by David Zierler

Bernie Brooks
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Remote Interview

DAVID ZIERLER: OK. This is David Zierler, oral historian for the American Institute of Physics. It is April 22nd, 2020. I am delighted to be here virtually with Dr. Bernie Brooks. Dr. Brooks, thank you very much for being with me today.

BROOKS: Ah, my pleasure. [laugh]

ZIERLER: OK. So can you start? Tell us your title and your institutional affiliation.

BROOKS: Well, I'm just as—I guess they call it Senior Researcher is the official title in the National Heart, Lung, and Blood Institute. I'm in the Laboratory of Computational Biology, and I run the section, the Computational Biophysics Section, which mainly focuses on simulation and modeling of macromolecules.

ZIERLER: OK, great. And now, let's take it right back to the beginning. Tell me about your birthplace and your family and your early childhood.

BROOKS: [laugh] Yes. OK, well, my family—I actually come from a long line of scientists. My father was a professor in meteorology. My grandfather was a famous professor in meteorology at Harvard. He founded the American Meteorology Society. His father was a famous electrical engineer at University of Illinois in Champaign Urbana. He was one of the contemporaries of Thomas Edison, and I hear they didn't get along very well.

So there's been a lot of scientists. On my mother's side also, both of her parents were professors: one a professor of music; the other a professor of botany. And he was actually partly responsible for the modern orange crop because he did a lot of grafting, and he had a farm in Coral Gables where he did a lot of his experimentation, and worked with producing the modern orange. And so I come from a long line of scientists with a very strong—you know, we had a lot science in the family growing up.

Education and science were always heavily pushed in my family. All of my siblings went to college. Most of them have advanced degrees. And I've tried to instill that in the younger generation. I have four children. They all have advanced degrees as well, and they're doing various things.

ZIERLER: And where were you born? Where did you grow up?

BROOKS: I was actually born in St Louis. My father was professor at St Louis University at the time. And I only lived there for eight years, and then I moved to Newton, Massachusetts, where I really did the most of my growing up [laugh] from there and on to when I went to college.

ZIERLER: Why did the family move to Massachusetts?

BROOKS: Ah, several reasons. One is my father wasn't really happy in his position at a second-rate university, and he wanted to move to a better location. At that time, there were a lot of government contracts, expensive government contracts looking for meteorologists to work on various projects, and my father jumped at the chance.

They also were building Route I66, which took about two-thirds of my street that I lived on in St Louis. And they didn't take the house we were living in, but my parents decided they didn't want to live across from a major interstate. And so that was—yeah, so there was a whole bunch of stuff going on there.

So they escaped there. And also, he grew up in New England, and all of his family, most of his family was in New England. His parents were living in New England, and so he was happy to go back closer to his family.

ZIERLER: And where are you in the order of the siblings?

BROOKS: I'm the sixth out of eight.

ZIERLER: Wow, eight kids.

BROOKS: Eight kids. I'm the sixth, yeah. I got sort of in there—yeah, it's tough being sixth. Six is a tough spot. [laugh]

ZIERLER: [laugh]

BROOKS: I can't think of a more difficult spot. Maybe fifth might be more difficult. But it's a tough spot to be in in a family of eight. But it was a spread out family. The age gap between oldest and youngest is about 17 years, so it's not—so it's a—and I'm sort of in the middle of that.

ZIERLER: And did you go to a public school or private school as a kid?

BROOKS: Public schools, public schools, all public schools. In St Louis, the public schools weren't so great, but I went there. And then I was fortunate to go to Newton High School (Newtown, MA), which at the time was ranked in the top 10 public schools in America. And I think that that was a real—I think that was really good at that time.

I think the Newton schools aren't as good anymore. They're not ranked in the—I don't even think they're ranked in the top 100 now. But at the time, they were ranked very highly. And Newton is the—it's not the first suburb West of Boston. Brookline is the first one, and then Newton is just beyond that. So it would be like Bethesda, you know. It would be like Bethesda in our area, whereas Brookline is more like Chevy Chase, you know.

ZIERLER: Right, and when did you start displaying an academic aptitude for math and science?

BROOKS: Ah, pretty early on. I mean, in middle school, I was—you know, I clearly realized I was way ahead of everybody else in the school. And in high school, I was in the top AP classes. And I took a little ma…I took a Math Olympiad test. And one test I ranked third in Massachusetts in the test, and that's about as high as I ever got. So I wasn't—I didn't study it judiciously.

If I had, I think I could've done far better. But I just sort of just did it for fun….I didn't have a tutor or anybody else that helped me. I just went to school and took the classes. So I think I could've done far better. I think my parents could've really moved me along. But I'm sort of glad I'm not a mathematician. I have—one of my nephews is a professor at MIT in math, and that's a tough—being a professor in math is a tough—that's a tough life.

ZIERLER: It's a highly abstract life.

BROOKS: It's a highly abstracted, very difficult life. But in middle school, I realized that I was more capable than everybody else around me.

ZIERLER: Yeah, and the decision to go to MIT, was that both the best school for you and the closest school for you?

BROOKS: No, actually, it was a difficult decision because I was accepted to—I applied to four schools: Boston College, RPI, I think University of Chicago, and MIT. And I was accepted to all four. But my father was a professor at Boston College, and I could've gone there for free.

ZIERLER: That's a very eclectic group of colleges to apply to. Usually it's like an MIT, a Stanford, a Caltech, that kind of thing.

BROOKS: No, I just applied to—I guess I did a reach, two matches, and a safety, you know, that's the way I saw it. And the safety was Boston College, and also I could go there for free because my father had tuition waiver for me. Whereas MIT, we would not get any kind of tuition benefit.

And so going to MIT actually was a family sacrifice because we had to pay for—except tuition back then wasn't as expensive as it is now in terms of fraction of income. It was only like a factor four. [laugh] If you actually look at the numbers in today's dollars, it's actually shockingly low compared to what we pay for our kids. [laugh]

ZIERLER: However, with tuition in your family, that's tuition times eight.

BROOKS: Yeah, but most of them—a lot of them went to Boston College, and a lot of them had full scholarships. Both my brother and sister had full scholarships at Harvard, and they did quite well. My sister was quite the exceptional student. And, yeah, she was like top—all 1600s on her SATs, and she was like top scorer in her math team. So she was like really, really good.

[laugh] But my parents really made use of the fact that we could save dollars by signing into schools either with scholarships or schools with a tuition-waiver program.

ZIERLER: Now, when you got to MIT, did you have a major in mind already, or you chose that later on?

BROOKS: No, I was actually one of the last students to choose my major. I was very indecisive. In fact, I don't even think I did choose it. I think my advisor—so [laugh] it was actually sort of comical. I was sort of indifferent and, you know, I didn't—I mean, it's not that I didn't care.

But I took a lot of math courses. I took a tremendous number of math courses. I took a lot of physics. I took a lot of computer science. I actually took the famous 6251 [computer] course, which is the only course I ever took that had headhunters. You had a gauntlet of headhunters to get your grade. So this was a compiler-writing course in the—this was early '70s.

There was a huge shortage of compiler writers, and companies were desperate to hire. And so this was a course where the course project was to write a compiler that compiles itself, and in a specific language. And if you got an A in this course, you were offered three or four jobs before you could even escape with your grade.

ZIERLER: [laugh]

BROOKS: In those days, they actually put your social security number [laugh] right up there on the board with—

ZIERLER: Sure. [laugh]

BROOKS: —the grade, you know. [laugh] It was just like—it was so quaint—if you think about it like today, they would never even dream of doing anything like that. [laugh] It was surprising MIT would even allow headhunters into the corridors to try to snap up students who were looking for their grades. [laugh]

But that was the only course I ever took where there was actually real headhunters trying to convince you you didn't need to finish MIT to have a good [laugh] life. And funny thing is I was actually a member of the NRSA (Non-Resident Student Association) during my years at MIT, I actually technically lived at home because my parents were away.

They were—they would spend—during that time, they spent a couple of years in Brazil, one year in Taiwan, and then three years in Saudi Arabia. So they were gone for a total of six years. And I managed the household, managed the house, and so I took care of the house and the bills and all that stuff while they were gone.

ZIERLER: Were they on visiting professorships kind of thing?

BROOKS: Yeah. So my father was a professor at Boston College at the time, and they encouraged him—they didn't really want to pay his salary. So they encouraged him to take lots of unpaid sabbaticals. [laugh] And so he had—so he went to Brazil that one year. He spent—oh, he spent two years in Brazil.

His job was to create a meteorology department at the University of São Paulo. They had no department, and they wanted one. And so he was a hired gun to come in and interview maybe 50 young people, and then hire a dozen to create a new department. And that's what he did. He wasn't going to be part of it afterwards, but his job was to identify the best candidates, and try to bring it forward into the, you know, 20…well, at that time, it was the 20th century [laugh] because the university had—they had no department, and they were trying to create one.

So he and I think one other—one or two other American professors went down, and ran the recruitment effort. And I think he enjoyed doing it. He learned a lot about Brazil. And some of my siblings went down. But instead I stayed, and went to MIT, and took care of the house.

But the reason I was telling you that, the background story on that is I was a member of the Non-Resident Student Association. And the NRSA at that time was a group that was probably most hated by the Dean, and most hated at MIT. It was the official group with the lowest GPA of any group on campus. [laugh]

ZIERLER: [laugh]

BROOKS: It was a bit of an—if you can imagine an MIT *Animal House*, that was sort of it.

ZIERLER: [laugh]

BROOKS: But one of the reasons the GPAs were so low is that some of these students were—these are the students that took the headhunters jobs but they didn't quit as students. And so they tried to make a lot of money working at the same time trying to continue with their coursework, and to slip through with grades to finish MIT.

And it's very difficult to do that, and they didn't do it all that well. But there were a handful of guys who were actually earning money doing programming or technical stuff while still trying to retain student status. And so that was the main reason, I think. It wasn't that we were like no good. [laugh] It was just that there were real-life pressures on some of these students to actually earn money.

ZIERLER: But you were not one of those in that regard? You didn't take a side job?

BROOKS: No, no, I took summer jobs. I took summer jobs. My first summer, I worked at the Union Boat Club helping—I was an oarsman. So I rowed for four years. All four years at MIT, I rowed on the crew, starting off on the freshman crew, and then moving up to the varsity in my second year.

And then one year, I tried out for the national team when I was cut a week before they went to the World Championships. So I was good but not great, you know. [laugh] But I worked at the Union Boat Club helping members with their boats, and taking care of them. That was an interesting summer.

And that was the summer they did the famous Fischer-Spassky chess match. So I used to just watch that on TV while—because there's a lot of downtime when you're managing a boat house. So I would have to watch the chess matches as a—I was on the chess team in high school, so I wasn't terrible at chess. But I wasn't great at chess but I wasn't terrible, but I enjoyed like doing that. And then in other summers, I worked at MIT doing various things.

ZIERLER: And when you finally got around to declaring a major, what major was it?

BROOKS: OK, so my—so I took—I was going to be a computer major, and I was going to—I was really good with computers. I liked computers. I wanted to be a program…I was really good at programming.

I had—but my advisor was a chemist. He was a Course 5. He was a chemist, and he says, "You know, we need computers in chemistry too. Maybe you could think about doing—you know, bringing your skills into a field where there's not a lot of people with that."

And I said, "Yeah, it makes sense." He says, "Why don't you be a chemist? I'll sign you up as a chemist. OK, you're a chemist." And so he did that to me, and I don't think I actually really decided. I think he just decided for me—

ZIERLER: [laugh]

BROOKS: —and he just basically said that "Oh, we need more computer people, and you'd be great for the course, you know." [laugh] And so he was one of the chemistry professors.

ZIERLER: And what was his insight that led him to believe that computational power was necessary in chemistry?

BROOKS: I don't know what was going on. It was in the early '70s. Computers were still very new, and there wasn't a lot of stuff in chemistry with computers. But I think it was recognized that there was a lot of potential. People with good computer skills were being recruited by the university departments at that time, in the mid-'60s—is it '60s?

You know, and my former advisor, Martin Karplus, went to Harvard. He went from Columbia to Harvard in the late '60s. So Harvard was—and a lot of it was for the computational stuff he was doing. And so the universities were hiring chemists with computational components, and realizing that there'll be a lot of computers in chemistry in the future [laugh] and stuff like that.

So my advisor convinced me to—and I said—you know, but I said, "But the only classes I get Cs in are chemistry." "There's a challenge for you then. You need a challenge. This will be an interesting life. It'll be a challenging life." [laugh]

So despite the fact that those were the only classes that I did horribly in, he convinced me to become a Course 5 major, and so that's what I did, and it was—yeah, I don't think it was a conscious decision. It was more of a I couldn't decide so he decided for me.

ZIERLER: Did you have a senior thesis?

BROOKS: No, I didn't. That wasn't—in chemistry, you don't have senior thesis at MIT. You just take a lot of courses. Well, I guess the closest thing to a thesis is you've got lab reports. You've got to do lab experiments and write lab reports. And that's I guess the closest thing to a thesis, and I certainly did that.

ZIERLER: And in your last year, you're mostly in the lab, and you're out of courses at that point?

BROOKS: No, I was never mostly in the lab. I hated lab work. I was mostly doing courses. And one mistake I did make is that MIT at that time had a policy that all freshmen were pass/fail. And so I decided to take a bunch of really difficult courses [laugh] my first year because I thought I could pass them, but I wasn't sure I could ace them. [laugh] And it turns out I aced most of them [laugh] and I kind of regretted not taking them later. [laugh] And there were other courses I probably should've taken my first year.

ZIERLER: So did you have to make up your degree, essentially? Were you a computer science major with a specialty in chemistry or vice versa?

BROOKS: No. No, I was a straight Course 5. I was a straight Course 5 chemistry in terms of my degree. I just took a lot of elective courses in computers, and I just took a lot of computer and math courses. I probably had more math courses under my belt than anybody else in the chemistry department, and I probably had more computer courses as well. So that was—yeah, and that was by choice.

ZIERLER: And then at what point did you determine that you wanted to go straight to grad school?

BROOKS: I always just sort of assumed. I just never really—I didn't really want to go to work. And so I would've had to get a job if I didn't. And I just didn't—there was no job I wanted to do really. [laugh] And so it was—I don't think it ever occurred to me to take a gap year.

ZIERLER: OK. And so given that you had this duality, you had the chemistry and the computation, how did that affect the kinds of programs that you were interested in applying to.

BROOKS: I applied—so for grad school, I applied to four grad schools: Berkeley, Stanford, Chicago, and Harvard. The only one I didn't get into was Harvard. My GPA was good but not great. As I said, I was a rower. I spent a lot of time on the water. My GPA was—at that time, they called it 4.5, which is a halfway between a B and a A, because 5 was an A, and 4 was a B. So I ended up with a 4.5, which is actually funny because I tend to not recruit people with my GPA now [laugh]—

ZIERLER: [laugh]

BROOKS: —when my own, you know [laugh]—so it's sort of ironic. I try to recruit between 3.7 and 3.9, between a 3.6 and 3.9.

ZIERLER: But that's out of a four-point system now, you see.

BROOKS: I avoid the 4.0s. So it's really funny. Every time I've hired a 4.0 student, I've regretted it. They're crazy. [laugh]

ZIERLER: [laugh]

BROOKS: [laugh] And every time I've hired somebody—anybody less than 3.6, I've sort of regretted it as well.

ZIERLER: So you've got your sweet spot?

BROOKS: So the sweet spot is 3.6 to 3.9. But that's where you want to recruit. I mean, I hired this one guy who was top in his class at Harvard. He was like top in his class in physics at Harvard. He was really superlative[?]. He was also the top prelim student at University of Illinois. But he couldn't stop pacing. He couldn't settle himself down.

He was like—I don't know—a compulsive—some kind of compulsive disorder. And I'd give him tasks to do, and he couldn't do them unless he fully understood them. And I said, "No, you don't need to fully understand this. You just need to do it." And he was dysfunctional.

There was a very strange level of—extreme level of intelligence coupled with a complete dysfunction when things didn't go exactly smoothly. So if everything was laid right out, everything was fine. But as soon as there was like a weird challenge or a weird something, then it just—everything fell apart.

And so actually I let him go after one year. I didn't continue with him. But it's strange. I mean, you meet a lot of people. And if you look at the little blurb I sent you, you can see I've had quite a few students and postdocs.

ZIERLER: Yeah.

BROOKS: So I get a sense for what works and what doesn't work. My first postdoc was a disaster. And I've had a couple other difficult—I had a disaster. This last year, I had a disastrous postdoc, not for technical reasons but for criminal activity and bad social skills.

ZIERLER: Whoa.

BROOKS: So that was a very ugly—very ugly. So he actually was fighting with other members in the group, and then police came to his door, and basically he got—he was—he actually escaped for China before he got arrested. But they collected evidence for child porn.

ZIERLER: Oh, boy.

BROOKS: And it was very ugly. And he put it all over my computers at work, you know.

ZIERLER: Oh, boy.

BROOKS: So it was a mess. It was a huge mess in the office. And, luckily, my boss didn't, you know [laugh]—didn't punish me for it. [laugh] He didn't like—I mean, I wasn't viewed as being accountable for his actions.

ZIERLER: That's good.

BROOKS: Certainly I had no knowledge of it. I didn't—you know. But it's also, you know, he—you know, his excuse was he didn't know it was illegal. He's from China. He was Chinese. It's illegal in China but he said he didn't know it was illegal. So I was just thinking maybe—you know, my recommendations to—when you have a new postdoc come from overseas, and you give them an—what's the thing? An orientation?

ZIERLER: Yeah.

BROOKS: What do you call it when you first bring somebody into an organization?

ZIERLER: Yeah.

BROOKS: Orientation? Indoctrination or [laugh] whatever you want to call it.

ZIERLER: Sure.

BROOKS: I mean, I think they should cover some of these legal—some of these criminal activities as well, particularly for—just to avoid this kind of mess in the future. But it was a huge mess. It was a huge mess.

ZIERLER: So these four schools, were they all the same departments you were applying to? Were they all chemistry departments?

BROOKS: Yeah, it was all chemistry—it was all strictly chemistry departments. But they all had good theory components and—

ZIERLER: And did you know that you wanted to work on computational stuff, to continue with that?

BROOKS: Yeah, or a theory or computation. I knew I didn't want to be in the lab. I didn't like lab work. It was too much like bad cooking, and I wasn't very good in the kitchen. You know, so, I—

ZIERLER: [laugh]

BROOKS: You know, it was—I just wasn't—it wasn't something that I wanted to do. So I wanted to be a computational or a theory person. I wasn't hellbent on computation, you know. There were some pretty good theory professors too. And I decided to go to Berkeley out of the three schools that accepted me.

They offered me the most money, and that might have [laugh] had something to do with it. But also they had over 60 professors. They had a huge program, and it was a top school. It was like—I think it was ranked number one or number two in the country at the time. And so I figured I couldn't go too wrong there. So I went to Berkeley, and at Berkeley—

ZIERLER: When did you connect with [Henry Frederick] "Fritz" Schaefer III?

BROOKS: I took one of his courses the first—my first semester there. So I connected with him pretty early in that course. I was probably the—again, I was probably the last student of my class to choose an advisor. I waited clear into January.

And there were several theory—there were five theory professors—four or five theory professors. One was inapproachable. But he actually looked like an interesting person to work for. But he would—you had to get past like getting thrown out of his office 10 times before you could convince him to [laugh]—

ZIERLER: [laugh]

BROOKS: —even consider you as a student. He was very eccentric. [laugh] Yeah, he was eccentric, very eccentric. [laugh] And there were other eccentric people there. But Schaefer begged me to join his group once January rolled around. And I guess he was—yeah, so he—and he signed me up, and I accepted [??]

ZIERLER: And what was he working on at that point?

BROOKS: He was working on quantum calculations. He was a highly published, well respected quantum chemist. He had probably more publications than any of his colleagues at the time. But he wasn't a programmer. He wasn't a method developer himself.

And, you know, we mocked his code that he had written at Stanford as a grad student. He had to do -1 to the N power. He had -1 * * N which is not the way you do it. [laugh] But he wanted to get more involved with methods and have method development. And so I joined his group.

My second year though he went to Australia for the year. He was gone, and I was left to my own devices, which was actually one of my most interesting years in terms of developing things. And I developed stuff. When he got back, I showed him all the stuff I'd developed, and he didn't want to deal with any of it. He basically said, "No, no, I want you to—I didn't want you to do this and this."

Some of it—I did quan…I did a really interesting Quantum Monte Carlo code, and I was one of the first to ever write this. And many people became famous later doing these Quantum Monte Carlo codes that I had first. But Fritz didn't recognize that there was any potential there at all. And, you know, I could've been the seminal—one of the seminal persons in that area.

The other thing I did was I did these solar system formation simulations. I did all of these sun, moon, Jupiter things. I started with like a dense gas cloud of gas, and I ran these simulations where these things would collide and stick. It was before anybody else had done it well, you know. It was like early ‘70s, and it was all very publishable.

It was all very interesting about how there was a propensity for forming large planets around an accretion disk. You could see it very clearly from these simulations. It just happened so many times, and it was just—it was sort of fascinating that it was just sort of a natural product of just a random collection of particles that fly around.

But Fritz looked at this and said, “No, we do chemistry. We’re not doing this.” So he threw all that code out as well. But that was all very publishable. It was all—it would’ve been interesting. It would’ve been an interesting paper. So I did a lot of the stuff which—you know, and in doing that, I also developed the leapfrog integration algorithm, which is actually published by others later as the leapfrog algorithm.

I never looked it up in a book. I just derived it. I just came up with it on my own. But it was a lot of fun because I came up with a lot of techniques, a lot of coding techniques. I wrote a lot of it in machine language to make it run fast on the four-megaflop machine we had. Four megaflops doesn’t sound like a lot but it’s—in those days, that was actually something.

But my second year was a year where I pretty much was on my own just developing things and writing code. I also wrote my CI code, the CI, configuration interaction code, which is quantum chemistry. And I worked on projects as well. So I had a dozen papers as a grad student, which is probably more than most people have in their graduate student career. And about half of those were methods papers, and about half were applications.

I did some early ozone work. At that time, the ozone hole was being discovered, and we were trying to understand the chemistry of the ozone in the upper atmosphere. And so I had papers like that. And so my papers are split sort of half and half in terms of this application-specific molecules versus method development papers.

ZIERLER: So if we look at your formal education, and then fast-forward to your position as Chief of Computational Biophysics, the obvious question is where's the bio and where's the physics in your formal education?

BROOKS: Oh, it's actually funny. You know, I'm Chief of the Laboratory of Computational Biology but I never took a biology course, not even in high school.

ZIERLER: [laugh]

BROOKS: I skipped—because in the bio track, if you wanted to take AP physics, you had to skip something or else double up or triple up on these courses. So I skipped the biology course, and I never took a biology course at MIT. I took a biochemistry course.

So biochemistry is the bio that I had. But I never took an actual biology course. I never studied some of the basics of biology. But I picked up a lot on the way, and I've read books. And, you know, you can learn a lot without a formal coursework.

ZIERLER: What about for quantum chemistry, though? Don't you need a foundation in physics for quantum chemistry?

BROOKS: Well, there's actually—quantum chemistry in physics is different than quantum chemistry in chemistry. If you take a quantum course in physics, it covers different material than a quantum course in chemistry. But most of my quantum, I learned as a graduate student. I took—did take the courses as an undergrad but they don't go into that deeply. It's not that in—a lot of it's more basic in terms of wave functions and wave packets and wave-particle duality. And, you know, there's a bunch of little projects and stuff.

But you really get the heart of it when you get to grad school. Oh, I guess I did take one MIT course which was actually very difficult in terms of the bra-ket operators and the—you learn all the math and the symbol—learn the notations and the symbols, you know, the bra-ket notation, and stuff like that. I took a course where I learned that quite well. And it helped a lot when I got into the unitary group stuff as a grad student.

ZIERLER: Was Schaefer's own background in quantum chemistry, or he developed that later on?

BROOKS: Yeah, but he was an application person though. So the real strength I had from working in his group is people would come on sabbatical with him at Berkeley. One year, it was Peter Pulay who was a top-flight method developer in quantum chemistry. And he was famous at the time for his analytic gradient work, you know, because before that, quantum chemists, they only computed energies. They didn't compute forces, so gradients.

So he developed the methods to do analytic gradients and so I'm on a paper with him. We were the first to do configuration interaction analytic gradients. But he was the one that helped me derive that though, taught me the math on that. We worked up the code. We got all that working.

And then Shi Shavitt came in, and he did the unitary group stuff. And then Nick Handy came in, and he did a lot of the—he was actually very inspirational in terms of a lot of the method development. So in terms of the method development, it was the sabbatical people that I learned the most from. I learned less from Fritz Schaefer on this—

ZIERLER: [laugh]

BROOKS: —because he didn't understand it deeply. But the sabbatical people did understand it, and they were good teachers, and they were very interesting to have around. And so those three professors actually had a huge impact on me. And that's one of the reasons I like to have sabbatical people come to stay at my lab now because I know it can have a huge impact on the development of the student, and the development of a program.

ZIERLER: Just because you're getting a diversity of ideas from all over the place?

BROOKS: Yes, and you also get knowledge that your advisor doesn't have. If you expect to learn everything from your advisor, you're going to know less than he does, and that's all you're going to know. [laugh] So that's a bad way of doing your education. [laugh]

So I think it's really important to interact with lots of people, and have a good—so I think Berkeley was a great place because so many good people came through there, either on sabbatical or other professors there. And I think that really made it a superlative place. And it's different.

At Harvard, we were more isolated in a sense. Karplus didn't have a lot of sabbatical people coming in. But we had a huge group. There was a group of 30 people, and it's very easy to get lost within a group, and you get a sort of warped perspective of the world that way. So Harvard was a very good place to have been. But at the time, I don't think it was organized as well as it could've been. I don't think it was—it could've been better.

ZIERLER: What was the process that led to your dissertation? What were you working on that led to that?

BROOKS: OK, so my dissertation as a grad student, it only covered the last 18 months of my work as a—so I actually started with Fritz Schaefer in '76, and I graduated in '79. So I was only in the group for not even three and a half years—about three and a half years. It was a very quick PhD. But only the last 18 months were in my thesis.

And by that time, Shi Shavitt came and he talked about his unitary group work, math worked out previously by Josef Paldus in Canada. And so my job was to code it up, and get it all to work. And I had to do a recursive algorithm which was very difficult to do in old FORTRAN, and I figured out how to do that using ASSIGNED GOTO statements. So it was kind of a mess but I finally figured out how to do it.

And I had the fastest CI program in the world at that time, and so it was—because it was based on this new math, everything before that was done with Slater determinants, which worked but they're slow as heck. And so—and then I also did some MCSC of multi-configurational self-consistent Hartree–Fock work. I did some—we did some density—we did a bunch of things. We did gradients.

So my thesis covers all the fun we had in the last [laugh] 18 months really developing this really big program. And a fast, big program that was very competitive with Gaussian at the time, except Fritz never really took it forward, at least not until well after I left, and that became the Psi program. You know, the Psi4 is a program we're working on now, which is a descendant of what I developed in the late '70s.

ZIERLER: And what did you see as your primary contribution with the dissertation?

BROOKS: Oh, my primary contribution was the unitary group CI, the recursive algorithm for unitary group CI. That was the primary contribution. I published a bunch of papers. Those are still some of my highly cited papers. They're on my h-index. You know what an h-index is, right?

ZIERLER: I do, yeah.

BROOKS: Yeah, so only the papers with lots of citations remain on your h-index, and these early papers from the '70s or a bunch of them are still on my h-index. And so they were well received, well noted. So that was—and the program—and you can—if you go to GAMESS-US now, and dig into the code, you'll find my name, you'll still find my code. So it has survived over the decades. It's still used in various places. Unitary Group CI is still probably one of the best ways of doing this kind of configuration interaction.

ZIERLER: Now the postdoc with Karplus, I mean, five years, that's a long postdoc. Was that sort of baked into the plan from the beginning?

BROOKS: No, well, I got—it's—well, I applied for an NSF postdoctoral fellowship, and I got it. So, at that time, it's—you know, NSF postdoctoral fellowships have always been prestigious, they've always been hard to get, and I managed to pull one down.

And I talked to my advisor about who I should go work for. And he goes, "Bernie, you're too narrow. You need to learn more." And he said, "Why don't you do some simulations? Go look at the—why don't you go do some BPTI simulations with Martin Karplus?"

And of course I'd never heard of Martin Karplus [laugh] because I was more narrow but I knew my stuff really well but I was very—you know. And one of the problems with Schaefer people is they do tend to be narrow, and I certainly was at that time. And so I went off to [laugh]—I went off to Harvard, and it was a complete shock because the standards for what is acceptable is just very different in the two subfields.

In quantum chemistry, if you make an error of a millihartree [atomic unit of measurement], you publish an errata. [laugh] You know, in the classical field, it was anything goes. My first job—in fact, this is an amusing story which I may not want you to include [laugh] in your final product.

But I told—my first job when I got there to Harvard, Martin Karplus was saying, you know, "I'm having trouble with this program called CFF/PI. And it's—we're doing normal modes of vibration, you're supposed to get six zeroes for the rotation translation, but they're not quite zero. Could you take a look to see what's going on there? It seems like a little bit"—so I dove into the code.

I quickly wrote some test code to test Hessian elements by finite difference of first derivatives, and then test first derivatives by finite difference of energies. I wrote—and I found—I quickly found about 10 mistakes. There were indices in the wrong order. There's an upper triangle matrix being indexed as if it was a lower triangular matrix. There's things that were swapped.

And then out of the six major terms in the Hessian, I could only find five. One was never coded. The most difficult one was never coded. And I can't believe that the person who did the math didn't have—he looked at the sixth one and said, "It's small. We're going to chuck it." And it only shows up in non-planar molecules, you know.

So it's a—so the code really—and so I fixed it up as well as I could. I didn't bother to write the sixth term because it was a mess. And I told Martin that just use the code for planar molecules. It doesn't work for non-planar molecules. That's the—you know. And, you know, he thanked me.

I believe that code was cited by the Nobel Prize Committee in terms of the—the code never worked. It had never been fully debugged. It was a junkyard dog. Yet, it's a—no, it's Nobel Prize work. And it's just sort of ironic to be given a Nobel Prize, you want to be first. You don't have to be accurate. [laugh] You don't have to be precise. [laugh]

ZIERLER: [laugh]

BROOKS: But you do have to be first. [laugh] And so that was the code written by one of the guys that won the Nobel Prize. So it was—yeah. But it was a shock to me because this would never fly in the hard quantum world.

ZIERLER: What was Karplus's style? Was he hands-on or was he—sort of he checked in?

BROOKS: No, he was very hands-off. He was very hands-off. We had a—yeah, he had a huge group. He had 25, 30 people, huge group. And he would let things fester within the group. There would be fights about how to develop—what's the proper way to develop code within the group. But he was—he didn't even resolve those very well.

So he basically—yeah, so he was pretty much hands-off. You know, I probably met with him maybe once a month early on. He was away a lot, too. He did a lot of traveling. He spent summers in France, and so—but he did give overall direction. So we were—when I went there, I started to work on the CHARMM project, and I dove into that and—

ZIERLER: Now how developed was the CHARMM project by the time you started working on it?

BROOKS: It was terrible. There were zero test cases. There was maybe one and a half pages of instructions. It was basically—there was also—it was two warring factions involved with this development, OK. And half the program was in FLECS, the other half was in FORTRAN, and there was all this copying that went on whenever you moved from one part of the program to the other. They always copy everything to the other format.

And it was basically on one side, it was a team of Barry Olafson and Swaminathan developing their code in FORTRAN, and then Bob Bruccoleri trying to write the whole thing in FLECS using structured programming. And it was just a mess, and they didn't get along. And I came into this, and it was like, oh, god, you know, it's like—so I sort of tried to bridge both worlds.

I tried to pull the thing together. We tried to bring some standards in. We made a lot of test cases. We basically started to do standardization. And so we brought the code along quite a lot. The original code came out of Bruce Gelin's work from his early BPTI simulations. It was also the parent code for AMBER. So AMBER and CHARMM split two years before I arrived at Harvard. That was the AMBER-CHARMM split.

ZIERLER: What was the overall goal of CHARMM? What was it trying to accomplish?

BROOKS: Oh, we wanted to do protein simulations—protein simulations and modeling, and basically any kind of energetic modeling of proteins and peptides. We wanted to do a simulation and mod…we wanted to do decent simulations.

ZIERLER: Now, working on proteins, I'm trying to figure out the transition point to NIH. Are you thinking about the value of this work in terms of human health sciences, or it's much theoretical than that?

BROOKS: I think it was more—for me, it was more theoretical. I wasn't really—I just assumed I was going to become a professor somewhere. And I had a couple of interviews. I had a bad interview at Columbia. I had another bad interview at Cornell [laugh] you know, and early on.

And then NIH basically offered me a tenure-track job after I'd been at Harvard for five years. Martin Karplus didn't really want me to go. I was the key developer of CHARMM. I was the key software guy. He was offering me a staff scientist position, a long-term staff scientist position at Harvard.

ZIERLER: But that's still not tenure track. That's still second-class, right?

BROOKS: It's still second-class, yes. But he wanted me in that role, and so he was—

ZIERLER: Was he not in a position to offer you tenure track?

BROOKS: No, he wasn't, and he wanted me—he needed me in that role to drive the program forward. He wanted the program to be—he wanted me in that role at Harvard to continue to push that code forward. And that was at a time that a lot of the other developers had already left, and he wanted me to train a new group of programmers coming in. And my wife wanted to move on to a better position with better options. And when NIH came up, I took it. I did have other job offers that weren't as nice as NIH, and I didn't take them.

ZIERLER: Now, did NIH find you or did you find them?

BROOKS: They actually—so it was actually interesting. So what happened was my good friend Rich Pastor, who I think you know—

ZIERLER: Yeah.

BROOKS: —he went to—he actually left the group a year before I did. He went to take a postdoctoral fellowship—

ZIERLER: Oh, so you worked with him at Harvard?

BROOKS: Yes.

ZIERLER: Uh-huh.

BROOKS: Yes. He was one of the few people to welcome me when I first came to the group.

ZIERLER: [laugh] He's a very nice guy.

BROOKS: Several other people just grunted, "Oh, not another person," you know.

ZIERLER: [laugh]

BROOKS: But Rich was very welcoming. He was a graduate student at the time I was a postdoc. And we worked on—yeah, we worked on a couple of projects, and I helped him with a lot of his stuff, you know, with his early subroutines. He had some needs that he wasn't—that I was much—it was easier for me to do, but difficult for him to do.

So I knocked off some code for him. I gave him some code, and I tried to get him involved with CHARMM. And there was a funny story about his early work with CHARMM. He actually tried

CHARMM for two weeks, and it wasn't doing what he wanted and stuff. At the next group meeting, he says—he just said—announced publicly very much, "CHARMM sucks." [laugh]

ZIERLER: [laugh]

BROOKS: So the "CHARMM sucks" comment sort of stuck with Rich, you know. [laugh]

ZIERLER: [laugh]

BROOKS: So every time like Rich has trouble with CHARMM, we say, "Yeah, Rich, we know CHARMM sucks." [laugh]

ZIERLER: [laugh]

BROOKS: So it's become a running joke over the last 35 years. But he was one of the few to welcome me. So he came to NIH. He worked with Attila Szabo, who you may know.

ZIERLER: Attila—I want you to know Attila is the one holdout of all of the people that I want to interview. He's the only one. It's a hard no. The mystique of Attila continues, particularly because so many people have said, "You've got to talk to Attila. He's a real physicist. He's somebody you got to talk to."

BROOKS: [laugh] Oh, yeah, I would certainly encourage you to get Attila if you could. But I can see why he might be reticent. He's got [laugh] some interesting stories, and he probably doesn't want the whole [laugh]—

ZIERLER: OK.

BROOKS: The story of his not getting tenure is an interesting story.

ZIERLER: Yeah.

BROOKS: I don't know if Rich told you anything about that.

ZIERLER: He alluded to it, yeah.

BROOKS: [laugh] Yeah, yeah, yeah, yeah. OK. And so he came down to NIH a year before I did, and he quickly got a job offer at FDA. And then Rich said, "They're looking for someone to code their"—so they—and then one of the persons with the Computer Division bought this $300,000 machine that you could only code with machine code.

And Rich knew that I was good with assembly language coding and stuff. He says, "This is the ideal for Bernie." And he called me up and said, "Bernie, they have this machine, and nobody knows how to use. They can't do anything with it. Why don't you"—so he recommended to the Computer Division they recruit me, and they did recruit me, and so I came down. So Rich was actually, you know, instrumental in getting me to come to NIH.

ZIERLER: And this machine, was it new, or was it new and really advanced?

BROOKS: It was new and advanced.

ZIERLER: Yeah, and this is attractive to you because you realized that NIH had resources that you could work with that were simply not available in an academic setting?

BROOKS: Oh, yeah, I got that thing to run at CRAY-1 speeds. It was a $300,000 machine that we made run as fast as the $3 million machines. And so it was a good run. I came down. I wrote 30,000 lines of microcode my first year, and got it working well. And it was actually a good thing for me.

ZIERLER: So help me with the abbreviation: Senior Staff Fellow OD/DCRT.

BROOKS: Office of the Director DCRT. I wasn't in any lab. I was a loose cannon. So I was pretty much free to—I was not—I reported directly to the Director. I didn't report to anyone else.

ZIERLER: And what were some of the benefits and pitfalls of not having that, you know, closer hierarchical relationship?

BROOKS: You avoid a lot of the pettiness that occurs within a lab, particularly if you're not a well-loved person in the lab. If he had stuck me in one of the labs, I think I would've been a much—it would've been a much harder go. So being a loose—being in a loose position meant that I could get resources without a lot of other people [laugh] knowing about it.

And I did have good resources. I had much better resources then than I do now, in fact, even though I have a lot of people now. I mean, I once wrote a paragraph, and got $1.9 million for [laugh]—you know, those days are over.

ZIERLER: Yeah.

BROOKS: And in those days, $1.9 million was actually worth something. [laugh]

ZIERLER: [laugh] And were you taking on postdocs and graduate students from the beginning?

BROOKS: No, not from the beginning. I took my first one after I'd been there about two years. Before I got tenure, my first postdoc was a disaster. He only lasted six months. I was advised not to take him by the person who knew him well, and I didn't listen, probably because I didn't have any other hot prospects at the time. The guy lied to me about what his skill set was, and was—

yeah, it was a—you learn the hard way. And then Martin Karplus told me early on having no postdoc is worse than having a bad postdoc.

ZIERLER: [laugh] Right.

BROOKS: And so I took that to heart, and that's one of the reasons I just did a lot of the work myself. And, in fact, the vast majority of my work I got to get tenure, I just did myself [??]

ZIERLER: Now, were you doing tenure—did you get tenure in that position, your first five years in that job?

BROOKS: I got tenure in '89. So after four years, I had gotten tenure through the NIH tenure system. And Alistair Stevens was the tenure—was on—Chair of my tenure committee, and that worked out. It all worked out pretty well.

ZIERLER: So the same question I posed to you when you were at Harvard about thinking about the potential use of your research in human health, did that become sort of a clearer connection when you got to NIH, or not necessarily?

BROOKS: Well, we were look…yeah, we were trying to—we did take on projects that were related. We took on a couple of malaria projects, and we were trying to help with the malaria vaccine. In fact, in one of my papers, I made three suggestions for how to develop a malaria vaccine—or maybe it was four sugg…we had four suggestions, I think, two of which were tried, and they both failed.

So we were trying. We weren't that experienced. And the other two suggestions, the experimentalists just said were too hard to do. That they weren't realistic suggestions. We didn't have the—they didn't have the capability to do what we suggested. So we did try. I mean, it's—connecting from what we were doing to actual health at that time was actually very difficult.

We didn't really see a clear path to helping with the health—real, you know, health. The malaria project probably is the only early attempt. There may be another one. I should go back and look at my papers. But that was sort of the obvious one where there was a clear health connection but we just—we tried to make the connection, but it just didn't work.

ZIERLER: And was that because the field was so new, like you were making it up as you were going along, essentially?

BROOKS: Well, it was—I guess the early models—I think the models were basically correct. But once you have a model, how do you go from a model to, oh, here's what we do to cure it? Just because you know what it looks like doesn't mean you know how to fix it, how to get rid of it. And so there's a gap. There's a large gap there.

And there was a—and some of our methods were actually fairly primitive. I also did a, you know, oxygen transport through a monolayer, you know, lung, you know, where we tried to predict the transport rates of oxygen through a monolayer. And we reproduced experiment. The fact that it increases and then decreases if you have too much cholesterol, as a function cholesterol.

So we were studying that. So we reproduced it but we didn't understand why. We couldn't—from our simulations, we couldn't figure out why [laugh] it was doing it. And only later did we actually realize that—you know, figure out why it was happening. But just because you can see it happen, just because you can reproduce it, doesn't mean you understand it.

And even if you do understand it, it doesn't mean you have an effective treatment. It doesn't mean you can go from there to an effective treatment. So I think—so I've always viewed the work we do as sort of a stepping stone towards better knowledge, but maybe not sufficient in itself to get all the knowledge you need.

But there have been—you know, a lot of codes have copied what CHARMM has. And CHARMM is still heavily used. And it is being used for a project, some real-world projects. I also tried to use it for some consulting, you know.

At the time, I was a consultant for Procter & Gamble, and we were trying to make better soaps that would last better in cold water. So we were trying to engineer—it was an engineering project that was very difficult to do. It was very difficult, and we were only partially successful.

But the question is how do you make a hot water detergent? They had a cold water detergent, and it didn't work in hot water because the proteins would fall apart. And they wanted to make it so it worked in hot water. They wanted the protein to be more stable. So the question is how do you change the protein to make it more stable?

And that's a difficult project [laugh] too. How do you increase a melting temperature? You know, and that's—we worked on that for a while, and that was difficult. So going from the models to actually real-world solutions is not a trivial thing. And that doesn't mean what we do is not useful. It just means that it's not easy.

ZIERLER: Right. Now, when you moved over to the Molecular Graphics and Simulation Section, was this a real change in your specialty, or this is a continuation of what you had been doing?

BROOKS: I guess that was a continuation. I guess it became a section because I started hiring postdocs. I had two, three postdocs.

ZIERLER: So you created the section?

BROOKS: Yeah, I was the—yeah, that was my section, and it became part of the Laboratory of Structural Biology, LSB, at the DCRT. So what happened was the Director of the Computer Division decided to put his science in one lab, and it became the Laboratory of Structural Biology. Adrian Parsegian was the Lab Chief, and then he—we pulled into—and I moved into that. I created a section. So that was my section. That was what we named what we were doing.

ZIERLER: And what is molecular graphics? What does that mean, molecular graphics?

BROOKS: Well, we did a lot of imaging at that time. We did a lot of pictures. We did movies. We did stuff. So we were simulating, and we were making—we were putting out pictures, you know, very much like the pictures you've seen in the—nowadays, it's—in those days, there were very few picture programs. There were very few graphics programs. Now, there's lots of them. [laugh] VMD is the most famous of the bunch.

ZIERLER: And what's the value of these programs? Who's the audience?

BROOKS: Well, you can see—the idea is you can learn by looking. So if look at a protein—for example, we were looking at this winter ice flounder protein, that it blocks—that it prevents ice from forming in the cells of fish at below freezing. You've heard about these proteins, antifreeze proteins?

ZIERLER: Yeah.

BROOKS: And the way they do it is they block the growth surface of ice. And you say, "Well, how does it do it?" Well, it turns out if you try to work out the math, it doesn't—but if you actually make a model, and you can say, "Oh, here, it fits right around the ice surface. Here's how it does it." [laugh] And by having a picture and a model, and being able to manipulate it, you can quickly see how the peptide blocks the growth surface of ice.

In fact, you can—it becomes sort of an aha, eureka moment. Oh, yeah, here it fits. It fights right on the ice, and binds to the ice, and prevents ice from growing. But having a molecular model or graphics really allows you to see that quickly. To try to do that without molecular graphics is somewhat difficult.

ZIERLER: And how is collaboration working? Who are the kinds of people across campus that you're working with, you're collaborating with?

BROOKS: Well, it turns out I don't collaborate with too many people on campus. I have done some collaboration. But most of my collaborators are out, off campus. And some of them are experimentalists. A lot of them are other theory people. And I've worked with a fair number of experimentalists over the years, and as reflected by the publication list.

Usually in the work I've done in collaboration with experimentalists, we're not senior author or first author. Most of the time, we're providing support, computational support for a larger project. And if you look through my publication list, you can probably find 20 or so papers like that, 20 or 30 papers like that.

And that's the kind of collaboration—that's typical of the kind of collaborations we do for those kinds of things. We also have other kinds of collaborators, yeah. I mean, it might be easier for me to throw up my CV, and we could talk about individual papers if you like. But I don't think you want to go to that level of detail.

ZIERLER: No, just keep it at the office level.

BROOKS: Yeah. But so very often, we will work with experimentalists or we will work with imaging people like the Cryo-EM people. We have a bunch of Cryo-EM papers where we helped do the computational work behind the structure determination under Cryo-EM. Or we can—we also have a lot of papers with other theory people where we would work on something together, you know, or—and certainly on these group papers like the big programs.

Like I work with helping with Psi4, the work with helping with, you know, some of the other big packages that are out there, Q-Chem. We did a lot of work with Q-Chem, so you can find Q-Chem—you know, some of these are like 50-author papers. But you're developing a larger package, and you're helping with that.

And I probably should have more collaborators. I think Rich has a richer set of collaborators than I have in terms of the experimental side. More of mine tend to be on the method side. And I view my work has always being more method-oriented, and less application-driven. If you look at my publication titles, you see a lot of it is method-based, a lot of method development.

ZIERLER: And why do you think that is? Is that just how you think?

BROOKS: It's what I enjoy doing. I enjoy writing code, developing methods, and pushing out these ideas. And it's also, in some respects, I think, a little bit cleaner. Real biology gets very messy very quickly, you know. And so—and—but I have—you know, we have papers like that.

But it's—you know, now we're doing the coded simu…we're setting up these CoV-2 simulations with the spike protein. And so we're doing stuff that's directly related to the—we're trying to understand the role that protonation plays in the action of the CoV-2 spike protein.

ZIERLER: Good. I'm glad to hear it. The more people who are working on this [laugh] the better it's got to be. [laugh]

BROOKS: [laugh] Yeah. Oh, this is pretty ugly out here, yeah.

ZIERLER: So that one-year stint you had as the special advisor to the CIO, now given—

BROOKS: OK. So that was an ugly—that was 18 months, actually. So after I jumped over to Heart, Lung, and Blood, I was asked to come help run the science program at the DCRT, what was left of the science—the science support program.

So it was a group of about 70 people, and they had a budget of about $5 million. So it was—and I was asked to come in and do a review. So the main function of—the main thing I did during that time was I did an exhaustive peer review. Like I have—I created like two thick binders' worth of material.

We had reviewers come in from all over the place to review the program. And at that time, several people, several people, several of the directors wanted to shut it down. And I guess I managed to—we managed to shut some of it down, but not as much as I think Dr. Balaban would've liked to have us shut down. [laugh]

Because I pointed out the good and the bad. And the good was actually pretty good. The bad was actually pretty bad. So they got rid of the bad. So we helped the program. But it was a horrible—I really didn't like that management job.

So the way I sort of paraphrase it now: there were four people in the organization who thought it was my job to listen to them complain about other people in the organization all day long. And there was some infighting going on, and they thought it was my job to be involved with the infighting and listen attentively to all of the crap that was going on.

And I just didn't want to have anything to do with it. It was just like—it was horrible stuff. They got lawyers involved, and it was just like—it just made me want to—so when Dr. Balaban—so I went to Balaban, and I said, "I just want to get back to the lab and back to my science." And Balaban brought me—so I got rid of that job after 18 months. But I was so glad to give that up. It was not so rewarding.

ZIERLER: But given the fact that you were advising on computational biosciences, was there anybody else that could fill in for you, or were you the guy for that?

BROOKS: No, it was mainly a management job. It wasn't doing actual science. It was managing scientists. So it was basically supervising—and not even the good level supe…bad—it was, you know, supervising at a level beyond the work. It was more of an administrative job. You're an administrator trying to keep the thing functioning properly, you know. And it's not interesting. It's not interesting work. It's like, you know—it's not that different from trying to run a supermarket—

ZIERLER: [laugh]

BROOKS: —you know. [laugh] And it's like it's not that different from [laugh]—you know, it's not science. It's managing people. And it's managing difficult people because these people are all difficult. And you have lots of constraints put in by the personnel roles and the civil service roles and stuff.

Basically your hands are tied, you're trying to deal with this stuff with your hands—two hands—one hand tied behind your back. You have limited resources. You have very limited help from anybody else. And it's a thankless—it seemed like a thankless job. And I was more than happy to run away from it.

I learned a lot doing it. In fact, I also—by going—I also went to Scientific Directors meetings every week or every time they had—you know, it could be twi…every—and so I learned a lot about what was going on at NIH. I got to know a lot of the movers and shakers at the NIH. I think it helped me in that regard, and it allowed me to—and even today, I'm still the Chair of the subcommittee, the tenure subcommittee on math, physics, sci…and computation, and bioinformatics.

So anybody who comes up for tenure in any of those fields comes through my subcommittee on the central tenure committee. And I think that was—and I think I got that position mainly because they knew me through that time I was at Scientific Directors. And it's not a difficult job, but it's one of my positions that I had.

ZIERLER: Now, when you came, did you create the Computational Biophysics Section also, or that was there before you?

BROOKS: Yeah, no, that we created. So I was—when I came over to the National Heart, Lung, and Blood Institute, I was moved into the Laboratory of Biophysical Chemistry. So we moved into an existing lab, and then we had to create a section, so we just called it Computational Biophysics Section.

ZIERLER: And what's the thinking behind that? What does computational biophysics mean?

BROOKS: Well, we try to understand how proteins work and act, the structure function relationship of macromolecules. And that's what really biophysics is. Biophysics is how—is trying to understand how things work based on what you can learn from modeling and structure.

ZIERLER: Yeah, I mean, I've had lots of conversations on what biophysics is. And as you can imagine, I've gotten lots of different answers. So do you see it as an even merging of bio and physics, or is it really physics with a bio component, or is it really bio with a physics component? Where do you come out on that?

BROOKS: I see it as chemistry. [laugh]

ZIERLER: [laugh] What does that mean? What do you mean by that?

BROOKS: [laugh] Well, I think a lot of biophysics relates to the actual chemical interactions that occur at the microscopic level. And I don't think you can understand biophysics without chemistry. And so I think, for me, it's strictly a—it's basically an application for which you can use your advanced chemistry tools.

ZIERLER: OK.

BROOKS: OK. So your advanced chemistry tools allow you to take biological systems and understand the basic physics of them. So it's a little bit of a twisting around of biology, physics, and chemistry. But I think my—I come at it from a chemistry perspective, and how do we use chemistry to study the physics of biological material?

ZIERLER: OK. So, I mean, there are biophysics programs out there, right?

BROOKS: Sure, sure.

ZIERLER: Could you do what you're doing if you came from a biophysics background?

BROOKS: So, actually, a lot of my students and several of my grad students are in biophysics programs. Right now, two of my graduate students are in biophysics programs at University of Maryland. OK. And so we are part of the biophysics programs. They have other things they have to do as part of the biophysics program. But most of what they're going to be doing is with me during their time as graduate students.

So I've had a wide variety of postdocs. They've come in from chemical engineering backgrounds, from—I had mathematicians. I've had physicists. I've had chemists. I don't think I've ever had a pure biologist come in. But I had a wide variety of people. And the people, the students I've had were also in a diverse set of departments. So some of my students are in chemistry departments. Some are in biophysics departments. Some were in math departments.

And so I've been fairly flexible about taking students. I don't really want to pigeonhole myself into one type of department. I mean, I can—I had a lot of fun with the mathematician. We did some really interesting stuff that I wouldn't have done without a mathematician grad student.

And the chemical engineers who have come into my lab have actually been very successful. They have a much higher professorship rate than some of the chemists have had. And I could send you—most of my—about two-thirds of my former postdocs are in faculty positions now. So I've had a pretty good rate of—because, you know, sending them into that—into the fields.

ZIERLER: Yeah. So this takes us, I mean, essentially up to the present. So now I want to ask you a few like broader questions about how you see your accomplishments sort of broadly conceived. So the first is if you can explain what's the process by which you take on new projects? I mean, obviously there are all kinds of things you can do. Resources are limited. You have to choose what you work on. So what kind of parameters do you—?

BROOKS: OK. So I usually—most of my projects I do either collaboratively or within—or as an advisor role. And early on, I tried to assign projects to students. And I find that that didn't really work unless they were—unless they really liked the project, it didn't really work very well.

And so I view new projects as a collaborative negotiation, if you like, a negotiation with a student or with a postdoc, and sort of negotiate where—what do you want to—you know, like where do you want to take this? What do you want to learn? What do you want to do?

And so very few of my projects are just simply—are mine to say I'm just going to assign this to somebody. Or very often, I will shop a project. Like when the COVID stuff came up, I sent an email out to the group. "Who wants to work on this COVID stuff?" And then we got a few takers, and now we got an active program going with the people who stepped forward.

But not everybody stepped forward. But instead of me picking somebody, I sort of threw open the doors and say, “Who wants to come running through and run on this thing?” And I’ve got some—you know, we got now an active program with two or three people involved as a collaborative thing.

So most of my projects I take on are done through negotiation and collaboration. Very few are assigned. I mean, I do have some assigned projects. If a student’s really green, you know, and I don’t trust their ability to choose their own projects, I will assign a project. But for the most part, most of my people are pretty advanced.

They’ve already either completed a couple years of grad student—grad schools or they’re postdocs, and they have very—or staff scientists, and they have very—you know, their own set of interests and such. Or I’ll have collaborators come in and say, “We want to work on this, you know.” And then we will try to find someone to work on those things. So I don’t know if I’m answering your question clearly.

ZIERLER: Oh, yeah, for sure, that’s the process. So—

BROOKS: But the process is a negotiation, and everything has an opportunity cost, because if you do project X, you’re probably not going to do project Y or Z.

ZIERLER: Sure, sure. I wonder if you could talk about the impact of advances in computational power over the course of your career. Do those advances drive—

BROOKS: Oh, they’re huge.

ZIERLER: Do they drive what you're able to do? Are you sort of ahead of the curve, and you need to wait sometimes to do something until the computer power catches up?

BROOKS: [laugh] Yeah.

ZIERLER: How does that relationship work?

BROOKS: Ah, things become—the kinds of things we used to do or used to be very difficult or expensive become cheaper and easier. But typically we will increase the size of the projects that we take on or the simulation time scale.

ZIERLER: But you're not conceptualizing new projects as a result of increased computational power?

BROOKS: Well, we do have some—some new projects came in, you know, particularly with sampling, you know, some—we do have some that are the new methods. So the question is are we applying old methods to new problems, or do we have new methods and new—it's a combination of things. So because the computers are so much faster or so much more in parallel, we do have new methods that exploit that.

The replica exchange is an example of that where we run maybe 30 or 50 simulations simultaneously and have them communicate with each other. And that's a new thing that we wouldn't have done in the old days because you just didn't have basically 50 computer clusters running at the same time. They couldn't[?] all talk to each other.

But nowadays, you have the ability to have a cluster of GPUs running, and you could do replica exchange in this manner. And we also have—our constant-pH methods are also very expensive.

And since we create multiple protonation states simultaneously, and that all—that doubles, triples, quadruples the cost.

We're doing things with polarization. That also quadruples the cost. So, you know, at the time when computer time was very expensive, we wouldn't have dreamed of taking a method that was 4 times slower or 10 times slower. But now it's OK. If the method's 10 times slower, if it gives a better answer, yeah, it's great.

ZIERLER: In talking about all of the projects that you've been involved in, do you see an obvious through line that connects all of them, like an overarching interest or a technological feasibility?

BROOKS: Yeah, most—I mean, if you look at my papers, I mean, much of it revolves around the development and production of CHARMM. So CHARMM has been sort of the base and the foundation of this, and things that relate are connected. CHARMM has been the thing. So CHARMM—I view CHARMM as my magnum opus.

I'm the first author on both the big CHARMM papers. It accounts for about half of my lifetime citations. And so I view that as my magnum opus, and it's still the foundation of a lot of what we do. Most of the methods that we develop first go into CHARMM, and then they go into other programs.

ZIERLER: And what has CHARMM achieved, and what hasn't it achieved that you think it can achieve at some point in the future?

BROOKS: Well, CHARMM's an old program. It's 40 years old. [laugh] It's probably—it's a large—it's got over 900,000 lines of code. It's a big—it's a dinosaur. It's a big—it's not the fastest code, you know. It's got a rich history. It has—probably has the most diverse methods, the most number of ways of doing things.

It's difficult to learn. It's not user-friendly. But it certainly has had a huge impact on the field. It's the highly—it's highly—it's the most highly cited program of any of the software packages out there. And it's had an impact.

Most of the methods that people use were in CHARMM long before they've been in the other codes. So it's been something that people have watched and followed, and then taken from, or redone in their own codes. And so it's been a leader in its field for decades. And it's had a huge impact on the field.

ZIERLER: And what is that impact? What do you see as its impact?

BROOKS: Well, you know, when I first came into this field of—you know, when I first started working for Martin Karplus, there was probably only—there were probably fewer than five professors in the world working on this kind of thing. And the number of people in the field were—was just in the—you know, it was probably—including all the students, it was probably less than 100 people. It was just a—you know, it was a nascent field with very—you know, without a lot of promise.

But now the field is huge, you know. There's thousands of people doing simulation and modeling. It's a much more involved[?] thing. There's whole entire subgroups of people doing very specific things with different kinds of simulations. But, you know, the field is clearly three or four magnitudes bigger than it was when I came into it. So the fact that the field has grown is a testament to the fact that the stuff is useful. People perceive its utility. People can recognize its ability to do things.

And also much of modern crystallography is a spin-off from CHARMM. The X-PLOR program is a CHARMM spin-off. These came directly out of the 1984 CHARMM split with X-PLOR. And so it's had a huge impact for crystallography, for Cryo-EM, for all these other fields.

A lot of the code that CHARMM has been used has been used or incorporated in other ways into other codes. So I think it's had a huge impact. I think if it hadn't been useful or hadn't had the impact, I don't think the simulation modeling field would be anything like it is today.

ZIERLER: Right. And so if you can just think about, you know, the sum of your career at NIH, to the extent that you think about the mission of NIH, how do you see your work fitting in and advancing that mission?

BROOKS: Well, I think NIH was an ideal location for me because it gave me continued funding without me having to spend a huge amount of time fighting or writing grants. It's allowed me to support the CHARMM program in its development while doing other research. I haven't paid a price for doing that, which may have been—it would be much harder for certain professors to do that depending on what kind of, you know, institutional setting they're in.

So I think NIH has been very good to me. They've given me—I've had good support. I've been able to hire the best people. I think my groups have been very strong. I have probably a better record—track record of placing people in academia than most of my competitors.

ZIERLER: But you're answering how NIH has been good to you. I'm asking you how have you been good to NIH?

BROOKS: [laugh] Ah, well, I've—

ZIERLER: Or is that a harder question to answer? [laugh]

BROOKS: That's a harder question to answer. NIH has been very good to me. I think I've been good to NIH. Certainly I've served on a lot of committees and things like that. But I don't think that's what you're asking about. I think it's—you know, NIH has very visible labs, [laugh] has very visible programs.

And, you know, the Laboratory of Chemical Physics I think is one of the premier labs at the NIH in terms of computation—in not just computation but in terms of chemical physics. And I think on the computational side, I think we—you know, Rich and I are both very visible, and I think we have a, you know, strong lab that is recognized worldwide. Both of us have a strong international reputation.

ZIERLER: And that in and of itself is good for NIH?

BROOKS: Yeah, that's good. You know, it's—we're—National Academy is probably not in the cards for either Rich nor me. It turns out that none of the people who stayed in the field with Martin Karplus have been inducted into the National Academy. And Martin Karplus carves out a big, big, you know, space, and I don't think that's going to happen until Martin fully retires. So it's actually funny in a sense, but it's—

ZIERLER: Is he still active?

BROOKS: He's still active, yes.

ZIERLER: Wow.

BROOKS: Still—he's still—yeah, he's still got his hands on CHARMM too, which is unfortunate, because I think he's making a lot of bad decisions with regards to CHARMM. All our competitors' software is free for academic users. But Martin still charges for use of CHARMM.

And I think it's kill—you're going to kill the—it's been very difficult to have to put up with that, especially since we're not getting any of the resources coming back. So there are a lot of bad decisions that will get changed as soon as Martin is no longer involved in the code. But for the moment, he still makes a lot of the decisions, and it's not always in the best interest of CHARMM.

ZIERLER: Well, I think, Bernie, for my last question, I want to ask you something that's sort of forward-looking. And that is, you know, what are you excited about for the future in terms of your field, in terms of what you want to accomplish personally about where this research can be applied—

BROOKS: [laugh] Well—

ZIERLER: —in ways that it can't be applied now?

BROOKS: [laugh] You know, you're asking a senior citizen about the future. [laugh]

ZIERLER: [laugh]

BROOKS: [laugh] You know, and this is the same problem you have with Rich, you know, that we're—you know, I see myself as being close to end career and—or certain…maybe not imminent but certainly not—you know, I don't think I've got 20 years left in the field.

ZIERLER: No. But what I'm asking is there's a momentum to your work that will continue when you're no longer working.

BROOKS: Oh, sure.

ZIERLER: That's what I'm asking about in terms of what's exciting.

BROOKS: Yeah, and I think there's certainly—it's certainly as I think—better physics models I think are something we're pushing. And I think that's going to be a rising star for the future.

ZIERLER: And who's going to do the better physics models? Who would you look to do that?

BROOKS: Oh, there's an entire team. There's an entire team involved with that. I think the Tinker community is one of them. But there are the advanced force field. The advanced force field efforts are out there. And I think the—it goes beyond the point charge fixed atom types of simulations. Also dealing with protonation states more better.

So I think moving the simulation field beyond the current balls and stick model we have on the computers I think is really what's going to change the field, change the way in which we do things in the future. More quantum chemistry, quantum free energies is something I'm fairly well-known for, and my former postdocs were actually making good inroads in that area. So I view the legacy as maybe getting better and better simulations with better and better software.

But doing it better with better physics I think is going to be the answer to—and we've been involved with these like drug-binding competitions. We've done really well. We've probably done as well as any group. You know, certain competitions we don't win. But I think overall I think if you've looked at the last few competitions, it's very—I don't think any group has done as well overall as we have.

But it's clear that we have deficiencies in what we're doing, and it's clear that only better physics is going to get beyond these. You know, we've sort of hit a wall at how well we can do without better physics. And so I think the legacy will be better physics, and pushing that way. I have several people in my group working on the better physics programs. And I think that's going to be the legacy there.

ZIERLER: Now, just as a postscript, you mentioned that, you know, your lab is working on the COVID-19 issue. And it's just a very exciting time to see all of these different, you know, scientists who are just, you know, getting thrown in on this because it's sort of an all-hands-on-deck situation. So I think in a way that for researchers and listeners to really get an appreciation for what it is that you do, it might—this might be a good like way to take this out of an abstract concept, and just explain what is it that your lab does that's useful to the overall fight against COVID-19?

BROOKS: OK. So one of the expertise we have is to be able to treat constant-pH, which would treat different protonation states simultaneously. And so with the spike protein, the CoV-2 spike protein, we're looking at specifically how multiple protonation states, how the action that was by protein may be instigated by a change of local pH. And so we're looking at specific hypothesis, and trying to understand those hypothesis in terms of structures.

If we can actually identify structures for these different things, those could be potential drug targets. And so we're looking at that from a—and lots of groups are starting to simulate this thing now. So there are many groups. So, you know, part of our motivation is not to be just metooism, like, “Oh, we’re going to simulate it too,” but to actually try to offer something different from what the other simulations are offering.

Because we can look at—we can address questions that they can’t address because they don’t have the more advanced methods that they’re applying to this. And so that’s where I see where we’re involved in. And hopefully we’ll have a paper out by the end of the summer on what we learned. And that’s where we’re going with that project.

ZIERLER: OK. Well, Bernie, it’s been a great pleasure speaking with you today. I really appreciate it.

BROOKS: OK, and if you have any further follow-up questions, please feel free to contact me [laugh] by email.

ZIERLER: Absolutely.

[End of recording]