Chris Mathews Oral History Interview, September 2, 2011

Title
“The Reflections of an Influential Biochemist, Administrator and Textbook Author”

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Location
Valley Library, Oregon State University.

Summary

In the interview, Mathews describes his family background and upbringing on two different coasts, his early interest in science and his particular infatuation with ornithology, his parents' backgrounds and sisters' lives, and his youthful involvement in scouting. From there he details his high school experience in Olympia, Washington and his decision to conduct undergraduate studies in Chemistry at Reed College. In reflecting on his undergraduate years, Mathews describes the climate at Reed in the mid-1950s, the evolution of his scientific interests, and his encounters with Linus Pauling as well as Pauling's youngest son, Crellin, who was also attending Reed.

Next, Mathews discusses his graduate education at the University of Washington, outlining his decision to move to Seattle and the research that he pursued there. Mathews also recounts his meeting and marrying Catherine Zitcer as well as becoming a father while working toward his doctorate. From there, Mathews reflects on his post-doctoral work at the University of Pennsylvania, during which time he collaborated with Seymour Cohen - who would become an important mentor - on the stimulation of metabolic pathways through virus infection.

Mathews' first academic appointment at Yale University is the next subject of the interview. He describes his arrival at Yale and the process of setting up his laboratory, recounts the research that he conducted (a continuation of his post-doctoral work), and notes the aspects of Yale's institutional culture that ultimately led him to look elsewhere as he continued his career. Mathews then recalls his subsequent decision to relocate to the University of Arizona, the new types of duties that he took on as a professor in Arizona's medical school, and the contours of his research during that time, including work on enzymology and the regulation of DNA precursors. He also touches upon his positive experience of the culture of the American southwest, a sabbatical that he took to the University of California, San Diego in 1973, and his perspective on various luminaries from the early study of DNA, including his mentor Seymour Cohen and Cohen's major professor, Erwin Chargaff.

A significant portion of the interview is devoted to Mathews' recollections of his years at Oregon State University. He describes his decision to move to OSU after eleven years at Arizona, the priorities that he established as chair of Biochemistry & Biophysics, his idea for creating a Center for Gene Research at the university, and the growth of the center in subsequent years. He likewise recounts his involvement with OSU's Environmental Health Science Center, the role that he played in helping establish the Linus Pauling Institute on the OSU campus, and his involvement with the planning of OSU's Agricultural and Life Science Building. Mathews also details the small shifts that occurred in his research on deoxynucleotide and DNA precursor enzymology and biochemistry during his Oregon State tenure.

As the session nears its end, Mathews shares the story of his highly successful textbook, *Biochemistry*, which he wrote with another OSU biochemist, Ken Van Holde, and first published in 1990. He recalls the initial idea for the book, the process by which it was written, and the acclaim that it received as it moved through three editions. The interview concludes with Mathews' thoughts on points of pride looking back, a lingering question that he still has concerning a career that he could have pursued in medicine, and the satisfaction that he has taken at the paths that his children have chosen in life.

Interviewee
Chris Mathews

Interviewer
Chris Petersen

Website
http://scarc.library.oregonstate.edu/oh150/mathews/

Transcript

***Note: Interview recorded to audio only.**

Chris Petersen: So, if you would just start by introducing yourself. Just let us know your name and today's date and where we are right now.

Chris Mathews: Ok. I'm Christopher Mathews. Today is September 2nd, 2011 and we are in the Valley Memorial Library.

CP: Ok, so let us know where you were born and where you grew up?

CM: Ok. I was born in 1937 in New York City. My father was about to start a medical practice in Bridgeport, Connecticut, so we moved from New York very early. He was stationed with the Navy during the war in a variety of places and moved to Seattle in 1944. The family moved with him. After the war, my family moved back to Connecticut again, but after three years they realized they'd made a big mistake leaving the west coast so we moved to Olympia in 1949 and that's what I consider my hometown.

CP: What were some of your hobbies when you were growing up?

CM: Well I was pretty interested in science obviously. I had a chemistry set and my friends and I used to make rockets and fire them off. I became interested in birding and nature study because my grandfather was a professional ornithologist. He was curator of birds at the American Museum of Natural History in New York so we had—we were very much exposed to natural history all my life. That's kept on. I was president of the Audubon Society of Corvallis for three years.

CP: So, there was a strong family influence in terms of science. I'm trying to understand where that early interest in science came from in your family.

CM: Right. Well, as my grandfather of course was an ornithologist and very broadly based biologist, my father was a physician and his father was a surgeon, so there wasn't—well let's say there was both medical and scientific achievement in our background and it was as natural, I guess, for me to have a career in science although I did consider medicine pretty strongly at various times.

CP: How about your mother?

CM: My mother?

CP: Yeah.

CM: She has a degree from Vassar in English and actually Dramatic Production. She never got involved in science, but she obviously encouraged what my brother and my sisters and I did. My brother ended up as a wildlife biologist and retired a few years ago from the University of Washington faculty in the College of Fisheries.

CP: And your sisters?

CM: My sisters are all younger and they—two of them finished college, but they finished in their thirties. My parents went through a fairly messy divorce when my sisters were teenagers and I think this kept them from being motivated to go through college. But they were all very bright and they went back and achieved quite a lot actually. My youngest sister, among other things, has published three books, one of which described her experience as the winner of the Pillsbury Bakeoff in 1998 with a one million dollar prize. It's a very readable book.

CP: Wow, very interesting. So outside of your family, were there other scientific mentors or influences in your life as a child?

CM: I guess so. I hadn't thought very much about that, but not so much toward the hard sciences. In fact, the chemistry course that I took in high school is probably my worst—my least favorite course, although the teacher, Mr. Gaines, was my merit badge counselor when I got the chemistry merit badge in Boy Scouts. This was my freshmen year in high school when he told me I shouldn't try for it until I was a junior and I had taken chemistry. And he helped me through it, but he wasn't a very good teacher. The botany teacher, Mr. Burke, also and the physics teacher, Mr. Keller, none of them I thought were particularly good teachers, but there was enough interest in what I was doing that I guess that provided some motivation.

CP: So scouting was something that you were involved in?

CM: Yes. When we moved to Olympia, we lived right in town, actually about two blocks from the state capitol building. It was very easy to be in Boy Scouts and my parents bought some waterfront land about seven miles out of town and we moved there to a house that they built in my freshmen year. It became much more difficult to be involved in scouting after that, so although I had always wanted to be an Eagle Scout, I just drifted out of it.

CP: How would you characterize the rest of your high school experience?

[0:05:37]

CM: Well that's an interesting question too. I had skipped the second grade, so I was younger and smaller than most of my classmates and it took me a while to catch up socially, but I worked very hard at it and ended up with a very nice group of friends. I thought that educationally, the high school experience was pretty mediocre. Maybe I was too hard on it. I worked pretty hard and obviously did pretty well. My daughter managed to make it through Corvallis High in three years and some—when I thought back on my high school experience, maybe that would have been good, but then I would have been two years ahead and the catching up socially would have been that much more difficult.

CP: Any sports, any athletic pursuits?

CM: I've never been very athletic, but I enjoyed doing things. I've skied—cross-country skied—and I jog regularly and you wouldn't call that athletics, but it's keeping in shape. Played a little tennis, but never was very good at much of anything in the way of sports.

CP: Ok, so after high school, you went to Reed College. How did you decide to go to Reed?

CM: Well, I was reading an article in the *Saturday Evening Post* in 1952, my junior year in high school, and there was an article in it by Richard Neuberger who became a Senator from Oregon. The title of the article was "The School for Bright Young Things." I guess that's sort of what I perceived myself as. I'd never heard of Reed College before, even though we lived just 120 miles away from Portland. It looked like a pretty exciting place and it seemed as though it would be right for me. So I applied to Reed and I applied to Stanford and of course, was accepted both places and Reed just seemed much more convenient and it was more affordable—quite a distinction between the two alternatives because our son eventually went to Stanford so I learned a lot more about it.

CP: I presume that you—you mentioned being somewhat dissatisfied with the environment at your high school. Reed probably presented a different sort of universe for you.

CM: Yeah, actually three of us from my graduating class went to Reed and one of them only made it two years. The other one, who'd been a very strong science student, ended up majoring in philosophy and going to law school and also becoming an extremely accomplished folk musician. He and his wife basically made their living. So Reed was interesting in terms of the fact that a lot of people went there moving in one direction and changed directions completely, or undirected and getting a direction. There was also very high attrition rate then, so there were a number of students who went there undirected and there wasn't much supervision and so a number of students just dropped out. I was one of the ones who had a sort of a vague idea of what I wanted to do and basically stayed with it.

CP: What was the climate like at Reed when you were there?

CM: I suppose pretty much like it is today. It was pretty intense intellectually, but students knew how to have a good time as well. The academic environment was very strong. The courses in liberal arts and social science all had a very heavy writing component, so in the freshmen humanities course, we had to write a paper every week and then we had an individual conference about every paper with the instructor. So any credit I can take for my ability to write today, I owe to Reed College. The science was very strong also. At that time, in the early- to mid-50s, I would say that the science wasn't as strong as it is currently. Reed, like many of the other high quality undergraduate colleges, has really made a push for a stronger research orientation in the science faculty. Although we were all required to write a thesis when I was a student, the theses—I would say—the theses weren't all cutting edge science, put it that way. In fact, one of my regrets about Reed was that I probably took more science than I really needed to and I should have taken more courses in liberal arts, philosophy, and literature, and social sciences than I did, but I ended up with an interest in a lot of different areas and to learn a lot of things through my own reading and that's what college is supposed to be for anyway, I think.

CP: How would you say your scientific interests developed as an undergraduate?

[0:10:59]

CM: Well I went there as a chemistry major because of—probably because of my interest that started with the reading about chemistry and playing with chemistry sets and so forth. It was sort of an unfocused interest, but at some point I read a science fiction anthology of short stories and the stories were grouped by scientific area that this science fiction dealt with. So there were two or three stories that were listed under biochemistry and I'd never heard of biochemistry before and I thought, hey, the idea of chemistry that has something to do with biology, I'm going to have to read these stories. I enjoyed them and my junior year, I took a biochemistry course and the reading I did both in class and out of class convinced me that this was a pretty exciting area to go into. During my sophomore year, I'd wrestled with the idea of going to medical school. I had a hard time with organic chemistry, the first term of it, and the fall term of my sophomore year and I like to tell medical students or premedical students this story. I began to wonder if I was bright enough to go into science and maybe I should go into medicine instead, but then the second semester of the main course for majors was quantitative analysis and I did much better. At the end of the year, I decided that I was bright enough to go into science after all.

CP: So was it at—while you were at Reed, or maybe when you were in high school—you've told me a story about a letter that you wrote regarding Linus Pauling. Can you recount that?

CM: I first heard of Linus Pauling the fall semester of my freshmen year. In chemistry class one day, there was a student who raised his hand to ask a question and he said 'Oh, Professor. Does what you are talking about have anything to do with the Pauling theory of resonance? Professor Livermore gave him a very respectful answer and I thought to myself, 'I've never heard of Pauling, but I guess I'd better learn something about this guy.' And then remarkably enough, within the next two or three weeks, it was announced that Linus Pauling had won the Nobel Prize in chemistry. So I realized that this student was a little bit ahead of me in terms of knowing major scientific themes.

CP: You later wrote a letter to the editor about Pauling?

CM: Right, I guess you and I talked about that a few years ago. Do you want me to describe that?

CP: Yeah, please.

CM: The *Oregonian* published an editorial a day or two after the Nobel Prize was announced. It was basically congratulations to a native son of Oregon who went on and achieved great things and won the Nobel Prize, but wasn't it a shame about his inaccurate thinking and his political associations that have led him to have his passport lifted. I thought it was pretty inappropriate to bring these political things into—at a time when we should be celebrating this person's intellectual triumph. I wrote my first letter to the editor ever and at that time, Reed College was in very bad odor in the Portland area because the Velde committee, which was the House Un-American Activities Committee, had toured the country in the spring just before I started college and three members of the Reed faculty were interviewed and refused to discuss their associations. This made a lot of people think that Reed was full of communists. So when I wrote the letter to the editor, I used my home address from Olympia which could be seen as being within the readership area of the *Oregonian*. Then I guess I clipped the editorial and my letter and mailed them home to my mother. Because my grandparents knew the Paulings—my grandfather was a member of the American Philosophical Society which Pauling was also—my mother mailed this to my grandmother and my grandmother mailed it to Pauling and Pauling eventually sent me a nice short note which pleased me a great deal.

Pauling's youngest son, Crellin, was a classmate of mine at Reed and then later on when I was a graduate student at the University of Washington and my wife was a graduate student in genetics, Crellin Pauling was doing his graduate work in genetics also. So Kate (my wife) and Crellin worked in the same lab and we used to see them socially fairly frequently. Somehow or another, I had a fairly close series of relationships with the Pauling family.

CP: That's—I had no idea about that. Can you reflect on your time with Crellin at all?

CM: I'm sorry?

CP: Can you reflect on your time with Crellin at all?

[0:16:21]

CM: Yeah. He was pretty immature and had a great sense of humor. He seemed to enjoy life a lot. He started as a chemistry major at Reed and he didn't do very well, so he switched to biology and it took him five years to graduate. He started graduate school at UW a year after I had and then I think it took him five or six years to finish his Ph.D. He actually published some fairly important papers from his post-doc and then later on when he was on the faculty at San Francisco State, if I remember right. He was chair of the biology department there for quite a few years. And so he was always a very likeable fellow and he was on sabbatical here in 1980 and '81. He worked with Dick Morita in the microbiology department and his then second wife, Kay Pauling, worked in our department as a post-doc with one of my colleagues. So we established contact and it was very pleasant.

CP: I didn't know that either.

CM: Well there was kind of an amusing—this doesn't have anything to do with the college era—but during that year that Crellin Pauling was here, I was called upon to be the organizer of the—what used to be the annual Biology Colloquium. I'm not even sure if that's still held. So I organized a two day meeting on the organization and manipulation of genetic information. This was 1981 and we had a party for the speakers and people who were participating. The President, MacVicar, was at the party and he came up to me and he said 'Chris, I'd like to have you introduce me to Linus Pauling's son.' So I took him over and introduced him to Crellin and he backed Crellin into a corner and wouldn't let him out. They were talking there for probably twenty minutes. I was trying to think of a way that I could rescue Crellin, but it didn't work.

CP: Interesting. So, did you ever meet Linus Pauling?

CM: Linus Pauling?

CP: Did you ever meet Linus Pauling?

CM: Yes. Probably the first time I met him—he came to Seattle for a lecture and I met him there, so that would have been 1960 or '61 when I was a student. But then, my first month here, I started my employment as chairman of biochemistry and biophysics in January 1978 and one of the first things that I learned in my first week on the job was that I had to get ready for a site visit for our department because the legislature in the previous year had made some sort of budget note or order of some kind that there should be reviews of academic programs that might involve duplication between Oregon State and U of O. Although the U of O didn't have a chemistry department, they had the Institute of Molecular Biology and they had a biology department and chemistry department. Chemistry and biochemistry were getting reviewed and Linus Pauling was one of the outside reviewers that was brought in.

It was fairly intimidating so I had to prepare for a day long site visit with, I've forgotten who the other reviewers were. We had a similar experience: we were site visited as a biology department as well, so I had to organize two site visits. I remembered the biology site visit—one of the site visitors was Herschel Roman who was professor of genetics at the UW. He's the one that my wife worked for. One of the other site visitors was a guy named Gordon Lark who was at Kansas

State University. He was quite a prominent bacterial geneticist. When he met with me early in the morning, he said 'Chris, why did you move here anyway?' It's sort of a—sort of wondering what the deal was, what was the attraction because I'd had a pretty good job at the University of Arizona before I'd moved here. Later in the day when I met with him again and they'd had a chance to talk with a lot of other people and learn about Oregon State, he said 'you don't have to answer me anymore.' He said 'now I know why you moved here.' So I felt pretty good about the decision I had made to move when that happened. That gets a little bit away from Linus Pauling, but I met him two or three times when he came to the campus either for the annual award of the Pauling Medal or for other things. Somehow, we were brought into contact. So I probably met him half a dozen times.

Did I ever tell you the story about Pauling and the joke that he told at the Pauling—do you want to hear that? It gets a little out of the chronology. So the three northwestern sections of the American Chemical Society give the Linus Pauling Medal every year, jointly, and there's a symposium and a banquet. The locale moves around from Corvallis to Seattle to Pullman, Washington, or wherever. In the fall of 1979, it was held here and—so Pauling used to come to all of these—and after the banquet, he would give a little talk about what he'd been doing during the previous year. These things were always hugely entertaining. The talk that he gave in 1979, and Mrs. Pauling was with him—she was still alive then—he said that he was encountering a lot of skepticism about vitamin C and the reporter was interviewing him and he said now, 'Professor Pauling, you take vitamin C, don't you?' 'Well of course, I do, young man.' 'Well then sir, do you mind if I ask you a few questions about your state of vigor?' 'No, go right ahead.' 'Well Sir, can you tell me then please, when did you have your last sexual experience?' 'Why,' I looked at him and I said, 'why 1956.' And he said 'why, that's terrible.' And I said 'what's so terrible about it?' And he looked at his watch and said 'it's only 22:10 now.'

CP: Ok, well, getting back to your life. So you mentioned at Washington and Seattle—University of Washington, Seattle—how did you make the decision to go to UW from Reed?

CM: Ok, that's a good question too. In the summer of 1957, I went back to visit my grandparents in Long Island and they were very interested in having me go to graduate school on the east coast. So they took me to visit various schools: Harvard and Brown and Johns Hopkins, but one thing that I did, since they lived fairly far out on the island, they'd arranged a visit for me at Brookhaven National Laboratory. I met with a biochemist there named Robert Steele and he told me about what he was doing and he said, 'I don't know why you're looking at all of these graduate departments on the east coast when one of the best graduate schools in the country is right out where you live.' I said, 'what's that?' And he said 'well, the University of Washington. It's a new department but it's really good.' So I figured, 'well I guess I'd better look at it.'

I ended up applying to Berkeley, Johns Hopkins, and the University of Washington and in those days, this was 1953-54, no excuse me, '57-58, you didn't get flown to departments to be interviewed at their expense. I had visited Johns Hopkins. I never did go down to visit—to Cal, but I was home for the weekend and drove up to Seattle. The department was small; it had just seven faculty members. But they were really nice and they represented a nice cross-section of the biochemistry of that era. They all had good records of academic achievement and it was pretty close to my family, all living in the state of Washington at the time. I figured, 'why not?' It worked out pretty well.

CP: What was your research focus as a grad student?

[0:25:22]

CM: Well, I was pretty unfocused when I began graduate school. I—when my fellow students would ask me 'what are you interested in?' I'd scratch my head and I'd say, 'well I guess I'm interested in enzymes, but I'd like to do some project in enzymes that has potential applications in medicine or biology, what have you.' So, we were required to talk to all of the faculty about their research and Frank Huennekens was doing work on folate enzymology. Folate is one of the B vitamins and it's converted to a coenzyme tetrahydrofolate, and tetrahydrofolate is a coenzyme that mobilizes single carbon functional groups. These are involved in methylation, for example methylation of DNA, methylation of certain amino acids and proteins and also the methyl group of thymine nucleotides in DNA. The Huennekens laboratory had just recently shown that the action of methotrexate, which is a folate analogue used in cancer treatment—it was discovered in the 1940s as a very potent anti-leukemic agent that acted by inhibiting an enzyme called dihydrofolate reductase that reduces folate to tetrahydrofolate, and I thought this was really interesting. There wasn't very much known about the enzyme at the time, but the fact that the enzyme was a target for a very effective drug meant that this whole area of folate enzymology had the kind of protein enzyme focus that I was interested in with potential applications of significance to medicine. So I went to work with Frank Huennekens and it worked out pretty well for me.

CP: So he was your mentor?

CM: He was my major professor. One of the other reasons that I was interested in his lab was that I learned that he'd had several students who'd managed to finish their Ph.D's in fairly short order. I was interested in getting my Ph.D and moving on. That worked out pretty well too. I completed my Ph.D requirements in a little under three and a half years, which is pretty fast by today's standards where a Ph.D in general is a five year program or so.

CP: When you were at the University of Washington working on your Ph.D, you got married.

CM: That's funny you'd—if I got married, is that what you're asking?

CP: Yes.

CM: Yeah that's an interesting one too because my wife was a graduate school classmate in biochemistry. There were twelve entering students in the entering class of 1958 and we ended up as lab partners in a lab course. Then, later in the year, as teaching assistants, we were assigned together to the reagent room—it was called the solution room—making up reagents for the biochemistry lab class for dental students. We were supposed to put in ten hours a week of effort in our T.A. duties and we worked pretty efficiently together so I think we worked two or three hours each per week. We didn't see each other socially at all at the time. She had a bunch of other boyfriends and I think we both had a feeling that you didn't get involved with people that you saw every day. But her interests were more biological and the genetics department was founded in the spring of 1959 so she transferred to genetics in her second year.

When we were not seeing each other every day, it became a little bit more natural and so we got married in the spring or early summer of 1960. It's kind of interesting because Kate grew up in Berkeley. Her mother was a research technician in the virus lab. She worked for Wendell Stanley who won a Nobel Prize for his work in tobacco mosaic virus. At Berkeley, the virus lab and the biochemistry department were in the same building at the time. Kate's mother tended to mother all the graduate students who were unattached, so if I'd gone to Cal as a graduate student, we've always wondered whether Elsa would have sort of mothered me and picked me out as someone suitable for her daughter and would have got us together. We had a laugh over that over the years, but you can only live one life at a time.

CP: Yeah. You also had your first child as a doctoral candidate.

CM: Right. That wasn't planned. Lawrence was born maybe nine and a half months after we got married and drank champagne from a glass on our first wedding anniversary. So Kate never finished her Ph.D and she claims—at various times I encouraged her to do it. She worked as a lab technician and she also worked—when I was at Yale—she worked as a teaching assistant in the department of biology where I was. She always claimed that she didn't really want a Ph.D anyway. She loves working in the lab and she's pretty good at it, but she says she's good at the tactics, but not so good at the strategy, at developing a long range line of research and applying for funding, and that sort of thing. So I think she's pretty happy with the kind of career she had.

CP: Was it difficult to sort of maintain a household and also be so devoted to a program of research somewhere?

[0:31:28]

CM: Yeah. Well, somehow it worked. I—a lot of my fellow students would go back to work in a lab in the evening and I just stayed home and Kate was very good about, after Lawrence was born, about seeing that I had a couple of quiet hours every evening. I don't remember what sitting arrangements—she was still working as a graduate student and a teaching assistant in the genetics department. Somehow it seemed to work.

CP: Ok. So you finished up your Ph.D at UW and then you did a post-doc at Penn. Tell me a little bit about that.

CM: Yeah. By the time I was approaching finishing my Ph.D, I knew that I wanted to work in a biological system that had more potential for genetics. I was getting more involved in the biological side of enzymology than the chemical or biophysical side. Reading the literature, I selected three people whose work I was interested in and I wanted to be able to go to a lab where the specific experience that I'd had as a graduate student would be useful. Seymour Cohen at the University of Pennsylvania was the one I eventually settled on. He was working on bacteriophages—bacterial viruses—and basically in the late 1940s, when he started with his own lab, he'd done what I would call the first biochemical experiments on what happens metabolically during a virus infection cycle using phages as model systems for plant or animal viruses, which of course were much more difficult to work with biochemically at that time. In the early 1950s, he and a post-doc had shown that DNA from certain bacteriophages had a very unusual modification in that all of the cytosine residues in DNA were modified by having a hydroxymethyl group. In the mid to late 1950s, they'd shown the biochemical basis for this; that there were new enzymes that were induced after a virus infection that put on the hydroxymethyl group and that phosphorylated the nucleotides to get it to the point where it could be activated and incorporated into DNA.

The whole idea that virus infection stimulated new metabolic pathways was really exciting to me and this enzyme that put on the hydroxymethyl group had a tertrahydrofolate co-factor, so it meant that I could bring some biochemistry to Cohen's lab that would help them out. It was a nice pairing, but again, in those days—now we're talking 1961—you didn't just hop on a plane to visit every lab that you were going to consider for a post-doc. So I wrote to three people and I was going to give a paper at the Federation meeting in April 1961. This was the Federation of American Societies for Experimental Biology which, at that time, included societies for biochemistry, physiology, pharmacology, nutrition and a couple of others. It was the big meeting for biochemists to go to and so the three people that I was considering would be at the meeting and I could meet with them there.

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This happened very shortly after Lawrence was born so I really owe Kate a debt of gratitude and also my mother and Kate's mother and my grandmother who all came in and helped out. But I was able to go to the meeting and meet with them. It was kind of amusing because on the first day of the meeting, I met Seymour Cohen for the first time and apparently, my major professor who had sent a letter of recommendation sent a two page letter and I didn't learn this until later, but the second page of the letter to Cohen had Dr. Boyer's name at the top of the page. Seymour knew that I was considering more than one laboratory and he'd recently had someone very good who had accepted a post-doc and then went somewhere else instead. So almost as soon as I shook hands with Seymour and introduced myself he said 'now see here. If I accept you in my laboratory, are you're coming or aren't you?' It really set me off and I wondered, 'who is this guy anyway?' Then I met the other two people during that week and by the end of the week I'd decided I wanted to work with Seymour. So I had another appointment with him and almost before I had a chance to say anything, he said 'well I've decided that I'd like to have you come and join my lab.' And I said, 'well that's funny, I've decided I want to join your lab too.' And then he insisted on driving me to Philadelphia—this was in Atlantic City which is about 60 miles from Philadelphia—so I could see his lab and meet the other people, which I did and it was very nice because then I knew them all by the time I joined his group six or eight months later.

CP: So from there you moved onto Yale. How did that come about and what was it like being a brand new faculty member at Yale and starting your laboratory?

CM: Things were much different back then. I used to get unsolicited offers of assistant professors—not so much offers, I'd get a letter in the mail from the department chairman that would say 'would you like to apply for an assistant professorship in our department?' Seymour Cohen would come into the lab on occasion with letters: 'would you like to...?' They'd want me to recommend someone for this place or that place. 'Would you like to apply?' Most of the time, I said 'well, no,' but Yale was interesting. My father had worked at the Yale Medical School after the war back in that interval between our lives in Washington state and I knew Yale was a pretty good place. I told Seymour, he could go ahead and put my name in if he liked. But I told him that I really hoped to get back to the west coast and he said 'well fine, I'll write to a couple of places. Where would you like me to write?' I said 'well UC Davis has a new biochemistry department that's pretty good. You could write to that. Also, the University of Oregon has this new Institute of Molecular Biology.' They had some terrific people there. So he wrote to both places and they both wrote back and said that they had positions and they were interested—I should send my CV and so forth, which I did.

In the meantime, I was invited up to Yale to be interviewed. It was an interesting day. I gave the seminar at noon and then I met immediately after the seminar with the search committee. They gave me a lunch to eat which I was trying to eat at the same time that I was trying to answer questions. It was pretty stressful. One of the search committee members took me to the train at the end of the day and I went back to Philadelphia and he said 'well, we have to go through a series of steps before we can make a decision on anything, so it may be a while before you hear from us again.' I thought, 'well that's fine. I'm not in a hurry anyway because I want to see what develops at Davis and Eugene.'

[0:39:33]

Within a week I had a letter from them saying that the search committee had met and they had decided that they were going to recommend that I get the appointment and so forth. Eventually, I did get a formal offer. The letter, I sort of stalled them as long as I could and finally—it was a good offer. The salary was pretty poor by comparison with what my cohort was getting at other places. It was the biology department. I didn't consider myself so much a biologist, but they were trying to build up biochemistry and molecular biology within the department. They wanted me to set up a lab class in biochemical research techniques that their graduate students could take. So that was a bit of a challenge. Anyway, I accepted the job on a Monday and then I wrote to the department chairs at Eugene and Davis and then on Thursday, the phone rang in the lab and I took the call. It was the department chair at the U of O and he said 'oh, Dr. Mathews. We just got your letter. I'm terribly disappointed. We got your last recommendation in and the faculty had a meeting. We decided you'd be ideal for the job. We were about to invite you to come out and give a seminar. Can we get you to change your mind?' 'You know,' I said 'I'm sorry, I made a commitment' and that was that. I went home thinking, 'I guess I'd given up my last chance to go to a good university in the Pacific Northwest.' Who would have known what happened years later?

So I went to Yale starting in January 1964 and today's assistant professors of course get almost the first year without significant teaching responsibilities to set up their lab. And the very first thing, I had to start setting up to teach this lab class that was beginning the end of the—well the beginning of the spring semester which is the end of January or early February. I had ordered almost everything I'd needed, but a teaching assistant and I had to set up the lab. I had to write the protocols for all the labs the students would do—this class of fifteen students. I was very busy with teaching. On the other hand, I also had my NIH research grant that started on January 1st. Grants were incredibly easy to get back then. So I was buying equipment and hiring a technician and getting my research lab set up at the same time.

CP: And what was the focus of that?

CM: It was sort of a continuation of what I'd done as a post-doc. One of the things is actually kind of an amusing story too. My Ph.D thesis had been on the enzyme dihydrofolate reductase which I told you is the target enzyme for methotrexate. There was another lab that had shown the enzyme that makes the methyl group of thymine reduces the methylene group to the methyl level. That requires two electrons and the rate of DNA synthesis after T4 phage infection goes up by about tenfold, which means there's a tremendous demand for DNA precursors including thymine nucleotides. Since there's a two electron reduction, it turns out that the tetrahydrofolate is oxidized to dihydrofolate. When I became aware of all this and I was talking to Seymour Cohen one day in the lab and I said, 'you know, with this big increase in demand for thymine nucleotides, there are all these virus induced enzymes that you and the other labs have been discovering. We should be looking for dihydrofolate reductase. There should be a virus specific form of dihydrofolate reductase as well. I know how to assay the enzyme—I worked on it for my Ph.D. Suppose I go ahead and do that.' And he said 'why don't you focus on the problem that we agreed that you would work on when you came to the lab.' I said, 'ok.'

Then Seymour was out of town for three days or so and I did the experiment. There was a twentyfold increase in the specific activity of dihydrofolate reductase in T-phage infected cells as compared to uninfected cells and it turned out to be really easy to show that it was a different enzyme from the corresponding enzyme that existed in the uninfected bacteria. So one of the things I did—we got a short paper out of it—but one of the things I did when I went to Yale was—it was a golden opportunity to get a free paper. We'd have to purify the enzyme and characterize it, make mutants that were deficient in the production of the enzyme to see what their phenotype was and so forth. There were a number of problems related to DNA precursor metabolism early in infection by T bacteriophages that got me off to a pretty decent start. I published six or eight papers in the first couple of years I was at Yale, even though I had a pretty heavy teaching load.

CP: So you were at Yale for four years, roughly.

CM: Roughly, yeah. It was actually three and a half by the calendar, but they started my appointment as Assistant Professor in July of 1963 and I was in absentia for the first half year. Then I taught that lab class and then in the Fall, they had me set up a lab for the—well it was an undergraduate cell biology course which was basically biochemistry in the Fall semester and cell biology in the Spring semester. So a colleague and I shared the Fall course where he did most of the lecturing and I taught the lab.

[0:45:33]

CP: Did your research agenda change over the course of that time in Yale, or were you essentially sticking with the same topic that you—

CM: About research?

CP: Yeah.

CM: Yeah. I stayed pretty much, but I was branching out a little bit more biologically and looking at questions such as the regulation—the time specific regulation of gene expression. Virus infection involves a very well scheduled program of events and gene activation and deactivation. So I was interested in what turns off the biosynthesis of these early enzymes that are involved in DNA metabolism and then the activation of the late proteins which are mostly structural proteins of the virus and proteins that help the virus assemble. I was pretty much sticking with what I knew, but branching out in slightly different directions.

CP: What was your sense of the culture at Yale?

CM: Yeah, that's an interesting question too. It was all male of course, as far as the undergraduate student body was concerned. There was a fair amount of self-satisfaction. The undergraduate students were really bright. At least, enough of them were really bright to make it worth the effort to teach them, to make it fun. The graduate students seemed like kind of a mixed lot to me. I wasn't hugely impressed with them at the time except for some of the very good ones. What's turned out in retrospect is that I maybe was a little bit too hard on them because a number of the graduate students that I thought were ok have turned out to have very successful careers. I see their names in the literature all the time. So I guess the students were as good as they thought they were.

In terms of the culture, my decision to leave Yale after a fairly short period was hastened—I knew when I went there that I wouldn't have my whole career there. I didn't really want to live on the east coast. I knew that most people who take non-tenured jobs in the Ivy League move somewhere else and I thought that it was a great place to start from. I might not have left so early, but we had a new department chair who came from Johns Hopkins and he was a fairly argumentative sort. He was someone who always wanted to put himself—he wanted to polarize discussions. So in my last year at Yale, the other biochemist in the department had gone on sabbatical and no arrangements had been made to take his place, so I was giving all of his lectures in the cell biology course as well as teaching the lab in the Fall and then teaching the graduate lab in the Spring. In addition, I'd become a pre-medical advisor. So I had several dozen advisees that I had to meet with and write letters of recommendation for. I was being run ragged and trying to keep my research going as well. There was a social function and I brought up to the department chair—there was a large department, there were about 45 people in the department so he barely knew me. I engaged him in conversation and I asked him, 'what are your thoughts about teaching versus research in an academic environment?' He said 'well of course you have to be a good teacher if you want to succeed at Yale, but the main objective was research.' He said 'if you want to stay at Yale, your research must scintillate. It must absolutely scintillate and if you ever want to be a full professor at Yale in this department, you have to be someone that we can confidently number among the top 50 biologists in the country.' So I went home and I figured with the amount of teaching and committee work I was doing, there wasn't any chance of my rising to the top 50. Then I also looked around the department and I didn't see very many full professors that I would rank in the top 50, myself. There were one or two. So that has something to do with the culture, I guess.

[0:49:55]

CP: So you mentioned that in 1967, you moved to Arizona?

CM: Right. That came about because the department chair at Arizona had been one of my professors at the University of Washington. He was on my committee. He was someone I'd liked a lot and he called me up one day and told me that the University of Arizona had a new medical school starting and that he'd just agreed to be chairman of the biochemistry department and would I like to join him? I knew nothing about Arizona at the time, but I liked—his name was Don Hanahan. He was in an area of biochemistry that's quite different from mine. He was an expert on biochemistry of fats and lipids.

And the idea of starting something new. There wasn't the matter of being interviewed, of search committees, anything like that. Basically, he just offered me a job over the phone. I arranged to go out and visit. I visited in January 1967 and Kate went with me. We had to pay her expenses and it was just a wonderful time. They put us up in a nice place and we got up in the morning and stepped out the front door and picked a grapefruit for our breakfast off the tree that was growing right next to our front door. The Dean and his wife took us out to dinner one night. In my years at Yale, I'd never met my Dean, the Dean of the Faculty of Arts and Sciences. Here was the Dean taking us out to dinner and telling me how much they hoped that I would decide to go there. It was a promotion in rank, to be an associate professor—big increase in salary and the opportunity to help shape something because the medical school was brand new. Everyone in Arizona was excited about the medical school that was starting. It just seemed like the right thing to do.

CP: And did it live up to your expectation?

CM: Yes. Yeah, I really enjoyed the time that we spent there. We were there for ten and a half years and there was a lot of excitement in the first few years, having the feeling that we were helping to build the place up. The medical school there was maybe a half mile from the main campus, maybe a quarter mile. It was a five minute bike ride or a ten minute walk. There was a little biochemistry group in the chemistry department that was pretty good and our department in the medical school was small. We had, I think, five or six faculty the whole time I was there, so we merged and formed a joint graduate committee in biochemistry. That was one of the things that I felt was a contribution on my part and the part of Don Hanahan that we wanted to build bridges to the main campus, whereas in other fields, like microbiology, there were barriers that were built up. The bridges, I think, really were beneficial to the University. Now they have a combined university-wide department that serves the main campus people and the medical school people mostly located on the main campus I think. There are a couple people left in the medical school building that focus on medical education.

CP: So your obligations changed a fair amount from Yale to Arizona?

CM: Yes they did. Of course, teaching medical students was quite a different experience, but I did also teach courses on the main campus in mostly the advanced undergraduate and graduate level course. Some colleagues and I originated some graduate level courses. I don't think I did any graduate teaching at Yale except for the graduate lab class, so I taught courses in biological regulatory mechanisms and nucleic acids and so forth, as well as teaching undergraduates and medical students. Overall, I think the teaching load was a little bit—I hate that term, teaching load. The teaching obligation—teaching opportunity was a little bit lighter than what it was at Yale. So there was a little bit more time to get involved in research and again, there was building the department, recruiting the other faculty members, being able to recruit graduate students, getting funding for graduate students support and so forth. It was a different experience.

CP: So what was your line of research pursuit in Arizona?

CM: Well, I continued with some of the projects that were underway when I left Yale and picked up some new ones, but they, for the most part, they had to do with the enzymology and regulation of DNA precursors. One thing that happened was that people involved in T4 bacteriophage genetics had generated a large number of mutants that were available. There were mutants in maybe 15 genes that were involved in DNA synthesis and it wasn't clear what the biochemical functions of all these genes coded for. So I got involved in that a little bit: to what extent might some of these genes have to do with DNA precursor metabolism and to what extent might they have to do with DNA replication itself? So at some stage, I became interested in the relationship between the synthesis of the four DNA precursors A, G, C, and T to make it simplest, and the replication apparatus because DNA replication is a very rapid process. In bacteria or in phage-infected bacteria, the DNA chain will grow at something like seven or eight hundred nucleotides per second. So I started thinking, how can the enzymes that are making the precursors throughout the cell, how can they channel precursors to DNA polymerase—the replication apparatus—fast enough to sustain this rate? I started working on the premise that there was a supramolecular organization within the infected cell with the precursor enzymes physically located close to the replisome—the machinery that synthesizes DNA—so that you could get channeling of precursors to DNA replication sites. That was a pretty big part of my research for several of the years I was at Arizona—for quite a bit of the time that I was here. We picked up some lines of research on comparable questions in mammalian cells working in tissue culture.

I also had a couple students who worked on theses quite independently on things that were quite different from anything that I did. One of them was sure that aging was a question of gene expression and that you should be able to learn something about aging if you knew something about the kinetics of nucleic acid metabolism. He did a thesis that was partly computational and partly biochemical on RNA metabolism that he published—one paper he published independently and one paper he put my name on as a courtesy gesture. After I came here, he joined my lab again. He had a grant and he needed a site where he could work fairly independently and he'd remembered that I'd let him have his own head. So he was here for a couple of years and then he got the idea of antisense as a potential drug and founded a company called Antivirals in his recreation room here in Corvallis. Then that turned into, ultimately, AVI BioPharma which is a biotechnology company in Corvallis. Eventually, he left them and formed another company Gene Tools, which is in Philomath and it's hugely successful. Even though all I provided was a supporting environment at Arizona, it's turned out having a very nice spin-off here.

CP: We're at about an hour. Are you hanging in there okay?

CM: Yeah, I'm fine.

[0:58:47]

CP: So this was your first experience of the Southwest and you mentioned the experience of picking a grapefruit. What did you think of the Southwest?

CM: We really enjoyed living there. Both Kate and I are pretty enthusiastic outdoors people. We found out that there's a lot more variety in Arizona than we'd ever believed there was. Tucson is ringed by four mountain ranges. We did a lot backpacking there and we went camping in Mexico. It turned out that there were some very nice beach areas on the Gulf of California that we went and did weekend camping at. So we really did everything we could to enjoy and profit from the southwest. We miss a lot of that; we miss being able to get into the out of doors twelve months of the year very easily. But Tucson was growing with very little planning and Tucson is one of the largest cities in the world that gets all of its water from underground. When the chance came to come here, of course it was professionally a very nice opportunity. We were happy in Tucson and I wondered, did we really want to move? But one of the features was how much longer is there going to be enough water to sustain the population? How much longer are we going to have these beautiful desert environments that real estate developments are crowding onto? So that all convinced us that we really enjoyed the ten years there, but maybe it was time to go. Every time we go back to Tucson, we're horrified at the additional growth that has occurred.

CP: You took a sabbatical to UCSD in 1973?

CM: Right. Kate still criticizes me on occasion for not having taken a European sabbatical then, because our children were something like twelve and fourteen at the time and they probably really would have profited from a year in Europe. But I still had a fairly small research group and wanted to stay in reasonably close touch with them. Of course, UCSD was a growing academic environment with some superb people and we lived near the beach, so it was very nice living for the year. I split the year between two different laboratories, so I had two different kinds of experiences. It was very nice. It was a good sabbatical.

CP: What did you do there?

[1:01:23]

CM: The Fall semester—the first six months, I worked with a guy named Gordon Sato who was an expert on culturing cells and maintaining their differentiated characteristics in culture. I wanted to learn tissue culture because I wanted to be able to branch out with our interests into mammalian systems so I could take what we were learning in microbial model systems and apply them to mammalian or maybe human systems, so I wanted to learn tissue culture. I did a project that had to do with growth factors in cell culture. And then in the second six months, I went to the Scripps Institution of

Oceanography where I had a very good friend who was an expert on the biochemistry of early events in fertilization using the sea urchin. Fertilization is a little comparable to phage infecting. There is a—among the metabolic changes that occurs is a huge turn on of DNA synthesis in the cleavage cycles—the cell cleavage cycles are very fast, so DNA genomes are reproduced in the order of half an hour or so. The question in my mind was where do the precursors come from? Are they stored or is there a turn on of synthesis. That was what I worked on in Dave's lab. It turned out that the sea urchin egg had huge supplies of deoxynucleoside triphosphates and then backup pools of the monophosphates and the triphosphates so the egg is really geared to activate DNA synthesis very soon after fertilization. I thought about going back and working that system a little bit on my own after I came here, but I never got around to it. There were plenty of other things to do.

CP: Was Francis Crick down there at the time?

CM: No, I don't think so. He would have been at the Salk Institute. I've forgotten when they moved there. I should know that because I reviewed the biography of Francis Crick just a few months ago for a journal. It made fascinating reading.

CP: Robert Olby's book?

CM: It was Olby's book, yeah. In my review, I wrote that this—I've been asked to review quite a few scientific books over the years. This is the first one I actually read word for word, cover to cover. It just read like a novel. But I'm pretty sure that was before Crick had moved to Salk.

CP: Yeah. Olby was here in 2003, I think. He spent some time.

CM: Is that right? I wish I'd known about that because I knew the name already. I knew he was a famous historian of science, a recent historian of science.

CP: Yeah, well he wrote the first big book on DNA, the history of the Watson and Crick story, I guess.

CM: Seymour Cohen was very interested in the early history of molecular biology. He was pretty unpopular with the crowd in that field because he was so aggressively pro-biochemical and didn't necessarily believe in genetics. Seymour Cohen was the first graduate student of Erwin Chargaff.

Chargaff who had promulgated the base composition regularities that helped Watson and Crick develop their model. Chargaff had been very bitter about being left out of the credit for that and I think Seymour shared Chargaff's bitterness to some extent. So when the Nobel Prize was announced, I was in Seymour's lab then—this was in 1962—and it went to Watson and Crick and Maurice Wilkins and so Seymour came into the lab and said 'well if they were going to include Wilkins in the Nobel Prize, they should have included Chargaff because his contribution was just as substantial.' I think he could make a pretty good case for that, but of course the Nobel Prize is limited to three awardees, so I'm sure that didn't do very much for Erwin Chargaff's mood either.

CP: He had a reputation for being kind of a difficult guy.

[1:05:55]

CM: Yeah, he was. In fact, Chargaff was the one who got me started thinking about Seymour Cohen because my second year in graduate school, Chargaff came into Seattle and gave a series of lectures. During the lectures, he talked about virus induced enzyme. He talked about work done by quote, my student Seymour Cohen, unquote. So I immediately went to the literature and started reading Seymour Cohen's papers. I'd never heard of him before. That was what got me fired up and the fact that Seymour was Erwin Chargaff's student. But at some point, I met the guy that was the chairman of biochemistry at Columbia when Chargaff had moved from Europe, I think he was a refugee, and Columbia took him in. So the chairman—his name was Hans Clark–he was quite a distinguished biochemist, said 'tell me what you're doing, Dr. Mathews.' And I said, 'well I'm a post-doc at the University of Pennsylvania.' 'Oh, who are you working with?' 'I'm working with Seymour Cohen.' 'Oh, yes. Seymour. He's one of my boys, you know.' It was very paternal or paternalistic. And so Seymour was Erwin Chargaff's student but it turned out that when Seymour was working on his post-doc, or on his Ph.D, neither of them was working on nucleic acids at the time. Seymour had done his Ph.D thesis on lung surfactant which is a phospholipid. It wasn't until years later that both Chargaff and Cohen independently started working on nucleic acid biochemistry. So, there's something kind of fascinating about the personalities involved in the recent history of science.

CP: Yeah, yeah. Cohen sounds like he was definitely a big figure in your life.

CM: He was, yeah. He taught a famous course in comparative biochemistry, I don't remember why I never sat in on the course. I should have. But he was very broadly based. He was very rigorous in his thinking. And he had a pretty pricklish personality so he was definitely a challenge to work for, but he was so broad and he had so many ideas that I think it influenced me too to read pretty widely in science and try to maintain a broad awareness. That's helped me a lot in writing a textbook. And also, since I became a member of the editorial board of the *Journal of Biological Chemistry*, I get sent papers to review that are way, way outside of my area because editors know that I can sit down and read something. I got a paper to review a couple of years ago on the biochemistry of body odor, if you believe that.

CP: Well, we referred to this a little bit. In 1978, you moved to OSU and it sounds like they made a pretty good offer to you. I mean, is that the primary reason that you moved from Arizona?

[1:09:08]

CM: Right, it was an interesting situation. I didn't have any real reason to leave Arizona. As I said, you can always find things to feel uneasy about, but I felt pretty well accepted on the campus. But my family was all still in the Pacific Northwest, so I kept my eye out for opportunities and OSU advertised for a chair in the department of biochemistry and biophysics and science so I sent my CV and eventually was asked for my references. So I sent them these references and eventually was asked to interview. I had enough information about the department to know that it was a pretty good department. They sent me data on the research funding of the faculty. There were 14 faculty at the time. Everyone except one had some kind of outside research funding, publication records looked pretty good. So on the days when I was interviewed, it was a two day—two and a half day process, I had a series of half hour talks with the faculty and each one, I would say 'you know, you've got a good department. Why are you looking outside for your chair? You could fill the chairmanship inside.' And I got told pretty much the same thing by everyone and of course, when you get consistency, that's a pretty good sign. What they said was, this is their only chance to bring in a senior level faculty person who could bring in a funded research program and give a jumpstart to our department's reputation, because if we appoint an inside person as chair, then we'd have to fill the vacancy at the assistant professor level. So that made sense and they said that the department was in pretty good shape scientifically. And personally, everyone got along which really seemed to be the case. What they wanted was someone who was a pretty active scientist and teacher who was willing to do some administration and leadership and that was sort of how I saw myself. I knew by that time I could probably handle the administrative details of being a department chair, but it wasn't the be-all and end-all of my existence. So it was a pretty good fit.

A few weeks after the interview, the Dean called up to offer me a job and it was my fortieth birthday, so it seemed like an omen of some kind. That was kind of amusing too because I'd put in a call—oh this happened later on. So I got the offer and then Kate and I were invited back to visit again and this time it was a recruitment visit and it was very pleasant again. Then I went back home. After a while, I thought things over, and decided that I would accept the job. So I put in a call to the Dean and he was out of the office and would call back. I sat there thinking that I was about to make a decision that would affect the rest of my life and the phone rang. I thought it was Dean Krauss calling me back. No, it was a guy from the biochemistry department from the University of California at Davis asking if I'd like to be considered for the chairmanship of the department there. I said you've got a great department, but I think it's a little too late.

CP: It's the second time this had happened.

CM: Yeah.

CP: So what was the set of priorities that you brought into the chairmanship coming into OSU?

CM: The main priority for me was for me to keep my research program viable and productive. It's quite a job to move a research program. I knew that the department would be in pretty good shape. There were a few things that needed to be done and I knew I could handle whatever teaching I'd need to do here. But not all the people that were working with me in

Tucson chose to come, so I had to appoint some more people and my major research grant had—I don't remember—a year and a half or so to run and I just wanted to make sure that I got enough papers out during that time, so I'd be competitive. Grants were already—it's now in the late 1970s—the grant situation was beginning to tighten up. So that was my first priority. It worked out pretty well.

CP: Did the administrative pressures change over time?

[1:13:49]

CM: Yes, but actually getting back to priorities for just a minute, there were some things in the department early on that I felt should get taken care of. One was the fact that graduate students—there was hardly any money in the department for teaching assistants, so there wasn't much state money that would support students who weren't committed to a lab. Almost all the students came on research assistantships which meant they were committed to the lab whose research grant was paying their assistantship. I thought that a first rate graduate program should have opportunity for students to come uncommitted. I thought it was a great strength that students could come here and start right to work with a person that they wanted to work with, but that many students come without a specific set of interests and they should have an opportunity to go through rotations. So a pretty high priority for me early on was to get an NIH training grant that would provide funds for tuition and stipends for half a dozen students or so, so that we could bring on a few and give them a year to look around and then go onto research assistantships.

My first attempt was unsuccessful. That was kind of interesting too because we got kind of a mediocre score on a grant application and really kind of a snotty critique in which whoever reviewed the grants said the training record of the faculty doesn't seem to be particularly strong. Most of the graduates seem to have taken jobs in industry. I wrote to the NIH and I said, 'what is this? It seems to me that Congress, which funds the NIH, might have second thoughts about the training program if industrial scientists are seen as second rate. So I'm going to revise the application and I'd like to have a site visit so you can see what we have out here.' The second time, we had a site visit and we got the grant and had it for two or three cycles. That was a, sort of an institutional priority for me.

Then, in 1981—so this is an opportunity that was sort of dumped in my lap, but it was an institutional priority for me. The Dean called me and said that the MJ Murdock Charitable Trust. Do you know about the Murdock Trust?

CP: I've heard of it.

CM: This is a large foundation that was created from the estate of Jack Murdock who was one of the founders of Tektronix. Murdock died prematurely in an airplane accident and he left most of his estate in trust to the foundation to support educational, charitable and community organizations of the Pacific Northwest. They used to give project grants to faculty here, but apparently the trust had told President MacVicar that they now wanted to focus their grants more on large multi-person projects that represented institutional priorities, and so the Dean and the President and others had then decided that it was time to make a push in molecular biology. They called me in as the person to—sort of the point person to write something up. It was clear that that was right, it was very much a time to make a push, even though there were a dozen pretty good people scattered around the university here in that area. It was clear to me that the multi-departmental cooperation is very strong on this campus. So whatever we did should be a multi-departmental—multidisciplinary framework.

I proposed that the university create something to be called the Center for Gene Research and that the grant then fund three positions and pay their salaries and start-up costs for two years, with the commitment by the university that their salaries would be continued at the end of that two years and that the search would be conducted in a multi-departmental framework. There was money also for projects grants for the faculty that was here. Then, when the grant was funded, we had a multi-departmental search that brought three excellent people in, one that came to our department is now the chairman of our department, Gary Merrill, one who went to botany, Carol Rivin, and one who went to microbiology and that's Dennis Hruby, Chief Scientific Officer at SIGA pharmaceutical. So very good people. In the meantime, the people in the Ag school wanted to form a biotechnology institute or a biotechnology center and President MacVicar told them that the campus wasn't big enough to have two competing centers and areas related to biotechnology and Ag better work with us. So we made this center. I mean, I had no idea it would grow to something that encompassed the whole campus the way it did. It's turned out to be very successful and the first several years, I think 1985, the center caught on so well that the legislature appropriated a pretty fair chunk of change as a continuing budget at that time with the CGRB. That was something else that worked out pretty well. Then I served as the Director of the Center for a year and a half or so after the first director left fairly abruptly.

CP: What is the status now?

[1:20:05]

CM: Well, it continued to get bigger and stronger and after—I resigned as director because I couldn't handle two administrative jobs and still keep a research lab going and keep my teaching going. So there was a sort of an interim appointment made while there was an outside search and Russ Meints came from the University of Nebraska and he built it up a bit. Then he retired and then a really big push came when Jim Carrington was brought in. Of course, he had a superb research program and I think his program attracted a lot of other people, and departments all over the campus were beginning to use molecular biology techniques. So the center—and then Jim changed the focus of the center with a big emphasis on genomics and computational biology. In fact, the name of the center was changed and I didn't realize it for a couple of years. It's still the CGRB, but now instead of being the Center for Gene Research and Biotechnology, it's the Center for Genomics Research and Biocomputing.

So five or six years ago, there was a university-wide hiring initiative in genomics and biocomputing and there was another multi-departmental search that I think brought five faculty members. They're outstanding people. One of them is Michael Freitag who came to our department and his office is right next door to mine. One is Todd Mockler in botany who's done extremely well. I think he left—Carrington left this year to become the president or the director of the Danforth Foundation in St. Louis. I just learned a day or two ago that Mockler went with him, but really outstanding people came and the focus of the center changed and it's well rooted in the university. The central service lab, which the center maintains, carries out multi-investigative procedures, nucleic acid sequencing, peptide synthesis. That it's been doing for years, but it also has a very large computational and second generation DNA sequencing capability grafted on, so it's got bigger and stronger over the years.

CP: So, getting back to your administrative responsibilities, how did they shift over the years?

[1:23:02]

CM: They shifted in that it got harder and harder to get money and there was a little bit more administration that had to get done. So the first year or two I was here, one of my colleagues got money in one of his grants—$100,000 to buy an electron microscope. This was when our department was still in Weniger Hall. He came to me and he said 'we need a room to put the electron microscope in.' And I said, 'well I guess we're going to have to see the Dean.' So we went to see Dean Krauss and it was maybe a fifteen minute conversation and he found fifty-some thousand dollars to renovate some space on the first floor of Weniger. So we got a pretty substantial amount of money on the basis of one short conversation. Getting money became harder and harder.

And at one point—so our department was very, has always been very heavily involved with the Environmental Health Science Center. This is a center that's funded with a core grant from the National Institute of Environmental Health Sciences. It was originally headquartered, basically, in what used to be the Department of Agricultural Chemistry. That again, is a center that has become bigger and stronger over the years and at some point, when the previous director retired, Don Reed, who was in our department, became the director, so we were heavily involved with that center.

One of the hardest things for me in my last several years of being department chair was accumulating competitive start-up packages when we wanted to recruit a faculty member. That's one thing to get a salary line, but around the country the amount of money you had to put together to attract someone was getting larger and larger because a new Assistant Professor couldn't count on getting his or her first grant funded and needed some money from day one. I remember one of the people who came in as Vice President for Research, which was of course one of the major sources we would go to, I think I've suppressed his name because I dislike him so much. Somehow or another, he never caught on to the idea that the discretionary funds that he had at his disposal, one of the highest priorities of them should be contributions toward set-up funds. And Don Reed who was still the director of EHSC and I talked ourselves blue in the face before we got a token contribution from him. We were just really irritated.

I remember another interesting episode we had with the Environmental Health Sciences Center. When Don Reed became director of the center, this was in the early 1980s, he also was pretty expansionist. He wanted to build and solidify EHSC. And this is sort of parenthetical, but in my opinion, one of the strengths of Oregon State, as I said something about the inter-departmental cooperation, you have strong individual departments, but you have these centers that span departmental boundaries. We have the CGRB, the EHSC and of course the Linus Pauling Institute and I think all of these centers have done nothing but good things for the university by bringing in more research.

So one thing that Don Reed wanted to do was to use the funds he had in the center to establish two or three new faculty positions that would be partly funded by the EHSC and partly funded by the university funds. One of the positions would be in our department. He wanted to get someone who was using cell culture to study, basically, areas related to environmental toxicology. The Dean at the time said, well our department was overstaffed already. We had too many faculty positions for the number of credit hours that we taught and you know the kind of thinking that administrators go through. Of course, both Don and I saw this as a great opportunity to strengthen the department research-wise and bring in some more money to the department.

Don was pretty aggressive so he set up an appointment—a meeting with president MacVicar and six or eight of us sat around a table, including Don and myself, and George Keller who was the Vice President for Research at the time and Dean Sugihara, the Dean of the College of Science and the President, maybe one or two others. Dean Sugihara went through his routine: that the department was overstaffed already and he couldn't justify putting even part of a salary into our budget under the circumstances. Then Don Reed gave his pitch. I don't think I said much of anything. I was just there for support. Don got all the negative brownie points from the Dean. At the end of Don's talk, president MacVicar said, 'well it sounds like a pretty good proposal. Let's go ahead with it.' And I thought the Dean was going to cry. So, from that point on, Don Reed's name was poison in the College of Science, but it worked out very well. He brought in David Barnes, who's no longer here, but that position was established and we got a research facility that's helped the whole campus community. Then he brought in Dale Mosbaugh in what then was ag chem and Mosbaugh had a superb research program until he died very young in 2004. The idea that you could use center funds to strengthen research programs within departments and to strengthen interdepartmental cooperation has been a keynote for the CGRB, the EHSC and the Linus Pauling Institute.

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In fact, the early history of the Linus Pauling Institute is pretty interesting too. Don Reed was Acting Director of the Institute while we had the search for a Director. I was chair of the search committee that brought Balz Frei here. That worked out extremely successfully. Balz is so good and the people he's brought in are just outstanding, but I think the only time I ever had a one-on-one conversation with President Risser was shortly—while this was all under way I think. I don't remember whether Balz Frei had arrived yet or if this was when we were still having the search. Of course there was concern all over the campus about LPI: how it would drain resources away from the administration and of course the Linus Pauling Institute in California was pretty mixed in scientific quality. That was a bit of a concern, but John Byrne really pushed the whole thing. It was his legacy at the university. We were—and so Risser and I were walking together from some function and it was just the two of us and he said, 'what do you think about this move of the Linus Pauling Institute anyway?' It's obvious he was pretty negative about the whole thing. I said 'it doesn't make any difference what you or I think about it; it's happening anyway.' At the time, I think I was one of the cautious ones about it too, but I've become nothing but a supporter because we were so fortunate in getting Balz to come here. He was our first choice. I thought the recruitment would be very difficult because the LPI occupied space that our department had occupied before we moved to Ag and Life Sciences. It was pretty—the space was pretty trashed, but Balz saw that it could work. They did a little bit of renovation and of course they said that a new building would be something that would be fairly high on the priority scale. But it took a long time, but it worked.

So you asked about the administrative load. The other thing that happened in those last several years was the planning of the Ag and Life Sciences building. That took a lot of time and in the initial planning I became aware that there were documents in the university that had five levels of space assignment depending on what kind of department or college you were in. Of course, Agriculture and Forestry were on the highest level—number of square feet per FTE of lab space, square feet per FTE for office space, and science was a level below Ag. We started having our first planning meetings and it was mostly Ag people of course, because it was Ag and Life Sciences and we were—biochemistry/biophysics was put into the department sort of accidentally.

The way I understood it was the administration was having trouble assembling funding for the building and this is all hearsay, but the way I heard it was that George Keller said, 'well, we don't have enough pizzazz in the building. We have range science, we have Ag administration, we have horticulture. They're all perfectly justifiable, but we need to put some more environmental science, we need to put some more biotechnology in there.' Apparently, Dean Horne was at the planning meeting and he said, 'well, you know, biochemistry and biophysics is heavily involved in both biotechnology and environmental health science.' So we were moved in very quickly. But then it turned out that they wanted to assign us space on the science level assignment and I figured if we're moving to a new building, we needed to have the same kind of space allocation that the other departments in the building had.

It was about that time that a friend of mine who was chairman of the search committee for the Dean of Science at Penn State invited me to come to look at the job. After I looked at it, I didn't want the job, but it was clear that they wanted me. So I went to talk to Graham Spanier, of course, who'd come here from Penn State and now is back there as one of the most successful university Presidents in the country. And Graham was very excited to hear that they wanted me to go to Penn State. He didn't talk to me about 'what can we do to keep you?' He wanted to know a lot about what was happening at Penn State and so forth, but he did eventually—you know, 'what would it take to keep you?' I had two things in mind that would benefit the department and one of them was space allocation in the new building. I said 'they're basically trying to knock us down in space. We have had adequate space in Weniger; that space is kind of second rate quality-wise, but if we're going to be asked to help plan a new building and move to a new space, we need to be assured that we don't have to accept any less square footage than what we have now.' So he put that on a letter and that helped me a lot as we went through the planning process, but that took a lot of time too.

CP: Were there any major shifts in your research during these years?

[1:35:33]

CM: Um, yes. Not major. I've always been involved in nucleotide—deoxynucleotide and DNA precursor enzymology and biochemistry. I can tell you yeah, the answer is yes. I'll get to that in a minute, but I'll tell you another story about the new building that you might find entertaining.

This has to do with the administrative load and you have to watch these guys all the time. Actually, two stories. One time, we were at a meeting in the administration building and we were being told that there wasn't enough money to build a building the size that was being discussed in the beginning. We were going all around the table—what can we do about this cutback and it was getting pretty late in the evening, you know 6:00, 6:30 or so. A guy named Ed Coate was vice president for the administration at the time. He was kind of a laughing stock in the faculty. And he was getting more and more impatient. He basically said, finally, 'hey it's getting late here. So let's just lop off a floor and we can leave.' So that solidified our view about Ed Coate.

And then somehow it ended up that the building was built. I think the university got a bargain. It's a very good building; it was done with the funds available. But at one point, the architect told me that we've built a prototype laboratory, so you and your colleagues can go over and look at it, look at the cabinets, look at the shelves, look at the bench top, look at the utilities and see what it looked like and I said, 'where is it?' 'Well it's in Moreland Hall.' There's a member of the psychology faculty, Bill Smotherman, who does physiological work and he needed an upgrade to his lab, so he built that as a prototype lab and you can go in and see what it looks like. So we went over and it was a nice lab and so we could see what kind of countertops that we were gonna have in the building and so forth and then it occurred to me to ask someone, 'hey, where'd the money come from to do this?' It turns out that Bill Smotherman had been offered a job at another institution and he needed—in order to stay—one of the things that he needed was an upgrade to his lab. So he went to his Dean, the Dean went to the then provost and somehow things had come about so that money was siphoned out of our building project to build this guy's lab. So we raised hell about it and they had to find the money from somewhere else and put it back into the building project. You had to be on your toes all the time about these guys.

So, getting back to research. I had a graduate student in the early—who finished in about 1982, who did his thesis on the DNA precursor supply for the mitochondrial genome. I'd seen a paper in the literature that suggested that the mitochondrial genome is fed by a distinct precursor pool that might be generated within the mitochondria. So Rick Bestwick did his thesis and a series of experiments that indicated that yes indeed, the pools were physically distinct in the regulatory sense as well. Then that sort of sat there until the late 1990s and another graduate student joined our group, Shiwei Song, a Chinese student who wanted to follow up in that work. He was—had a medical degree from China and a number of diseases had been described that have genetic effects within the mitochondrion. Some of them are mutations within the mitochondrial genome; some of them are mutations in the nuclear genome that encode proteins that are transported into mitochondrion and function there. So there's some very interesting diseases and of course now there's also the idea that accumulation of mutations in the mitochondrial genome is partly responsible for cancer and aging. Since we knew that aspects of DNA precursor metabolism are mutagenic determinants—that is metabolic derangement, if you will, of deoxynucleotide metabolism can affect the mutation rate, we wanted to learn more about the mitochondrial pools of DNA precursors: where they came from, how they were regulated and how this might affect the mutation rate. It turns out that the mutation rate for the mitochondrial genome is much higher than it is for the nuclear genome. Why should this be?

So Shiwei did his thesis on this and he was one of my last graduate students to finish, but by the time he started publishing papers from his thesis, we began to get some notice for this. I got funding actually after I retired and was hoping I would be able to keep this research funding going because it was turning out to be a pretty productive line of research. In fact, that has been the total of our research since about 2003 and had pretty decent funding for that and during that time, the three graduate students that I had, at the time I retired in 2002, took two or three or four years to finish and they were done. After that, I kept my lab going with a technician and a post-doc and one or two undergraduates most of the time. Now I decided to let my funding expire and let a—there's a new faculty member in our department who's going to take over our lab. So my last grant expires end of the year. For the last year—last few years it's taken the knowledge and the background I've had in deoynucleotide metabolism and just applied it to mammalian cells and mitochondrial metabolism.

CP: The last sort of big topic I'd like to talk about is your textbook, *Biochemistry*.

CM: Alright.

CP: So what was the process in which you and Ken van Holde decided that you were going to do this?

[1:42:24]

CM: In 1983 and '84, there were two major texts that came out and we have two sort of advanced level undergraduate courses, BB450, 451, which most students take as a two course sequence and then BB 490, 491 and 492 and these can both be taken as an undergraduate or graduate. These two books came out. One of them we assigned to the 450 course and one we adopted for the 490 course and they're both terrible. At some point in the Spring, I was eating my lunch in my office and a publishing representative came in. I sort of set my sandwich to the side and I told them how disappointed we were with all the textbooks that were on the market. He said, 'well you know so much about what's wrong with all these books, you ought to be writing your own book.' I said, 'are you crazy? I don't have the time or the expertise to write a whole book.' He said, 'well get a co-author.'

Well I was about to go on sabbatical leave to Sweden and I thought 'well, maybe I could write in the evening and work in the lab during the day so it's not a completely crazy idea.' I was talking to my colleague Bob Becker about this and he said, 'well why don't you talk to Ken van Holde. He's talked about writing textbooks from time to time.' Ken and I had taught graduate level courses together and I knew he was extremely articulate, a brilliant scientist. He had a good sense of humor and also was much more of a physical biochemist than I am. His Ph.D is actually in physical chemistry. So I went and talked to Ken and he said, 'well I'd have to be crazy to even think about something like this, but yes, I am interested.' So we went down and visited the publisher and talked to our editor—the woman who would be our editor—and she said that each of us should write a sample chapter and we should write a chapter outline and a prospectus and sample chapter. She bought each of us a Compaq computer. This is just before Macintoshes came out, but there were slightly portable computers. I took one with me to Stockholm and by the time I'd finished writing my sample chapter, I thought, 'this is more work than I want to let myself in for.'

But we sent the material in and in December, Diane called up. She said the reviewers all liked what we'd read and they thought we ought to go ahead, so they wanted to sign us to a contract. I thought, 'oh God, what do I do now?' I called Ken and he said, 'oh yeah?' He says 'I think it's terrific. Let's go.' So there was no alternative. We went ahead with it and many times during the writing process, I thought I was crazy to get involved in this. If I could quit, I would. In retrospect, I'm glad that we stuck with it. It took a long time because it was 1984 that they first started talking to us about the book. It was early '85 when we signed the contract and then I had a lot of things that got me behind schedule when I came back from sabbatical. We didn't really plunge into work on any kind of schedule basis till Spring or so of 1986. We had the first draft done maybe in Spring of '88, no, must have been—I don't remember the date now because it took a year or so to produce the book after the chapter drafts were done. The whole thing was about almost a five year process and the subsequent editions were much easier.

CP: Was it a difficult process to establish the point of view, with two authors, that you were going to be writing this book from?

CM: Actually, that was the easiest part. Ken and I split up responsibility for chapters very easily. We agreed to read each other's chapters. I did most of the metabolism. He did most of the structural biochemistry and we sort of split the molecular biology and the genetic biochemistry. The editors were very concerned about merging our prose styles. I think we did pretty well, although now that I'm writing some for our fourth edition, which he's not involved in, I'm rewriting some chapters he wrote and I'm seeing some differences between his writing style and mine. The difficulty we had in the first edition was some pretty spirited arguments with our editors. They kept a pretty heavy hand on us and we disagreed with them pretty frequently. They ended up being pretty good friends and we had a different editorial team with each of the editions, but that was where the energy came out. But Ken and I had nothing but a good relation. The one thing that was a little disappointing was that he spent almost half the year at his summer home in Woods Hole that he established when he was at the University of Illinois before he came here. In Massachusetts. So it wasn't always a matter of just walking down the hall if I wanted to talk to him but it worked out pretty well.

CP: How was the book received?

CM: It did pretty well. I can't tell you how much—what percentage of the market it captured, but the publisher was very pleased. In terms of the royalties, we were very pleased and I'd been told by quite a few people, I mean this is not something I should be talking about, but I've been told that it's the most clearly written book on the market. I know it brought us a lot of attention. I know when I was on sabbatical leave in Sweden, I got a call one day from someone at the University of Uppsala. They wanted me to come and meet with a group of their biochemistry teachers to tell them my thoughts about teaching biochemistry. I gave a talk in South Africa a few years ago at their biochemistry meeting. Students were coming up and wanting to be photographed with me because they'd used our book. So a lot of things happened that were very gratifying to the ego, so from that standpoint, I guess our book was received well enough that it was worth the effort—worth the effort after the project I thought was dead after the third edition was done, that it was worth picking up for the fourth edition.

CP: As you look back on your career, what are some of the things that you're proudest of?

[1:49:36]

CM: I guess the first thing is the fact that I trained thirty-five Ph.D students and most of them have done very well in their careers. That's like being a parent and most of them have stayed in enough contact that I have the feeling that I made a difference in their lives. Another thing that I've been satisfied with is maintaining a balance of teaching and research through all the positions I've had because I always enjoyed teaching. I'm pretty enthusiastic about the field. I like to know what's going on in the field. I like to explain it to others whether it's in writing or speaking. I like to set an example for colleagues who might be focused only on their research and you can be a successful research scientist and still maintain personal communication with students, with colleagues, with people in other departments on the campus. Science can be a social activity. So I'd say the breadth of interests and associations I've had is something else I take satisfaction in. Being able to stay funded for years in a very difficult—increasingly difficult environment. And the book, I mean, that's a pretty big part of my life—put a pretty big strain on our family situation for a long time, but now Kate is just—she just is as supportive about the whole thing as I am. She likes it when I come home and tell her stories about the experiences we had. So it's been a big plus also.

CP: Is there anything that we've missed that we should touch on?

CM: Well, yeah. I guess there's always been the thought about what—and again parallel, lives parallel universes—what if I'd gone into medicine? That's hit at several times: when I was in college trying decide which way to go. Of course, my father was a doctor and I thought the world of him and I'd talk on occasion, 'you know, maybe we could go into practice together.' That could have been fun, but Dad was very good about not putting pressure on me. He said it was my decision whether to go into science or medicine.

You asked about the Reed College culture earlier and pre-meds were sort of frowned on as being grade grubbers, even though Reed gave grades, but the students—we weren't told what the grades were. The idea was to make you less grade conscious, but the pre-meds were a little more narrow in their interests and I saw there was something about the culture that the highest level of acceptance was the people that wanted to go on and be university and college professors. So that helped. And then I was pointed in that direction.

But when I went to Arizona and started teaching medical students, I realized that biochemistry in that context is a lot different. My father had actually—never actually conveyed to me the intellectual stimulation of medicine as a multi-disciplinary scientific activity. It was partly that he was in practice. He was an internist, but a lot of his patients were—they just had routine troubles that didn't give him much stimulation. So he didn't convey that part of it, but once I had to learn to teach biochemistry in a way that medical students would accept and once I started interacting with them, I realized that medicine is a lot different from what I thought it was. At some point after I'd been there a few years, early 70s, I read that the University of Miami had created a fast track M.D. program for Ph.D's in the biomedical sciences. You could finish an M.D. degree in a year and a half to two years. I was pretty interested in this, so I applied for it and was accepted and then I went to talk to the department chairman, the idea being that one of the years, I could get partial support by being on sabbatical leave and we'd use our own resources for the rest.

When I told him about it, it looked like he had been kicked in the stomach. Then he talked to my colleagues, which I always felt was improper. I thought that my conversation was just one-on-one, but after a week, he said that the department had decided they really didn't want me to do this. Obviously I could have done it anyway, but I would have had to resign. I could have resigned. You know, I thought it over and by that time our children were eight and ten and we were pretty well settled in Tucson. There wasn't any—and I enjoyed what I was doing—there wasn't any real—there wasn't any reason that I had to do this. But I've always wondered what it world have been like if I'd had a career in medicine. Would I have gone into medical research or would I have been primarily in practice? Would I have gotten the intellectual stimulation? Would I have enjoyed the kind of breadth—the awareness of what's happening in cutting edge science and all the rest of it? It'd be nice if you could live two lives, but that's something I just have to live with I guess.

[1:55:51]

So obviously, we're also very proud of our two children: Lawrence, who—as I said—was born very shortly after our marriage, and then Anne who was born a couple of years later. Lawrence ended up going to the University of Washington for a Ph.D in biochemistry, so he was in the same department I was. The department had changed a lot since then. He's now out of science, but he got a great start to his career. He did a post-doc in Sweden and then a second post-doc at the Salk Institute. He did a piece of work than made him quite well-known. He had four excellent faculty offers and he and was an Assistant Professor at the University of Michigan for several years. He had an epiphany and now he's a teacher in the Waldorf school system. I won't go into detail about that, but he is much happier doing that than he ever was as a university faculty member.

Our daughter graduated from Oregon State with a degree in psychology and no clue to what she wanted to do. She happened to talk to a naval recruiter on campus and ended up going to naval officer candidate school after she graduated and becoming an ensign. She had a—she did very well in the Navy, but she ended up secretly getting married to an enlisted man under her command and that was a no-no in the Navy. When they found out, they were both in trouble and again, making a long story short, they both left the Navy and Anne was in the reserves. She got promoted in the reserves so she was in good standing as far as the Navy was concerned, but they had two children and she was basically a soccer mom until her two daughters were in college. Then she went back and got a certificate as a paralegal assistant, so she's working in that field. So both of our children are doing things they enjoy a great deal. Each of them has two children who have done very well. So that's something that Kate and I can look at with some satisfaction also.

[1:58:01]