO: So, I'm guessing then, this played an important factor into why you decided to go to med school instead of pursuing a Ph.D.

STRYER: Yes, and it was that there was almost the assurance of financial security along that path. But also, I was really very interested in helping people, and it was clear to me that if I did medical research in a medical context, that I'd be able to help people and also carry out science. So, I would not say that it was purely an economic decision. It was also that, for someone like me, the medical route was just a culturally more acceptable or conventional route. Being a Jewish kid, medicine is exalted, whereas a Ph.D., what does that mean? And so, the M.D. was, for a number of reasons, the way to go.

CARUSO: And did you at all want to be seeing patients? Or did you just want to be helping people in the sense of doing science that would ultimately...?

STRYER: Well, initially I thought it'd be interesting to see patients.

CARUSO: So, a researcher who was also...

STRYER: Yes, some combination. And I actually, because the physiology department was right in the medical school, and it was right at [Albert M.] Billings Hospital, I would see physicians, and I'd see some of them were physician scientists, and so there were some models. For example, [Leon O.] Jacobson was doing his work on erythropoietin. He was a very good hematologist, but he was also opening new vistas in terms of stimulating red cell production. And so, I had some examples of people who were physician scientists.

CARUSO: Was there anyone counseling you against going into an M.D. program?

STRYER: Yes, the Ph.D.s. [laughter] Yes. They predicted that I would be hopelessly bored in medical school. Daniel Harris predicted that. And their goal was to rescue me from that, but when I decided to go to medical school, they were good sports about it.

CARUSO: They just thought that it was not going to be intellectually interesting to go through an M.D. program?

STRYER: That's right.

CARUSO: Was there any concern that [...] if you go through an M.D. program, you won't necessarily know how to do science? Doing science is something that's very distinct from doing medicine.

STRYER: Correct.

CARUSO: Was there any of that at the time?

STRYER: That feeling? Very definitely. Now, one should say that in Europe many M.D.s—for example, George E. Palade —got their scientific training concurrent with the end of their M.D. period or shortly thereafter. [...Many European scientists] who made major contributions in biochemistry and physiology [had only an M.D. degree]. One could see that tension here in the United States. I already experienced it as an undergraduate. But at that point, there were no M.D./Ph.D. programs. That came later.

CARUSO: Right, okay. And so, there was no temptation for you to do an M.D. and then do a Ph.D. or something along...?

STRYER: Wasn't thinking that far ahead. That came up a little later.

CARUSO: Okay, so we'll get to that.

STRYER: Right.

CARUSO: All right. So, you're going through your college career. One advisor lets you know that you can probably graduate a year early. You, I assume, jump on the chance to do so.

STRYER: I jumped on it because [it shortened the path]. Having been through World War II, having seen my parents dislocated, there's a tremendous feeling that one has to get on with life and make one's place and be successful. I look at the students here at Stanford, and most of them seem pretty relaxed to me and [do not have the kind of drive I had at the same stage]...They're doing wonderful work, and they're going to make major contributions, but that sense of urgency, that "War of time against the soul of man," that was something that was certainly pressing me on. And you hit it right on the mark when you said I just snatched that possibility of just going on to medical school after three years.

CARUSO: So, did you...what medical schools did you decide to apply to, and were there specific reasons?

STRYER: Well, it's very funny in retrospect because I applied to two medical schools—just two. Today, people apply to thirty, forty, who knows how many? I applied to Harvard, and I applied to the University of Chicago. And the University of Chicago was very keen on having me, but it was Harvard...so I applied, it must have been...

CARUSO: 1956?

STRYER: So, let me see. I graduated in 1957, so I applied, right, sometime...

CARUSO: Fall of...

STRYER: In 1956, in the summer. Okay. And the first week of September, a few weeks after I sent in my application, I get a telegram from Harvard admitting me with a scholarship. And Chicago had not yet acted, and they were chagrined. [...] I had wanted to go to Harvard as an undergrad, and so here was a great opportunity and I seized it and, of course, went off to Harvard Medical School.

CARUSO: So, what materials did you submit to them as part of your application to...

STRYER: I think it was a very simple...things were much simpler in those days. It was a very simple application. I think there was an essay on why I wanted to become a doctor, and a statement of what I've done, and the transcript, a few letters of recommendation, and that was it.

CARUSO: Just the fact that they telegrammed you, admitting you, giving you a scholarship, I was wondering if...maybe it's the letters of recommendation. Do you remember who?

STRYER: Yes, I had...one came from a physicist, another came from a biologist, and I think a third from a chemist. And that was it.

CARUSO: And so, you didn't want to wait around to hear what the University of Chicago might say?

STRYER: No, no.

CARUSO: Was it a full scholarship to Harvard or partial?

STRYER: It was a very [good scholarship] plus a loan. It was a [very] good package. I could have probably gotten a better package at the University of Chicago, but I felt, at this point, that I really wanted to go to Harvard. It was, at that time, a more eminent medical school, and I thought it would also be good to go to a different place for the next stage of my academic life.

CARUSO: You mentioned that you did laboratory work for the three summers. So, I'm guessing at the end of that last summer is when you moved out...

STRYER: I actually spent...I spent another summer at Argonne National Lab, which was very good.

CARUSO: And so, right after that is when you went to...

STRYER: September of 1957. Right.

CARUSO: That's when you went out to Boston [Massachusetts]. Nineteen years old, starting medical school...

STRYER: Right, nineteen years old. Exactly.

CARUSO: ...when most people are in their sophomore year of college. Was age an issue when you started medical school? Did you let people know that you were nineteen, or did everyone just assume you were at the same age level? Was it a concern?

STRYER: Oh, it was clear that I was a young one, and I think patients would react to my youth, some quizzically, some enthusiastically. But it was something I certainly was aware of. And also, I have a funny story in a moment, but it was also an issue at the University of Chicago with my fraternity buddies. There were two bars. One was well lit, and I couldn't go to that one because they would see that I was underage. The other one was very dimly lit, and they didn't check IDs in those days, and there I passed through. So, I was definitely aware of it.

CARUSO: Can you tell me a little bit about what your medical school education was like? Was Harvard co-ed at this point?

STRYER: Yes. There were five women in the class, and they were a group unto themselves in a sense. I mean, they interacted with us, but they were regarded as strange critters by some of the faculty. It was a very sexist environment. They were a wonderful group. One of them was Tenley [E.] Albright, who was a figure skating champion in the [1956] Olympics, and they were all just terrific people. The class...we had a lot of fun with them. They were funny, and we enjoyed them, and we accepted them, but a lot of the faculty did not, and it was tough going for some of them.

CARUSO: They were clearly treated differently, or was it just...?

STRYER: Clearly treated differently.

CARUSO: In what ways?

STRYER: Well, it was said that "they wouldn't have the stomach to be in the operating room," which was absurd because Tenley's dad was a surgeon and she had been exposed to a lot of medicine at home, and it was that "maybe their place was in the humanities or in the ballet or something like that." But it was tough for them. It was a subtle kind of thing sometimes.

CARUSO: Were there any of your classmates that expressed those values? Or was that just a minority?

STRYER: No, I don't remember any of the classmates expressing that. We were very enthusiastic about [the women in our class], and they were very much a part of the team.

CARUSO: So, what was your medical education like? Was it two years of classes and two years of...

STRYER: Well, it started off, I would say, dismally. First I left my fiancée, Andrea, in Chicago.

CARUSO: So, you did have some outside activities while you were at the university.

STRYER: Yes, I-[laughter]. Oh, yes. Yes. Right, right. Yes, I...

CARUSO: Was she an undergraduate there?

STRYER: She was an undergraduate there. That's right.

CARUSO: Same year or same time frame as you?

STRYER: Andrea was there at the same time. We met in a group called Orientation Board that helped incoming students learn about the university. So, we were part of the welcoming group [...].

CARUSO: What was she majoring in?

STRYER: She was majoring in history and then education, and she came from a medical family. Her dad was an internist and lived in Chicago.

CARUSO: All right. So, it started bad?

STRYER: So, it started off I'm separated from her, I'm generating these huge phone bills, and just as the Ph.D. people predicted, medical school is really boring. And here I am, again, locked up in class from 8:00 am to 5:00 pm, very different than college and much more rote learning and very little inquiry, [...] surrounded by very bright people but a really dull [curriculum].

Before I left the University of Chicago, I had visited several times the home of [Nathan] Goldblatt. His son Stan[ford J. Goldblatt] was a classmate of mine, and we would go to his house, sometimes for fun, sometimes we would study together and prepare for exams. We had an interesting group. One of them was Leon [R.] Kass, who later went into bioethics. And so, Stan's dad [Nathan] owned a department store in Chicago and was a philanthropist and was very interested in medical research. [He] had set up a number of laboratories at the University of Chicago. When he heard that I was going to Harvard, he said, "If you need any help, you should look up my friend Sidney Farber."

Sidney Farber was a pioneer in cancer chemotherapy. I remembered that, and so after about six or eight weeks of medical school, I couldn't stand it anymore not doing research [...].

I figured, "Well, I should talk to Sidney Farber, head of the Children's Cancer Research Foundation." I called his secretary and told her that [Nathan] Goldblatt suggested that I call him, and I had an appointment with him that evening. I told him what was troubling me and he said, "Well, there are two people I want you to talk to." One of them was Elkan [R.] Blout, and I saw him, and we hit it off right away. Now, Elkan, at the time, was vice president of Polaroid [Corporation]. He was in charge of their program to develop color film and color instant photography. He had been at Polaroid almost from the start of the company, and had a very close relationship with Edwin [H.] Land, and he was the one who really guided their [chemical] research and some of their development.

But Elkan had broader interests—he had a laboratory at Harvard Medical School, at Children's Cancer Research Foundation, which in those days was also called The Jimmy Fund [...]. The Jimmy Fund was a fundraising [entity] associated with the [Boston] Red Sox that provided funds for cancer research. [Elkan] had a large lab at Children's Hospital [Boston] that was devoted to synthetic polypeptides. Now, the immediate goal—and what provided a lot of support for the lab—was to use synthetic polypeptides as plasma expanders. The Army was interested in having a material that could be the equivalent of plasma in terms of its osmotic properties. But Elkan's interest was really to learn the secrets of protein structure, to understand the relationship between amino acid sequence and three-dimensional structure, conformation. He was interested in making an artificial enzyme. He had this program with maybe fifteen people in it, and he would run that at night, and his day job was Polaroid. This was amazing.

[When Elkan came to the lab in the evening], I had a lot of time with him. It was perfect for my schedule. My day job was as a medical student, and so I would do my research in the evening, and Elkan would come there in the evening, and we had just an incredible group of people there. In addition to Elkan's lab, there was an independent lab that Carolyn Cohen, who's now a professor of biophysics at Brandeis [University], ran on muscle. There was a lot of terrific science in that building. Also in that building were people like John [F.] Enders, who won the [1954] Nobel Prize [in Physiology or Medicine] for his contributions to tissue culture, to getting vaccines and so forth. And so, once I started there, I was very, very happy again. And then, the rest of the medical school day was fine. I would learn lots of useful things.

That was my start of research as a medical student. I worked on the conformation of polypeptides, and the technique we used was optical rotatory dispersion. We measured optical activity [as a function of wavelength]. For example, when poly-L-glutamate is mostly unionized [at low pH], it's in an alpha helical form. When it's ionized [at higher pH], it goes into a random coil [because of electrostatic repulsion]. We could follow the helix to coil transition as a function of pH and monitor the optical rotatory dispersion and see a large change. That is an example of the kind of [research that was being carried out]. Elkan was very good at synthetic organic chemistry, he developed ways of making copolymers and long polymers.

And what I got interested in, as a result of my work with Douglas Smith at Argonne National Laboratory, was dye-binding to proteins and polypeptides. I was interested in dyes because they were the photosensitizers in the photodynamic action that was causing cellular destruction [...]. So, I was very interested in following what the dyes were doing on synthetic
polypeptides. Dyes were also of interest because their spectroscopic properties changed on binding to proteins and synthetic polypeptides, and so here was a way of probing molecular interactions. The dyes were in a sense surrogates for substrates or inhibitors.

I started looking at the optical rotatory dispersion of dyes and, very early in my medical school research, discovered that symmetric dyes, acridines for example, become optically active when they are bound to helical polyglutamic acid but not when they're bound to the random coil form. That was very exciting. I spent my medical school research years on conformation of synthetic polypeptides, on induced optical activity, and I learned a lot of spectroscopy. I would go across the river, and while I couldn't take a real course, I would go to some lectures by William E. Moffitt on quantum chemistry. I would go across the river to George Wald's laboratory and talk to him about vision. I really got hooked on spectroscopy.

CARUSO: So, you were doing this, within two to three months of starting your medical education, throughout the entire four years.

STRYER: Yes, throughout the [four years]. In the second year of medical school, we started seeing patients, and I actually enjoyed that. I really enjoyed the diagnostic puzzle. The third year was very much a clinical year. I had less time in my third year for research, but in the fourth year, the dean's office recognized that my heart was really in research, and so they fashioned [my schedule] so that I could spend about six months of my fourth year full time on research—not quite full time. There was a requirement, for example, that you had to deliver twelve babies and spend a month on obstetrics: but they arranged it so that when a baby was ready for delivery, they would give me a call, and I'd come and deliver the baby. So, they were very, very accommodating. This was before, as I said, before M.D./Ph.D. programs, but they went out of their way to make it possible for me to do as much research as possible.

The dean of students, Joe [Joseph W.] Gardella, very much wanted me to intern, but I told him that [I wasn't going to]. At some point during medical school, maybe in the third year, I realized that being a good clinician was very demanding and being a really good research scientist was very demanding, and to try to do both would be perhaps impossible. And so I decided that I would forego clinical medicine and devote myself to research entirely. Then I decided it made no sense to take an internship, and Elkan Blout, who was a Ph.D.—a Ph.D. in chemistry—very much reinforced that. The dean's office warned me that I'd be walking the streets if I didn't get an internship, but eventually they agreed to my plan. So, at the start of my fourth year of medical school, I knew that I was going to go into a pure research career.

CARUSO: Looking back on the classes that you were taking in medical school, was there any attempt to incorporate some of the current trends or the new advances in science that were going on? In many ways, you're going to medical school during maybe the tail end of the real revolutionary period in terms of pharmaceutical developments and things like that, but was there an attempt to broaden the medical education to make it more of a scientific investigator type of

curriculum, which I've heard some people mention that they had more of during medical school...

STRYER: Right. Yes, and it depended very much on the instructor, and it depended on the department so that, for example, microbiology and immunology, which was led by Bernard [D.] Davis, had a very modern outlook. When we were learning about the control of bacterial metabolism, we [were exposed] to a lot of modern genetics. In physiology, modern instrumentation was coming in. I still was doing [experiments] on smoke drums, but right around the corner, there were [scientists using new] electrophysiology [equipment]. So, it was coming in, but it had not really made its full impact. I'd say I experienced something between a traditional medical education and the kind of medical education that we offer now [...].

CARUSO: And how did your classmates respond to your interest in research? Were you just the odd man out in that sense? Were there others?

STRYER: [...] We had a very gifted class. So, in our class, we had John [E.] Dowling, who is a distinguished vision scientist. He's a professor at Harvard. Howard [C.] Berg too is now a professor at Harvard. Howard and John left medical school after two years and went into Ph.D. programs. Howard went into a Ph.D. program in physics and worked on masers, the microwave equivalent of lasers. And John Dowling went to George Wald's lab [...]. I would visit John and get to meet George Wald. And so, they left the class but while I was there, in the first two years, we had a group that was very dedicated to research. [Another gifted classmate was J. Michael] Mike Bishop, who went on to win a [1989] Nobel Prize [in Physiology or Medicine].

There were [quite a number of] students in our class who, at the time, were doing firstrate research, or who would be doing it and were very receptive to it [...]. It wasn't that I was an oddity [...]. Everyone was very supportive.

CARUSO: Did you have much time for anything else during this?

STRYER: Well, I got married in the summer after my first year. Here's an amusing story. We got married in Illinois and I was twenty years old—and Andrea was also twenty—and because I was twenty and a male, I needed parental consent. She was twenty and a female and did not need parental consent.

CARUSO: Interesting.

STRYER: Clearly. We got married early; we celebrated our 50th anniversary a few months ago. Andrea came [to Boston], which made life so much better. But it was very, very intensive. We didn't have much money. We didn't have a car. We would occasionally go to a movie. We would take walks. It was not easy living at all.

CARUSO: You mentioned that she was doing history and education.

STRYER: She was teaching.

CARUSO: So, she did...

STRYER: She taught and then she became a librarian.

CARUSO: So, she was...

STRYER: She was supporting me. She was putting me through medical school. Not quite [in the style to which I would like to become accustomed]...yes, she did a great job of supplementing the scholarship and the loan that I took from Harvard.

CARUSO: Was this the Helen Hay Whitney Research Fellowship?

STRYER: Ah, the Helen Hay Whitney Fellowship came in my first post-doc full year. So, what happened was that one day Elkan Blout, in my fourth year of medical school, tells me that he's made arrangements for my next two years, and he had spoken to Ed [Edward M.] Purcell, distinguished physicist at Harvard, co-discoverer of nuclear magnetic resonance, [1952] Nobel prize winner [in Physics]. Elkan thought that I needed to strengthen my knowledge of physics and math if I was to do anything worthwhile in research, and that I should go across the river and be tutored by Ed Purcell. Wonderful idea. It actually happened. And then, I'm to go to Cambridge, England, and he's spoken to John [C.] Kendrew, and he's made arrangements for me there. And so, this was a time when, if that's what your mentor tells you...

CARUSO: That's what you did.

STRYER: Well, that's what you do. It turned out that Elkan chose wonderful mentors and wonderful people, opened up great new worlds for me.

And then I got a Helen Hay Whitney Fellowship, which paid, if I remember, about six thousand dollars. So, here I was going from poverty to this sudden splendor. And then, when our first child was born, Michael, we got a five-hundred-dollar bonus, and so that was high living. We lived in Cambridge. We had a nice apartment there. And now, it was, kind of, the feeling that I had back in college. It was totally unstructured. I had all this time, and it was a matter of putting it to good use to learn some physics and to learn some chemistry. I did research. I continued at Children's Hospital and learned some x-ray diffraction in preparation for my year in Cambridge, England, and worked on the fiber diffraction pattern of fibrinogen and fibrin. I continued my interest in spectroscopy with a chemist at Harvard. We were studying the [...] fluorescence properties of porphyrins .

And so, in addition to auditing courses on math, I took E. Bright Wilson's course on quantum mechanics and went to a lot of seminars. And then I would have discussions with Ed Purcell, and the shortest discussion was an hour—never less than an hour—and the longest discussion that I remember was about six hours. And there were little projects, little things like he would say to me…he said, "Well, you're interested in the binding of dyes to polypeptides. Why don't you model it? What are the interactions between the dyes?" And then he said, "You really ought to learn some computing." The computer center at MIT [Massachusetts Institute of Technology] had an early IBM [International Business Machines Corporation] machine, and I got an account there, and so I got into computing. Purcell very much encouraged me to do simulations and just to really get into computing, which was a wonderful thing.

I just had a great time talking to him. I maintained my contacts with Elkan Blout. And it was [...] much more fun living in Cambridge near the Harvard College Observatory than it was living in Boston across from Sears. So, we had a great year in Cambridge, Massachusetts.

CARUSO: What I'd like to do is just find out a little bit more about what lab life was like in Dr. Blout's lab, because one of the things I'm interested in is how different mentors mentor their students and how lab life exists over periods of time. You mentioned you went to med school during the day, you went to lab at night. By your second year, you had your wife with you. When was your son born? That was...

STRYER: After medical school.

CARUSO: That was after medical school but while you were still in the U.S.?

STRYER: I was a first-year postdoctoral fellow.

CARUSO: Okay, okay. So, what was your schedule like in the lab, and how did other people respond to you while you were in the lab? I'm assuming there were a lot of other Ph.D. students or post-docs.

STRYER: There were a lot of post-docs. At the time in Elkan's lab, there were no graduate students. I was his very first student. He ran with staff; his model was very much a corporate model. That is, the kind of thing that he was doing at Polaroid. He replicated that model at Children's but he deviated from it in taking me, for he wasn't looking for students. [...] My guess was that Sidney Farber said, "Oh, here's a young man that I'd like you to talk to," and when that came from Sidney Farber, implicit in it was probably, "If he seems reasonable, take him." But Elkan was delighted that I was interested in dyes...I was telling him about what I was doing with dyes. Now, here at Polaroid, his life was dyes. Also, I knew some spectroscopy, so he right away [reacted positively] to me.

I was different from the others, who were post-docs or research associates with a certain degree of permanence in the lab. And it was run very differently from the lab in the physiology department at the University of Chicago, from Dan Harrison's lab. It wasn't five people; it was fifteen, twenty people. Very focused objectives: "You're going to make a copolymer of glutamic and serine," and, "You're studying the viscosity," and, "You're doing this or that." I had the most freedom, but my research was very, very disciplined. Once I hit some pay dirt, it was very clear what to do. And so, it was much more formal, less exploratory, less free-form, but very, very effective. It was an engine that was really producing things. And Elkan had a series of papers in the *JACS* [*Journal of the American Chemical Society*], and it was polypeptides one, two, three, four, a whole succession of papers, and it was a body of work with great coherence and a lot of impact.³ Elkan was well known. He had a lot of interactions with first-rate chemists. He would play poker with Bob [Robert Burns] Woodward every Tuesday night.

And so, [Elkan's lab was] very different from [those I previously encountered]. I would almost say it was the difference between a corporate lab in the case of Elkan, to, kind of, a Bohemian lab in the case of Dan Harris. A different kind of science, but very effective. And occasionally, I would visit Elkan over in Cambridge at Polaroid, and I would see the Polaroid environment, and occasionally I would meet Edwin Land, who was a very imposing figure and quite something to meet [...].

CARUSO: And how much was Dr. Blout involved in your day-to-day research? Was he guiding you through things? Was he just...?

³ For example, M. Idelson and E.R. Blout, "High Molecular Weight Poly-α,L-glutamic Acid: Preparation and Optical Rotation Changes," *Journal of the American Chemical Society* 80(17) (1958): 4631-4.

STRYER: Not day-to-day. I had lots of freedom, and I also had access to him any evening I wanted, and if I had something exciting or something puzzling or something wasn't working, I would go see him, but otherwise, I would not.

And there were interesting visitors. We had people, like Ephraim Katchalski from the Weizmann Institute of Science in Israel, who came for a mini-sabbatical. There were a lot of people to talk to and get advice from. It was a very different kind of lab experience and showed me a different aspect. It showed me big science in operation.

CARUSO: Part of the reason I was asking about the relationship is one thing that's very noticeable about your list of publications is that early on you were sole author on papers, which is not something you see, really, today. Being in someone's lab, that person's name is almost always on the paper. But there are some papers that you have that seem to be co-authored with him. So, I was wondering what your role was in those experiments, what his role was in the experiments that you were doing.

STRYER: The experiments were done with my hands. The conceptual framework of synthetic polypeptides and the study of their conformation, of course [was] Elkan's. The discovery of induced optical activity was mine, but an understanding of what it meant, Elkan played a key role. When I showed him a Cotton effect, where the optical rotatory dispersion, instead of varying monotonically, suddenly goes up, swings down and swings back up...I mean, I had never seen anything like that. The books that I had had no mention of it, and so it was just wonderful sharing that with him and having him help me interpret that. And so, it was very much where my research had tremendous guidance and intellectual input from Elkan.

CARUSO: So, what were the papers that were coauthored? Was he doing some of the handson work?

STRYER: Never. Elkan probably stopped doing hands-on work maybe fifteen years earlier. Now, I remember one evening, though, we actually did an experiment together, but that was very rare. In fact, that was like at 2:00 in the morning. That was something we were very excited about, and his wife was out of town, and so we were working very, very late. But he had a big program. At Polaroid, he was running several hundred people, so he was beyond the point of actually doing things with his own hands, but he was very conversant with what went into each experiment.

CARUSO: Okay. So, how did the paper writing go for those early publications? Was it something you just did, you submitted and got published? Or, did he have any guidance for you or input for you in these papers?

STRYER: Elkan cared very much about the writing of papers. He made it very clear to his lab that how you write a paper, the clarity was crucial and the same for talks. And what he would emphasize is, "What are the three main points you want to make?" And you don't even have to make three; "What is the point of it all?" And that everything is subsidiary to the main point or main points. That was very good intellectual training. Now, that was complementary to what I got earlier in the day. One of the things that I really liked about clinical work was the diagnostic puzzle. After you examined the patient, you had two minutes to present to the physician in charge, the attending, the history, the [physical exam] findings, the lab findings, what the differential diagnosis is, and how the patient should be treated until further information is acquired. You had two minutes to do it. And that, I think, is fabulous intellectual training. It forces you to focus and to be concise and to get the essence. And so, that plus Elkan's point about, "What is the major new thing here?"...

Again, he gave tremendous freedom. I would write the first version of the paper, and then I would hand it to Elkan, and he would criticize certain things. He would not rewrite the sentences. He would say, "This sentence is unclear. I don't see the relationship of this first sentence to the second one. Isn't there a paragraph that's missing here? Isn't there a gap in the logic?" And he would work very hard also on the right figures. And so, figures had to be very clear, and you also had to tell how you did the experiment. That was a wonderful part of being in Elkan's lab...the papers that came out of his lab were extremely clear.

CARUSO: Before moving on to your time as a post-doc, just one simple question. I think it's a simple question. Were there any women in these scientific labs?

STRYER: Definitely. First, at Children's Hospital, there was a lab run by Carolyn Cohen. In her lab, there was Susan Lowey. In Elkan's lab, there were several women: Alice [J.] Adler, there was Liz [Elisabeth R.] Simons. So, that was very natural and very comfortable.

CARUSO: Were they researchers in the sense of being post-docs? Were they technicians?

STRYER: No, Carolyn Cohen was a principal investigator, had her own grant. She was operating very much as a faculty member. Harvard, in those days, kept people in academic slavery [...]. Fritz [Albert] Lipmann, when he won the [1953] Nobel Prize [in Physiology and Medicine], was an instructor in medicine or something like that. So, Carolyn may not have had an exalted title, but *de facto*, she was running a lab in the full sense of the word.

CARUSO: I guess I'm just trying to get a sense of what...you mentioned that the faculty at the medical school had some negative connotations towards the female medical students, and I was

wondering if the same, sort of, mentality persisted when it came to more pure sciences, not necessarily medical.

STRYER: No. That's a very interesting distinction. Certainly not at Children's Cancer Research Foundation. There, women were in positions of responsibility and treated very much as equals.

Now, when I was in the physics department at Harvard, they had a lot of students. They had almost no post-docs. And so, I was in a strange category, and for some reason, I was invited to the faculty luncheons that they had once a week, and there were no women in the physics department at that time, and right now there are a few. So then, George Wald's associate was Ruth Hubbard—he eventually married her—but Ruth was doing outstanding work, some of the groundbreaking work on the photoisomerization of retinal...so, I would say there were many of examples of women doing terrific science.

CARUSO: Prominent positions. And there wasn't a...

STRYER: Prominent. There was a real distinction between what we saw in the medical school class and what we saw in research.

CARUSO: Okay. You mentioned that your post-doc was...well, your post-doc positions were, sort of, assigned to you...

STRYER: Assigned.

CARUSO: ...by your advisor during medical school. And this was supposed to be a time of learning for you.

STRYER: Tremendous.

CARUSO: Especially those first two years. You were still doing research in Blout's lab at that time? Or had you moved into...

STRYER: No, I had [moved out of Elkan's lab]. In my first postdoctoral year, when I was with Ed Purcell, I was doing research in Carolyn Cohen's lab on x-ray diffraction. Elkan felt that I needed to broaden my education. It would have been very convenient for me to continue with

him, and it would have been good for his lab, but he put my development first and foremost, and he felt that for my development, I needed to learn x-ray diffraction, x-ray crystallography to broaden my understanding of conformation. And so he made sure that I was working with Carolyn.

CARUSO: So, could you compare the two labs in terms of how things were being organized? You mentioned that Dr. Blout's lab was more of a corporate style. So, what was it like moving into Dr. Cohen's lab and doing...

STRYER: Dr. Cohen' lab was a fascinating lab because literature was very important as was cutting edge science. [...] It had wonderful people like Andrew [G.] Szent-Györgyi, the nephew of Albert [I.] Szent-Györgyi. Andrew was at Brandeis. He would come over, as would Hugh [E.] Huxley. The very best people on muscle in the world would come there. It was a watering hole for investigators interested in muscle contraction. It was also a very literary lab. There was a lot of discussion of Jane Austen. There was a lot of discussion of [Sidonie-Gabrielle] Colette. So, along with intense science, it had very much a humanistic and artistic component. D'arcy [Wentworth] Thompson's *On Growth and Form.*⁴ They had books lying around, and it wasn't [Linus and Peter] Pauling's *Chemistry.*⁵ The books dealt with science, but [they might be] on symmetry and art, or something like that. And it was a very intellectual place, much more free form, and more similar to Daniel Harris's lab, but with this strong literary component. And again, it was a lot of fun.

And a tremendous amount of time was spent [together in intense discussion]—coffee and tea were real rituals. [...] We would typically spend an hour having tea and coffee, and discussion was wide-ranging. It would cover non-scientific topics as well as scientific.

CARUSO: What were your days actually like when in...or what were your post-doc days like in terms of, were you doing 10:00 a.m. to midnight days during that period of time? Were you working more standard hours?

STRYER: Well, the year in the physics department was totally free-form. So, there were some days that I'd hang around the house and read math. Then there were days that I would go in to the physics department. I had an office there and I would go to either a math course or a quantum mechanics course—I would sit in on at least one lecture a day. But which experiments I was doing, what I was reading, just varied from week to week, and there was a lot of time for discussions. I remember the genetic code was being cracked then, and there was a scientist, a physicist John [R.] Platt, who had been at the University of Chicago. He was a very good

⁴ D'arcy Wentworth Thompson, <u>On Growth and Form</u> (Cambridge [Eng]: University Press, 1917).

⁵ Linus Pauling and Peter Pauling, <u>Chemistry</u> (San Francisco: W. H. Freeman, 1975).

polyene spectroscopist. And John was very interested in the genetic code, and we'd talk about the latest experiments and what it all meant [...].

There was time for lunch at the faculty club, and it was really a dream year. I haven't had that kind of a year until just recently, when going emeritus. I again [...] have that free-form style. [Another change from medical school was] suddenly having six thousand dollars. That was a lot of money in those days. One could live very well. And it was, having a child and all, it was very good and intellectually very intense and very unstructured.

CARUSO: Did you pursue things outside of science? You mentioned that the lab itself had more of an intellectual feel to it and that people were talking about things beyond just scientific experiments. Were you doing things outside of lab? Were you getting into any hobbies? I know you had a child, so that's going to be...

STRYER: We had a child, right, and we had a play reading group that we'd get together and take some good play and maybe eight or ten of us would read it. That was a lot of fun. It was just fun walking around Cambridge—Cambridge, Mass. and then later Cambridge, England. We had enough money, we were able to go to the theater and to the movies. I did not really have time to really dedicate myself to a hobby. The return to the hobbies came later, but there was time for the arts. There was time to enjoy things and to have a broader life than science.

CARUSO: And did having your child impact or transform your time in the lab in any way? Or was that...I assume your wife stopped working?

STRYER: She stopped working.

CARUSO: Okay, she became a full-time...

STRYER: And that made a tremendous difference. Andrea was very supportive of my research. She would sometimes try to get me to calm down a little bit and spend some more time at home. But I was always home for dinner. Sometimes home for lunch, maybe half the time. So, there was time for the family, and there was a lot of time to do good things. That's something I remember from my post-doc years.

Shall we take a break?

CARUSO: If you'd like, sure.

STRYER: Yes, that'd be great.

[END OF AUDIO, FILE 1.1]

CARUSO: So, I'd like to pick up with talking a little bit about your time moving to Dr. Kendrew's lab as, I guess, that's the next sequence. But before actually getting there, one thing that I was curious about. You did have a *Nature* publication come out of your time in Cohen's lab.⁶

STRYER: That's right.

CARUSO: Talking to contemporary scientists, they tell me, of course, that *Nature*, *Science*, those were the big publications. Was *Nature* as big, or considered as big at the time.

STRYER: Nature was very big then. I should say, in those days, *Proceedings of the National Academy of Sciences* too was regarded as a choice place to publish.

CARUSO: And that was your second publication.

STRYER: Right, and it was a great honor to publish [in *PNAS*]. After all, Pauling published his great papers, many of them, there. [...] Robert Woodward communicated [my paper with Elkan] to *PNAS*, and that's something that I, of course, cherish.

Yes, *Nature* was [very big the]n. It's very interesting how that paper got into *Nature*. I wrote the manuscript and sent it to—I was in Cambridge, England at the time—sent it to Carolyn Cohen and Bob [Robert] Langridge, and just before I went on winter holiday, I gave it to John Kendrew to look at for his criticism. John said, "This looks pretty good. I'll send it to *Nature* for you." [laughter] I get back from a ski holiday in Austria, and the proofs of the paper were on my desk.

CARUSO: Wow.

⁶ L. Stryer, C. Cohen, and R. Langridge, "Axial Period of Fibrinogen and Fibrin," *Nature* 197 (1963): 793-794.

STRYER: Okay? Carolyn says, "No, no. We've got to make some changes." And it was different in those days. So, it's an example of where, if you had the right people backing you, things were much simpler; the filter there was John Kendrew.

CARUSO: So, how was it transitioning into his lab, but also how was it transitioning into life in England and life at the MRC [Medical Research Council Laboratory of Molecular Biology]?

STRYER: It was a fantastic time at the MRC. The quality of the scientist there was just absolutely amazing, and it was a wonderful time in science. Max [F.] Perutz was the head of the laboratory, and Max was doing his wonderful work on hemoglobin. John was doing the groundbreaking work on myoglobin. The year we were there, John and Max won the [1962] Nobel Prize in Chemistry. [Francis H.C.] Crick was there, and that year [James D.] Watson and Crick won the [1962] Nobel Prize [in Physiology or Medicine]. Fred [Frederick] Sanger was running a laboratory. Aaron Klug, who went on to win a [1982] Nobel Prize [in Chemistry], was running a laboratory.

There were maybe only thirty-five, forty scientists in the lab, many of whom went on to win Nobel Prizes, all of whom, just about all, distinguished themselves in their careers. And it was just a great time in science, a time of great ferment, discovery. Major discoveries were being made about gene expression. New tools were developed in the structural arena in terms of ways of handling complex protein structures, solving the phase problem. And then we had Sanger developing new sequencing technologies, turning his thoughts from the sequencing of proteins to the sequencing of nucleic acids. It was one of the best times in my scientific career, and it was just a great privilege to be there.

And Cambridge, England is a delightful place. We enjoyed the town. We enjoyed the people at the lab. It was a very international group, a very lively group and just a lot of fun people. We went into London [England] frequently, saw some great plays, a wonderful performance of [King] Lear with [David] Paul Scofield, and it was just one of the best years of our lives.

It was very thrilling, and I had a wonderful time in research. [...] The structure of metmyoglobin was solved by Kendrew by the time I got there. And so now the interest was in solving the structures of the deoxy and oxy forms. I tried very hard to get crystals of oxymyoglobin, but they went over from the ferrous to the ferric form rather quickly. I decided I'd have to work on something in the stable ferric form. The ferric state forms complexes with a variety of ions, such as the azide ion, that gave stable isomorphous crystals. And so, I wanted to see how the azide ion goes in, and I carried out the first difference Fourier synthesis that revealed the binding of a small molecule to a protein. And that project was suggested...the idea of using the phases of the original protein and, as long as the crystal lattice dimensions were the same, using the phases of the native structure to solve the structure of the derivative, that was given to me by John Kendrew. Interestingly, Max Perutz did not think it would work. He thought that there'd be too much noise. So, it was a real thrill [to see the difference Fourier

method work]. We had the first indication that it would work around Christmas time with a two-dimensional difference Fourier, and then I solved the three-dimensional structure a few months later. It was just a great year, a wonderful time.

CARUSO: Did the culture of that lab differ at all? Or, in what ways, from the labs that you'd been in the United States...was there a different way of doing science at all?

STRYER: Yes. Now, let's see. How to categorize it? Well, first it's very English, and that means that what you accomplish in a year is not what counts. What counts is what you do over a longer period. So, this is a laboratory that grew out of the Cavendish Laboratory, with its incredible scientific tradition—the Medical Research Council Laboratory was the continuation of the Medical Research Council unit at the Cavendish Lab, and originally that was run by [William Lawrence] Bragg. And right behind you [here in my office] are the portraits of Perutz and Kendrew drawn by Bragg, and he was a good artist in addition to being a great scientist.

Now, Bragg was still very alive and well, and he ran the Royal Institution [of Great Britain] in London, but he would visit the [MRC Lab in Cambridge]. It's very special to have someone come up and be interested in what you're doing, and where the goal is to transform science to make the major discoveries, to address the most important problems and not to worry about time and to keep working on a problem. And that's what Perutz and Kendrew did with tremendous courage and with great support from Bragg. And this kind of great support will come up again in regard to the Pew, and let me remember to talk about it when I talk about Torsten [N.] Wiesel and Rod [Roderick] MacKinnon. I want to come back to that.

And so, there was very much the feeling of choosing an important major problem and just keeping after it, so that was absolutely critical. There was a tremendous amount of discussion at coffee and tea. What was expected was that you would go to coffee and tea twice a day, and then, if you wanted to, you could have lunch at the canteen. But these were times of great scientific discussion, and one would sit not only with the people in the structural group. That was not considered appropriate. You sat where there's the first opening at a table, and Crick or [Sydney] Brenner might be at your right, and Sanger might be at your left. And it was expected that the conversation would not be frivolous, that it would not be about the weather. You were expected to discuss serious science, and a lot of wonderful science was discussed. A lot of experiments were discussed. You learned things way outside your area of expertise, and it was an amazing year.

CARUSO: So, in some ways, breaking down those disciplinary boundaries that might get set up in individual laboratories to provide cross-fertilization for scientific ideas.

STRYER: Absolutely. Very much so. Very much so. And so, the importance of material science and engineering...I mean, a lot of the reason that the x-ray group succeeded is that they

had a rotating anode generator. There were new technologies coming in. They were at the forefront of using computers to process the data. We would process the data at IBM London. We would go in to IBM, which was located in SoHo, and we would bring our pack of cards—punch cards—and we would deliver the job and hopefully did not mis-punch. Once we saw the job was running, we would go off to lunch, talk some science, have a nice ethnic meal in SoHo, come back, pick up our results, and then ponder them on the train back to Cambridge. It was a very enjoyable life.

CARUSO: You mentioned that you were there for about one year.

STRYER: A little over a year.

CARUSO: During this period of time, based on what you've described to me, you were involved in...not necessarily extremely different, but somewhat different scientific projects from your medical school days to your time at the MRC. Were you developing any sense of an area of science that you wanted to pursue as your career?

STRYER: [...] I would say that spectroscopy, using light to probe biological macromolecules was very much in my mind, a great interest before I went to Cambridge. Cambridge, it was a very deliberate choice to learn a new technique, a new approach. The commonality is that it was on proteins, and I did not do much thinking about nucleic acids. [I was very involved] in protein structure.

And so, what I learned in Elkan's lab about relations between amino acid sequence and three-dimensional structure very much carried over to Cambridge. So, with Elkan there were certain rules that glutamic and alanine are helix formers, whereas serine and aspartic are beta sheet-formers, so that I was very interested in the protein folding problem. And so, having the structure of myoglobin and hemoglobin right there in front of you every day, you would think about that. There was a common thread, but there was something very new, as you pointed out.

CARUSO: During this little-over-a-year period, clearly...I'm assuming that Dr. Blout was not telling you where you were going to start your professorship.

STRYER: No. [laughter]

CARUSO: So, that was a decision you were going to be, sort of, making on your own?

STRYER: Well, then John Kendrew said, "Hmm." He said, "I got a letter from Arthur Kornberg, and Arthur wants to know who are the good young people here. Should I put your name in?" And I said, "Sure," although I had intended to stay longer at the MRC. My fellowship—Helen Hay Whitney fellowship—had two more years going. But he responded to Arthur, and before very long I got an invitation from Arthur to come to Stanford and, essentially, give a job talk. So, once again, it was the mentor, and again, it was the mentor looking out for my interest rather than having someone keep doing research in his laboratory.

CARUSO: Right. It would have benefitted your mentor more to just keep you there and put you to work.

STRYER: Exactly. Why not? By then I knew some crystallography, so exactly.

CARUSO: Had you heard of Kornberg before this incident? Had you heard...

STRYER: Yes.

CARUSO: Was Stanford on the map for you for a place you may want to go and do work?

STRYER: No. It was not, but I had, of course, heard of Kornberg, and the reputation of Stanford at the MRC was very high. Crick and Sidney Brenner thought it was a very good place. Sidney was very funny. He said, "Well, Arthur's house is high up on the hill, and he can watch you at every moment." But Sidney, with whom I still have contact, thought that it'd be worth going there.

CARUSO: So, you flew out just by yourself, or with your family?

STRYER: I flew out just by myself and visited [...] Arthur and talked to Paul [N.] Berg and talked to others in the department, like Buzz [Robert L.] Baldwin, and was very much taken by the spirit of the department.

And when word got out that I was going to visit Stanford, two other institutions invited me to come give talks. Melvin [E.] Calvin invited me to [University of California], Berkeley, and I was invited to the University of Oregon. And within a few weeks, I was offered jobs at all three places, and I decided on Stanford because I really liked...so, Berkeley had a lot of excellent people, but it was kind of vast, and what I liked was the intimacy of Stanford and the fact that Arthur had brought together a group of people who really were working very well

together. I recognized that I would be different, in that I'd be almost the first with no expertise or particular interest in nucleic acids, but it was precisely because of that—my interest in structure and proteins—that Arthur brought me into the department. And so, I very soon after that accepted the position.

Once again it was an example of where you were handed from one mentor to another. I didn't spend a lot of time applying for positions. There was no application. I gave a talk, met with the members of the department, spent a couple days with them, and it was done.

CARUSO: So, you started your position at Stanford in 1963?

STRYER: That's right, 1963. September of 1963.

CARUSO: Did you have time off in between? Because I thought your fellowship...oh, no, it ended in 1963 at the MRC, so it was pretty much straight from the MRC into Stanford.

STRYER: Via Italy, which was nice. And it was via Rome [Italy], where there was an international crystallography meeting, and there were maybe fifteen or twenty protein crystallographers there. Essentially, everyone in the world—or nearly so—who was working on protein crystallography was there, and I remember having a farewell dinner in the Piazza Navona, and what we all sensed was that everything was going to be transformed. This was the last time that you'd have a group of people who knew each other, who had grown up together in the field, and now it was so successful that it would just break open, and there would be a multitude, and this, kind of, thing would no longer be possible. So, it was both a moment of triumph led by Kendrew and Perutz, and before that by Bragg, and what has followed—the tremendous harvest that has followed. And I remember being very conscious of that, and then coming to Stanford.

CARUSO: What were your requirements as a new professor at Stanford? Did you just...was it a pure research position? Was it a combined research/teaching position?

STRYER: No, teaching was very important. Arthur cared very much about teaching. We had a biochemistry course for the medical students. That was a first-class course. We were encouraged to innovate. We were encouraged to pick certain topics that we thought were particularly interesting. And so, I developed a series of lectures on proteins, giving the latest of what was known on protein structure and protein function. Arthur came to every lecture, and he would say what was good, what was not good. And we also would give a graduate level course, so I would have a course on protein structure where we would have some mock data and students learned how to use a computer and to process the data. We recently had a reunion of

the biochemistry department, and a number of the people who had taken my course still remembered the examples and the problem sets, and we talked about it a few months ago.

Research was very important. We had journal clubs that we would rotate and talk about papers that were not our own, and then, of course, we had a lot of time for research, and it was a wonderful environment. But now I was on my own, and this was where I returned to my [interests in light and] life. I did not do protein crystallography in the department. I had ideas about fluorescence energy transfer and the use of fluorescent spectroscopy generally to study protein structure and dynamics that I pursued.

CARUSO: And how was it actually, physically setting up a lab? Were you given just an openended budget to equip yourself, equip your lab? How many people, in those early years, did you have in your lab?

STRYER: So, the way the department worked was that you did not have what was formally your own space. Postdoctoral fellows and students from different labs, different faculty members, might be in the same room. And so, yes, you were given [what was needed]...I had a small office. I had a lab. I had a place to put some more instrumentation. But everything in the department was available for my use. And likewise, my instruments as I developed them became available for use by other members of the department.

There was no fancy negotiation or discussion about the resources needed to set up a lab. There was no start-up budget. It was just the idea that Arthur would take care of you. Very simple [...]. And he did. And then you'd apply for grants, but you didn't have to wait for grant awards. I was able to hire a technician right away. You could recruit a post-doc right away and graduate students came in through the department, and they selected the labs they wanted to be in. And so, it was right away getting right down to the research on a small and very personal scale. That is, it was where I was really doing things with my own hands for quite a few years and also working closely with post-docs, medical students, and graduate students who did things with their hands [...].

[I recall vividly my first day as a faculty member in late September 1963. That was] a moment of truth. I remember the excitement of walking into the building and also the trepidation. Suddenly the golden post-doc years were over, and now the clock is running, and you have a finite number of years to succeed. And you're now truly on your own, and I remember the sudden feeling, both of exhilaration and of worry, and of pressure, in coming in and walking into the department.

CARUSO: Succeed in terms of...are you talking here about getting tenure? Are you talking about becoming a researcher in your own right? What was it that was...?

STRYER: Standards in the biochemistry department were very simple. You had to make a major contribution in your field of choice, and the standards were those set by Arthur and Paul Berg and Buzz Baldwin and the others. They're all superb scientists. And again, it was not a feeling that you had to publish a lot of papers. So, after getting to Stanford, within about a year or so, I published a paper on a fluorescent probe that could look at non-polar sites, again using a dye.⁷ And the paper was published in a good journal. I wrote the paper and was ready to send it in, and the department administrator, who also [typed manuscripts], said, "Lubert, you can't send it in until Arthur looks at it, and she was really worried [laughter] that I would do something terrible. And she showed it to Arthur, and Arthur thought it was terrific. He had one or two suggestions. But again, Arthur was looking out for the faculty, and he wanted to make sure that everything that left the department was of very high scientific quality.

Then I collaborated with an investigator who had visited the department, and when I published a paper on that, Arthur said, "Why did you publish the paper?" He said, "There's nothing wrong with that work, but it's not the most important thing." [...] What I had published turned out to be correct, but he was right that it did not truly advance science. It's fine for other people to publish stuff like that, but what Arthur wanted was for the people in his department to be publishing papers that really made a difference. It was not publish or perish. It was, rather, to be very careful about what you publish, and that was a wonderful thing. That's great support.

CARUSO: [...] So, you come into your time as a professor. For the first three years, you're doing much of the work, or you're in your lab doing work. You start to take on graduate students and post-docs. How do you envision your role relative to those students? Are you more of a Blout, where you have ideas but the students sit in the lab and do the work themselves? Do you contribute somewhat to that, but you're not necessarily going to be as much at the bench anymore? Or do you want to be at the bench alongside your students and your post-docs? How do you want to participate in your lab?

STRYER: The answer is very closely, and I was doing experimental work. At that time, I got a joint appointment in chemistry, and I had space over in chemistry. One of my first students was Richard [P.] Haugland—Dick Haugland—and Dick would carry out many of the syntheses over in chemistry where we had a lab, and he would carry out some of the experiments over in biochemistry. And so, when he was doing the synthetic organic chemistry of making new fluorescent probes, I wasn't there, and he was using an expertise that he had that I did not have. He was also drawing upon the wonderful synthetic organic chemists that we had then, and have today, in chemistry at Stanford. I had started the synthesis of oligomers of poly-L-proline, [and then] he was carrying them out. I was right next to him and helping with some of the steps. So, it was very much hands on, very much shared. It was only years later that my students and fellows did things experimentally quite separate from my direct participation.

⁷ L. Stryer, "The Interaction of a Naphthalene Dye with Apomyoglobin. A Fluorescent Probe of Non-polar Binding Sites," *Journal of Molecular Biology* 13 (1965): 482-495.

CARUSO: During this period of time, were the politics going on, the broader—not just departmental politics or university politics—but were you at all being affected by broader social and political changes going on in the United States at this point?

STRYER: Well, it was the Vietnam War. Because I had an M.D., I was liable for the doctor's draft. I received an induction notice, went to Oakland to take my physical—which I passed—and meanwhile, the medical school was, through its dean, Robert Glaser, working hard to get me a deferment based on my teaching of medical students and my involvement in important research. And my draft board was in Forest Hills, New York. They were not very sympathetic, but the California Appeals Board reversed the induction, and so I stayed on here.

The Vietnam Era certainly had an impact on science. I would say that we began to have a lessening of the kind of authority structures that were both good and bad. I had benefited from them immensely with Elkan and with John Kendrew and with Arthur. But authority was becoming more dispersed. More of the money was coming from Washington [D.C.]. More investigators were becoming more entrepreneurial and more administrative; they [were involving themselves more in] fundraising. And so, the nature of science was changing while I was an assistant professor. I would say, through my post-doc period, it was a golden era of science in the older mode, where the resources and the talent were, very much, in fewer hands, and if you were in those hands, it was very straightforward to progress. And then things changed—the scientific enterprise became more open, but scholarship was diminished and entrepreneurship was ascendant.

CARUSO: You mentioned your international conference in Italy, and it sounded like it was not just international in the sense that everyone that you knew from the United States and the United Kingdom went to Italy for a conference, but my impression was that you had people from different countries coming together.

STRYER: Exactly.

CARUSO: Did that at all also start to change during this period of time. I know that Russian scientists probably were not participating much in the broader spectrum of things, but with the whole...this is obviously after the end of the McCarthy Era, but the fear of Communism, the Vietnam War itself, did that have an impact on science during your early years at Stanford?

STRYER: Arthur invited the head of the biochemistry department in Moscow [Russia] to come here for a sabbatical, which he did. We certainly did not see much of Russian scientists. I never traveled to the Soviet Union until the Gorbachev era. But we had wonderful contacts with scientists from Japan, from Western Europe and Israel. And [we] went to meetings overseas.

So, it was very international. China was not yet in the picture, and Russia was very specifically excluded from the picture, but part of the international character of science that I had experienced while I was a student was fostered, very much continued, and particularly by the setting here at Stanford.

CARUSO: I know we're pretty much out of time for today. One thing that I definitely want to ask you—and maybe it would be best to pick up with this tomorrow—is [about] your biochemistry textbook.⁸

STRYER: Oh, sure.

CARUSO: It's something I used as an undergraduate, my brother used as an undergraduate.

STRYER: Well, that's great. We'll do that tomorrow because it actually comes chronologically...it starts with Yale [University].

CARUSO: Oh, it does?

STRYER: Yes.

CARUSO: Oh, okay.

STRYER: Well, it starts at the end of my first time at Stanford and then going into Yale. So, it'll come up there.

CARUSO: Okay, all right. Then let's stop there for today.

STRYER: Great.

CARUSO: Thank you.

⁸ L. Stryer, <u>Biochemistry</u> (San Francisco: W.H. Freeman and Company, 1975).

[END OF AUDIO, FILE 1.2]

[END OF INTERVIEW]

INTERVIEWEE:	Lubert Stryer
INTERVIEWER:	David J. Caruso
LOCATION:	Stanford University
DATE:	4 December 2008

CARUSO: So, I think we can pick up where we left off yesterday. We had been talking about your time here at Stanford. One thing I wasn't exactly clear on, you mentioned the birth of your first child in the end of your graduate career, beginning of your post-doc career, but I know you do have two children. Was your second child born...

STRYER: While I was a faculty member at Stanford on the first round.

CARUSO: Okay, so this was?

STRYER: Right, 1964.

CARUSO: 1964. And did that have an impact at all, in terms of the research that you were doing, or affect your scientific lifestyle in any way? Did you have to commit less time to the lab at all?

STRYER: No, my wife was at home full time until the kids were both in school, and so I would say that the momentum of my research, the number of hours I spent was still very much the same. A difference was that we did take fairly long summer vacations, sometimes combined with scientific meetings. That's when we started to visit Aspen [Colorado].

CARUSO: And the students in your labs, were they mostly single individuals? Or did you have married students as well?

STRYER: They were mostly single and often they got married shortly after leaving the lab, so we went to quite a few weddings.

CARUSO: Because one thing I've heard a lot of the younger scholars talk about is some of them wound up being married during their post-doc years or their graduate student years, and that in some ways changed the dynamic that they had with their mentors. But I've never gotten to speak to the mentors and hear what their perspective was on students who were married, or if that changed the dynamic of them working in the lab. But clearly...you received tenure while you were at Stanford.

STRYER: At Stanford, right.

CARUSO: You became an associate professor in the department of biochemistry. But at some point—and this is what I'd like to talk about a little bit—you decided that you wanted to go to Yale University. How did that come about?

STRYER: It came about, I think, for two reasons. One is that I was thinking about the next phase of my research. At Stanford, I was working on fluorescence spectroscopy, developing fluorescent probes, developing fluorescence energy transfer as a spectroscopic ruler. And then I wanted to apply the physical biochemistry to some important biological problem. And indeed, Buzz Baldwin, one of the members of the faculty at the biochemistry department, one day had a chat with me, and he said, "Lubert, what you're doing is very nice, but why don't you go for something really, really important."

I thought about it, and in the course of my teaching, I became fascinated with the problem of visual excitation: how does a retinal rod cell get stimulated by a single photon? And I decided I'd make that the next major effort of my career. And to do that, you need dark areas where you can isolate visual pigments. You need a good deal more space than was available in biochemistry. The biochemistry space was very much set up for enzymology. One could do a little bit of physical chemistry, but it would have been very difficult to have really mounted a major effort and expanded my research group beyond the five or six people that I had in it.

And at the same time, Yale made me a most attractive offer of a full professorship, and with all the space I needed, and so I went there though still feeling that Stanford is a great place and I retained my close ties with Stanford and mounted a new research effort. I think it was very much the right decision for me.

CARUSO: Had you been receiving other offers from other universities during this period as well?

STRYER: Yes, MIT. It was really between MIT and Yale at that point.

CARUSO: And were these in responses to talks that you went out to give? Was this just people knew your reputation, so they contacted you and said...?

STRYER: Right. It was by reputation, and then they would invite me to give talks.

CARUSO: So, how was it moving all the way across the country, back closer to where you had spent so much time for high school?

STRYER: Well, it was very exciting to have my own turf. Shortly after arriving at Yale, it was evident that people looked to me to exert leadership in teaching and to help develop the new department of biophysics and biochemistry. What happened then was that biophysics was located in the non-medical school part of the campus, and biochemistry was, for many years, at the medical school. And the two departments merged—it was the first department that [bridged across...] different schools of the university. Fred [Frederic M.] Richards, a wonderful protein physical chemist, was leading [the new department]. It was very exciting that, [in addition to doing research], I had the opportunity to help build and develop an institution.

I very much enjoyed having the additional space and the scope to mount my research program on visual excitation, which began the day I started doing research at Yale. So, the move gave me an opportunity to suddenly say, "Ah, now's the time to work on something more biological," and that's when I got started on the problem of visual excitation.

CARUSO: Did any of the people who were working in your lab in Stanford make the move across country with you? Was that an option?

STRYER: Yes. A couple people came with me, and but one of them [...], said to me [a few weeks after arriving at Yale], "My gosh, I really like being in your lab, but it's just hard leaving Stanford," and he returned.

CARUSO: And he just worked in someone else's lab under that mentorship? Or did you maintain a tie?

STRYER: We maintained a tie, but he carried out independent research. Now, interestingly, the mover...Stanford allowed me to take a lot of my equipment, and the mover who brought it over to Yale said to me on delivering it, he said, "You come here, and you have a very different feeling. You feel that there's a lot of tradition here, and it's a different feeling from Stanford." And then he looked at me with a smile and said, "And if you ever want to go back to the West

Coast, I'll be glad to take your stuff there." [laughter] There was something impish in that, and I don't know whether he was prescient or just joking. [laughter]

CARUSO: How was it getting involved in a new university setting, with different faculty around you, starting this new biophysics and biochemistry program? It must have been a different feel from the way things were at Stanford.

STRYER: Very definitely. And one of the new elements was college life. So, Yale—like Harvard has its houses—Yale has its colleges, and the collegiate life at Yale is very nice. I became a fellow of Morse College. Vincent [J.] Scully [Jr.], a distinguished historian of architecture, was the master of the house, and I enjoyed going there for lunch once a week or dinner occasionally and partaking in the college life. By being on the main campus—my lab was in Kline Biology Tower on the main campus—I had contact with people outside the medical school. I also had an office over at the medical school. It was a broadening experience. I met humanists and social scientists. It was a broader range of faculty contact than I had at Stanford, and that was very good.

Now, at the same time, I never really liked New Haven [Connecticut], and it just bothered me to be in a less bucolic environment than [Stanford]. But we lived in Woodbridge [Connecticut], which is a lovely area about 30 minutes away from Yale, and I enjoyed our home there. The kids liked the schools, and we had a very good time there. But New Haven was, sort of, like a bone in my throat, and in the end, when I got an offer to return to Stanford, going back to Stanford was really irresistible.

CARUSO: Did your responsibilities change in comparison to what you were doing at Stanford, in terms of number of students you were supposed to supervise or teaching outside or other departmental activities?

STRYER: It was just broader scope, and it was really up to me what I wanted to do. For example, instead of being one of eight fine faculty teaching a biochemistry course at Stanford, I was given the opportunity at Yale to lead the teaching of biochemistry. And that was actually crucial in the development of my textbook of biochemistry, because I decided that I wanted the course taught by just two people. So, the first year I did it, I taught half of it, and Sofia Simmonds—who had a wonderful command of intermediary metabolism—she co-authored with Joe [Joseph S.] Fruton, her husband, a fine classical textbook of biochemistry quite a number of years earlier.⁹ And so, I taught the course with her. The following year, I taught the course with Joan [A.] Steitz, who was a new faculty member that we had recruited and that I participated in recruiting along with her husband Tom [Thomas A. Steitz], and that was a great joy. So, the biochemistry course was a really integral part of my life and a key step in writing the textbook

⁹ Joseph S. Fruton and Sofia Simmonds, <u>General Biochemistry</u> (New York: Wiley, 1958).

of biochemistry, because the notes for the biochemistry course that were handed out to the students—the handouts—became, in essence, the outline of the first edition of my textbook of biochemistry. That was a major change.

I had much more space, so that meant I could have more students, a larger lab, which I did have. Also, my opinion on university matters was given weight, and I was invited to participate in a number of important committees. It was really stepping up in responsibility and broadening the scope of what I was doing.

CARUSO: [...] I noticed you had roughly the same number of publications come out. I don't know, of course, how much scientific time was invested, but roughly the same number of publications. But I was wondering if you were still in the lab. You mentioned that you were taking on more responsibilities. Were you able to be doing your hands-on experiments as much as you had been?

STRYER: Less so. Very definitely...you know, there is a conservation theorem about how much energy and time you have, and it was then that I was making the transition to not doing experiments with my own hands. Now, there were evenings, weekends where I would have a little project...what I would like is to start a little project on my own, and when it looked like it was working, then turn it over to a postdoctoral fellow.

CARUSO: Really? I would have assumed the opposite, that you get the post-doc to get things working to begin with.

STRYER: No, if the idea's really crazy, you have to carry it out yourself. But you're quite right.

Now, the other thing I discovered was that you double the size of your lab, you do not necessarily double your productivity. Also, it was a time that I was exploring new terrain, so that it was not the most productive time scientifically for me. As I think back to the Yale years, I don't recall a truly major publication. If I would set aside five papers, say, "What are the most important papers that I wrote in my life," Yale may not have contributed one of those papers. Yet, what I did there was absolutely critical for my eventual discovery of the first stage of amplification in vision. So, it set the stage, and that's very crucial.

Now, fortunately, the granting agencies, the institution were all very tolerant, and I think one of the wonderful things about growing up in science in the 1960s, 1970s was that you had time, and you were not expected to produce a *Cell* or *Nature* paper every year. Yale was really wonderful for that, very supportive of it, just as Stanford was very supportive of me at an earlier stage of my career. Going to Yale was really the right thing. And then teaching half of a biochemistry course and having responsibility for the entire course—leading into the textbook,

of course—was something that, as I look back, a great part of my life. So, I'm very grateful to Yale for the years I spent there.

CARUSO: You sent me a list of what you considered major publications, and just glancing at it right now, it is noticeable that between...you sent me an article from 1968.¹⁰ The next article was 1980.¹¹ So, it is skipping over the Yale period except the publication of your biochemistry textbook. But is that your perception of your productivity, or were you receiving feedback from other faculty members? Was there someone—similar to Buzz that you mentioned—who came to you and said, "You need to be working on the big thing, not just these papers?" So I'm wondering if it was external to your getting criticism about the science that you were doing, or was that just something you were feeling about your own productivity?

STRYER: It was something I was feeling on my own. I kept getting very good grant support. I kept being appreciated by the scientific community. Stanford wanted me back. And so, I would say that, in those days, people were willing to wait. Once they saw that you could do some good things, they were willing to wait. And what I'm concerned about is that today people are less willing to wait.

CARUSO: From what I've heard from many scholars, it really is publish or perish out there. So, if you're not doing something important immediately, you're going to be out of a scientific career pretty soon, which is interesting to make that comparison. It's only a 30-year period with that transformation.

What was the response to your biochem textbook? As I mentioned yesterday, it's something that I used as an undergraduate. My brother used it as an undergraduate. How did people in the scientific community respond to this new textbook coming out?

STRYER: I think with the first edition, the response was bimodal. First, I think there was a broad recognition that I had broken new ground didactically in using color, and there's a story on that. I really wanted a visually appealing book, and in my teaching, I would draw simple transparencies, simple slides that would depict the essence of a biological process or a metabolic transformation or an enzymatic step. And this goes back to the presentations at the bedside, where you just have a couple of minutes to present something important. So that...I think there was very broad recognition that I had broken new ground in terms of how biochemistry should be taught.

Then there was a division. Those who taught courses for graduate students and those who were going to biochemistry as a profession felt that my book was not on a sufficiently

¹⁰ L. Stryer, "Fluorescence Spectroscopy of Proteins," *Science* 162 (1968): 526-533.

¹¹ B.K.-K. Fung and L. Stryer, "Photolyzed Rhodopsin Catalyzes the Exchange of GTP for GDP in Retinal Rod Outer Segment Membranes," *Proceedings of the National Academy of Sciences* 77 (1980): 2500-2504.

advanced level; that it was not sufficiently mechanistic. And I think they meant that in the sense of catalytic mechanisms, enzyme mechanisms, and metabolic regulation. Albert [L.] Lehninger had a very fine book, and his book did a gorgeous job with metabolism.¹² Mine was, initially, very strong on three-dimensional structure, and so that was my Medical Research Council background. I would say that the response was bimodal, very appreciative, but it made a stamp almost immediately, within a year. Sales were strong, and a lot of people were talking about the book.

CARUSO: And so, this was, pretty much, at the end of your time at Yale that it came out. 1975, 1976 time period?

STRYER: Exactly.

CARUSO: So, as you mentioned, you did wind up going back to Stanford. Actually, you were the chairman of the new department of structural biology. Is that how they got you to come back?

STRYER: That's how they got me. This building that we're in was built in 1976, so there was new space. There was a new opportunity, and it was to lead a department of structural biology that included the division of human anatomy that taught anatomy to medical students. The department had the responsibility for the teaching of cell biology, and the idea was to develop a faculty group who would be studying three-dimensional structure, who would be interested in the dynamics of biological processes. And so, I was recruited to head that department.

CARUSO: Were you at all nervous about taking on the additional responsibilities associated with being chair?

STRYER: Yes, very definitely, particularly because it involved a broad range of responsibilities, and anatomy was not exactly my strength or my major interest in medical school. So, it required that I pay attention to an area—to make sure that it was done well—where I did not have an instinctive feel for it.

CARUSO: And how did you...

¹² Albert L. Lehninger, <u>Biochemistry: The Molecular Basis of Cell Structure and Function</u> (New York: Worth Publishers, 1975).

STRYER: And also, when you become a department chairman, you get into the minefield of medical school politics. So, I recognized that it was new opportunities and new problems that I was stepping into.

CARUSO: And what impact did this new position have on your research? Because you did mention that the time at Yale set the stage for the application research, and I'm assuming it really started to take off after you got back, or once you got back to Stanford.

STRYER: It did. And actually, though I had all this administrative stuff going on and a lot of challenges (administrative), my research program flourished. A lot of things that I had initiated at Yale came to fruition. But without the Yale background, it would not have worked. Those were terrific years [at Stanford]; the work on transducin, the elucidation of the first stage of amplification and vision came in those years.

CARUSO: [...] Did people in your lab follow you from Yale back to Stanford?

STRYER: Only one person came, amazingly, because they were at a stage in their career where they went off to new positions, some to academic positions. So, I was again starting from scratch, but I got some very good fellows. I got some good students and everything worked out.

CARUSO: Your lab was still relatively well populated even though you were starting off.

STRYER: It took a while, but that may have been very good. In other words, I was back down, for a few weeks, to a lab of one, and then it began to increase in size.

CARUSO: You were still in the lab doing experiments. Even with the new responsibilities, you didn't have that...

STRYER: I was doing experiments that involved instrumentation but not experiments that involved biochemistry or chemistry, so that it's much easier...to be specific, I was still very interested in the dynamic of proteins, and I was using fluorescence spectroscopy, and I would carry out fluorescence experiments, and I'd carry out nanosecond flash experiments. That I would do with my own hands, because you can go in there, do that for an hour, then take care of some administrative stuff. But if you're in the middle of an enzyme preparation or doing things with rhodopsin, you can't stop in the middle of the day. And so the nature of what I did with my own hands changed.

CARUSO: How did you feel about that change? Were you becoming more comfortable with not being in the lab?

STRYER: Yes, I would say so, that the idea of having students, colleagues who would really be developing a project more on their own. I became very comfortable with that. I did not have to micromanage. I realized that I was contributing to the university, helping the medical school with many things outside of the department.

And then, of course, once you write the first edition of a textbook of biochemistry, it's almost something for life, and so no sooner are you done with the first edition than you begin to start thinking about the second edition. And what happens is that whenever you go to a seminar, whenever you hear about a new work of science, you ask yourself, "Now, how does that fit into my textbook? Should I include it?" And so, it was very much on my mind.

CARUSO: [...] I'm guessing you were working on it probably earlier, but the second edition didn't come out until 1981.

STRYER: That's right. Either six or seven years between editions.

CARUSO: And you remained chairman of the department until 1979?

STRYER: Very short time because it really wasn't fun, and then I turned it over to one of my colleagues who I brought here, Jim [James A.] Spudich, and Jim carried the ball on it.

CARUSO: What was it about the chairmanship that wasn't fun for you? Was it just all the added responsibility?

STRYER: I think it was the politics. Sitting through executive committee meetings of the medical school, which occurred very often, was just excruciating. I never really liked committee meetings. I enjoyed taking care of things administratively by having a short chat with people, coming to a consensus, and then executing on it. I like to consult people, but I hate having to sit in the room for many hours and have a painful discussion that often leads nowhere. I realized then that, while a position of chairmanship or a higher position in the university had a certain prestige and gave certain opportunities, that it really was not my thing.

CARUSO: Did you feel that, in any way, the dynamics of the university politics had changed? I'm just thinking back to some of your descriptions about what Dr. Kornberg was able to do. He liked a scientist; he brought a scientist in. Was there still that open system of...?

STRYER: No, it had become much more, I would call it, corporate, much more...authority was fragmented, coalitions were constantly changing, the ground was never quite firm.

CARUSO: And do you think this was at all in response to any broader social and political changes going on in the United States at the time? Or was this just within the Stanford system, these...?

STRYER: Oh, no, it was much broader, and as we discussed yesterday, I think the Vietnam Era brought in quite a few changes, some towards a more open democratic process, but at the cost of collegiality and being able to move very quickly with a minimum amount of formal administrative stuff. And also, the nature of the university community changed and epitomized by...I was thinking back. When I came to Stanford, we knew nearly everyone on the faculty, both the clinical and basic science faculty. There were social events where the faculty came together, and it was a very, very nice community. But then the hospital expanded, many more people came in, and it got to a size where the circle that you knew was much smaller, and that changes things.

And also, I think, more of the resources came from grants, and so people were spending more time away from Stanford. The amount of time people are on the road increased dramatically in those years. Before that, you would stay at your lab unless you were giving a seminar or going to a major federation meeting or something like that. But then, people had to promote themselves in order to create the reputation and the buzz that would enable them to get large grants.

CARUSO: So, when you say they were on the road, do you mean that they were visiting other labs, doing work in other labs? Were they giving talks?

STRYER: They were giving talks, and they were being very visible, and we see that very strikingly today. If I go to Washington or New York, come back on a plane, there's always a Stanford person on the plane. I have met many Stanford people at the Frankfurt Airport. It's quite amazing where you meet the faculty...in Tierra del Fuego. They're on the move, and this is true of the entire academic community.

CARUSO: After stepping down as the chairman, I'm assuming that gave you a lot more time, well, one, to work on the next edition of your text book.

STRYER: Exactly.

CARUSO: But did it also give you a chance to get more into your lab and the activities of what your post-docs and students were doing?

STRYER: Very much so, yes, and those were very good research years. I enjoyed them tremendously—the 1980s.

CARUSO: And what role were you taking with regard to the research that was going on? Were you still more hands off, in terms of just letting the lab run on its own? Or were you more in there on a regular basis, talking to people and looking at their experiments?

STRYER: I think both. I liked it when a post-doc would get an idea and really flesh it out and develop it. So, an example was that one day I saw an article in *Nature* where an English scientist described calcium spikes from liver cells that were stimulated with a hormone.¹³ Instead of getting a sustained rise in calcium, what he observed were oscillations. I discussed this with one of my postdoctoral fellows who had just arrived, Tobias Meyer. He had a very good background in physics, and he looked at it, and said, "There must be some positive feedback. There must be some delayed deactivation." And he started putting together a model of what might be going on. And then, for the next few weeks, we talked about the model, and we talked about experiments. And so, this was a case where he clearly had a critical new idea that I did not possess and where I gave him the freedom to pursue it and then very much participated in the development of the model and its experimental realization and in the writing of the paper.

In other cases, the research was something where I would carry out a pilot experiment with my own hands, and I would tell a student, "Well, here's what I've found. Does this interest you?" And then I would follow it more closely.

CARUSO: So you really wanted to have a mixture of involvement? You were not necessarily in every single project from the basic level, from the beginning, but varied it depending on the type of project and the stage of the person working on it, I assume, as well.

¹³ N.M. Woods, K.S. Cuthbertson, and P.H. Cobbold, "Repetitive Transient Rises in Cytoplasmic Free Calcium in Hormone-stimulated Hepatocytes," *Nature* 319 (1986): 600-602.

STRYER: Right. But I was really in the lab actually looking at data acquisition and fixing computers and...fixing things was very much my job. [laughter]

CARUSO: I've heard from a few scholars that computers weren't necessarily something that was adopted readily in the labs that they were working in. Their advisors didn't necessarily know what the box was supposed to do. Some students I know of—Scholars that I know of—went in, and they were the ones tinkering with the computers to show their mentors what it is the computer was for. But it sounds like you were very much an early adopter of having those technologies in the lab. Was there a reason?

STRYER: Yes. First, as I said yesterday, Ed Purcell got me going with computing. He indicated that it was a great way of doing simulations, that I have got to learn it, and immediately I took to it and enjoyed it. Then, at Stanford, in addition to Arthur Kornberg, Joshua Lederberg was a big influence. He was the head of the genetics department, and Josh was a very early user and developer of computer approaches to problems of biology, and he said, "You need to have a computer at home." I remember being networked to Stanford. This was around 1966 and there was this huge IBM terminal in our home. A phone connection was made over an acoustic modem, where the computer actually made different tonal sounds that were carried over the phone line. And the phone people, it took them two days to install it. The phone truck was parked outside our home [for two entire days]. Now, the only place we had in our small home in Palo Alto [California] to put this thing was the bedroom, and after a few weeks, Andrea said to me, "It's either me or the computer," and the computer was sent back to Stanford. [Having a computer at home] was very disruptive. In the middle of dinner, I would jump up to see a job finished or start one—it was not the greatest thing for home life. But I was very much tuned to computers early, starting as a postdoctoral fellow and then at Stanford. We used computers to handle our spectroscopic data and were always at the cutting edge of computers. I especially like computers that were not centrally located and having a HP [Hewlett-Packard] computer-or then a DEC [Digital Equipment Corporation] computer-right in the lab was very important, I attracted post docs and graduate students—some were in electrical engineering—who loved this kind of stuff and wanted to put it to work on biological questions. So indeed, computers were very central to our research very early.

CARUSO: In those early years, or at least when the PC—personal computer—revolution really started to take off in the late 1970s, early 1980s, were you doing your own programming? Were you creating your own...?

STRYER: Oh, yes, and this goes back to my days with John Kendrew. I was writing FORTRAN programs for processing crystallographic data, and I always wrote my own programs. I used some packages later, but I very much enjoyed programming, and that's something I still enjoy. It's almost a form of recreation to write programs, and I'm involved in that maybe a couple hours a day right now.

CARUSO: Since you have a lot going on in the next few decades, I figured it might be easier to talk about decades as a whole since parsing it out to individual years or time periods would be a little difficult for me.

STRYER: Great. Yes.

CARUSO: So, in the 1980s, this is when you're working on the amplification research.

STRYER: Correct.

CARUSO: What are you discovering during this period of time? How's the work going for you in terms of that?

STRYER: Well, there was a really magic moment where, in the course of two days or so, we elucidated the first stage of amplification in vision. We discovered this GTP [guanosine triphosphate]-binding protein that we named transducin, and we found—this was with Bernard [S.] Fung, a wonderfully gifted post-doctoral fellow, and then James [B.] Hurley came into the picture—we discovered that a single photon can lead to the activation of five-hundred molecules of transducin. So, for the first time, we knew what photoexcited rhodopsin was doing, and after years of working on [visual excitation], it was just great to have the answer. It's one of those magic moments that comes only maybe two or three times in a lifetime, and it was a wonderful moment.

And then we worked out what activated transducin does next in the transduction cascade: it activates a phosphodiesterase that hydrolyzes cyclic GMP [guanosine monophosphate]. So, in the course, initially, of a few days and then of a few weeks and months, we worked out a key part of visual excitation.

CARUSO: Was this prior to being elected a member of the National Academy [of Sciences]?

STRYER: Shortly before. That's right.

CARUSO: So again, a lot is going on during this period of time. I also know that you're rewriting your textbook, which comes out in 1981. You also are on the scientific advisory board of the Jane Coffin Childs Memorial Fund [for Medical Research]?

STRYER: Right.

CARUSO: And president and scientific director of—and please correct me if I'm wrong—Affymax, [Inc.]?

STRYER: [...] That came right at the end of the 1980s.

CARUSO: That's right. 1989 is when that happened.

STRYER: And so, one could look upon that as the next era. That's a good demarcation to the next era.

CARUSO: And member of the National Academy of Sciences. How was it being elected as a member to the National Academy? Did you know about it in advance?

STRYER: Well, I was hoping for years and years, and I had a few clues, but it was a lovely feeling but almost the kind of thing that I felt, "Oh, it should have come a few years earlier," but I certainly did enjoy it, and yes, it was very nice.

CARUSO: And what's involved? I actually haven't spoken with a National Academy member, but what is involved in being a member of the National Academy of Sciences?

STRYER: Well, it was set up by Abraham Lincoln to provide advice to the government during the Civil War. So, it's the nation's advisor on science. It's quasi-governmental, [while being a] private club, a self-perpetuating group. And the Academy does many wonderful things in education, in public policy, in providing impartial and highly informed advice on important questions of science and technology. And so, in addition to being an honor, the Academy carries with it an obligation to contribute to this country in terms of providing advice, so that I was particularly interested in the educational aspects. And some years later, I led a study called BIO 2010 on the future of undergraduate biology education for people who are going to become research biologists.

[In the] Academy there's a nice fellowship. The annual meeting is very enjoyable. There're usually good talks, and the biochemistry section—that was the one that I initially joined—was a place where I had an opportunity to meet other biochemists. So, it was a very nice watering hole, and the annual meeting has a garden party where you get to meet a lot of your friends in one place. It was a very nice event, and I think it's very moving to sign the Great Book, where each member signs on being inducted, and it includes [Albert] Einstein and many heroes that I have.

CARUSO: And one question before we move on to the next stage, as you had just mentioned. In 1985 Dr. Lederberg is involved with this Pew [Scholars Program in the Biomedical Sciences], which I know you become part of—an advisory committee member—in 1991. Did you have any awareness at this period of time that Dr. Lederberg was involved with the Pew Charitable Trusts and starting this scholarship program?

STRYER: No, I did not. Now, Josh had moved to the Rockefeller University—I forgot which year—to become president of the Rockefeller. [I] maintained contact with him, but I was not aware of his Pew activities until he called me and asked me to join the advisory board.

CARUSO: Okay. Because I know that...I'm pretty sure that from the first year the Pew was an institutional-level grant, and I'm assuming that Stanford was probably one of the institutions, so I wasn't sure if...?

STRYER: I was not really aware of it.

CARUSO: Okay. So, as you mentioned more in 1989, this is the end of the 1980s, you become the president and scientific director of a research institute. So, can you tell me a little bit about [that]?

STRYER: I was interested in the biotech industry. I saw some exciting, thriving biotech companies develop here, though I was not part of them—companies like DNAX [Research, Inc.], that was in immunology. And during the 1980s, I developed with two collaborators—Alex [Alexander N.] Glazer at Berkeley, and Vernon [T.] Oi, a postdoctoral fellow in my lab—we developed a new class of fluorescent labeling reagents that took advantage of an algal protein [that harvests light in photosynthesis]. These are the phycobiliproteins, and they are intensely fluorescent when they're taken out of the cell and not transferring their energy to the photosynthetic reaction center. And we coupled these [brilliantly fluorescent molecules] to biological recognition molecules such as antibodies, and these became very nice reagents for labeling of cells and molecules, and they were patented by Stanford. So, I became aware of the potential for applications of the sort of things that were going on in my lab, and I was interested in that.
And then Alex [Alejandro] Zaffaroni, a wonderful scientific entrepreneur-he had helped start Syntex and develop the contraceptive pill, he then started a number of companies here—wanted to develop a company devoted to combinatorial synthesis. He felt that the drug industry needed to have a much larger repertoire of molecules, of chemical diversity, and he wanted to develop facile ways of generating chemical diversity. And some of these would, of course, involve the use of light, so he invited me to come on board as a scientific advisor, and within a few weeks I was meeting some of my colleagues from electrical engineering here and applied physics and some people from Berkeley. It was just a very exciting group and people were bubbling with ideas, but nothing was getting focused. I was really enjoying it, and one day Alex said to me, "Lubert, why don't you take a leave of absence from Stanford and spend a year here and help get things going? I think you might enjoy it." And I thought about it, and at the time, I would say that nothing truly exciting was going on in my lab, we had solved something I had wanted for many years—how a photon leads to a nerve impulse. So, this new opportunity looked very interesting. I accepted the challenge that led to my recruiting people. It was a remarkable environment. I was given great scope. It was located right here in Palo Alto, so I was able to return to this building one day a week to maintain my research program at Stanford. [At the same time], I was able to—with a very talented group of people—develop lightactivated parallel chemical synthesis, which made possible the synthesis of DNA arrays using light to direct the pattern.

That was an extremely rewarding year. I [subsequently continued as a scientific advisor to] Affymax—the part that led to DNA arrays became Affymetrix, [Inc.], and Steve [Stephen P.A.] Fodor, the extraordinarily talented post-doc that I recruited, grew tremendously, both as a scientist and as a leader, and he eventually became the chief executive officer of Affymetrix and led its development of DNA arrays.

CARUSO: I know you mentioned that you technically took a leave of absence from Stanford, but you were still coming to your lab. How was it handling the issue of this university and private industry divide? You did have two things going on, which I'm assuming that by this time universities were starting to get a little more involved in terms of patents that were coming out of the scientific work of their professors. How did you handle [and] how did Stanford handle the fact that you had your foot in, seemingly, two different...?

STRYER: The first is that there was a wall [between my laboratory at Stanford and Affymax]. I never had a student or post-doc visit me at Affymax; I would always come here. Second is that nothing that was carried out in my [Stanford][lab would be used at Affymax, and later at] Affymetrix, unless there was a formal technology transfer licensing agreement. We had developed some single molecule detection methods, and so Affymax licensed that from Stanford, so Stanford knew exactly what I was doing. The way it was handled was that you avoid the grey zone. You totally avoid the grey zone so that there's a complete separation. My program then was pretty much vision, and vision was not what Affymax [or] Affymetrix was doing. Now, there was a little bit involving high-sensitivity fluorescence detection, and that was open on the basis of a licensing agreement.

CARUSO: Okay. Because I can see it being a difficult thing, even if you want to make that grey area that you don't want to get into, there is, of course, the potential that you're sitting in on something in one location—you're the source of knowledge—and it's kind of hard for you to go back to your lab and not necessarily talk to your students who might benefit from that. So, it must be a difficult...or, it could be a difficult position for one to be in.

STRYER: That's right. And I would say that I was so careful about that in the years following that we never used DNA arrays in our research, and I think something was lost by that.

Now, right now, there are members of the department who use it, and I can look with pride on it. I can help them in terms of my insight into the arrays. So, there is, in fact, a downside if one is too careful, and it's a very fine line. But I'd rather be on the side of the line of having a gap, losing something, than where you get into a situation of a really bad conflict.

CARUSO: Better to be a bit more cautious, even if there's...

STRYER: Be a bit more cautious. There are enough things to do in science. [laughter]

CARUSO: You did mention that this period of time, in some ways, marks a transformational point in your career. You solved the problem that you had been interested in for quite some time, you started in this new research institute to develop arrays, and it also looks like you started to take on, in the 1990s, a fair number of other commitments.

STRYER: Exactly.

CARUSO: [...] Were you making this shift consciously? Is this something that you wanted to pursue? Or was this that many more or other doors were opening for you, and you decided to take on these opportunities? Because I know that ultimately they would take you away from your lab. They had to take you away from it.

STRYER: Yes, but they took me away, perhaps, because I wanted to be taken away. And I think, by and large, people are not truly coerced; they may be seduced, but they're not coerced. And I think that, you know, I've always been interested in the broader picture. My textbook certainly always looked at the broader picture. And so, yes, I think that I found these broader responsibilities and opportunities attractive, and I think there was nothing that grabbed me the way, "How does a single photon lead to a nerve signal?" And that, perhaps I had not thought

about what I would do once that was solved. [My vision program had] a long incubation period, and just as my fluorescence energy transfer work had a very long incubation period, the incubation for my fluorescence energy transfer work came in my freshman year at the University of Chicago.

I was a waiter at the Quadrangle Club, the faculty club. James Franck, [1925] Nobel Prize [in Physics] winner and the discoverer of fluorescence energy transfer—going back to 1923—I served him dinner every night, and he always ordered the same thing—a lean veal sandwich—which made it possible for us to talk about other things. He wanted to know what courses I was taking, and I told him I was taking chemistry from Harold Urey, and then he started talking science to me, and then we started talking about excited states and about energy transfer. And with a glint in his eye, he said, "and someday, Lubert, maybe you'll work on energy transfer." And when that day came, when I was a medical student, really got closer to it, I did visit him and told him about it. So, I think the most important scientific projects in my life had a very long incubation period. There is a moment when you get the answer, but it's preceded by a commitment to the problem and the development of techniques to solve it, and also there's a big element of a random walk, where we were in the wilderness many years with rhodopsin; we were clueless as to what it was doing. But if you stay on the court long enough, you're rewarded…and so, I don't think I had in the 1990s a developed plan for pursuing another area of science.

CARUSO: So, these were opportunities that...obviously you were still intrigued by science, but you didn't necessarily have that one thing.

STRYER: A passion. The one thing, a passion. Right. And I also think there are a finite number of these that you can have in a lifetime.

CARUSO: You did mention that Dr. Lederberg called you up one day and asked you to be a part of this Pew Scholars in the Biomedical Sciences Advisory Committee. You started as an Advisory Committee member in 1991 and stayed on through 1996.

STRYER: Correct.

CARUSO: And yesterday, you also...while we were talking about the MRC, you had mentioned that you wanted to revisit something about the great support at the MRC in relation to this Pew Biomedical Scholar program. And so, what I'd like to do is just spend a little bit of time exploring more your involvement with the Advisory Committee and the program more generally. So, can you tell me a little bit about what Dr. Lederberg told you about this program? Do you remember what he...?

STRYER: Well, first, when he called me and told me he'd like to have me on the committee, there was just no question. I always admired what he did, beginning with his fantastic experiment with Esther [M. Zimmer] Lederberg, the velvet transfer experiment of bacteria that showed that antibiotic-resistant bacteria were there before they were ever exposed to antibiotics. So, I knew about his research perhaps when I was in high school or shortly after that, and he was a figure that I was, just, in awe of. And then when I came to Stanford, we would get together quite often. We had lunch together maybe once every two weeks,[...]—sometimes with others—[a] very freeform discussion. It could be about anything [relating to] science. Sometimes it was about ethical problems in science—about transplants—and sometimes it was about computing.

So, when he told me that he was interested in nurturing young scientists, would I join him on this advisory committee, I of course said yes, and it was extremely rewarding being on the committee with Josh and with another of my heroes, Torsten [N.] Wiesel. And so, our job was to, first, pick the most talented young faculty members in the biomedical sciences, and second, and I think equally important, help nurture them by giving them a broader support community. The annual meeting too is a critical event because it brings together the Advisory Committee with the fellows, some of the alums, and it was always just a fabulous meeting hearing the talks. But also, just the informal discussions that took place on the beach—always held in a nice place. I can remember the exact spots where I had stimulating discussions. For example, Peter [S.] Kim, I remember we were waist high in water, enjoying the warm water, and I remember talking to Rod [Roderick] MacKinnon at a particular rock [on the beach at Cozumel]. I also remember exploring Costa Rican rainforests with Harvey [F.] Lodish and Bertil Hille and their spouses...[The advisory committee meetings had a] wonderful scientific intensity and very serious deliberation about who are the most talented people, and then [we had the pleasure of interacting] with them.

And I was looking at the list of people who had been there the years, and I realized that I've maintained contact with quite a number of people like Rod McKinnon, Steve [Stephen J.] Elledge, and John [J.] Ngai at Berkeley and Bill [William I.] Weiss, of course, right here at Stanford, Seth [A.] Darst and Kevan [M.] Shokat, just a wonderful group. And so, it's the start of a lifelong broader community, and you see people develop. You see them...so, I served for quite a number of years on the Howard Hughes committee, and you see people at different stages of development. With the Jane Coffin Childs, they're applying for a post-doctoral fellowship. With Pew, you see them a few years later. There were some in the Jane Coffin Childs group who then became Pew Scholars. Then some of the Pew Scholars became Howard Hughes investigators. And so, you watch them, and you're associated with them for 20, 30 years, and that's really wonderful. I admired the leadership provided by Josh and then by Torsten.

CARUSO: What year did Dr. Wiesel take over?

STRYER: Maybe halfway, something like that, yes.

CARUSO: Early 1990s, but like 1993, 1994, around.

STRYER: Yes, right.

CARUSO: So, a couple of questions that I hope you could talk a little bit about. Of course, every year institutions submit candidates for nomination to receive this award, and every year the Advisory Committee has to go through a number of applications. I know, based on what Torsten described, I think the Advisory Committee had to go through...things were weeded down to a certain number beforehand, and then the Advisory Committee went through a smaller batch and then narrowed those people down to twenty. Did Dr. Lederberg have the same, sort of, practice, or did you see all the applications that were submitted when Dr. Lederberg was...?

STRYER: I think some may have been taken out administratively. But I think that if an application met the formal criteria and the person came from an eligible institution and it looked real, we saw it. I don't think there was a stage of weeding out before we saw them.

CARUSO: You mentioned eligible institution. Do you know what made an institution eligible?

STRYER: I don't remember [...].

CARUSO: Okay. Yes, from what I understood, I think it had to do with...the levels of NIH [National Institutes of Health] funding at the institution made an institution eligible, and I wasn't sure of the origin of that idea, because in some ways it seems like there might be some biomedical scholars who are not eligible just because their institution hasn't done a whole lot in terms of applying for NIH funding.

STRYER: But my recollection is it was broad, and if you actually look at the institutions where the fellows came [from], it was a very broad cross-section of the biomedical world in the United States.

CARUSO: [...] In your mind, did [the applications] differ at all from some of the grants that you had submitted or some of the other committees that you might have served on—whether or

not they be graduate student committees or things like that—did the applications in some way differ or read differently?

STRYER: By 1991, the applications were often longer, although in the case of Pew they may have still been fairly brief. But they had more technical detail, and the one thing that was striking was that for many of the fellows, for the scholars, they were [carrying out research that was] related to what they had done for their thesis or in their postdoctoral years. So, there wasn't a total break.

Thinking back to my career, Elkan Blout: optical rotatory dispersion of synthetic polypeptides. Then I went to the Medical Research Council, worked on x-ray and crystallography. Came to Stanford and did something different: fluorescence energy transfer, fluorescence spectroscopy.

What we saw then, certainly by 1991, was a more conservative path in which students and then applicants for the Pew would be, by and large, proposing things that were related to what they had done at an earlier stage in their career. In order to get an NIH grant, you had to have preliminary data, and you can get...I never would have gotten a fluorescence energy transfer grant at Stanford in the 1960s had they applied that requirement. So, that was a major change. Another was that technically I think this group of scientists by 1990 were just terrific. They had command of many techniques and they were perhaps stronger technically than our cohort, let's say, for the Helen Hay Whitney fellowship back in 1962 or so. So, there was a change.

CARUSO: And what was the overall decision-making process like, and did it change depending on who was chairing the committee?

STRYER: There were either two or three primary reviewers who would present, in some depth, what the applicant's background was, what the proposal was about, and what the evaluations, the letters of recommendation were. And with letters of recommendation, you have to know who's doing the recommending. So, if Fred Sanger said someone is good, well, that means this person walks on water. And then, with other people who did the recommending, we knew there was a lot of hyperbole, so there's an element of discounting based on your knowledge of who's writing the letter. You've been around. You've seen a lot of these letters, and so it's a very important part of the process.

And then, you come up with, "This is one of the best applications we have," or, "This person's just not on the level," or the more difficult case, "The person's somewhere in the middle," and then everyone in the room really starts paying attention because these are the critical decisions. Then the second person can either agree/disagree, and then you had a pretty lively discussion of people who knew something either about the field or about the applicant or about the people who were writing the letters of recommendation. And there was usually a very

good consensus at the end of this discussion. And then, of course, exactly where the dividing line is is always somewhat arbitrary and subject to chance, but I would say that we all felt good about the process.

CARUSO: So, I'm guessing, roughly, let's say fifteen to eighteen were pretty easy to say, "They should be funded." There was probably a fair number that you said, "Well, those aren't going to be funded." But there was that little portion that was on the edge that it was hard to decide between?

STRYER: Well, no, it's a broader portion that's on the edge. For ten [of the applicants], it's absolutely clear, and then there's a group of twenty that are really in contention for the next ten awards. And these are, of course, rough numbers [...], but it's a bigger group because everyone applying is really very competent, and what they're proposing is quite worthwhile.

[...] I, first of all, look for an early spark of creativity and all I care about is, "Let's put on the table the one best thing that the person has done before." And now, let's ask, "What is the person trying to do?" And if the person is trying to do something exciting and the person has done something important before, well, that's a sure thing. I don't care what they say about how they're going to accomplish it. I'm just not interested in the methods they use, their approach. They'll figure that out. But what I care about is the goal, and the past is a predictor, to some extent, of the future.

CARUSO: So, in some ways, it sounds like you were interested not necessarily in funding the science, per se, but the scientist.

STRYER: The scientist, the person. Exactly. Very much so. Very much so. Exactly.

CARUSO: And did that change at all under the leadership when Torsten started, or was it pretty much the same?

STRYER: Very much the same.

CARUSO: Same process, same idea.

STRYER: Oh yes. No, his scientific standards, his outlook on young people, were very similar to Josh's. Very similar.

CARUSO: Okay. Would you say—since you have had a fair amount of experience with other foundations and awards—does the Pew stand out in some way from those other private foundation awards? Or is it along similar lines to...I know, for example, Howard Hughes is funding someone in a later stage of their career, but beyond the age of the scientist or the period in which you're funding the person, is there something that stands out about the Pew compared to other awards that you've been involved with? Or are they all really trying to achieve the same thing in terms of pushing...?

STRYER: Well, fortunately, they have chosen [to support scientists at] different stages of their development. These foundations are a wonderful expression of something that is truly American in character. Private philanthropy in this country has just been absolutely incredible, and so you have the Jane Coffin Childs and the Helen Hay Whitney for the post-doc, and then you have the Pew and a few others in the first academic appointment stage.

CARUSO: The Searle [Scholars Program] things like that.

STRYER: The Searle and ones like that.

Now, I think what I really appreciated about the Pew was that, at the highest level— Rebecca [W. Rimel]—a deep interest and commitment, and that was felt from the very start. And so, you're not wondering, "Is this thing going to go out of business in a year or two?" There's a feeling that the parent entity is really committed and really wants to know what is going on and participates, and that's a great feeling.

They each have their personalities in the very best sense of the word, and it's been a great privilege serving on each of these, and they are different, but they have a common purpose, and they do a great job.

CARUSO: The annual meeting that you did mention about the Pew, did other organizations have meetings similar to...?

STRYER: Some do, and some don't. Now, the ones I've been on, yes, they all do. But, for example, I was shocked to find that the MacArthur Fellows do not get together. I would think that would be a blast. To have Mary Zimmerman talk about theater, it would be incredible. So, I think they're missing something at MacArthur [Foundation]. But the ones that I've been associated with, each of them has these annual meetings, which have different flavors, but they are a key part of creating a sustaining community. Absolutely wonderful.

CARUSO: Also during the 1990s, just to move on a little bit, board of trustees of the Helen Hay Whitney Foundation, board of directors for the McKnight Endowment [Fund] for Neuroscience, and by the end of the 1990s, you also received an honorary doctorate from the University of Chicago. I'm assuming because you were a former student there?

STRYER: An alum, yeah. Right.

CARUSO: But you also received the [Intellectual Property Owners] Distinguished Inventor award, and you also became the chairman and chief scientific officer at the end of the 1990s for Senomyx.

STRYER: Correct.

CARUSO: So, during this period of time, did you...I know that publications were still coming out.

STRYER: But more slowly.

CARUSO: But more slowly. How did you envision yourself as a member of the scientific community during this point? Clearly, you were still participating in research, but it seems like you were really taking on new and different roles with regard to science.

STRYER: They were roles of creating new structures that were doing interesting things, rather than have my laboratory do interesting things. So, I had mentioned that I had an aversion to administrative work, but I did take over—first with Affymax—but I did it for a year. Once again, three years as department chair of structural biology here, then just one year as president and chief scientific officer of Affymax. But it was a critical year; I got it going.

Then I got Senomyx, a taste and olfaction company, going; there I was interested in chemosensation. That complemented my interest in light. The techniques used involved receptor discovery. It involved combinatorial chemistry. So, scientifically it was part of a continuum, but with a goal of actually affecting the real world: making more healthful foods, salt enhancers, sweet enhancers, things like that. Once again, I took a leave of absence, spent some time in that. But at that point, my laboratory was winding down [...] as these activities became a much bigger part of my life, and the pro bono side became a bigger part of my life.

CARUSO: Given that, why did you only stay on for two years at Senomyx? Was it that you had the taste for getting things started, but you didn't necessarily want to remain in those administrative...?

STRYER: Well, unless you're Secretary of State, Stanford limits a leave of absence to two years.

CARUSO: Were you enjoying the work there? Was it ever tempting just to say, "You know what? I've had my time at the university. I got to do what I wanted to do. Now I'd like to play a little more in this private industry"?

STRYER: No, I still very much value [academic life though] I don't have a lab now. I've been emeritus for about four years or so, but I care very much about Stanford. I spend time helping Stanford retain good faculty, attract young people. I enjoy talking to my colleagues here. I pick which ones I talk to. I enjoy the university life, and I value the connection, and I like doing things in the nonprofit sphere as well as the for-profit sphere. I did not want to lose my connections.

So, what I did was I stayed on as chairman of Senomyx's Scientific Advisory Board. Actually, it was only yesterday that I concluded that relationship—and it was very satisfying seeing where they've come to—because I decided that I wanted to have more time for photography and more time for adventure travel, which I'm doing a lot of with my wife Andrea. We go to interesting places around the world, and I don't want [too many responsibilities]. So, this is now another transition. I also retired from the Howard Hughes Medical Advisory Board just a few months ago. Those were two things that I shed as part of a plan.

CARUSO: Part of my line of questioning comes from a lot of the other interviews that I've conducted with Scholars, and it's something that I am curious about, but many of the Scholars have...or see the university/industry divide as a potential major decision—especially now, for the students that they're advising. [...] A lot of the Scholars, kind of, look down on going into industry. It's not entirely clear why, and they make it sound like their mentors are the ones that fostered that negativity towards going into private industry. And so, I'm wanting to see things from someone who has held positions in both, and clearly you returned to the university as your preferential area. That's what I was trying to get an understanding of with my questioning. But clearly, by the end of the 1990s, you were still serving on the scientific advisory boards, but you were clearly shifting away from things, and you were taking on other new things. This is when you became the chairman of the BIO 2010 committee for the National Research Council. Can you tell me, in a little more detail, what occurred over that two-year period and what it is that you were trying to accomplish with looking forward in terms of, I believe you said, education...?

STRYER: Right. So, this initiative was set up by Bruce Alberts, who is an outstanding scientist. He was president of the National Academy of Sciences for 12 years. His textbook, [Molecular Biology of the Cell], is an outstanding work. Bruce recognized that there was a real disparity between the advances in science and how our educational system was responding to them.¹⁴ And so, he asked me to chair a National Research Council [of the] National Academy committee that would make recommendations about what education should be like for future research biologists.

This was a study supported by the National Institutes of Health, so it was one of the last things that Harold [E.] Varmus did before leaving the NIH. They put money into it, and Tom [Thomas R.] Cech and the Howard Hughes Medical Institute put money into it. And we had a two-year study involving about 20 or so committee members, drawn from chemistry, physics. We had outstanding chemists like Ron [Ronald C.D.] Breslow. We had John [J.] Hopfield, who's a terrific physicist with strong interests in biology. We had mathematicians, computer scientists, molecular cell biologists and so forth.

And we had many meetings where we brought in other experts: people from liberal art schools, people from large state universities, people from institutions like Harvard, Yale, and Stanford. And we really explored, in depth, the kind of curriculum and research opportunities that were needed, and we presented a plan that involved, one, a much more interdisciplinary education. Two, instead of dry didactic teaching, that it be oriented around solving problems, that it be project-oriented, that it involve students in a very active, hands-on sense—not just hands-on in a laboratory, but hands-on with getting hold of...so, if they were learning statistics, they would be looking at interesting data and trying to make sense of the data, and these would be real data that pertain to things that we all care about. And we gave examples of programs that already do this well. It was a study that came out with a book, [which] made a real impact because Howard Hughes then gave grants to educational institutions around the country [...] to implement the vision of BIO 2010.¹⁵

So, I'm very gratified by the outcome. It's a continuing process, but within a year, it was already being implemented. Shirley [M.] Tilghman at Princeton was a big force in this. At Stanford, of course, we implemented parts of it very quickly. And so, it was very satisfying seeing this transformation of undergraduate education occurring. And we're thinking about additional ways of making it happen. So, that was a major endeavor.

CARUSO: [...] Was that consuming most of your time during this...?

STRYER: At least a half. I was thinking about it a lot.

¹⁴ Bruce Alberts, <u>Molecular Biology of the Cell</u> (New York: Garland Pub, 1994).

¹⁵ National Research Council (U.S.), <u>Bio 2010: Transforming Undergraduate Education for Future Research</u> <u>Biologists</u>, (Washington, D.C.: National Academies Press, 2003).

CARUSO: And still doing some bits in the lab, but that was petering out.

STRYER: Some bits. Certainly petering out, yes.

CARUSO: [...] I'll use that as, sort of, the next stage in your scientific career. After that, you had the Howard Hughes Medical Institute Advisory Board from 2005 to 2008. You also received the Molecular Bioanalytics Award in 2002, the European Inventor of the Year Award in 2006. You became a member of the American Philosophical Society in 2006.

STRYER: Yes, next door to you [in Philadelphia, Pennsylvania].

CARUSO: Right, right. And you received the National Medal of Science in 2006.

STRYER: I did, yes. Right. I actually got the award in 2007.

CARUSO: 2007, but you were 2006...

STRYER: I was the class of 2006. That's right.

CARUSO: So, tell me, during this period of time, I know that your involvement with your lab...you were taking a step back, eventually became emeritus professor. Did you have any specific scientific goals in mind? Were there things that you wanted to achieve during those years that you hadn't necessarily had the time to do while you were so heavily invested in the research that was going on in your lab, or the chairmanships of the department, and things along those lines? Did you have any, sort of, vision for what you wanted to achieve scientifically?

STRYER: No grand vision, but there are projects that I've had. One of them is to understand human diversity and to understand population genetics using the information we now have from DNA arrays. I've had a very interesting time, and still am having a very good time looking at the rich data that are coming out with massive genotyping of an increasing number of people of different ethnic backgrounds as a way of retracing human history. I find that absolutely fascinating, and it's a very good computing problem. These are massive datasets, and I'm learning a lot of new math, and I've always enjoyed math. So, that's a case of where I used my Affymetrix connection [...].

CARUSO: Oh, that's right.

STRYER: And that gives me access to these very nice data. Some of the data are also available in the public database.

I continue to be very intrigued with olfaction. How is it that we're able to sense the vast number of odors? How do they affect our emotions? And here, it's more a matter of thinking about it, modeling, looking at other people's data. But it's something that very much intrigues me.

And in the case of vision, I'm very interested in the evolution of the eye. [Charles R.] Darwin recognized the challenge posed by the eye for the theory of natural selection in Chapter 6 of *Origin of Species*, and so I enjoy thinking about that, talking...and there's some nice new data.¹⁶ I'm in touch with Jeremy [H.] Nathans at Johns Hopkins [University]. Jeremy was originally an M.D./Ph.D. student at Stanford, did his wonderful work on the cloning of the visual pigment genes, and so we maintained contact. Denis [A.] Baylor, who developed wonderful ways of looking at single-retinal rod cells and cone cells—he's also emeritus—we talk about vision. Brian Wandell, in the psychology department here, works on vision at a higher level. So, I'm interested in perceptual processes. I'm interested in art and the brain. Are there forms to which we respond powerfully at a subconscious level?, as Henry [S.] Moore posed the question many years ago. I'm very interested too in how the brain processes music and the evolutionary development of the musical faculty.

So, I would say, if there is something that unifies all of this, it's human evolution, and I have fun with that, but I'm under no pretense that I'm going to solve a particular problem. Rather, I'm having fun just exploring it for its own sake, and there's no need to write a manuscript. A number of times, people have asked me to join them on a manuscript, and I've said no. I just enjoy calculating things until I figure it out or not figure it out.

CARUSO: How was it receiving the National Medal of Science?

STRYER: Well, that was very moving, I think, going to the White House, to the East Room with [Gilbert C.] Stuart's painting of George Washington on one side, and stepping up and shaking hands with the President as the citation is read. And as I said to the President when the medal was placed around my neck, that I'm especially grateful because I'm an immigrant to this country. So, it was a very, very special moment. It was great having some members of my family there, and it really indicated to me what a great land of opportunity this is and how important it is to maintain those opportunities, both for those who are native born and for those who come into this country, and to keep the doors of opportunity open. And I am very

¹⁶ Charles Darwin, <u>On the Origin of Species, 1859</u> (Washington Square, N.Y.: New York University Press, 1988).

concerned that young people in science are having a harder time getting independent positions now. Science has been so successful. We're producing many wonderful scientists, but they're not initiating their own research programs at an earlier stage of their career. There are these wonderful years when everything seems possible and is possible, and those years have to be captured. My concern is that those opportunities are not open today as they were open so wonderfully to me when I grew up in science.

Now, one of them is the fact that we no longer have mandatory retirement. We no longer say to a faculty member, "You've attained the age of sixty-five, and now is the time to retire." Now, many people say, quite rightfully, that they still have great intellectual prowess; why should they be forced to retire? What's so magic about the age of sixty-five? And I would say in response that it doesn't have to be sixty-five. It could be sixty-seven, maybe even seventy, but there has to be a finite point at which you do not apply a test. The great thing about tenure is that it gives great freedom, but if we are to preserve that, we also need to have a time limit on it [...]. I think the only other position that is as privileged as a tenured university professor is a federal judge, and federal judges have tenure for lifetime, but they've worked out a terrific system of becoming a senior judge, getting the same pay, sometimes retaining an office and retaining the powers of the position at the call of the chief judge of a district. We need some way of making room for the younger generation. Every tenured faculty member who keeps his or her position after age sixty-five is denying an opening to a young faculty member. So, a major part of my decision to retire the day before my sixty-sixth birthday was that I wanted to create an opening for someone who, like myself, had terrific ideas and deserved to begin research. Unfortunately, the view that I've just stated is a minority view, and so you have a lot of people who talk about, "We've got to do this for young people, et cetera, et cetera," but there is very little talk about the root cause, and I think the root cause is that we have eliminated mandatory retirement. So, I think this is a very serious issue for the country, and I think we're going to lose out on extraordinarily talented people unless we change things. We just cannot keep adding the number of positions and just wait for people to die.

CARUSO: It's actually very interesting that you are talking about this in the way that you are because one thing that a fair number of Pew Scholars complain about is funding, right? The NIH doesn't have enough money, they're cutting back, it's going to destroy science. Shirley Tilghman, since you mentioned her, spoke at the Chemical Heritage Foundation last year—I think it was last year—and raised this issue of the impact that funding in the United States is having on the next generation of scientists, that either people are not staying in academia—they're going into private industry—or, what's also happening is that you have a lot of students who come to the United States to get the education and then leave the United States to secure positions elsewhere because it's better for them. But no one that I've spoken to has ever brought up this notion that one of the potential solutions to the problem is making more open spaces. If the senior faculty aren't applying for grants anymore, if they move out of their tenured positions and take other perspectives in terms of science, that would actually create greater room for the younger scholars.

STRYER: Exactly, and I think it's fundamental. The things about sustaining federal funding [are] very important, but the community of scholars has within its hands a solution, and it can be exercised, without an act of Congress, first by simply people retiring sometime between sixty-five and seventy. And I would hope that more of my friends and colleagues would do that. Because the striking thing is that you look at the research careers of most scientists, and you ask, "What is their single best contribution, single outstanding contribution," and it occurred before they were forty, usually...maybe, in the case of biology, maybe forty-five. In the case of math, it occurs before thirty, and physics occurs a few years later than that, and then chemistry and then biology. Now, that's not to say that people are no longer able to think, but the creative genius occurs quite early, and that's what we have to capture.

CARUSO: But I guess, just thinking of it from another perspective, one thing that would be lost is truly a fountain of knowledge. If the faculty member leaves after a certain period of time, after...most of the people I've interviewed, their priority is doing research, right? They're not at an institution to educate. I think there are a fair number of more senior scholars, not necessarily Pew scholars but scientists, more senior scientists, who you could actually benefit the younger generation in terms of if you became more of the educators at institutions, and that is something that would be lost. I know Cornell tries to, or has been trying to recapture some of the faculty who have retired, bringing them back in as educators.

STRYER: Absolutely. No, I'm not advocating that retirement means you lose your office and all your connections with the university. Quite to the contrary. Right now, I'm doing things that are helping the provost accomplish certain important things here. So, this is where my knowledge of the institution, where my years as a faculty member, as an administrator, as someone in industry come into play and help the university. I've spent a lot of time talking to young faculty and helping nurture them.

What I'm saying is that what is important is that the tenure position become open, because there are only a finite number of tenure positions, and that space become available so that a person who contributes to the university, like myself, need not take a lot of space. My space right now is right here. It's not three thousand square feet. That's a big difference. That enables my younger colleagues...they're using space that I stepped out of. That's a really significant thing. And they're getting NIH grants that I had previously gotten. But there's a lot that I could do intellectually, and there are a lot of ways the university can draw upon me, without costing a lot of money.

CARUSO: Okay. So, in terms of this overall interview, I actually only have two questions, and one of them is just something I meant to follow up on but did not. Your children, what do they do?

STRYER: Well, our younger son, Dan, died of a glioblastoma four years ago.

CARUSO: I'm sorry to hear that.

STRYER: He got an M.D., became a resident in medicine, and then was interested in the public policy side of medicine, and he, after spending about three years on an Indian reservation—a Navajo reservation in Arizona—went to the Federal Agency for Healthcare [Research] and Quality. [He] then became head of their [Center for] Quality Improvement and Patient Safety. So, he was very interested in developing and improving medical care, and also enhancing hospital safety.

My other son, Mike, was in international trade for many years but always had a yearning to get into teaching, and about five or six years ago he decided that he would take some courses and get his teaching credentials. He now teaches history and economics at a high school in Los Angeles—a public high school—and is having a wonderful time with it. He's running for the L.A. Unified County School Board, and he's making an impact on education in Los Angeles.

CARUSO: So, the only other question I have, and this is what I tend to end my interviews with, is clearly I came in with a list of things that I wanted to cover. Is there anything that you would like to discuss or talk about, and of course the answer can always be no, but is there anything that you would like to talk about as an issue, or a statement that you want to make that hasn't been brought up yet?

STRYER: Well, I think we touched on many of the things that I care about, but again, to come back, I think that it's absolutely crucial to seize the phase of people's lives when they're immensely creative and to do everything possible to nurture that. Everything was open to me. I came here as an immigrant kid, and I always felt that all of the doors were open and that there was nothing holding me back, that it was up to me. And I think we need to strengthen that. We need to make people feel that way. We need to actually have the opportunities there, and we need to be mindful that a major source of our strength in science—and outside science—is the vitality of young people. I think the older scientific community has to get a more realistic assessment of itself. Some of my friends have no idea that they are not as creative as they were years ago. There is a biological clock. There is an ageing process, and one has to look at where one is and take advantage of it.

You asked me about my hobbies. Well, I'm now able to do many things that I simply could not do because I was on a very fast trajectory coming out of Shanghai. I'm now able to spend many months of the year in Aspen. I love the mountains. I love hiking. I love music. I love being able to get up some days and have them totally unstructured. There's nothing on my calendar because I keep it that way, and to really have fun with that. And so, I'm now preparing a photo show that will be exhibited at Janelia Farm, the Howard Hughes laboratory. I'm

passionate about photography and going places in the world. I was in the Arctic a few weeks ago. My wife and I were in Borneo looking at orangutans and bushwhacking with our guide, and doing these things now is just a fantastic thing. And so, there's a place, you know, "to everything there's a season," and so I think that the scientific community would be even stronger if people recognized that and saw what they can contribute and what they cannot contribute at different stages of their career.

I would say that I've had an immense amount of fun in science. Lots of very hard work. I've had fun through my research. I've had fun through my textbook, because it has opened many doors in terms of meeting students around the world. It enabled me to learn a tremendous amount and to give back to people who taught me and to the broader community. So, I just hope that the kind of scientific environment [in] which I grew up, that we can maybe go back to some of that. There are wonderful things today in being wired and having the internet and having all these wonderful techniques and having a huge scientific community, but there was also something terrific about being a young crystallographer at a time when there were twenty or so in the Piazza Navona [...]. I think that the scientific community and its leaders [can help restore that spirit]. Certainly Howard Hughes is doing that, and Pew is doing that and quite a number of others too.

I think this is a great time to be growing up in science. We're going to have a deeper understanding of human nature. We're going to understand more of the relationships between nature and nurture, the interplay of environment with our genetic endowment. I think there are going to be major new principles emerging from that inquiry. I think we're going to see in this century something [that is equal to the] importance of Darwin's contribution. What Watson and Crick did was truly monumental, truly major, but I think it will lead to a totally new principle that will enable us to understand our cortex better. So, I think there are great things to be done. I must say, I slightly envy people who are just entering science today. I think that covers it.

CARUSO: Okay. Well, thank you very much.

STRYER: That's great.

[END OF AUDIO, FILE 2.1]

[END OF INTERVIEW]

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