THE BECKMAN CENTER FOR THE HISTORY OF CHEMISTRY

HAROLD A. SCHERAGA

Transcript of an Interview
Conducted by

James J. Bohning

at

Cornell University

on

10 February 1987

THE BECKMAN CENTER FOR THE HISTORY OF CHEMISTRY

Oral History Program

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Oral History Program

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> Harold A. Scheraga, interview by James J. Bohning at Cornell University, Ithaca, New York, 10 February 1987 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0064).

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

HAROLD SCHERAGA

1921 Born in Brooklyn, New York on 18 October

Education

1941 B.S., chemistry, City College of New York
1942 A.M., chemistry, Duke University
1946 Ph.D., chemistry, Duke University

Professional Experience

1946-1947 American Chemical Society Postdoctoral Fellow, Harvard Medical School

Cornell University
1947-1950 Instructor of Chemistry
1950-1953 Assistant Professor
1953-1958 Associate Professor
1958-1965 Professor
1965- Todd Professor of Chemistry
1960-1967 Chairman, Chemistry Department
1970-1980 Visiting Professor, Weizmann Institute, Rehovoth, Israel

Honors

1956-1957 Guggenheim Fellow and Fulbright Research Scholar, Carlsberg Laboratory, Copenhagen
1957 Eli Lilly Award, American Chemical Society
1961 Honorary D.Sc., Duke University
1962 Welch Foundation Lecturer, University of Texas
1963 Guggenheim Fellow and Fulbright Research Scholar, Weizmann Institute, Rehovoth
1966 Elected Member, National Academy of Sciences
1967 Elected Member, American Academy of Arts and Sciences
1968 Harvey Lecturer, New York
1968-1969 Gallagher Lecturer, City College of New York
1970 Townsend Harris Medal, City College of New York
1973 Lemieux Lecturer, University of Ottawa
1974 Nichols Medal, New York Section, American Chemical Society
1976 Hill Lecturer, Duke University
1977 City College Chemistry Alumni Scientific Achievement Award Medal
1978 Kendall Award, Division of Colloid and Surface Chemistry, American Chemical Society
1981 Venable Lecturer, University of North Carolina
1983 Linderstrøm-Lang Medal, Carlsberg Laboratory

1983	Kowalski Medal, International Society of Thrombosis and Haemostasis
1985	Pauling Medal, Puget Sound and Oregon Sections, American Chemical Society
1985	Honorary Life Member, New York Academy of Sciences
1989	Honorary Member, Hungarian Biophysical Society
1990	Mobil Award in Polymer Chemistry, American Chemical Society
1990	Repligen Award for Chemistry of Biological Processes, American Chemical Society

ABSTRACT

Harold Scheraga starts this interview by recalling his childhood in Monticello, New York and then in Brooklyn, where he attended Brooklyn Boys High School. There he was attracted to Latin and to mathematics and he decided to concentrate on chemistry only when at the City College of New York. The atmosphere surrounding CCNY in the late thirties was such that their graduates met some difficulties in continuing to graduate studies. However, Scheraga was offered a place at Duke University where the chemistry department was chaired by Paul Gross, himself a CCNY graduate. As well as his graduate research on the Kerr effect, Scheraga contributed to the wartime projects on the frangible bullet and on gas-phase halogenation. Influenced in part by the Cohn and Edsall book Peptides, Amino-Acids and Proteins, Scheraga consolidated his growing interest in biochemical areas by a postdoctoral year at Harvard. From there he was appointed as an instructor in the chemistry department at Cornell, where he has spent the rest of his career, including a period (1960-67) as chairman. During the 1970s, he was also a visiting professor at the Weizmann Institute. During the second part of his interview with Bohning, Scheraga describes the development of his research activities; first with the hydrodynamic properties of polymer solutions which then led to his extensive work on protein structure and function. He also recounts his achievements as departmental chairman, with the construction of the new chemistry building and the appointment of new faculty. International collaboration has always been important to Scheraga and he details his sabbaticals at the Carlsberg laboratory and his later association with the Weizmann Institute.

INTERVIEWER

James J. Bohning holds the B.S., M.S., and Ph.D. degrees in chemistry, and has been a member of the chemistry faculty at Wilkes College since 1959. He was chair of the Chemistry Department for sixteen years, and was appointed chair of the Department of Earth and Environmental Sciences in 1988. He has been associated with the development and management of the oral history program at the Beckman Center since 1985, and was elected Chair of the Division of the History of Chemistry of the American Chemical Society for 1987.

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INTERVIEWER: James J. Bohning

LOCATION: Cornell University, Ithaca, New York

DATE: 10 February 1987

BOHNING: Professor Scheraga, you were born in Brooklyn on October 18th, 1921. Could you tell me something about your parents?

SCHERAGA: My father was born in Rumania but came to the United States with his family when he was three and grew up in Brooklyn. My mother was a first generation American, born of immigrant parents who had come from Russia. The early part of her life was spent on the lower East Side in Manhattan but then later on also in Brooklyn. They married in Brooklyn and shortly after moved to Monticello, upstate New York. The fact that I was born in Brooklyn was simply an accident. My mother had gone back to Brooklyn to visit her parents at the time and I was born in my maternal grandparents' house. After a month or so, I was brought back to Monticello, where I grew up from 1921 to 1930, when we left Monticello to move back to Brooklyn.

My father, Samuel, was a machinist. My mother's name is Etta. They're both still alive and are each ninety-one at the moment although, unfortunately, living in a senior citizen's home since my mother had a stroke about three years ago. He was a machinist but he wanted to go into business for himself and, since there were some relatives in the Catskill area, he decided to go up there and take a fling at it. He had a store in Monticello where he sold radios; this was at the beginning of the radio business in the early 1920s. I remember every time he sold a radio, he had to climb a telephone pole to put up an aerial. Also, during the summer hotel trade, he was very active in servicing the hotels with radios and with the automatic record changers that they were using; he would also repair the instruments of the hotel orchestras. But, in the 1929 crash, he lost the business, and that's the reason they moved back to Brooklyn.

BOHNING: You didn't have any formal schooling in Monticello?

SCHERAGA: Yes, I did. I entered school at the age of five. At that time they weren't very strict about the starting age, so I was one year ahead from the beginning. I was put in the first grade at the age of five. I had almost four years of schooling in Monticello. I continued in the fourth grade when we moved to Brooklyn.

BOHNING: With your father being in the radio business, did you have any interest in early radio?

SCHERAGA: No. I was much too young for that. I just did all the things that young kids do. I have a brother three years younger than I am and another one born much later. We were very mischievous kids.

BOHNING: Were you living in the country? Monticello is not a very large town.

SCHERAGA: Monticello is not a very large town. We moved several times and I lived in two or three places. The last one was in a rather rural part of the town, in fact, right next to a large field with a hill, where I remember going sleigh riding in the wintertime, running around the fields; just the things a kid does normally.

BOHNING: What was it like for you to go from that environment to Brooklyn?

SCHERAGA: We adapted quite easily. I never felt any cultural jolt or anything like that. Of course, we had visited fairly frequently since both my parents' families came from there; they both came from very large families. My mother was one of eight and my father was one of six, so there were plenty of cousins and aunts and uncles. We were accustomed to that environment. In fact, we lived with grandparents for the first few years after we moved back. My father had to find work and it wasn't easy in 1930 as you can recall.

BOHNING: Did he ever start another business then?

SCHERAGA: He worked on and off as an employee and then he went into business for himself. A brother, who's long since deceased, had a number of supermarkets in New Jersey and he helped my father get started in one of the concessions in the supermarket. But my father was never a successful businessman. He went broke in everything he tried.

BOHNING: Where did you go to school in Brooklyn?

SCHERAGA: In Canarsie, P.S. 114. I think I was there for about two years, through the sixth grade. Then I went to Junior High. At that time we moved away from Canarsie and I went to John Marshall Junior High, P.S. 210 in Brooklyn. It's in another area of Brooklyn. I went through Junior High there, which meant getting through the ninth grade, the equivalent of the first year of high school, and then went to Boys High in Brooklyn. At that time Boys High was a rather prestigious high school academically.

BOHNING: I'm not familiar with it. Did you have entrance exams to get into it?

SCHERAGA: There were no entrance exams. It wasn't like Townsend Harris High School. I thought of trying out for Townsend Harris High School which was a prep school for City College; the school doesn't exist anymore. I decided not to and, since Boys High was closer to home and it had a very good reputation, I was happy to go there.

BOHNING: Were there any teachers during this period from junior high to high school that you remember?

SCHERAGA: Yes. I remember right from the start in Junior High, that I was very much interested in Latin. In fact, I got the Latin medals when I graduated both from Junior High and from Boys High. My career seemed headed for an arts degree with a major in the classics. I remember Mr. Jacob Shack who stimulated me very much in Junior High. Then in high school I began to develop not only my interest in classics, but also mathematics. I had some excellent teachers of both mathematics and Latin in Boys High. I remember that in the Latin department there was Dr. Mann -- I think he had a Ph.D. -- and Mr. Gross. I can still remember him reciting Virgil very passionately. Then there was an old professor we used to call Dad Edwards, who was remembered very fondly by generations of alumni of Boys High; he also taught Latin. Andrew Child was another. These were all people who at least made me feel very much at home in the subject and like it very much.

Then my interest was growing in mathematics. At that time there was an interscholastic mathematics team which used to compete with teams from other schools, but I never made the team. I was always on the squad of substitutes, never a regular. Mr. Panem directed the math team. My interest in mathematics was certainly stimulated there; as a matter of fact, so much so that I remember that during the summer after I graduated from high school I decided to study math on my own. I taught myself analytical geometry and calculus.

BOHNING: What range of math did you cover at high school?

SCHERAGA: At that time the curriculum didn't go up to calculus, ending at advanced algebra. I took all the math that was offered through advanced algebra. Then that summer I did differential calculus by myself. I didn't get through integral calculus. However, I was still very much headed for a classics career when I entered college.

BOHNING: Had you had any science courses at Boys High School?

SCHERAGA: I think two years of science were required. I had one year in Junior High: introductory biology, which didn't excite me one way or the other. Then I took chemistry in high school. It was a terrible course, which I found very dull and had no particular interest in it, although as a kid, I had a chemistry set and had played around with it at home, but I had no interest in the high school course. Unfortunately I was never exposed to physics in high school. I was clearly headed for a career in classics, but mathematics was lurking in the background.

BOHNING: Did you have any laboratory experience with your chemistry course?

SCHERAGA: There were a few experiments but I never found it very interesting.

BOHNING: Did your younger brothers go to college? Did you have forerunners in your family that preceded you?

SCHERAGA: Both of my brothers went to college; one, like me, to CCNY and the other to Cornell. None of my mother's brothers and sisters had been to college. My father has a twin brother, Morris, who went to Cornell. Morris went through the Vet college here at Cornell and became a microbiologist. When he left Cornell he went to the University of Kentucky and for many years he was head of the Department of Bacteriology. Then it became Microbiology. He retired at sixty-five and became emeritus. He was the only college educated person in the immediate family, and he clearly was a role model when I was growing up. As a matter of fact, I at one time had thought about going to Cornell but the expenses were out of the question. My father was unemployed a very significant fraction of that whole period of the 1930s while I was going to school. In fact, for two out of the four years when I went to college, he was unemployed. I wanted to quit school and help support the family but he was very strong in insisting against it. I'm forever grateful to him for that because my career would have been derailed if I had dropped out of school.

BOHNING: Did you have much interaction with your uncle?

SCHERAGA: No. He was in Kentucky and in those days people didn't travel much. In fact, I had never been to Lexington until many years later when I was on the Cornell faculty; I was invited to give a seminar there and of course he was in the audience and very proud of his nephew. I wasn't giving a seminar in his department, but in the Biochemistry or Chemistry Department. So we saw them on rare occasions: every two or three years. I got along well with his children. He has a daughter my age and a son who is my next brother's age. That son was a Cornell undergraduate and is now the advertising manager of Science magazine.

BOHNING: Had you given any thought to career plans as you were leaving high school?

SCHERAGA: You must remember the times. It was in the depths of the Depression and the only real professional models were not so much my uncle but the teachers that I had. High school teaching was the kind of career that I was looking for and I thought of becoming a Latin teacher, even though my Latin teachers had told me that the State hadn't given an exam for certification of teachers for years but that didn't bother me.

BOHNING: How did you come to choose CCNY?

SCHERAGA: Before we get to that; I graduated from high school, I got the Latin medal and was going to become a classicist. Being near the top of my class, I had aspirations to obtain a scholarship. Well, a Cornell scholarship didn't pay all expenses so that was out. There was something called a Pulitzer scholarship which covered all one's expenses for Columbia. That required taking the college entrance boards exams. Unfortunately, I didn't obtain the scholarship and so I fell back to going to City College, which at that time was a very prestigious school. I found it to be a very stimulating place.

BOHNING: This would have been about 1937?

SCHERAGA: Yes. I was at City College from 1937 to 1941. When I entered you had to decide on whether you were going to follow a science or an arts career. Being interested in Latin, I opted for arts, but I also wanted to do mathematics. They said that I couldn't do that, and that the only way that I could take mathematics would be if I enrolled in the science school. So I enrolled in the science school.

But I wasn't completely committed to mathematics. I didn't feel that I wanted to be a math major. So I just picked chemistry essentially at random. That's the way I got into it because my high school experience in chemistry had been a terrible one. I had a very dull high school chemistry teacher. I remember his name; Mr. Cook. He droned on and on and put everybody to sleep, stimulating no interest in the subject; he actually killed it.

BOHNING: You didn't have any physics in high school?

SCHERAGA: I had no physics. My only experience in science aside from that early biology was with mathematics and this one chemistry course. So I opted for a chemistry major and, as soon as I started taking chemistry, I got excited about it. I had very good teachers. In fact, in my freshman course, I had a teacher named Edgar Leifer, who had just graduated from City College a year or two before and was doing his Ph.D. work at Columbia under Harold Urey. He was building a mass spectrometer for studying gas-phase reactions; I guess that was what was going on in Urey's lab at the time. He got me very excited in chemistry. At that time, he didn't have a teaching assistantship at Columbia which was why he was teaching at City College. By coincidence, he lived near me in Brooklyn. So after labs at night, we used to ride home on the subways together and I would hear a little about what he was doing in his graduate work. Just as these coincidences go, I had also known his uncle because all during my elementary school and high school days, I had gone not only to public school but also to a Hebrew school. These were after school activities five days a week. His uncle had been one of my teachers in Hebrew school. This was purely coincidence.

BOHNING: Did you have any professional encounters with him?

SCHERAGA: I had him for the lab and recitation. Now you would call him a TA, but he was called a lab instructor at that time. The lecturer was dull; his name was Joseph A. Babor who wrote the textbook that everybody had to buy (1). But I think it was Ed Leifer who really got me interested. First of all, he made the lab recitations very exciting, and then there were the personal conversations with him going home.

BOHNING: What kinds of things were you doing in the lab?

SCHERAGA: Normal freshman experiments. Making hydrogen and so on; what you did in the old style freshman chemistry. But for some reason it was interesting whereas in high school it wasn't. And then hearing about the kinds of things that Ed was doing, I started to realize that chemistry was going to be my career.

BOHNING: Could you tell me something about the facilities and what CCNY was like when you were there?

SCHERAGA: The chemistry building was called Baskerville Hall. Baskerville had been an old faculty member at City College. It was in a state of considerable decay at the time that I was there, and the labs were horribly antiquated. They didn't have enough lab space to cover all of the courses. The uptown campus was at 137th Street and Convent Avenue, which is where I went to school, and involved a one hour commute each way from Brooklyn every day on the subway. City College had a School of Commerce at 23rd Street and Lexington Avenue and they had labs down there for the spillover. Those labs were more modern because the building was more modern and it was at the 23rd Street Center where I took all of my freshman chemistry and the third semester, qualitative analysis. It was only in the fourth semester, when I took quant, that I actually entered the labs at the uptown campus.

BOHNING: Did you continue your mathematics at the same time?

SCHERAGA: Yes. I took mathematics and happily I also got into physics. Ultimately, I had enough math and physics to have had a major in both of those areas. So, while I was nominally a chemistry major, I had quite a bit of math and physics. Actually, I found the math teachers at City College rather dull, but it was an interesting subject. My freshman calculus teacher, William H. Fagerstrom, was the only good math teacher. After that, it was dull. I remember a course in complex variables that I took in which we used a German text [Knopp: Funktionentheorie] and the instructor spent half the lecture translating the German for us. [laughter]

So I had plenty of math and physics. An outstanding physics professor that I remember was Mark Zemansky, the author of a very famous book on thermodynamics.

BOHNING: Is it Sears and Zemansky? (2)

SCHERAGA: No, Sears and Zemansky is a freshman text, but he wrote a rather famous book, Heat and Thermodynamics (3), which is still cited. When the modern textbooks list the references for further reading at the end, they always cite his book. I had several courses with Mark Zemansky. Physical optics was one. Another good physics teacher was Henry Semat. But of course, it was in chemistry where I felt at home, I began to live in the chemistry building. I had some very good teachers there. Unfortunately, most of them are gone. I remember David Pearlman, Percy M. Apfelbaum. I did undergraduate research with two of them; Alex [Alexander] Lehrman and Morris U. Cohen. I did senior research and honors so I got my degree with honors. With Lehrman, I did research on the phase rule and with Morris Cohen, on X-ray diffraction. That was both a stimulating and a sad time because I was in my senior year in 1940-1941, when the state legislature started one of these communist witch hunts. They went into the City Colleges and a lot of professors were subpoenaed and ultimately lost their jobs. Morris Cohen was one of them.

I used to see Lehrman in the years since my graduation, but I never saw Morris Cohen again, although I heard rumors that during the second world war, he was making a lot of money in defense work as a defense contractor. [laughter] So much for communist witch hunts. The committee was the Rapp-Coudert committee, named after those two legislators [Herbert A. Rapp, Frederick R. Coudert]. Incidentally, quite recently, there was an amnesty and all of the City College professors who lost their jobs in that witch hunt were all, so to speak, rehabilitated. It took all of that time to rectify the situation. As an alumnus, I get the alumni news and it was maybe two or three years ago that I recall reading that this had taken place.

BOHNING: Do you have any idea how many professors were affected?

SCHERAGA: I would guess about twenty-five when you count both City College and Brooklyn College. It was much like the later McCarthy period.

BOHNING: I hadn't realized that this occurred. Was it unique to New York State?

SCHERAGA: Yes. It was the New York State legislature. This was separate from the Dies committee, which was a federal one. Martin Dies was a congressman. So, there was the Rapp-Coudert committee which was a state thing, and the Dies committee which was a federal thing, and then the McCarthy time. City College was ripe for this because all the students were very poor and were experimenting with political philosophies. It was called a hot bed of communism but I suspect the number of communists was very small, although there was always a lot of political activity. I remember that some of the boys went off to fight in Spain. The Spanish Civil War was going on at that time and the campus back home was trying to drum up support for the Spanish government forces. It was the period of Nazism, and Fascism. There were rallies against Nazism and Fascism; lots of ferment going on, protest rallies and so on. I was always on the periphery; I never joined but I must say, my sympathies were there. But I never got involved in any of that political activity.

BOHNING: You said you did your research on the phase rule and X-ray diffraction. Did you have any leaning specifically toward physical chemistry at that time?

SCHERAGA: Oh, yes. I was definitely heading toward physical chemistry. That's why I also took a lot of math and physics. Incidentally, I stayed far away from biochemistry. I sort of looked down my nose at it. There was a rather well-known biochemist there, Benjamin Harrow, who wrote a textbook which I understand was used in all the medical schools and biochemistry departments (4). Some students were doing undergraduate work in biochemistry but all I remember was that they were studying detoxification. They would swallow pills and then collect urine so the johns always contained big buckets filled with urine. That made a very bad impression on me.

BOHNING: Did you have a formal course in biochemistry?

SCHERAGA: No. I didn't want it. In fact, my uncle in Kentucky had suggested it, but I didn't think it was a rigorous scientific discipline. I've since done a 180° phase shift on that one.

BOHNING: What student colleagues do you recall?

SCHERAGA: Quite a few of my classmates have since become famous chemists. Ernie [Irwin B.] Wilson and I worked together with Morris Cohen. He subsequently was on the staff at Columbia and in more recent years moved to Colorado. Saul Roseman at Hopkins was a classmate of mine. Oscar Touster; I believe he is at Vanderbilt. Seymour [Z.] Lewin at NYU; Henry Freiser at the University of Arizona.

BOHNING: That's an incredible list.

SCHERAGA: It was a very good class. Either Ernie Wilson or Seymour Lewin were first and second and I was third in the class.

BOHNING: Do you remember how many there were in your class?

SCHERAGA: The whole class of 1941 might have been about 500 or 600 people. There were maybe fifty chemistry majors. It was a rather large group.

BOHNING: As I recall, there was a period of time when CCNY was noted for its chemistry majors.

SCHERAGA: I think they were one of the biggest producers of bachelors degrees. A very significant fraction of those who went on for Ph.D.s, came from City College. There was no graduate school at CCNY at that time; it was only undergraduate and it was an all-male school. There were no women. In fact when I was there, a woman broke into the engineering school and that was the start. It became co-ed and then they took on the graduate school. I still have mixed feelings about whether the latter should have happened or not. It was a very good undergraduate school but not a top-notch graduate school.

[END OF TAPE, SIDE 1]

BOHNING: Were those classmates that you mentioned personal friends?

SCHERAGA: My relations with them were just friendly through school; they were not my after-school friends. I would have been happy to be friends with them but we didn't live near each other, although Henry Freiser and I later became friends (and roommates) in graduate school at Duke. My social life revolved around a cultural club in Brooklyn that I had joined, which was made up of students from both City College and Brooklyn College. This was a Jewish cultural club and most of us have become lifelong friends. In fact, I met my wife there. There were a number of marriages from that club and the couples have continued to be friends. We see them quite frequently.

BOHNING: What was it like growing up in Brooklyn?

SCHERAGA: I can remember the after-school activities before I went to college. I was very much interested in sports. I played a lot of handball whatever the season; we played punchball in the street. We played baseball in the schoolyard and in the fall we would play touch football. In fact, I had aspirations of going out for the baseball team at Boys High but I was too short. I was rather short in my high school days. Only in the latter part of high school did I suddenly shoot up. In college, through this cultural club that I belonged to, I began to get very much interested in tennis. I played a fair bit of tennis which I kept up for many years. I also had an uncle, a brother of my mother's, who was a golfer and he started to give me golf lessons although I couldn't afford the greens fees and was never able to take it up then, until I actually got to Cornell and then started up again with golf lessons and became a golfer.

BOHNING: As you were completing your degree at CCNY, had you already decided about graduate work? How did you make that decision?

SCHERAGA: There was no doubt that I was going to graduate school; I just took that for granted. Again, you must go back to the times. City College was known as a hot bed of radicalism and it was very hard for a City College man to get into graduate school. I graduated in June of 1941 before we got into the war. I sent out twenty-five applications for all the good graduate schools and I got only one favorable reply. Remember I was third in my class and I know I had very good letters of recommendation because the professors who wrote letters had no secretaries, so they gave me the letters to type. I typed the letters and then they signed them. I got just one offer for graduate school, from Duke, and that only because of a fluke. That in itself is an interesting story. The chairman [of chemistry] at Duke was Paul [Magnus] Gross. He himself had been a classmate of Alex Lehrman at City College, I think it was the class of 1917 or 1918. He went down to Trinity College. Maybe he had some knowledge that it was going to become Duke University with the endowment. He was sitting at the right place at the right time so he was head of the chemistry department. I wouldn't say "chairman" because he ran the department. Along about the late 1930s, he began to take one City College man every six months; at City College you could graduate at midyear. Being a young graduate school, he must have had trouble getting graduate students. Some of the best undergraduates from City College went to Duke for that reason. Dave [David S.] Breslow, who went on to Hercules, Phil [Philip S.] Skell, who's at Penn State, and Henry Linschitz, now at Brandeis, were amongst my predecessors there. That was the offer I had. Henry Freiser had preceded me there by six months; actually I roomed with Henry at Duke.

Incidentally, after I had accepted the Duke offer, in the summertime I got an offer from the University of Chicago. Obviously, somebody dropped out and they were scrounging, but I had already accepted the Duke offer. I remember, even though it was my only offer, I was still worried about going to Duke. I remember Zemansky telling me, "Fritz London is there, so you go there." London was really one of the best teachers I had there. He gave a year course in quantum mechanics. I took that my first year. Then the next year I took his year course in statistical mechanics. Because I felt I had a lot more to gain from it, I sat through the quantum mechanics in the third year when he taught it again. The group taking his courses consisted of only five or six students, so it was a very personalized kind of instruction. We felt we never got enough of him, so we prevailed upon him to give us an extra course at night. He was working on superconductivity at the time, so he gave us a series of lectures on superconductivity.

London had come from France a couple of years before. Gross was very smart in snatching him up. London had left Germany as soon as Hitler came to power and Langevin made a home for him in Paris. I remember London telling me that he saw the handwriting on the wall in 1939. He was going to leave France because he could see Hitler was going to invade. As he tells it, Langevin said, "On les resistera." And London's reply was, "Non, non. On capitulara." London left on the last boat in 1939 that got out, so he was at Duke for about two years by the time that I got there.

I wanted to work with him but he was a loner. He wouldn't take any graduate students; he worked by himself. Outside of his paper with W. Heitler, I think all of his work was published on his own. I don't think he ever had a student. He might have had a postdoc in the years after I was at Duke. He felt that students weren't sophisticated enough in research to waste time with.

BOHNING: He was still willing to give you that extra course when you asked him for it.

SCHERAGA: That he was willing to do. As a teacher, he was very willing to do it. So I did my research with Gross. Gross was very busy running the department so he always had a helper who was Marcus [Edwin] Hobbs. Hobbs was either an instructor or possibly an assistant professor by the time that I arrived there. This was the time shortly after London had made the quantum mechanical theory of van der Waals forces, which involved the polarizability of molecules. London was very much interested in polarizability and particularly anisotropy of polarizability.

Gross had a background in that direction too because he had spent a sabbatical leave in Leipzig with Debye. He was a very close friend of Debye's and in fact, that's how I got my job here at Cornell, but that comes later. Under London's stimulation, Gross wanted an experimental program to determine anisotropic polarizabilities. So he put me on a research problem, the Kerr effect; electric birefringence in molecules. I started to do experimental work on the Kerr effect on small molecules. I started that when I got there in September of 1941. On December 7th we got into the war and the whole picture changed. Everything was in a state of flux but I managed to continue for the remainder of that academic year on it. They gave me a masters degree for what I had done. I really had to scrounge for equipment because in those days, you couldn't get any money for any kind of equipment. For example, to study birefringence I should have had an optical compensator. They couldn't afford to buy me one so I used another Kerr cell which I had made in the shop, so I could make only relative measurements. In one cell I placed a fluid, with a known Kerr constant, and used that as the compensator for the other one. It certainly stimulated my interest in molecular structure as related to optical properties and so on. Ultimately, I got back to that a little in my postdoctoral work. Because of the war, we all had to go onto war work. So I was put on a war project but I was still able to continue my graduate work. I worked on the war project during the daytime and on my graduate thesis at night, which was related to another war project. I was on two war projects. The first was sponsored by the Navy. They had a problem with fires onboard ship which used to generate a lot of smoke. The smoke particles would get into the filters of the gas mask and destroy the impermeability to poison gases so that the gases could get through the filters to the adsorbent. The problem was to study the interaction of smoke particles with cellulosic matter, paper, in fact. I think this was also in collaboration with Columbia because Victor LaMer there was a colloid chemist. I know he was one of the people related to this project. We would measure particle sizes of smokes in electric fields; essentially a Millikan oil drop experiment.

After that, there was a big project which was essentially a Duke project run by Paul Gross called the frangible bullet project. The problem was this. By that time we were making bombing raids over Europe with the B-17s. There was no way to train the gunners. You know that in the B-17 there were gunners in the nose, tail and in the waist. The only way they got their training was in combat; if they survived. The only other training was to have somebody tow a sleeve and have the gunners shoot at it. Well a sleeve is not a fighter coming at you, and they had no way to get proper training. What was developed on this project was a 30 caliber plastic bullet. It had a bit of lead inside it because it had to have some additional mass; a lead and plastic composite. The idea being that in training a fighter could make a simulated attack on the bomber as if in combat and the gunner could shoot at him, but the bullets would break up on impact with the fighter so it wouldn't damage the fighter or injure the pilot. In the B-17s, they had 50 caliber machine guns. That was too big even for a plastic bullet, so we had to modify the 30 caliber machine guns to simulate a 50 caliber so that the gunner would think he was firing a 50 caliber. However, even a 30 caliber projectile at the normal velocity would still penetrate the fuselage.

First of all, we armored the fuselage of the fighter with extra armor and attached a microphone on every plate so it would pick up a hit and the nose would light up so the gunner knew as soon as he scored a hit. In fact, it was nicknamed the pinball machine. But even with the extra armor, at the velocity that the 30 caliber projectile was fired, it would still penetrate. So we had to cut down the velocity but then the gun wouldn't recoil. My part of the project was to do the calculations and some supporting experiments on the interior and exterior ballistics of these projectiles. We had to get enough force for the recoil. What we did was to put a flange on the nose of the barrel and put a cylinder around it so that, as the gases came out of the muzzle, there was enough back pressure against this big flange to develop sufficient force to make the gun recoil. It looked like a monster; a 30 caliber machine gun with this great big thing at the end of it. Then we altered the sights so that the gunner would think he was firing a 50 caliber gun. With that kind of training, the number of hits that were scored on first combat went up tremendously, so it was a very worthwhile program. When the war was coming to an end in Europe we were using B-29s for the bombing raids in Japan. The velocity of the B-29 was sufficiently greater than the velocity of the B-17 so that, when added to the muzzle velocity of the bullet, it was already too high even for this scheme to work. We never solved the problem but the atomic bomb ended the war before we were faced with the need to improve our method.

I worked on both of these projects during the day and I worked on a third project at night. This was very remotely connected to the Manhattan project. There was a fluorine chemist, Lucius Aurelius Bigelow at Duke, who incidentally trained one of my colleagues here at Cornell; Bill [William Taylor] Miller had been a graduate student with Bigelow and Bill himself developed Kel-F, that fluorine polymer for the Manhattan project. As a consequence there was a lot of gas-phase halogenation studies going on at Duke which were related to the role of fluorine in the Manhattan project. I never quite understood the connection, but we were asked to study the kinetics of halogenation of toluene. My lab partner at that time was Milton Manes, who has since been a lifelong friend. He went on to Kent State University and has just recently retired. You know, when those students were killed at Kent State, he continued to run his Pchem lab. He had previously been at one of the government bureaus in Pittsburgh, so he took his students from Kent down to Pittsburgh and he ran his Pchem lab down there.

Milt Manes and I both had the problem of studying the chlorination of toluene. I was given the project of studying the thermal chlorination, whereas he had the photochemical chlorination. We quickly modified the problem. We figured that was too complex; there were three hydrogens on the methyl group. So we decided to study benzal chloride, which had only one hydrogen, and that was our thesis work. I never enjoyed it. First of all, there were the circumstances under which we did it: we worked nights, very often through the night. Our wives would bring us our suppers and go home. I decided that this was a hell of a way to make a living in chemistry; somehow gas phase kinetics never excited me. Somewhere along the line, I was browsing in the library and I picked up a book which changed my whole career. That was the book by Cohn and Edsall, Peptides, Amino-Acids, and Proteins (5). It was a multiauthored book, but most of the chapters were written by Cohn or Edsall. They were at Harvard Medical School where, incidentally, they were in a physical chemistry department. There were also chapters by Scatchard and Kirkwood. I said, "This looks like interesting physical chemistry done on interesting physical systems." So I wrote Cohn a letter and asked him if he would consider me for a postdoc. He never answered the letter. He just turned it over to Edsall and Edsall answered it. Edsall said he would be glad to take me if I could come with my own money.

Toward the end of the war, the American Chemical Society seemed to be concerned that they wouldn't get enough people back into academia so they set up a postdoctoral fellowship program. They awarded ten fellowships for the whole country and I got one of them. You must remember this was before NSF and NIH postdoctoral fellowships. I got this ACS postdoctoral fellowship, with a stipend of $2500. The terms were that the school where you went had to supplement it with $1000. So they made me a glorified TA at Harvard and that's how I got the other thousand. I was a TA for Edsall and for Jeffries Wyman, both of whom gave a course in biophysical chemistry. It was a lecture course and as a TA all I did was grade the problem sets.

BOHNING: Before we get to Harvard, let's back up to Duke a little. You were really working on three projects at one time, yet one was allowed for your Ph.D. project.

SCHERAGA: No, the Navy gas mask and frangible bullet projects were in sequence. The Navy project lasted for six months and then the frangible bullet must have gone on for about two years. Besides all of this theoretical work I was doing, we had to test it out. We had a firing range in the attic and we used to fire the machine guns up there. We had to decide on how much powder to put into the shells to get a certain velocity in the gun. You could calculate it all but, in the end, you had to check it because in the last analysis, there was a fighter pilot in that plane who was going to be shot at with live ammunition. In fact, I wasn't there when the system was ultimately tested, but I was told that when Gross and the Army Air Force people went to test this contraption out and when the fighter pilot heard they were going to shoot live ammunition, he refused to get in. So Gross got into the plane on the ground and let them fire the machine gun at him. I must say I always felt he had a little too much confidence in my calculations. [laughter] Then the pilot took the plane up.

All of this was going on during the day and it was only at night that we did our Ph.D. research. That was a separate research problem given to us, we weren't getting paid for it but I think the motivation came out of the fluorination work that was going on at the time.

BOHNING: Did Gross assign you to that project?

SCHERAGA: Yes. Gross ran everything. We called him the Great White Father. The war ended in 1945 and then I had a year of full time research to finish my Ph.D. I didn't get out until 1946.

BOHNING: What were the facilities of Duke like then?

SCHERAGA: The old chemistry building has long since been abandoned as a chemistry building. The labs were more modern than what I had known at City College. Manes and I shared a two man research lab, but it was hard to get money for supplies. As I recall, we even paid for our own supplies as graduate students. We didn't pay the full price. I think they gave us some. But I had to settle up a bill for ten or twenty percent of all that I had spent in my years at Duke before I left. That's unheard of now. All of this gas phase kinetics required a lot of high vacuum work. We were doing a lot of glassblowing and putting up and taking down high vacuum systems.

We needed liquid air for the diffusion pump. Over at UNC, Chapel Hill, which was very close by, they had a liquid air machine. We used to go there and get 15 litres of liquid air and bring it back to Duke. But their machine broke down and during the war, you couldn't get parts to replace it. So that was the end of the liquid air supply at Chapel Hill. We located a source in Washington, D.C. They used to put a 15 litre Dewar on the Southern Railroad which went through Greensboro and from where there was a spur that came into Durham. Very often the transfer wouldn't get made and the liquid air went on down to the south. By the time it was recovered.... Well you never got 15 liters from a 15 liter Dewar. And you could never make a run until you got the diffusion pump going. These were the conditions under which we were trying to do research at Duke.

BOHNING: How many students were there? Were they all working on war effort projects?

SCHERAGA: [Charles R.] Hauser, an organic chemist, had a war project. Dave Breslow and Phil Skell came back during the war to help Hauser with his project; I think it was an anti-malarial project. Then there was the fluorination going on and the frangible bullet project. I'd say there must have been about twenty graduate students there at the time.

BOHNING: What kind of courses did you take?

SCHERAGA: I told you about London's courses in chemistry. I had to take a year course in organic; one term was taught by Hauser and the other by Bigelow. Then I took a course in thermodynamics which Gross and Hobbs gave out of Lewis and Randall (6). That was about all the coursework in chemistry. I didn't do any more mathematics because I had had plenty but I did a lot of physics as a graduate student. In physics, there were two other German refugees besides London. Lothar Wolfgang Nordheim was a well-known physicist and I took three semesters of electrodynamics with him. I had already had electricity and magnetism as an undergraduate. Then I took a year course with Herta Sponer. She had been a student of James Franck, and incidentally, married him later on when his wife died after the war. I took a year course in atomic and molecular spectroscopy where we used Herzberg's books (7). I took quite a bit of physics at Duke.

BOHNING: Was that group of twenty students pretty stable during the war?

SCHERAGA: Yes. Gross was very successful in getting and retaining draft deferments for all of the people. It was all legitimate as everybody was doing war work. As I told you, I wasn't luxuriating in my Ph.D. work since it was being done at night. I was working full-time during the day. We weren't even allowed to take vacations. I got married in 1943 during that period. I was allowed a few days to go home and get married but my honeymoon consisted of a days stopover in Washington, D.C. on the way back to Durham.

Then my wife had to work to support me because I couldn't support the both of us. She worked for Nordheim. She was trained as a sociologist but Nordheim had a war project and she operated a Marchant calculator. He was a theoretician so she would punch the keys on the calculator. Then he went off some place. I don't know whether it was Los Alamos or some other place. So she lost the job and then she worked in the chemistry department on a tobacco project. It had been there for some years but the war had influenced it in the following sense. As I understand it, American cigarettes are a blend of Virginian type tobacco and Turkish tobacco and, during the war, the supply of Turkish tobacco was cut off. As a matter of fact, there was a story that Hitler was trying to corner the market on Turkish tobacco and use it to trade tobacco for munitions. The North Carolinians decided that they were going to try to grow the Turkish tobacco in NC and so there was a lot of chemical analysis to be done. As a matter of fact, after the war when my war project had ended, I had to earn some money during my last year at Duke and Manes and I worked on that tobacco project. My wife was doing analytical work for which she was trained by the person she worked with. She had no training as a chemist so she was a technician. Then she became pregnant and we had our first child about four months before I left Duke to go up to Harvard.

BOHNING: When you moved to Duke, had you arranged the research work before you arrived?

SCHERAGA: No. I went there because Zemansky told me that London was there. That was the attraction. I wanted to work with London but he wouldn't have any part of it. Gross, running the show, told me that I was going to work for him. I didn't have a choice. As a matter of fact, there was a semblance of choice. [Warren C.] Vosburgh was working on magnetic susceptibility which appealed to me. I had practically signed up to work with Vosburgh but then Gross informed me that I was going to work on the Kerr effect. I was certainly willing to accept that. He was a strong man who ran the department his way but I think that was a department that couldn't be run any other way. Only two or three others would have served as chairman. Marcus Hobbs was a good man and Gross recognized that. All of the students who worked for Gross really worked for Hobbs and all the papers came out authored by the student, Hobbs, and Gross.

BOHNING: But your paper on benzal chloride only had Hobbs name on it (8). It didn't have Gross's name.

[END OF TAPE, SIDE 2]

SCHERAGA: Is that right? After I arrived at Cornell in September of 1947, Hobbs came up here in the spring term to spend a sabbatical leave with Debye and it was then that we finished that paper. But, I don't remember why Gross' name wasn't on it.

BOHNING: Then you and Manes had two other papers (9,10).

SCHERAGA: Yes. These were just small things, outgrowths of techniques that we had developed in order to purify the materials that we needed.

BOHNING: Gross's name didn't appear on those either.

SCHERAGA: No. The frangible bullet project was Gross's really big thing. I think he got a Congressional certificate of merit for it.

BOHNING: Were there other student colleagues who were there at that time?

SCHERAGA: I was friends with Henry Freiser who was a graduate student there. Henry Kamin, who is still on the faculty there, is in biochemistry. There was another person in physiology, Art [Arthur K.] Saz. Both he and Kamin, I think, were not so successful at their draft deferments. I think that in order to avoid going in as privates, they enlisted and became officers. Then they came back after the war and finished up. Hans Neurath, who later became head of biochemistry at the University of

Washington, was a young faculty member there at the time. I remember the whole group of us used to sit out under the tree after lunch and with lots of chit chat. Neurath was always there with his students. Being a young faculty member he mixed more with postdocs and graduate students than the older guys.

BOHNING: You still avoided biochemistry until you read that book?

SCHERAGA: It was that book of Cohn and Edsall that got me interested. I had never had any contact with biochemistry, so I had a lot to learn when I got to Harvard. All during the 1930s they had been doing physical chemical studies on amino acids, peptides and proteins. This book was a kind of summary of all that work. George Scatchard from MIT was collaborating with them and Kirkwood, who had been Scatchard's student and was then on the faculty at Cornell, was also a collaborator. In fact, I was very sorry that, just as I came here, Kirkwood left. When the war came, Cohn started a big blood plasma fractionation program because they needed plasma components, specifically serum albumin for shock treatment. When I got there, it was after the war, in 1946, they were still operating a pilot plant. They were doing blood fractionation on the order of 200 litres of plasma at a time. The way they broke in all the new postdocs was to have them spend two or three weeks in the pilot plant. So here I was, never having handled any of this, and I immediately got thrown into learning how to fractionate blood plasma on that scale. I had to do a lot of reading. Larry [John Lawrence] Oncley, who was on the faculty at the time, gave a course in biophysical chemistry. That opened up all new vistas. Then there were the weekly lunch meetings in Cohn's lab where I saw Scatchard, who was a regular there; Kirkwood would come occasionally. Then there were visitors. That's where I first met Irving [M.] Klotz from Northwestern; he was an invited speaker there. Alex [Alexander] Rich, who is now at MIT, was a medical student halfway through medical school while I was a postdoc; we did a little work together (11). Harry [Arthur] Saroff, who just retired from NIH, was there. I actually worked very closely with Geoffrey A. Gilbert and I was working with Edsall, not with Cohn. Gilbert and I worked on something which was an outgrowth of the plasma fractionation (12) -- something called cold-insoluble globulin which was part of the clotting system -- fibrinogen and this cold-insoluble globulin. It has since been renamed fibronectin and is a very hot topic now but in those primitive days, all we were able to do was to determine the size and shape. I had written my proposal to get that ACS postdoctoral fellowship, trying to resurrect some of my old interest in the Kerr effect, electric birefringence. I knew Oncley was doing dielectric dispersion on proteins and Edsall had done flow birefringence on proteins. I tried to make a combination out of these. When I got up there, Oncley didn't seem too interested in pursuing that at the time so I worked with Edsall on flow birefringence, and Geoffrey Gilbert and I collaborated on preparing cold-insoluble globulin. That's where I got my hands wet with proteins, aside from that pilot plant training. Then we did the flow birefringence measurements.

During that time we noticed an anomaly in that the ascending and descending limbs of the Tiselius electrophoresis apparatus were giving different behaviors. It was Gilbert who figured out what was going on and he went on to utilize the phenomenon and make some very fundamental contributions in the transport properties of proteins. He was from the University of Birmingham in England and he went back to Birmingham.

BOHNING: How long were you at Harvard?

SCHERAGA: I went there in September of 1946 and left in August of 1947. I had a fellowship for only one year. It wasn't a renewable fellowship, so I started looking for a job. I went to the spring ACS meeting and I ran into Gross. I told him that I was looking for a job and he told me that [Peter] Debye was looking for a man. I told you he was a friend of Debye. So Debye had Professor [A. Washington] Laubengayer, who now is emeritus from this department, contact me through the ACS clearinghouse and I had an interview with him. On the basis of that, I was invited up to Cornell to give a seminar and go through the usual interviewing. I spent a full day talking to people and at the end of the day I gave my seminar. Nowadays, the candidate goes home and hears weeks later but Debye was a no-nonsense guy. Professor [Simon Harvey] Bauer of this department was seminar chairman and said, "Debye wants you to wait in the library." I waited in the library and he called the faculty together. They had a meeting and in about a half hour Bauer came down and said, "Debye wants to see you." He called me in and said, "We are going to offer you a job," and he wanted my answer right away. Of course I was ready to accept it but I sort of felt that I ought to at least let my wife know. I promised to let him know. This was on a Thursday; I called him on Monday and accepted the job.

BOHNING: You came in September?

SCHERAGA: Yes. It was exciting to have Debye here because birefringence was a close interest of his and he was very much excited in what I talked about in my seminar. But I was disappointed that Kirkwood had just left to go to Caltech. Then things got really exciting when, in the following spring semester, [Paul J.] Flory came as the Baker lecturer. Those Baker lectures were very stimulating. He was supposed to write a book but he didn't write the book until several years later. He came in 1948 and I think his first book was published in 1953 (13). At that time when he was writing it, he was using Leo [Mandelkern] and me as guinea pigs. We read chapters and told him what wasn't clear and what was clear. I found Flory a very stimulating person, in fact, he and Debye just made this a very stimulating place.

BOHNING: What kind of interaction did Debye and Flory have?

SCHERAGA: We used to have polymer seminars at night, once a week and of course, Debye and Flory would dominate these. There were three competing theories of the hydrodynamic properties of polymer solutions, all developed at Cornell at the time. Kirkwood-Riseman (14), Debye-Bueche (15), and Flory-Fox (16). Each of them thought the other's was nonsense and there were very strong discussions, but it never interfered with their friendship. They could argue and then go off as pals and drink beer together. That was always an admirable quality. As a matter of fact, Flory just got a posthumous award at the September ACS meeting and Leo Mandelkern was called upon to make some remarks. He just recited the same story I told you. For all I know, it might be in the transcript that you got from Leo.

BOHNING: He did mention something that was very similar to that.

SCHERAGA: It was very stimulating. I remember the time when computers were just coming in and I was trying to solve a partial differential equation which was involved in interpreting flow birefringence data. It involved Legendre polynomials. This was just up Debye's alley and I'm sure that, plus some other things that I did with Leo, were the reasons why I got tenured here because, at that time, there were about fifteen assistant professors who had marched through here and never got a tenure appointment. The first tenure appointments in the period when I was here were Mike [Michell J.] Sienko and myself. Unfortunately, Mike died a couple of years ago. Did you know Mike?

BOHNING: Not personally, but I used his textbook for my first teaching assignment (17). It was brand new.

SCHERAGA: He and I came together in September of 1947, together with three or four others. We were the only two that survived. There were literally about fifteen that went through here. By the way, I was hired here to teach quant. That was where the position was. But I wasn't forced to do my research in that area. I taught quant. and qual. up to 1952, as did Mike. That qualitative course had been developed by Frank [Franklin A.] Long and Si Bauer. Mike put all of that stuff into freshman chemistry and that's where that textbook really came from. So it really goes back to Long and Bauer. The reason I got into physical teaching was that Tommy [Thomas R.] Briggs who taught the physical chemistry course for the engineers, got lung cancer and died. Frank Long, who was chairman at that time, moved me over into physical and I've been there ever since.

But right from the time that Flory came, it was a very stimulating place. We had a lot of interaction. We collaborated a lot in research, both with Flory and with Leo and with Bill [William R.] Krigbaum, who is now at Duke. In fact, I remember recommending Krigbaum to Marcus Hobbs for a job. Unfortunately, Bill Krigbaum is critically ill right now. I don't know whether you know about that. He has Lou Gehrig's disease. That's really sad. But we worked on hydrodynamic properties of polyisobutylene and nitrocellulose (18, 19); Flory was just getting interested in proteins and we did some collaborative work on collagen. He was interested in the phase transition properties and the regeneration of collagen.

BOHNING: Was Debye a dominating force in the entire department?

SCHERAGA: He certainly was. People had great respect for him. Being a young faculty member, I didn't appreciate the situation as much as some of the older ones did but I had the impression that he was not a very good administrator. He let his secretary run things and it was only in 1950 when he stepped down as chairman and Frank Long took over that this department really got turned around in the way it was administered. Frank was a terrific administrator. He was chairman from 1950 to 1960, two five year terms.

On the other hand, Debye was very approachable when you had a scientific question. I could walk into his office without an appointment, ask my question, he would take out the yellow pad and start working. He didn't have to consult a textbook; he could write out the solutions. It was very stimulating to see him, so I appreciated that kind of interaction very much. With Flory, on the other hand, it was almost a daily contact. You could talk to him about problems. We traveled together once on my first trip overseas. We went to a macromolecular symposium in Sweden in 1953. Of course, they made very much of Flory at the time and he was a leading person at the symposium. That was at about the time he was writing his book. Then he tried it out on Leo and me as guinea pigs and it turned out to be a bible.

BOHNING: Absolutely. That was one aspect that I didn't get from Leo.

SCHERAGA: Well if you look in the foreword, he acknowledges our reading it (13). Maybe Krigbaum did too; but it's in the acknowledgments.

BOHNING: How was Debye in terms of bringing in outside support to the department?

SCHERAGA: Debye had support for himself. During the war, with the Rubber Reserve, he had developed the application of light scattering to polymer solutions. But as far as I am aware, he was never very helpful to other faculty -- as far as getting grant support was concerned. In that respect, I think Frank Long, when he became chairman, was much more encouraging in the sense that, while he didn't go out and get it for us, he at least pointed out where we could go. You must realize there wasn't much outside support in those days. My first grant came in 1950. I was here for three years before I had a grant, before I had a graduate student; it came from O.N.R. Long had the contacts and at least the interest to help the faculty along. I don't think Debye had much of that interest.

BOHNING: Your first paper with Flory was on sedimentation behavior.

SCHERAGA: Yes. It might have been the polyisobutylene paper. I think Krigbaum and Mandelkern are co-authors on that (18).

BOHNING: You were already here when Flory came; how did you develop that relationship with him?

SCHERAGA: I was interested in hydrodynamic properties of macromolecules, that is sedimentation and viscosity and so on. Flory never had any experience with the ultracentrifuge although he had done viscosity with [T. G.] Fox. It was just a natural bringing together of mutual interests. Now while I was primarily interested in proteins at the time, I was still getting into the so-called macromolecular field so that I was perfectly willing to work on any large molecule. It was big molecules that intrigued me although it gradually became focused on proteins. So with Flory's interest, it was natural to go to the natural and synthetic polymers. That is the polyisobutylene and the nitrocellulose work. Actually, Debye was working on soap micelles at the time and the question of their sizes and shapes arose. I had the technique to do that with flow birefringence, so I put one of my first graduate students on a flow birefringence study of detergent micelles (20). This was something that both Debye and I were interested in. He was always receptive to hear about results and was helpful in that respect.

BOHNING: When did you first meet Leo Mandelkern?

SCHERAGA: Probably just as soon as I came here. He was a graduate student of Frank Long's at the time. He was already married and Birdie and my wife became friends; Leo and I became friends. We both had young children of the same age. Then when he decided to stay on as a postdoc with Flory, the mutuality of interests cemented both our professional and social contacts. While I was doing mostly soap micelles at the time and also working on the blood clotting system, that was my protein activity, I was hearing mostly from Leo and a little bit from Flory, what was going on at the time in the polymer field. I mentioned that there were these three competing theories and Flory was looking for experimental tests. In fact, the polyisobutylene study was one of the experimental tests. We tried out all three theories and showed that it was the Flory-Fox theory that best accounted for the data. That was the framework in which this was all going on. Flory having done the viscosity, and I doing the sedimentation. Flory and Mandelkern put the theory together.

I tried to see how their treatment would apply to proteins, which were rigid particles. It turned out that there was a shape factor that you had to take into account for proteins that wasn't necessary with the flexible chain polymer because, being a random coil, it was basically a spherical object. I started to fiddle around with the equation, got all excited and called Leo up one morning. We decided that we had better look into this. Of course, Flory was very sympathetic; he wasn't a part of it but he encouraged us to keep going with it and we finally worked it out and sent it in. It turned out that it flew in the face of established ideas at the time and we had a difficult time trying to get it published. We sent it to the Journal of the American Chemical Society [JACS]. Albert Noyes was editor at the time and he was sending us these horrible referee reports. Flory kept encouraging us not to give up and to write rebuttals. During the course of writing the rebuttals we did some more calculations, which only strengthened the paper and finally they relented and published it (21). According to Current Contents it became a "Citation Classic" although people always refer to it as a controversial piece of work. It's still referred to that way. I don't see that there's any controversy. [laughter]

BOHNING: How long did it take to finally get it through the referees?

SCHERAGA: As I recall, it took about a year and, in fact, that's when Leo left and went to the Bureau of Standards. He came up to Ithaca in the summer and our families went out for a picnic at Taughannock Park. They picnicked while Leo and I worked on one of the picnic tables and finally put the finishing touches on the paper. I presented it at an ACS meeting in Minneapolis and some people, John Ferry for one, were very much taken by it. I know Flory was very appreciative of it and I'm sure that that, among other things, led to me being granted tenure at Cornell.

BOHNING: What year did you get tenure?

SCHERAGA: 1953. I was an instructor from 1947 through 1950, and assistant professor from 1950 through 1953. In 1953, both Mike Sienko and I got tenure and we were promoted to associate professors. Then Long nominated me for the Eli Lilly award in biochemistry, which I received; I'm sure that the hydrodynamic work that I did with Leo, and the blood clotting work with Mike Laskowski, were a significant basis for that award.

BOHNING: How much input did Flory have on the hydrodynamic work?

SCHERAGA: We showed it to him and he said that it all looked reasonable to him and told us to stick to it. But Leo and I developed the whole thing. Flory had no input in it other than that he and Leo had done the precursor.

BOHNING: You actually had another paper on bromination of hydrocarbons about this time (22).

SCHERAGA: Yes. This was a carry-over from my Ph.D. thesis. When I arrived here, I thought I wanted to do physical chemistry of proteins, but, at the same time, I wasn't one hundred percent committed, so I decided to pursue this area too. There was a person on the staff, [Erwin Robert] VanArtsdalen, who had worked with [George] Kistiakowsky and had done his thesis on the bromination of methane about the same time that I had completed my thesis, so it was natural to continue in that line. He was one of those who didn't get tenure. He and I had two graduate students, Bernie [Bernard Hans] Eckstein and Herb [Herbert Rudolph] Anderson. The idea was to determine carbon-hydrogen bond strengths. That was something that really just wound down, and I never did anything more with it.

BOHNING: At this time, you really started to look at proteins in great detail. You worked with Michael Laskowski.

SCHERAGA: Michael Laskowski was my first graduate student, although not my first Ph.D. He came in as a fresh graduate student in 1950. That was when I got my first grant and so I had a research assistantship available for him. John [King] Backus was my first Ph.D. because he had already been here several years and transferred to me. He had been through all of the coursework so he got out first. So Backus was my first Ph.D. but not my first graduate student. Laskowski was one of my best students;

he's now a professor at Purdue. We worked on the mechanism of the thrombin-induced conversion of fibrinogen to fibrin, a subject on which I am still working. We also worked on the thermodynamics of protein reactions, focusing on hydrogen bonding. We were able to account quantitatively for the effect of internal hydrogen bonding in proteins on the pK's of ionizable groups, on the reactivity of covalent bonds, including peptide and disulfide bonds, and on protein stability. We also showed how hydrogen bonds could stabilize peptide bonds so that proteolytic enzymes could be used to catalyze not only the hydrolysis but also the synthesis of peptide bonds. Hydrogen bonding later seemed to go out of favor but now is coming back. Then we were trying to identify internal interactions in proteins in order to determine the three dimensional structure. Amino acid sequences were just coming out; insulin was the first one, so we started to work with that. This was long before the X-ray structures were known and our idea was that, if you knew the amino acid sequence and if you could find out about some specific noncovalent interactions, you could determine the three-dimensional structure. So we set about to try to carry out thermodynamic and spectroscopic studies to identify local interactions. Thus, we published some papers on insulin, but we were always thwarted by the fact that insulin is insoluble in the neutral pH range, between 6 and 7. For a lot of the experiments that you want to do, it drops out of solution, but it was the only protein that was sequenced. We had heard that the amino acid sequences of lysozyme and ribonuclease would soon be available so I started working on lysozyme and ribonuclease.

Lysozyme work was started while Laskowski was still here; Jack [John W.] Donovan also participated. But I started the ribonuclease work myself when I was on sabbatical leave in the Carlsberg Laboratory. Then I came back and started a whole series of experiments involving many graduate students and postdocs and, before the X-ray structure was known, we actually had identified three specific tyrosyl···carboxyl interactions, that is, between groups that were near each other. Three out of six tyrosines were abnormal because they were interacting with something. There were also three out of eleven abnormal carboxyls. There are over 19,000 ways to pair three out of eleven carboxyls with three out of six tyrosines. We proposed a specific pairing based on a whole series of experiments. When the X-ray structure came out, we were right on the nose. I think that was a triumph of protein physical chemistry. It was only years later that we could demonstrate the validity of the conclusions from those experiments.

But all of that had its origins in the work with Michael Laskowski. It's dangerous to cite your good graduate students because, by inadvertent omission, I would hate to see the others feel hurt. Certainly three stand out, and Mike was one of them, but there were many others. I'm jumping ahead, but as I said, I took a sabbatical leave in Carlsberg with [K.] Linderstrøm-Lang. One of the visitors there was Walter [Joseph] Kauzmann from Princeton whom I found very stimulating. There was lots of discussion about what at that time was becoming known as the hydrophobic bond. You're not supposed to use that word anymore; it's hydrophobic interaction, and the solvent water plays a dominant role in this interaction.

When I got back to Cornell, I acquired a new graduate student, George Némethy. George had come to Cornell to work with Flory but just when I got back to Cornell, Flory left for the Mellon Institute. So I inherited George and he did a beautiful thesis on the structure of water and hydrophobic bonding, and the solubility of hydrocarbons. He was another one of my very good students. Shortly after that, Doug [Douglas] Poland came along. With Poland we did a fair bit of work, mostly on helix-coil transition theory in homopolymers and copolymers. We wrote a textbook together (23). He's now chairman of chemistry at Johns Hopkins.

Némethy thought he would like to go into industry, for reasons I never understood. He went to G.E. but as soon as he got there he knew it wasn't for him. So he took a postdoc with Dan [Daniel Edward] Koshland at Rockefeller. Koshland was at Brookhaven at that time but with a joint appointment at Rockefeller University. When he went to Berkeley, he left Némethy behind at Rockefeller. By the way, Némethy did with Koshland one of the theories for allosterism. Némethy is a co-author of three "Citation Classics." His papers with me on the structure of water (24) and hydrophobic bonding (25) were "Citation Classics" and his paper with Koshland was also a "Citation Classic" (26).

[END OF TAPE, SIDE 3]

I've had a large number of other very good people. Dick Ingwall who is now at Polaroid. Hal [Harold E.] Van Wart at Florida State. Chuck [Charles F.] McWherter whom I tried to encourage to take an academic job but he went to industry. Bob [Robert R.] Matheson is at Du Pont; I sent him to Flory for a postdoc. Fred [Frederick Rowland] Maxfield was an outstanding one and he's now on the faculty at NYU but that whole department is moving to Columbia. Jack [John C.] Owicki at Berkeley, Peter [N.] Lewis at the University of Toronto. As I say, I have been blessed with many good graduate students and it's unfair to name some and not others.

I also had an outstanding group of postdocs and senior visitors. My first senior visitor was Syd [Sydney J.] Leach from Melbourne, Australia who at that time worked at CSIRO and later got the chair of biochemistry at the University of Melbourne. He has just retired. I'm talking about the early days. Some postdocs were Jan Hermans who is now at Chapel Hill [U.N.C.], John [A.] Rupley who is at the University of Arizona in Tucson, and Seymour Ehrenpreis who is at one of the Chicago medical schools, and Shelly Rackovsky who is at the University of Rochester.

Then I've had a large number of foreign postdocs. Through Syd Leach I've had a very good pipeline of people from Australia. One of the outstanding ones is Tony [Antony W.] Burgess who is now head of the Ludwig Cancer Research Institute in Melbourne. Maurice Huggins, of Flory-Huggins fame, had a close Japanese connection and advised one of their polymer chemists, somebody from the polymer chemistry department of the University at Kyoto to come here, Akio Nakajima. Nakajima has just retired last year from Kyoto University. He was my first Japanese visitor and that was the start of my having a Japanese person in my laboratory almost every year. Several of them were outstanding, such as Tatsuo Ooi, who came from Nagoya, but later moved to Kyoto University -- he's just about ready to retire from Kyoto University. Nobuhiro Go who is at Kyushu University and just this April is getting a chair in quantum chemistry at Kyoto University. He's a younger person. Then a very young person who is not yet established in Japan is Akinori Kidera. He actually came from Nakajima's laboratory. Nakajima also sent me another very good person, Seiji Tanaka who unfortunately died of lung cancer about ten years ago.

Besides the Australians and the Japanese, I've had a number of very outstanding ones from Israel, including Izchak [Zevi] Steinberg who is now in the chemical physics department at the Weizmann Institute, Noah Lotan, who is now at the Technion, and Hagai Meirovitch, who is now at Florida State University. More recently, I've started to get postdocs from China, Korea, and Hungary. It mushrooms. Once you get one or two, they keep coming.

BOHNING: Chronologically, we were talking about your early papers with Flory. It was at about that time that you went to Carlsberg.

SCHERAGA: I had a Fulbright and a Guggenheim fellowship to spend the 1956-57 year at Carlsberg with Linderstrøm-Lang. That's probably the last time that I worked with my own hands in the laboratory. As you get more and more students, there is less time and for a while you just show them things, and after a while, you just talk to them. I did ultraviolet absorption spectroscopy on ribonuclease which started the ribonuclease story I told you about. Then I also learned from Linderstrøm-Lang some of the techniques for studying deuterium-hydrogen exchange, which he had developed. I did some work on insulin at the time. It was the phasing out of the insulin work that we had been doing.

Aside from the stimulation of Linderstrøm-Lang, I think the other thing about that sabbatical leave was also the stimulation from him and Walter Kauzmann to get going on the hydrophobic interaction. That included Némethy and many other people afterwards; experimental work to test the theoretical parameters and so on. Unfortunately, Linderstrøm-Lang died, I think from medical malpractice, a year or two later. In fact, I got Frank

Long to invite him to become a Baker lecturer at Cornell and he had accepted, saying that he would be happy to come if he survived. He had been a diabetic and that complicated things. During my year at Carlsberg he celebrated his sixtieth birthday and I thought of him as an old man. Now I'm sixty-five and I have a much different view. [laughter] But it was a great birthday party; Niels Bjerrum was there; Niels Bohr was there. It was a banquet right at the laboratory with plenty of wine, beer, aquavit (not vodka); and toasts. The way they celebrate is that everybody gets up and makes a little speech. Some of the people at the lab thought I ought to make a speech in Danish on behalf of the foreign visitors. So I memorized a speech in Danish and now it's a family joke; my children still recite it. I remember Niels Bohr coming over and telling me that he appreciated my speech in Danish. Niels Bohr was an outstanding scientist but a lousy lecturer. I had heard him lecture on several occasions. You had to sit in the first row and you still couldn't hear him. He whispered. He always gave one the feeling of a very gentle sort of a person. Of course for a young scientist, just to be in his presence was very stimulating. And old Niels Bjerrum was there. In fact, he used to come to all the weekly seminars at the Carlsberg Laboratory. He had very sarcastic remarks to make, you couldn't slip anything past him. Lang was more of a diplomat and a gentleman when he criticized. For me scientifically, this period of the hydrophobic interaction was important.

By the time it came around to my next sabbatical, that was in 1963, I was lucky enough to get another Fulbright and Guggenheim. I had already met the Katchalsky's but Linderstrøm-Lang's place was the Mecca for protein chemistry in the 1950s, and that's why I went there. Actually, I met Aaron Katchalsky at a meeting that Flory and I attended in Stockholm. I was very much taken by Aaron Katchalsky. He was a charmer and you could just see that he was an outstanding scientist. Then I met his brother, Ephraim, a year or two later at a Gordon conference and was equally taken with him. Then they had a very bright student, Michael Sela who subsequently became president of the Weizmann Institute. Already I was developing an attraction for Israel although I opted to go to Denmark at the time.

I mentioned earlier that I had been to Hebrew school, and had a strong Jewish cultural background at home, and had acquired very strong Zionist feelings so that, plus the scientific interest in the Weizmann Institute, made it the natural place to go in 1963. But having spent a whole year on my previous sabbatical, I felt it was too long to be away from my students, so I took only a half year as I have done on subsequent sabbaticals. That was also very stimulating. I worked with both Katchalskys. This was all theoretical work. I also worked with Shneior Lifson who was in the chemical physics department.

BOHNING: What had transpired here between Carlsberg and the Weizmann sabbatical? Where had your work gone in the interim? Your work started to include theory.

SCHERAGA: I'll tell you where the theory started to come from. We were carrying out experiments to look for noncovalent interactions to define structure. It then became apparent that if you had enough of these, you could determine the structure from the amino acid sequence; that was the push into the theory. Némethy had left here after getting his Ph.D. As a graduate student, he had studied the structure of water and hydrophobic bonding and we still maintained some contact. I thought there was something to be learned about D_2O and the effect of deuterium substitution, so we continued to collaborate while he was at Rockefeller. Just before he left Cornell, I was already chairman at the time, around 1962, I was sitting in my office chatting with him and John Rupley. John Rupley worked on ribonuclease; he was one of those who contributed to the ribonuclease story. We began to think that we ought to be able to determine protein structure theoretically, by making use of experimentally determined distance constraints such as those three tyrosyl···carboxylate interactions that I already mentioned. So, with George, who was waiting around to take his Ph.D. thesis exam, we decided to take a loop of ribonuclease and write out the analytical geometry, generate a structure and that was the start of it. It was a long series, involving Syd Leach, Roy Scott, Doug Poland and others. Némethy collaborated from a distance and then, when he came back to Cornell, he got into it full time. That was part of the theory, that is to try to figure out how proteins fold, but we also became interested in the helix-coil transition. It's hard to remember how that interest developed. Certainly as a model system for understanding interactions. When Némethy was doing his thesis, we already saw that with a helix and neighboring nonpolar sidechains, hydrophobic interaction could stabilize a helix. At the Weizmann Institute with Lifson and one of his students, we did a quantitative treatment of the helix-coil theory (27). He had done a helix-coil theory before with Antonio Roig (28), as had Zimm and Bragg (29), but they focused only on the backbone. I wanted to focus on what the side chains were doing, how they contributed to the stability. Since we had already proposed a specific type of interaction involving side chains, we extended the helix-coil theory and showed that the melting point of a polyalanine helix would be a hundred degrees higher than that of a polyglycine helix, if it existed. So you had tremendous stabilization. That started a whole series of studies of the effects of side-chain interactions on helix stability which I then picked up with Doug Poland. That also led us into random copolymers because most helices weren't soluble in water and we wanted the interactions to be in water. The only way you could beat the solubility problem was to make random copolymers with a water soluble host, and the residue of interest as a guest.

We were helped along with this random copolymer work about that time in the 1960s by one of the postdocs from the Weizmann Institute, Noah Lotan, who had developed a good model system which we used as a host. With this host-guest technique, we obtained experimental parameters to characterize the helix-forming tendencies of all 20 of the naturally occurring amino acids.

BOHNING: You did some work on blood clotting?

SCHERAGA: That's been going on all through the years. More specifically, the interaction of thrombin with fibrinogen. In the early years, thrombin was simply just a reagent to get the reaction started and I focused on what the fibrinogen was doing. It got activated, then it polymerized and we studied the distribution of polymers and the energetics of the polymerization reaction which told us about what functional groups were involved from the pH dependence of the interactions. In the subsequent years, we began to worry about what the enzyme was doing. We looked at the mechanism and action of thrombin. It hydrolyzes a peptide bond but the question is why is it so specific because trypsin will hydrolyze after every arginine and lysine in the protein whereas thrombin hydrolyzes specific arginine-glycine bonds. That kind of work is still going on. More recently, we think there are special conformational features in the fibrinogen molecule which allow it to fit into the active site of the thrombin. Now, we're doing NMR experiments to demonstrate those conformational features. Of course, as the years go by, new techniques come in, you apply the new techniques and you get new answers to old questions.

BOHNING: You were at the Welch conference in 1964. I read the remarks you made as a discussion leader (30).

SCHERAGA: That was just when we were starting on the theoretical approach to the folding of polypeptides and proteins. We had a very simplified model when we were just getting started. We just treated atoms as billiard balls, the hard sphere approximation. They couldn't overlap and so many stereochemical conformations were eliminated. I remember Debye getting up at that meeting when he said, "But atoms aren't hard billiard balls." [laughter] Of course we knew that; but then we had to make the potential functions for the interactions much more involved. The only way to know that you had good potentials was to paramaterize them on real experimental data, namely on known crystal structures so if you could calculate crystal structures and lattice energies and rotational barriers, then you could have some comforting feeling that the potential functions are reasonable.

So what you heard in those remarks was simply the start, within the framework of a hard sphere potential, of a field that has occupied most of my interest in the years since.

BOHNING: You also got into the structure of water.

SCHERAGA: That goes back to the hydrophobic bonding. We realized that water was playing a very important role in determining the hydrophobic bond strengths so we felt we had to understand, as a model for the hydrophobic bond, hydrocarbon solutions [in water]. If you want to understand hydrocarbon solutions, you better first understand the solvent and what the hydrocarbon is doing in it. The model that we proposed, which was based on some earlier qualitative discussion of Frank and Evans (31), was one in which a clathrate forms around the hydrocarbon. This was the work with Némethy. Then we made a statistical mechanical treatment of that model. Twenty-five years later, that model now arises naturally as a result of the intermolecular potentials. We now have good potentials and we -- and lots of other people -- do Monte Carlo or molecular dynamics calculations on a methane molecule in water. You can see the clathrate develop. That's the model that we had assumed but now it arises naturally as a result of the potential function.

BOHNING: I noticed that you have some papers on internal rotation barriers with Roy Scott (32).

SCHERAGA: We started with Némethy and the hard sphere potential, that I referred to in those remarks at the Welch Foundation conference. Then we began to realize that we had to get much more realistic potentials, one component of which was the rotational energy. We subsequently developed much more realistic potentials, and used them together with various optimization techniques to calculate polypeptide and protein structures. Roy Scott had been a graduate student of mine working on the ribonuclease project. He wanted to stay on and get involved in this new work and Roy did some of that early investigational work on rotational barriers.

BOHNING: I want to ask you about your term as chairman of the department and what had occurred at Cornell over the years that you have been here.

SCHERAGA: I think of the administration of this department as undergoing a very great change when Debye retired as chairman. He stayed on as a professor and Long became the chairman. I think for the first time in the history of this department it was in very good hands. Long was not an autocrat. He ran the department democratically but he was genuinely interested in guiding it in the proper direction. He was a good leader and a good model for me to follow as chairman.

About the time that I took the chair, the staff was roughly twenty and when I stood down it was about thirty. During those years I was able to bring about the change: I wouldn't take the credit, I would say that I was providing leadership. It was all done democratically. We made some very good appointments in those years. We got Roald Hoffmann, Michael Fisher, George Morrison, Gordon Hammes, Jack Freed, Elliott Elson, who unfortunately has left us. But it was a period in which we made some excellent appointments which really enhanced the reputation of this department.

The first thing I realized, and here I had to push, that you can't bring in people like that unless you have good facilities. Baker Laboratory is a fine building. It's solid. The walls are thick but inside it was run down. It was almost as bad as Baskerville Hall at the City College campus. During all of the years of the Depression, it was built about 1924, it was neglected and it went to pot. There weren't proper electrical outlets; D.C. was piped in from batteries in the basement. This wasn't a building that you could bring outstanding people to. I was aware that there was NIH and NSF money available and I must say I had to push people to go after it. There was resistance on the part of some of the old faculty, but I managed to convince them and so we made applications. We got both NIH and NSF money but it was geared to two programs; I was involved in initiating one and I was pushed into the other. The one I initiated was to get the chemistry department moved into the biological direction. It was certainly my interest but I felt this was where chemistry was going. The one I was pushed into by the physicists was solid state chemistry. Mike Sienko also pushed in that direction too because they were getting the Material Science Center at Cornell funded by ARPA [Advanced Research Projects Administration] and a lot of the chemists wanted to be part of it.

So here were these two new directions in chemistry that I was able to talk up. We were going into the Cornell centennial campaign and so I went around and talked to alumni groups and got them convinced to help out. You just don't decide that you're going to build a building. You have to convince the administration. It has to get dragged screaming and kicking in that direction. I managed to get us into the centennial campaign, so there was fundraising there. We managed to write grant applications which got us grants from both NIH and NSF. NIH because of that biological interest in the chemistry department. Then it turned out that the president of almost every chemical company in the United States at the time was a Cornell alumnus. We defined them as chemistry alumni but some were really chemical engineers. But that didn't matter and so we managed to get some contributions out of Dow and Carbide and Du Pont and Monsanto. The Monsanto episode was a joke. It involved Bob [Robert Allen] Plane, who succeeded me as chairman and helped me along in this, and the Cornell president, who at that time was

Jim Perkins who subsequently lost his job in the student unrest of the later 1960s. Anyway, he, Bob Plane and I went down to St. Louis to visit the Monsanto president, Edgar Monsanto Queeny, who had left Cornell. I think he dropped out halfway through as an undergraduate. He was a grumpy guy. I'm surprised he even let us in. He told us, "Look, there's a half million dollars in my will and at my age, you won't have long to wait for it." We were happy. We left and as we walked out Jim Perkins said to me, "Okay Harold, this tips it. Your project is go." We started the building project but when Queeny died, it wasn't in the will. He had apparently put everybody off this way, so Cornell was left holding the bag.

Incidentally, at the time we started there was still several million to raise but president Perkins figured that they could get that. Ultimately, Cornell picked up the tab. First of all, we built this building -- the "new" wing. Then we completely gutted the old one and remodeled it.

BOHNING: Wasn't Olin a graduate of Cornell?

SCHERAGA: Olin was another one. I forgot to mention him; John Olin and Spencer Olin. John Olin gave some money. He was the first contributor. He was a little more inclined towards Cornell. Spencer had a wife who didn't seem to like Cornell. Anyway, it was harder to get money out of Spencer, but we eventually did. It is Spencer's name that is on this building. I don't like to use the name Olin and I'll tell you why. There is an Olin Hall somewhere else on this campus and my mail would frequently go to the wrong building. So I say I'm in 660 Baker Lab because if you get to Baker there's no sixth floor so you're bound to get up here.

To come back to my chairmanship, this may sound a little egotistical but I feel that I played a very important role in building the reputation of this department. I got these facilities and the appointments that I already mentioned, besides the people who were here and got promoted to tenure, like Andy Albrecht, Jerry Meinwald, Dick Porter, Bob Fay, David Usher, Charlie Wilcox and Ben Widom.

BOHNING: What about the undergraduate program?

SCHERAGA: We never separated our faculty into graduate or undergraduate faculty, everybody teaches in both. There has never been any distinction. We have also paid a lot of attention to making sure there was good instruction right at the freshman level. Mike Sienko was an excellent teacher and that book he wrote; you know how it influenced chemical education in the United States. I think we've paid a lot of attention to trying to do good teaching. When we make a promotion, we pay serious attention to evaluation not only of research potential, but also as a teacher. We have a faculty committee that goes around every year and visits most of the faculty members in their courses. They sit in and write a report, so we have faculty evaluating teaching. We have student evaluations at the end of every semester. All of these data are collected in every person's personnel file and, especially for those coming up for tenure, these come into the decision. I remember one case of an outstanding person, he's well-known now, whom we let go because his teaching was not very good. That divided the faculty but, ultimately, we decided that we just couldn't tolerate a poor teacher on the faculty.

BOHNING: That's got to be a difficult decision to make.

SCHERAGA: That was a hard one and in fact, it is the only one that I can remember like that. I remember another case where a person was a very outstanding teacher but we weren't dancing up and down about his research ability and we promoted him. It turned out alright. You win some, you lose some.

[END OF TAPE, SIDE 4]

One other thing I managed to do: in those days, it doesn't happen any more, now the budgets come down from the administration, but then they were negotiable. I think I was a lot more successful in negotiating than was the physics chairman. There was one time when the math chairman and I teamed up and we just refused to accept the bottom line and we held out long enough. I know in chemistry I was able to push salaries up.

Another thing I'm very proud of is that I increased the services of this department. I got the position of Executive Director upgraded, so that we could hire a scientist with a Ph.D. Incidentally, we now have an excellent person in that position, Earl Peters. We didn't have a glassblower when I came; I got a glassblower. I got a draftsman; now a draftswoman. I increased the personnel in the machine shop and I got an electronics shop. All of these kinds of services which you had to have to run a first-rate research group. Then we started into getting instrumentation. As the federal programs came along we were grabbing them; the instrumentation facility programs and so on.

So between building, faculty, services, and facilities, I think I did a pretty good job as chairman.

BOHNING: I would like to look around the building before I leave.

SCHERAGA: One thing about looking around the building which reflects our interest in undergraduate education. Bill Miller played a very important role as chairman of the building committee. They introduced an entirely new concept of an undergraduate teaching lab. We built a mockup and tried it out for a couple of years in the old building and used the design from there. So you'll see that the undergraduate teaching lab is quite different. In traditional labs you have students on both sides of the bench and they face each other. Here they all face one way and the laboratory doubles as a recitation room. The teaching assistant can just stop in the middle of an experiment to make a point. Everybody is there and the blackboard is up there. There were a lot of features which they developed which I had nothing to do with.

BOHNING: I have worked in many laboratories which I felt weren't teaching facilities because you didn't have that option. To try to stop a lab and make a point is very difficult in those facilities.

SCHERAGA: That was one feature that they wanted to work into it and I think they did a pretty good job of it. I know it was written up in some of the chemical education journals at the time.

BOHNING: When you first came to Cornell, what were you teaching?

SCHERAGA: I taught quant. Pete [Melvin L.] Nichols was the analytical chemist at the time. He gave the lectures and I gave the recitations and ran the labs. I had to earn money in the summer so I taught qual. in the summer. Within a couple of years I was given a qual. assignment along with quant. and I was in analytical chemistry until 1952. So that was five years teaching both the academic year and the summer. I taught summers until I had a grant which could pay me a summer salary. I moved into physical chemistry in 1952 when Briggs went into the hospital and I took over his course.

Then I began to teach graduate courses. I taught two types of graduate courses. One was the physical chemistry of proteins which has evolved over the years and which I still teach. For several years I taught a course in colloid chemistry but the interest for that seemed to have disappeared although, now, it has become a hot topic again. However, I certainly don't want to start a new colloid course and there doesn't seem to be anybody else around who is interested in doing it.

It's hard to know the direction that things are going to go. We now are resurrecting our polymer program with an IBM grant. IBM had a competition with about thirty or forty different schools competing. They gave twelve grants of $2 million each;

one million in cash over five years and one million in IBM equipment and we were one of the twelve. Roald Hoffman and I wrote that application with much help from a senior research associate, Ken Gibson. With this funding we are rejuvenating our program which had lost the tradition of Debye and Flory. One of the things we proposed was to go out and try to hire a major polymer figure. We have just made that appointment. He is Jean Fréchet, who is a man in his mid-forties, a Frenchman who now is at the University of Ottawa and a synthetic polymer chemist. I think our chairman has been able to raise some other money for fellowships in polymer science and with him arriving on the staff, I hope we can start to resurrect the polymer activity in the department.

BOHNING: Do you see this as being an important direction?

SCHERAGA: I think it is an important direction for chemistry. I was on an NRC committee (33) which looked at the status of polymer science and engineering in the United States. One of the conclusions we came to was that universities are derelict in their duty to train polymer scientists. They're leaving it to industry, whereas most chemists who go into industry do polymer science or engineering. Outside of two or three well-known polymer institutes, polymer is a dirty word at most universities.

This situation is changing gradually and we're hoping to resurrect it here at Cornell. Other directions which I mentioned earlier when I discussed being chairman; the biological macromolecules and solid state chemistry. Any lively, vital chemistry department has got to keep asking in which direction the field is moving; we should be leading and not just following. Polymers is one direction in which we feel we, as a teaching and research department, ought to be involved. It's nice to have that IBM grant to help us along. The University has made a commitment to pick up that position when the five years are up.

BOHNING: You had made the comment earlier that you felt chemistry was moving in a biological direction.

SCHERAGA: I personally think that's a very exciting area of chemistry to be in. I was able to convince a significant number of my colleagues so that we made appointments in that area. For example, we appointed Gordon Hammes and Barbara [A.] Baird. There are others in this department who are traditional chemists in the sense that they are organic or physical chemists but they work on biological systems. I used to tell the alumni when I was trying to raise money and convince them of this, "What's the difference whether the white powder in the bottle that you make measurements on came out of the side of the mountain or whether it came out of the tissue of some organism." You still do the kinds of experiments you're doing on, in this case, large molecules. In addition, there's the excitement that it has biological relevance. That's one of the reasons that I like to keep my blood clotting work going on. Most of my contributions in protein physical chemistry were within the framework of the blood clotting system and at the same time I felt we were contributing towards a very important medical problem. In fact, in recent years I have now joined that project together with a similar one at the University of Rochester Medical School, so we now have a combination of basic research and the applied research in the medical school. They are now trying to apply some of these ideas. They have a project in which, if they can catch a heart attack victim early enough, they can dissolve the blood clot in the heart and open up the blood vessels so that that portion of the heart doesn't die. It's very tricky because this is a kind of plasminogen activator system. If you give too much, you not only destroy the clot but you destroy blood-clotting ability when it is needed, so it's a really delicate balance. This goes back to much basic research but now you have clinical applications going along with it. I find that an exciting aspect of chemistry. There are various other disciplines in the department here, each doing their own thing, but on biological systems. We're not making biologists out of them. They're chemists but the systems they choose to work on are exciting biological systems; and the chemistry is exciting.

BOHNING: Do you see more and more traditional chemists moving into that area?

SCHERAGA: Yes. In fact, we have people that we label bioinorganic chemists. We have people we label bioorganic chemists, biophysical chemists. These are actually subdisciplines within the department. For example, [James] Lynn Hoard, who has since retired, for years was doing X-ray crystallography on boron. We got him interested in heme groups. So he joined our group and he was the one who showed that iron was out of the plane of the heme. This was very important when Max Perutz worked out the structure of hemoglobin.

In addition to getting the NIH grant for the building, we were also successful at that time in getting an NIH training program which provides fellowship money for those of us whose students are in health-related science.

BOHNING: How do you find attracting graduate students today? How do you find the undergraduate market, so to speak?

SCHERAGA: This is a serious problem. First of all, we train very good undergraduate students but we send them away. Unfortunately, I'm finding that not only ours, but all over the country as I visit and talk to friends, the really topnotch students are not going to graduate school. That's a strong statement but, by and large it is true. They are going to medical school, business school or law school. I don't know what the reasons are for it although I have my own guesses. They see how hard it is to get grants now from the government. You have to scrounge; it's a cutthroat business. If you take an academic position and you don't get a grant, how are you going to get promoted if you don't produce research results? On the other hand, financially, I think they perceive that medicine, law, business are more financially rewarding disciplines. The result is that I don't think we are getting as good graduate students as we used to get. That's one thing. The other thing is that by and large, the United States is not turning out such good Ph.D.s in science, and so the postdoc pool is down. We're getting our postdocs from abroad. We get very good ones from Japan and only an occasional one from the United States. The result will be that the Japanese are going to walk away with biotechnology like they did with cars and electronics. I visit Japan quite frequently. They've just set up something called PERI -- Protein Engineering Research Institute -- a consortium of industry and government. It has put in $100 million for a ten-year project to develop this. We don't have that kind of thing in the United States where government and industry are working closely together.

BOHNING: The wartime Rubber Reserve project was an example.

SCHERAGA: That's right. And the sad thing is that many of the Japanese scientists who are leading their effort are my former postdocs. For example, Go is the scientific consultant for PERI.

BOHNING: I teach a course in chemical literature and I was giving out some patent assignments from the 1987 Chemical Abstracts. I was just randomly selecting patents from different sections in Chem Abs and I was amazed at how many Japanese patents there were.

SCHERAGA: Look at Macromolecules. Until recently I was on the editorial board and I remember Stretch [Field H.] Winslow, who is the editor, commenting about the phenomenal percentage of the papers that he receives from Japan. I think this is a point we may have made in our NRC report. In contrast to American universities, there are many more polymer scientists per capita or even in absolute terms, in Japan than there are in the United States. The Polymer Science Society in Japan is a big society. I think the biotechnology effort is better there. Everybody is getting into the act all over the world but especially in Japan. I hope we don't lose out to them. I think the whole training of scientists in America, in my view, needs a big shot in the arm. The Japanese study mathematics right from kindergarten on. It doesn't matter whether you are going to be a humanist or a scientist, they're going to be comfortable in mathematics. Their education system is geared to it. We've seen what they've done to Detroit.

BOHNING: As you got into more and more theoretical work, when did you get your introduction to computers?

SCHERAGA: That started just as I left Harvard as a postdoc. There was something called the Harvard Computation Laboratory where they had assembled the Mark I computer. As I remember it, the computer sat in a room that was twice the length of my office. It had vacuum tubes and mechanical relays and it chugged away. The printer was a typewriter which typed one letter at a time. We'd stand there and watch the typewriter and the numbers coming out. It took two weeks to solve a problem on which I was working. I was working on a partial differential equation and had worked out all of the equations here and talked to Debye about them. Then, with Edsall, I had the entree into the Harvard Computation Lab. That's the early paper of Scheraga, Edsall, and Gadd (34). We were able to get numerical solutions so that you could interpret flow birefringence data. Until then, you could make the measurements but you couldn't interpret the data in terms of rotational diffusion coefficients.

That was my first use of the computer but I didn't have any interest in doing the programming; [J. O.] Gadd was the programmer. I was more interested in doing the science. I've never really had an interest in programming. I felt I had to learn Fortran and write a program just to keep up with my students but I don't like when they become enamored with programming and forget about the science. Maybe that's why I resist it. Then I did a follow-up on non-Newtonian viscosity (35). I did that myself because it was basically the same theory. I had no further contact with computers until Némethy got involved; he was doing the statistical mechanics of water and hydrophobic bonding for his thesis and we had a primitive computer here which he was using. Since he knew how to use the computer he ran the hard sphere calculation on ribonuclease that I mentioned earlier.

BOHNING: Was that a computer in the department?

SCHERAGA: No. It was a university computer. At that time, graduate students could get free time so we weren't paying for it. Suddenly, things started to change. You had to pay for your computing and that's when I was having a very difficult time because I couldn't get money out of the agencies to pay for computing. It wasn't appreciated at the time that computing was important. The University wouldn't let you buy your own computer even if you had the money; if you put an order through the purchasing department it was stopped. They wanted it all to go to the central facilities and there was a long running battle on that. That battle has been won now and I have been able to get some money out of the agencies to buy my own computer. That's pretty good but now Cornell has been designated a supercomputer center. It's one of the four or five. We have our own computer full-time, 24 hours per day unless there's something to be gained by going to the supercomputer. So we're using both facilities now. The University has matured a bit and it's mostly because the need for the supercomputer was demonstrated by scientists. Ken Wilson was the moving figure in that; previously, the computer was driven by the business people. That's why it was IBM all the time. Now, the supercomputer is still IBM but coupled to array processors. It's being supported by a consortium of IBM with NSF. We're IBM not Cray the way some of the other supercomputer centers are. Obviously, the computer has played a major role in our development of the field of conformational energy calculations on proteins.

BOHNING: You had a paper on polypeptide nomenclature which had both Edsall's and Flory's name on it (36).

SCHERAGA: When we started to do the hard sphere calculations, there were three groups that were active. One was mine; one was G. N. Ramachandran in India and one was that of A. M. Liquori in Italy. Flory started to get interested and then Lifson. These were the main groups. Since each of us was starting up on our own we had our own nomenclature and it became a real zoo. At some meeting, somebody suggested that we get together and agree on a nomenclature. John Kendrew who is a crystallographer was in on it. John Edsall's only interest in it was because he was editor of the Journal of Biological Chemistry at the time. He wasn't doing any work in this field. George Némethy was interested and I don't remember all the other authors. It was an international committee. After several meetings, we agreed on a nomenclature and then we found out that it flew in the face of what Vladimir Prelog and [Robert S.] Cahn had set up for the organic chemists (37), so we had more meetings to try and reconcile that. I remember Flory never gave in on one terminology. He didn't like the word conformation. He wanted to use configuration; as a statistical mechanician, it was configurational space. The protein chemist distinguished the two terms. Conformation indicated what happened when you rotated about bonds. Configuration was what happened when you break bonds as you convert from an L to a D form. I think that's a useful distinction. Aside from that Flory went along with it. The zero point was fixed as the cis conformation. Originally we had it trans but we reconciled with Cahn and Prelog.

It started as a private group and I think it may have even started at a Gordon conference. Then we got the blessing of the International Nomenclature Committees and finally, it was adopted. So there is an official nomenclature for polypeptides. I think it has carried over to polysaccharides and polynucleotides, although I haven't been as actively involved in that. That's how all those names got together on that nomenclature paper.

BOHNING: You actually went to get sanctioning after rather than before. In other words, you weren't asked to do this, you did it on your own.

SCHERAGA: It was done by the workers in the field just to keep from confusing each other. Edsall was an editor of a journal so he had access to other editors and to the International Union of Biochemistry, the International Union of Pure and Applied Biophysics so it was easy to bring them in and one or two others. I was involved in one of those international unions myself. It was easy to get the blessing from those groups.

BOHNING: How long did it take you to work out your differences with Prelog?

SCHERAGA: I think once we became aware of it, then it wasn't so difficult. None of us had even considered it.

BOHNING: Who discovered that first?

SCHERAGA: It might have been Kendrew. I don't remember. Vladimir Prelog had been here as a Baker lecturer. It surprised me at the time, but a lot of his Baker lectures were devoted to nomenclature when he had so much good organic chemistry to talk about.

BOHNING: Was that about the time of the R & S nomenclature?

SCHERAGA: Yes. He was pushing all of that.

BOHNING: You also had a note that intrigued me (38); when you responded to something that [Joel H.] Hildebrand had said.

SCHERAGA: That's funny. I forget how this went but he had a different view of what a hydrophobic interaction was, so Kauzmann, Némethy, and I responded to him. I thought that was where the matter lay. Ten years later, he went back and did the same thing all over again but we never responded. I think he put it in PNAS the next time (39). [laughter] By that time Hildebrand was close to one hundred. I should be so active at that age.

BOHNING: Going back to your work with Mandelkern; Tanford attacked what you had been doing.

SCHERAGA: Yes. We had a running battle with Charles Tanford for many years. It was mostly over the work I had done with Mandelkern. What we had done was challenge a view that actually goes back to Oncley, and Tanford tended to support that view. That's why I say that it's referred to as a controversial issue. I think it sort of died out as a controversy, although I must say, I still find people using the old procedures, even in papers published today. Most people will make use of our method. Indeed they use it in a way that we never envisioned. We were using our theoretical treatment to determine size and shape, but people turned it around and use it to get molecular weights. I don't recommend it. We had assumed the molecular weight to be known. There are more direct ways to get molecular weight. Put it in an ultracentrifuge and do sedimentation equilibrium; or light scattering.

BOHNING: Is there anything in your notes that we might have missed?

SCHERAGA: You asked me what my activities were when I was young. I played a lot of chess, especially the summer after I graduated from high school, with Ruby Schaeffer who is now at the Bureau of Standards, and Cy Sroog who recently retired from Du Pont. I want to mention some of my other colleagues at Duke. Henry Linschitz who is now at Brandeis was there. Henry finished up a little before I did and went off to some mysterious place. We never found out until after the war that that was Los Alamos. In fact, he was very much involved in assembling one of the bombs that was dropped.

Another one was Harry Soodak. He worked for Nordheim and he's now a professor of physics at CCNY. In fact, when Henry Freiser got married, I roomed with Harry Soodak. I hardly ever saw him because he worked at night and I worked during the daytime. Another person who was a colleague in my postdoc year was Chris [Christian Robert] Sporck. He had been a Ph.D. with Kirkwood at Cornell and was a postdoc in the department at Harvard, obviously from Kirkwood's connection. I shared an office with him and had lots of stimulating discussions. At that time I also became friends with Harry Saroff who recently retired from NIH.

There were two people in that lab who came the year after I left, but because I was going back doing this computational work, I had close associations with them. One of them was Charles Tanford. The other was Harold Edelhoch, who unfortunately died last year. He was at NIH and Harold and I were very good friends.

BOHNING: Where did Tanford go?

SCHERAGA: Tanford went to Iowa and was there for many years, but then wound up at Duke. Tanford is now at Duke; he was in biochemistry but I think he moved over into physiology. I haven't seen or heard of any of his work for several years. He's moved into membranes and I just don't read that literature.

[END OF TAPE, SIDE 5]

BOHNING: What was Cornell like when you first arrived?

SCHERAGA: When I first came here in September 1947 with my wife and daughter, it was shortly after the war so we couldn't find an apartment. We had to live in Watkins Glen which is thirty miles away. All of the veterans were coming back and there wasn't enough housing, so the University took over a resort hotel in Watkins Glen and converted it into apartments. They bused us back and forth to the campus, a thirty mile commute each way every day. I was finally able to find an apartment in Ithaca in May, 1948.

As I said earlier, the faculty was much smaller than it is now, and very formally divided into enclaves, physical, organic, inorganic, and analytical, with a semi-formal head of each group. Happily, those formal divisions are long since gone. I've already mentioned the run-down condition of the laboratories. Research funds were almost non-existent. Nowadays, a newly appointed faculty member gets a sizeable amount of start-up money to get his research program going. In those days, we didn't get a cent. I managed to obtain a $200 grant from the American Academy of Arts and Sciences to pay for the precision machining of the concentric cylinders of my flow birefringence apparatus which was done in a Boston machine shop. Socially, there was very little interaction between the older and younger faculty. However, long-standing friendships were established among the younger faculty, who are now the old timers. My initial appointment was as Instructor, a rank which is no longer used, and I became an Assistant Professor only three years later. I've already mentioned the evening polymer seminars. Besides this, there were, and continue to be, an active seminar program and annual Baker lectures.

Another person I would like to mention from the Weizmann Institute is Arieh Berger. This leads me to something that I left out which is an important part of my career. Arieh Berger and Michael Sela were contemporaries. They were students of Ephraim Katchalski and so naturally I had interaction with them too. I was there in 1963 for a sabbatical and I was there again in 1970 on sabbatical. At that time, remember we were in the middle of the Vietnam War, there was turmoil, my three children were growing up, I was beginning to think about emigrating. Now, to do that there has to be a push and a pull. The push was what was perceived as an intrinsic breakdown in American society because of what was perceived of as an unpopular war and the pull was Zionism. But I didn't have the guts to make the move. They [the Weizmann Institute] were interested in having me come there because they're always interested in attracting mature scientists so we settled on a compromise where I would spend half a year there every year, but Cornell balked at that. Cornell was willing to settle for me to take a leave for six months every other year, so I was there in the Spring semesters of 1970, 1972, 1974, 1976, and 1978. The idea was that I would collaborate with Arieh Berger and Ephraim Katchalski and Aaron Katchalsky. I would have a research group over there and when I was there for six months I would be directing it; when I wasn't there I would make some visits but they and my postdoc, Noah Lotan, who was originally Arieh Berger's graduate student, would have hands-on guidance. That didn't work out for a variety of reasons. First of all, Aria Berger died. Aaron Katchalsky was killed in the Israel airport massacre in 1972. You remember there was a Japanese terrorist with a machine gun who sprayed it, killing about seventy, including Katchalsky. And Ephraim Katchalski became President of Israel. Finally, Noah left the Weizmann Institute to go to the Technion. So all the structure that we had envisioned collapsed; nevertheless my wife and I enjoyed being there. Our children were grown at the time so that was no longer an issue. If we had made the move permanently, we would have been away from our children and what soon became grandchildren. The research wasn't going right because there was no group developing. So as not to waste my time there, I brought students with me; I would always take two or three students from Cornell. I had close contact with them and worked closely with them at that time. I must say it was a great sacrifice to myself because I worked there on an Israeli salary. I took leaves of absence here, giving up a very good Cornell salary. An Israeli professor makes $7000 a year. I was there half a year, so I got $3500, plus an apartment. As you can imagine that's nowhere near the salary that I gave up here at Cornell.

Nevertheless, there were other things. The attraction of being in Israel because it's a very exciting place. The Weizmann Institute is scientifically an exciting place. 1978 was the last year that I did it. Then we decided that I could continue collaboration but instead of taking a leave of absence, I would do it for one month every other year, during the winter break, and so I have done that. I was supposed to go this past winter but I had to postpone it. I've had that kind of scientific relationship with the Weizmann Institute for many years. It didn't work out the way we all envisioned it for the reasons I told you but there still is collaborative research. When Ephraim finished as President, that was in 1978, we started to talk about starting up some collaboration again. But his interests were moving more towards biotechnology at this point. As President he began to be aware of the social needs of the country. But he was still interested in listening and being involved in a project that I had proposed. He called in his former student, Izchak Steinberg, who had been my postdoc. He was also interested but, by that time, his interest had turned away from the things we had been doing, to neurobiology, which is another exciting area. So, he called in his student and we were down to the next generation already, Elisha Haas. Elisha and I have been collaborating ever since. I mentioned a student, [Charles A.] McWherter; I sent him over to Israel for one summer actually to work in Haas's lab. That kind of collaboration is continuing. That's one of the collaborations that I have going right now at the Weizmann Institute. I've had two Israeli postdocs, a husband and wife team, Hagai and Eva Meirovitch, who both spend time here and I've collaborated with both of them. Eva actually works with my colleague Jack Freed but we did something together. In fact, we just sent a paper off to the <u>Journal of Physical Chemistry</u> this week. Hagai was working with me. They're just in the place where their careers are being determined, whether they make tenure or not. So I have that collaboration with both of the Meirovitches and with Haas.

I've had a few good senior people visiting. I already mentioned Leach, Nakajima and Ooi. Then there was Wayne [L.] Mattice who has taken the chair in polymer chemistry at the University of Akron; while he was at LSU, he spent a very productive year here when he worked out the theory of the beta-coil transition. Dennis Rapaport, from Bar-Ilan University in Israel spent a very productive year here, doing molecular dynamics studies.

I should mention another person who first came to me as a postdoc, Ken [Kenneth David] Gibson. He's an Englishman who came here in the late 1960s and then went to the Roche Institute of Molecular Biology in Nutley, New Jersey, and has just in the last couple of years taken early retirement and has rejoined me. He's a very stimulating person to have in the group. He's a biochemist but an unusual biochemist. He's very soundly trained in mathematics and physics, the way training in England used to be.

Another person that I collaborate with is Matthew Pincus, who was a postdoc of mine. He is now on the faculty at the Medical School at New York University. One of the things I've done with him is to work out the structure theoretically of an enzyme-substrate complex and then prove it with experiments. This particular one pertains to how a hexasaccharide sits in the active site of lysozyme. We calculated the orientation of the substrate in the active site (40) and then validated it with experiments (41). There's a whole series of good postdocs that I could name but I don't think you'd want a catalog.

Another interesting study that was done with two Japanese coworkers, Yasuo Konishi and Tatsuo Ooi whom I mentioned before, where we worked out the pathways of folding of ribonuclease and found out that there are many pathways depending on the solvent conditions (42). Then I mentioned our theoretical work on protein folding. We've produced a whole literature on that. I don't think we have time to go into all of the details of that but, ultimately, we are trying to understand how the interactions between the various parts of a polypeptide chain dictate, first of all, how they should fold and, secondly, how they should interact with substrates. I just mentioned the enzyme-substrate interaction, and we also solved a number of problems theoretically and verified them subsequently by experiment. These include the structures of open-chain and cyclic peptides, fibrous proteins such as collagen, and homologous globular proteins. These are proteins which have similar amino acid sequences and presumably similar three dimensional structures.

I would say our main research interests right now are in both experimental and theoretical studies of those two areas; the folding of the protein and then how it expresses its biological function. Besides that, I have an ongoing interest in the mechanism of the thrombin-fibrinogen reaction in blood clotting and the structure and mode of action of various growth factors such as the epidermal growth factor. Those are the things that are exciting us most at the moment.

BOHNING: One of the things I've been struck by as you've been discussing this, and you've given at least two specific cases, in which the theory came first and the experiment came second, which is not always the case. It's usually the other way around.

SCHERAGA: As I say when I give lectures, I believe they go hand in hand. I don't believe you should ever calculate anything unless you can check it with an experiment and we've got numerous cases where we have done the calculation and then checked it. On the other hand, very often you do an experiment and it looks like you have an anomalous result which you don't understand until you can do a calculation which provides the understanding. So it goes both ways. One good example of that is in the helix-coil transition. You would think that polyvaline and polyisoleucine would behave the same because they both have branches on the beta carbon. The only difference is one extra methyl group. Well they have very different helix-coil transition behavior, which we first observed experimentally, didn't understand it, and then one of the Go's, Mrs. [Mitiko] Go, she's also Dr. Go, who had done the polyvaline calculation earlier (43), became involved in the work. When we got the polyisoleucine results, I invited her to come back and spend a summer here and we worked out the theory and understood what was going on (44). I have a number of papers with both Go's. It's Go-Go-Scheraga. [laughter]

BOHNING: I think on that note, if there is nothing else you wish to add at this point, we'll close here. I'd like to thank you again for a delightful afternoon.

[END OF TAPE, SIDE 6]

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