SPB by David Zierler

Sergey Leikin 24 March 2020

Remote Interview

DAVID ZIERLER: It is March 24th, 2020. This is David Zierler, oral historian for the American Institute of Physics. It is my great pleasure to be here with Dr. Sergey Leikin of the National Institute of Health. Dr. Leikin, thank you so much for being with me remotely today.

SERGEY LEIKIN: Actually, NIH has closed its intramural program. I don't know whether you've heard it or not. So I have to be at home. We're not allowed to be in the lab except for basic maintenance functions.

ZIERLER: Right. You are referring, of course, to this period that we're in right now, which is the crisis relating to the coronavirus.

LEIKIN: Yes, yes, of course. As of today. I mean, yesterday, we had to finalize shutting down all experiments. But as for today, all the labs that are working on coronavirus are allowed to continue experiments. Other intramural labs were asked to shut everything down in order to minimize interactions between people.

ZIERLER: So as a historical document, when researchers from the future will be listening to this interview, this will be a real-time reminder of what life was like during this particular crisis. So as a historian, that's something that I think about.

LEIKIN: OK. [laugh]

ZIERLER: Dr. Leikin, would you please tell us your title and your affiliation at the NIH?

LEIKIN: I am a senior investigator, which simply stands for fully tenured investigators. And I am a chief of the Section on Physical Biochemistry at the National Institute of Child Health and Human Development (NICHD).

ZIERLER: Does that mean that you are focused exclusively on child health, or does your research have reach beyond children's health issues?

LEIKIN: Primary function of most Child Health (NICHD) principal investigators is to work on either basic science or translational science, or applied science that's related to developmental diseases, childhood diseases, pregnancy, that kind of stuff. But you cannot really separate that from a lot of basic science. So all of us do some that's related to child health and some extends way beyond that.

ZIERLER: Right now, we are going to start at the beginning for you, for this oral history. Would you please tell us about your birthplace, where you are from?

LEIKIN: I was born in Moscow. Back then, it was still Soviet Union, because I was born in 1961.

ZIERLER: At the height of the Cold War.

LEIKIN: At the height of the Cold War, and at the height of—at the beginning of some of the most difficult period for Soviet Union.

ZIERLER: Tell us about your parents—where they were from and what they did for a living.

LEIKIN: Well, my mother was an economist all her life, and she was doing mostly research. She was economist as a scientist. She was working at the Institute of Economics of back then Soviet Academy of Sciences. And my father was an electrical engineer. Both of them died long time ago.

ZIERLER: Tell me a little bit about the kind of school you went to as a small child.

LEIKIN: Well, initially in primary school, I just went to regular public school. But then starting from sixth grade, which would correspond to middle school and high school in U.S., I went to a very special school in Moscow. It was School Number Two, specializing in physics and math. I don't know, maybe you've heard about it, because it's world-known. And so I graduated from that school.

ZIERLER: What's the name of that school?

LEIKIN: Very well-known for very large number of people trying to fight Soviet regime, so it was shut down in '78, when I graduated.

ZIERLER: What was the name of the school?

LEIKIN: Do you want me to say it in Russian or in English?

ZIERLER: Both would be great.

LEIKIN: Both? In Russian, it would be [speaking in Russian]. In English, it would be Second Physical Mathematical School, or Physical Mathematical School Number Two probably is a more accurate translation. It was in Moscow. It was only middle and high school, unlike all other Russian schools. And it was very special in many ways, but in particular in the ways we were taught mathematics. Like for instance, at the time I graduated that school, the level of my education in math was higher than a standard four-year college in U.S. specializing in math and even six-year college in Russia. I didn't learn any math after the high school. Nothing else was needed, even though initially I worked as a theoretical physicist. All my math education came from high school.

ZIERLER: So even as young as sixth grade, it was already obvious that you had an aptitude for math and science.

LEIKIN: Yes. And to get into that school, we had to pass a special math exam. Otherwise, you wouldn't be accepted. It was specifically for kids gifted in mathematics, yes.

ZIERLER: I wonder if in the 1960s during the height of the Space Race, if the Soviet ideology to take on the United States was something that you felt as a small child in terms of emphasis on math and science?

LEIKIN: [laugh] Probably. But I wasn't much interested back then in those years, in the '60s. I got a bit more savvy in understanding all of that in '70s, once I entered that school. I believe it was '72, because I graduated in '78. It was a five year school. There, I began to learn more.

ZIERLER: Were your parents engaged politically and ideologically with Soviet Communist issues, or not really?

LEIKIN: Not really. My mother was a member of Communist Party but only because otherwise she would be fired. But she was always apolitical.

ZIERLER: Now when you said that this school that you attended was known for—would it be refuseniks? What would be the right term for the students that this school produced?

LEIKIN: Well, yeah, there were quite a few—well, the refuseniks, not so much. It was more—you know, [laugh] I forgot the Soviet term for that.

ZIERLER: Dissident—?

LEIKIN: Dissidents, yes.

ZIERLER: I remember the Russian word for dissidents. They use—they picked [?] that up right away.

LEIKIN: It has been so long since those times. Yes, dissidents. And at any particular time, a number of our students and/or teachers were investigated by KGB. If you're interested in those stories, I can tell you more.

ZIERLER: Absolutely. Why don't you tell us that story now?

LEIKIN: OK. That's fine. Our math teacher, who was teaching us this high level math, college level math—so we have regular algebra, geometry, and that kind of stuff, but we also have calculus. And so the math teacher who was teaching us calculus, he was also a very well-known dissident in Russia. And he was teaching us life, and he was teaching us what Soviet regime is, also, and how awful it is. And he was teaching us in subtle ways, sometimes. So I can give you one example. I was probably still in sixth grade when he told me, "Why don't you read this particular article, a short letter, by Lenin?" And he told me which one. And I said, "I've never seen it." Even though we were forced to learn all that stuff. That was '72, or maybe early '73. He said, "Of course you've never seen it, because it exists only in very early editions of Lenin's books. It was later removed." So he gave me a copy. And the letter was essentially stating—I don't remember exact numbers. I may not be accurate, OK, so don't hold me to it. And I don't remember the exact language. But the point of that letter was that it represented Soviet regime that was formed—by the late 19-teens or maybe early '20s—again, I don't remember the exact date. But the letter was to the extent that intelligentsia, which is a Russian term—maybe you've heard it, OK?—they think too much. And they have too many ideas. So we need to arrest and execute several thousand of them so that others would not be tempted to think too much. That was unbelievably revealing of what the whole Communist idea was about.

ZIERLER: So your teacher wanted to show you this. The idea was that Communism was rotten to the core, even from Lenin.

LEIKIN: Absolutely. From the very beginning. Yes, the whole idea. Yes. And then he also [gave us prohibited books to read]—but again, he was careful, because there were a couple of kids in my class that could not be trusted. So nobody—and he warned us—"Don't talk to them. Don't show them any of the stuff I give you." And that kind of stuff. So he was reasonably careful. But to the kids that could be trusted, which was 90% of my class—it turned out later; I didn't know—that will be my KGB story in ten minutes—

ZIERLER: [laugh]

LEIKIN: —he brought us all prohibited literature and all kinds of stuff. And he talked to us. And for me, it was incredibly important, because my parents didn't talk to me about it. Why they didn't, they explained later. When I later talked to my mom about it, she explained that, “Look, I didn't want you to get arrested and executed. OK? Not that I object to those ideas [laugh] but it’s just a pure survival skill.” And so our parents didn't talk to us, but he did. And he taught us to be careful, not to discuss it outside, but he wanted us to understand what we're dealing with. And so he helped us. You got disconnected for a moment.

ZIERLER: I'm here.

LEIKIN: Can you hear me?

ZIERLER: Yeah.

LEIKIN: OK, then that’s fine. It’s probably just video got lost. At times, the systems get overwhelmed. Anyway, so if you get disconnected and you can’t hear me, please type in the chat window.

ZIERLER: Yeah, I will.

LEIKIN: That, I’ll be able to see. And so he brought us all kinds of literature and stuff. Once I graduated in ’78, within about half a year, maybe couple of months, when I was already at the university, I got a call from my dean that I need to come see him. So I came to the dean and he told me that, “Well, you need to call this number.” I am asking him, “What’s that phone number?” He said, “Call them; you'll find out.” So I called them. Turned out it was a local KGB. They wanted me to come in, as they said, for an interview. It got me scared to my bones, of course, but I had no other choice, so I went. In about five minutes it became completely clear that they were investigating that particular teacher, although they were framing it in a different way. And so just as he taught us, I simply played dumb. You know, I said, “Yeah, I haven't heard anything.” Whatever. Just played dumb. And he taught us that no matter what, no matter how innocent their questions might be, never cooperate. Play dumb. Because if they hook you, they hook you for life [?]. And I've later read all of those stories multiple times, so I simply played dumb, and I was of no use to them, so there was no even follow-up. Well, as it turns out, all of us did the same thing, just as he taught us, and he was not arrested at that time. He was arrested maybe about a year later, or two years later, when he was protesting something. Because school was now closed, he had no kids to teach stuff he taught. So he thought as it’s fine if he now gets arrested and that kind of stuff. So he got arrested later. He spent many years in Soviet concentration camps. Because this was still late ‘70s. It was height of Afghanistan war and all of that awful stuff. But what’s really amazing is that none of the kids who he taught all of these things gave him in.

ZIERLER: They protected him.

LEIKIN: Yeah. Nobody! Apparently. I mean, I don’t know for sure, but he would be arrested if somebody did.

ZIERLER: In high school, was your education purely physics, or did you also study chemistry and biology?

LEIKIN: Oh, no, no. We had general education. We had normal general education. But outside normal, we had math and physics, in addition to normal education. So we had pre-calculus in sixth grade, calculus in seventh grade, calculus two in eighth grade. In ninth and tenth grade, it was way above that.

ZIERLER: Amazing.

LEIKIN: Like probably theory of complex variable functions was probably eighth grade. Something like that.

ZIERLER: And you knew at this stage that you wanted to focus on math and physics for a career? You had already settled on this?

LEIKIN: Yes. Well, it's kind of hard to—I had a lot of fun doing math, so in eighth or ninth grade, I settled on what I thought at the time I wanted to do, which would be theoretical physics. Which would be math and physics.

ZIERLER: So when you graduated high school, what were your options? What were you thinking? You clearly understood that there were problems with the Soviet Union. Were you thinking you could leave for college, or that wasn't an option for you? You had to stay?

LEIKIN: Oh, not that—not leaving Soviet Union—I had no option of leaving Soviet Union—again, it was 1978. It was the peak of awfulness of that evil empire. So the only way to leave was to go into that category of refusenik with all kinds of repercussions for the family. And some people tried to do that. For me, that was not an option, because you do those kinds of things only when the whole family wants to do that. And my mother and grandfather didn't, and so I couldn't do that to them.

ZIERLER: Now with the looming invasion of Afghanistan in December 1979, were you ever concerned about being conscripted into the army?

LEIKIN: Well, I never wanted to be, but again, that story is a little more interesting and complicated.

ZIERLER: Please! That's what we're here for.

LEIKIN: [laugh] It depended on where I went for higher education, the choice of which was very limited for me, because I'm Jewish. And based on what I am seeing on your head, I guess you know a little bit about that as well. [laugh] OK? But depending on which university you went into, in most cases, they had a military department, and you would not be conscripted into the military. And only those universities were on my radar anyway, so I wasn't concerned about being conscripted. So initially I tried to get into the Moscow Physical Technical Institute, which was the best university for becoming a theoretical physicist. But they accepted very few Jewish kids in that year—it depended year to year. In some years, when there was an international committee investigating, they would let some Jewish kids in, even if they didn't have anyone [an insider] to pull them in. But in that particular year, there were no international monitors, so unless you had somebody inside to help, there was no way. And so, it didn't work for me, I was not accepted.

ZIERLER: So you were qualified to go there, but because there were quotas on Jewish students, it was just not available to you.

LEIKIN: I wouldn't call it quotas, because if you did not have relatives in there who would somehow get around that limitation, the quota was zero. Do you call it quota? [laugh] I don't know! I can give you an example, again, if that's interesting for you, of what would happen.

ZIERLER: Please.

LEIKIN: So we had to pass exams. It's not like in U.S. It's not your score and you submit documents. No. It's after you graduate from high school, you would submit your application, and then you had to go through exams. In that particular university, it was five exams. To be more precise, four exams and then one kind of not graded exam but rather oral conversation with an examining committee. Everybody was separated into groups and had to be in a specific group for all exams. There were two written exams and two oral exams, that were graded. Everybody who applied was assigned into a group of maybe 20, 30 people for all [?] exams. And so we had to go through that process. It was done based on when you submitted the application. So I had a friend in my class, in my high school, who was a complete genius. I mean, a true genius. And unfortunately he died very young. But even though he died when he was only maybe 22, 23—I don't remember how old he was—at that point, he was already internationally recognized as a genius theoretical physicist, and he already had a theory named after his name.

ZIERLER: What was his name?

LEIKIN: Knizhnik. You can find him on Wikipedia. His first name was Vadim, last name Knizhnik, K-N-I-Z-H-N-I-K, I believe, this is how one would spell it in English. If you want, I can send you a link later on.

ZIERLER: Sure.

LEIKIN: He was an absolute genius. So he submitted his documents maybe a couple weeks later, but we were in the same group. OK? And he absolutely—in the exams in mathematics and in physics, he absolutely knew more than the examiners. No question about that. And yet, both him and me were rejected.

ZIERLER: He was Jewish?

LEIKIN: Yeah, yeah. Same reason. [laugh] Same reason. But by that time, he already passed couple of exams of so-called Landau Minimum. I don't know whether you've heard about it, what Landau Minimum is? He already passed several exams of Landau Minimum. And he let those people know what's happening. So they went to the rector of Moscow Physical Technical Institute, and it didn't help. Then they went to Kapitsa. You know the name Kapitsa?

ZIERLER: Yeah.

LEIKIN: Not younger Kapitsa; the older Kapitsa [the Nobel Laureate physicist]. He was still alive. And they told him what's happening. And he said, "No, that's not acceptable. I'll go and beat the"—literally, the translation—"and beat the shit out of the rector of the Moscow Physical Technical Institute." What he really did—he called him up and said, "If you don't accept this kid—he already has an invitation from U.S., from Harvard. You can't do that. That will be a scandal."

ZIERLER: How did he get his reputation international? How did Harvard even know about him?

LEIKIN: There was a very famous mathematician, academician, his name is [Arkady] Migdal [?]. I think his son is still active and a member of National Academy in the U.S. And so my friend Knizhnik thought

that he has proven one very famous theorem in mathematics about four color maps and I forgot what it is, because I went into a different field. And so he showed his proof to a number of mathematicians. Nobody could find a hole in it. But it's a theorem that has been out there for like hundreds of years. And only the academician [Arkady Migdal] found a hole, one he eventually went through steps. But he still saw that the kid was an absolute genius, maybe beyond genius. Like on the level of one in a century in the whole world or something like that. I mean, all of us were gifted, but none of us was even close, even an order of magnitude close, to that kid.

ZIERLER: Why did he die young? What happened?

LEIKIN: Aneurysm. Aneurysm in his brain, which could be part of the reason why he was genius, because of a different blood supply. He died suddenly—he was on Metro in Moscow and an aneurysm suddenly ruptured. He just fell and was dead by the time he hit the ground, from what I know. But he was just—I mean, pure genius. And so in the end, he was allowed to enter that Institute. I went the roundabout way. I didn't fight it. Instead I resubmitted my application to a university that was called Moscow Steel and Alloys Institute. It had a department of theoretical physics that was chaired by Abrikosov. I don't know whether you know this name. He got Nobel Prize in physics in 2003, after he immigrated to the U.S. He was a very famous theoretical physicist from the Landau school of physics. He was one of Landau pupils. And he got his Nobel Prize for theory of magnetic vortices in superconductors. And I believe it was 2003 Nobel Prize in Physics. So I went to his department, and he was officially my university advisor. And so I figured that would be good enough. And then my university allowed me to develop what they called individual study plan. So I was allowed—because I was straight A student at the university, and I was allowed to take courses from different universities. So actually most of the courses I took was together with my friend Knizhnik at [laugh] Moscow Physical Technical Institute. So in the end, my education didn't suffer much.

ZIERLER: Now, Moscow Steel and Alloys Institute did not have restrictions on Jewish students?

LEIKIN: Well, it did, but they were not as severe. So it accepted Jewish students. It would generally—for general education—accept Jewish students. If you wanted to become a graduate student there, then that was a different story. But that's a different tale.

ZIERLER: Now, given the name of the Institute, it would look like you would go there to study metallurgy. But apparently they had a robust physics department?

LEIKIN: Yes, well, and it would be called physics of metals, OK?

ZIERLER: I see, I see.

LEIKIN: And physics is very important. It's not just engineering. I mean, it was the science of metallurgy. And I was able to get rid of all but one, I believe, metallurgy courses in my curriculum, and replace them with straight physics courses.

ZIERLER: And you were able to pursue theoretical courses there?

LEIKIN: Yes.

ZIERLER: It seems like given the focus on metals, that it would have more of an emphasis on applied physics.

LEIKIN: For most departments there, yes. But there was one department which was purely Department of Theoretical Physics, and it was really concentrated on condensed matter physics, and metal physics in particular. And Abrikosov was the chair of that department.

ZIERLER: Now, I'm curious—how international was your exposure to what was happening in physics in the United States and elsewhere in Europe? Was your education aware of what was going on in places like Harvard and Caltech and things like that? Or was the emphasis really on discoveries and advancements that were made by Soviet physicists?

LEIKIN: Well, no, no, no. The science that we were learning, that was entirely international, in fact. In most cases, it was what was done in the U.S. [??]. No limitation. Now, I don't know how common that would be for other departments and other places and other universities, but the courses I had, they were pure science. It had nothing to do with politics.

ZIERLER: Now, your master's degree was in 1984. Was your bachelor's degree also there, or was a bachelor's degree just incidental toward the master's?

LEIKIN: Incidental towards the master's. Because what we had—well, yeah, it's all more complicated. My university was a six-year university, not a four-year university. So essentially, everybody would get an equivalent of master's degree. And we had a diploma work that is—actually, the requirements were probably more stringent than for master's degree in U.S. Now, not every university was a six-year university, but mine was, and so was Moscow Physical Technical Institute.

ZIERLER: Now, how much of your time was split between coursework, and how much was split between lab work?

LEIKIN: Well, I didn't—well, again, my case was special, because first of all, I was in Department of Theoretical Physics, and second of all, I had this individual course plan. So I was able to minimize labs. Little did I know back then that that's what I really loved doing! [laugh] Not back then—it completely changed. These days, it's 100% lab work for me. [laugh] But back then in the '70s and early '80s, I thought that I wanted to be a pure theoretician, and I didn't think much of lab work. So I was able to minimize it, so I would say in my case, it was probably 95% course work and theoretical work.

ZIERLER: And as a pure theoretician, were you thinking that you would become a faculty member at a Soviet university? Was that basically the career option that would be available to you as a pure theoretical physicist?

LEIKIN: That never occurred to me, because that would be almost impossible for a Jewish student without having parents being faculty there. So I was hoping that I would be able to get into one of the research institutes of Soviet Academy of Sciences, which in the end, what I was able to do.

ZIERLER: Which would be a less prestigious appointment than a faculty member?

LEIKIN: No, actually in many ways it would be a more prestigious appointment.

ZIERLER: But open to Jews, you're saying?

LEIKIN: In some of those institutes. Not fully open. Nothing was fully open to Jews back then. Those were really bad years. It became open later, but '84 was still not—nothing was open. But easier to kind of sneak in.

ZIERLER: What was your master's thesis on?

LEIKIN: It was condensed matter physics.

ZIERLER: What was the thesis? What did you work on?

LEIKIN: I don't remember the exact detail, but I think it was something like localization of non-linear waves in randomly inhomogeneous media. I think that was my first paper in an international journal that was published based on my thesis.

ZIERLER: Now was the expectation for the master's thesis that you would do original research, or were you synthesizing literature at that stage?

LEIKIN: Original research.

ZIERLER: And you had a pretty good idea that you were—

LEIKIN: Plus synthesizing literature. As I'm saying, it's more stringent than master's here. Original research. Essentially my master thesis was published in a well-recognized international journal.

ZIERLER: Which one?

LEIKIN: I can look up. I would have to look up. Let me see. Just second.

ZIERLER: Sure.

LEIKIN: I'll look up. I should be able to access it. I just need to connect. I just need to connect to VPN—can't actually look up. I'll send it to you later. [Physics Letters]

ZIERLER: We can add that in later.

ZIERLER: After your master's thesis, you were at the A.N. Frumkin Institute? Is that right?

LEIKIN: Yes. Again, the story was complicated.

ZIERLER: Please.

LEIKIN: If you want to hear it, I can tell you.

ZIERLER: That's what we're here for.

LEIKIN: Because the way the Soviet system worked back then—at the end of—after you defend your master's thesis, there was what they called assignment, if I may use that word, of all the students to different places of work. You were not free to go wherever you want. You would be assigned where you go. The way it worked—people would be—the dean and representatives from these organizations would sit in a room, and students would be called in, in the order of their grades. First, the best students, and et cetera, et cetera, et cetera. And representatives from these organizations—so a student would be given a choice where he would want to go, and representatives from these organizations would interview the student, and either accept or whatever. But if they denied the student, they would have to kind of close down their request. Then the university didn't have to fill their request. And that was for the whole Faculty [of Physical Chemistry of Materials]. So all students would go through that process one by one. There were two of us, both Jewish, who had straight As. So I was

called in first. The other guy who was in about the same boat as me, we were from the same department, was called in second. And both of us who were Jewish, we closed all of the positions [requests] for [laugh] the entire Faculty.

ZIERLER: Wow.

LEIKIN: They didn't have to fill any positions [requests] after that. And after that, it was kind of free choice. [The organizations could not demand any student being assigned to them]. But because I closed half of the open positions—because the organizations didn't want to have a Jewish student—and I kind of had to go somewhere, I was given an option to have what they called the free assignment.

ZIERLER: Free assignment.

LEIKIN: Meaning that I had to find a position for myself. I didn't have to go to any of those places.

ZIERLER: So this is like a golden ticket, essentially. You get to go where you want to go.

LEIKIN: I got it. OK? [laugh] And my friend got it. So there we go! Was it beneficial for that purpose, being Jewish? Probably.

ZIERLER: [laugh]

LEIKIN: It worked entirely backwards! But then a particular institute, which was not the Frumkin Institute, which was the Institute of High Temperatures of the Soviet Academy of Sciences, had provided a letter that they'll accept me. I had this letter in my hands when I went through the assignment process. This is where I did my master's thesis research, in theoretical department. And so I was allowed to go there. But then something else happened, because the department I was heading to had lots of Jewish scientists and the head of that department had a conflict with their Institute director. The head of the department called me up and said, "Yeah, the Institute will accept you, but because I now have a conflict with the Institute director, you will not be assigned to our department. You will be assigned somewhere else. And you will be assigned into a place where you don't really want to go. So you better decline." And because it was a "free assignment", I was allowed to decline, which I did. And then I started talking to my friends, whose parents were working at different institutes of the Academy of Sciences. One of my friends said, "Why don't you go and talk to my father?" (Who was a department chair at the Frumkin Institute). So I went there, presented my master's work.

ZIERLER: What was his name, the chair of the Institute?

LEIKIN: Department chair. Chizmadzhev. Professor Yuri Chizmadzhev. He later became a corresponding member of the Russian Academy of Sciences. And he was the head of Department of Bioelectrochemistry, I believe, at the Frumkin Institute. The department was half theoretical, half experimental, and it was more or less focused—because the Frumkin Institute was the institute of electrochemistry, the department was focused on biophysics and what they called bioelectrochemistry.

ZIERLER: Now was this your first exposure to the field of biophysics? Had you heard about biophysics before, or this was new to you?

LEIKIN: It was new to me. In a funny way, it was a second exposure, because the first time—my first exposure was when I asked Abrikosov, who was my official supervisor at the university, I asked him what he thinks about biophysics. He was very arrogant, so he told me [laugh] not surprisingly—

ZIERLER: It's not real physics, right?

LEIKIN: Yeah. For theoretical physicist who later got a Nobel Prize, not surprising, right? [laugh] And he told me an anecdote why biophysics is a junk science.

ZIERLER: Please share with me. I want to hear.

LEIKIN: The anecdote?

ZIERLER: Yeah, please.

LEIKIN: So I asked him, what does he think about biophysics? He said, "Well, let me tell you a story. Scientists"—and I forgot where, but it was a biophysicist somewhere, maybe in the U.S.; let's say in the U.S. just to make it an anecdote—"they were studying the effect of magnetic field on the brain, and so they decided to make an experiment. They took two solenoids—" You know what solenoids are, right?

ZIERLER: Yeah.

LEIKIN: Did I pronounce that correctly? "Put it on two sides of a chicken head, turned on the current to get the magnetic field, and the chicken was yelling. And then of course they forget that the two solenoids would attract each other the way they were configured." So it's just squeezing poor chicken's head. Which is why he was yelling.

ZIERLER: [laugh]

LEIKIN: And he [Abrikosov] said, "That's biophysics for you!"

ZIERLER: [laugh] That's great! [laugh]

LEIKIN: [laugh] Anyway, but I was contrarian. So exactly because of this story, the very first interview I went to was the one in Frumkin Institute, exactly because it was biophysics. [laugh]

ZIERLER: So were you already interested at this point in sort of moving into human health research? I mean, were you interested in moving into biology?

LEIKIN: Not health, but rather biophysics. At that point, it had nothing to do with human health.

ZIERLER: So you're still thinking you can operate—?

LEIKIN: At that point, I was interested purely in applying theory of condensed matter physics to the problems of biophysics.

ZIERLER: I see.

LEIKIN: That's what I wanted to do. And that's exactly why I went there. I mean, actually, several of my friends suggested to see someone they know and get an interview there. But that's why I've chosen Professor Chizmadzhev from the Institute of Electrochemistry as my first interview. And after that, I didn't go anywhere, because I really liked it, and he offered me a job right away.

ZIERLER: How was your background in biology? Did you have to learn a lot of biology on the fly, or you felt pretty solidly grounded in biology?

LEIKIN: I knew zero biology. I mean, zero. To give you—again, I can tell you another anecdote, which is a real-life story. To defend my PhD, I had to pass exams which would be called minimum exams for PhD if I translate. Like four or five exams. And because my PhD was in biophysics, one of the exams was in general biology. And I had to study for it. By that time, that was three years into my research, or maybe two and a half years in, at the Frumkin Institute. I don't remember exactly. So I was exposed to quite a bit of biology by that time. And I got interested and I started studying it, but still, I had zero background. So I went to that exam, and the examiner was somebody from another Academy of Sciences institute. It was an oral exam, and had a bunch of questions which were more related to biophysics, and I had no trouble with them whatsoever, because I got exposed. But then for the last question, he decided to ask me a general biology one. And so he asked me—and I remember the question very well—"Name a mammal that lays eggs."

ZIERLER: [laugh] I hope you said platypus!

LEIKIN: Well, now I hope I did!

ZIERLER: [laugh]

LEIKIN: But I had no clue! I think I named some snake.

ZIERLER: [laugh]

LEIKIN: He like almost fell off his chair. [laugh]

ZIERLER: [laugh]

LEIKIN: He said, "It's so funny, you pass!"

ZIERLER: [laugh] Perfect. That's great!

LEIKIN: [laugh] Now I know it's platypus, OK? [laugh] Now, after another 30 years of biology research, [laugh] I know.

ZIERLER: That's great.

LEIKIN: But back then, I didn't.

ZIERLER: Now your background in theoretical physics, was that usually the point of entry into biophysics? I'm assuming in Russia, this is a relatively new field. Are there people in biophysics who are being taught by professors whose degrees are also in biophysics?

LEIKIN: Oh, yeah, yeah, yeah. There was a biophysics department in Moscow State University. That's actually where I defended my PhD. Because my PhD was in biophysics, I could not defend it at the Frumkin Institute. There I could defend a PhD in chemistry. I could defend a PhD in electrochemistry. But not in biophysics. So I had to defend my PhD in biophysics at Moscow State University Department of Biophysics. And that was a true biophysics department.

ZIERLER: So your affiliation was more closely with the Frumkin Institute or with Moscow State University?

LEIKIN: Oh, no, it was purely Frumkin Institute. The Moscow State University was only to defend the thesis, so they hold the exam. Again, PhD thesis defense in Russia was a bit more stringent thing, than the PhD in the U.S. So I had to submit my thesis, there would be a bunch of reviewers, and then there would be a real stringent oral exam and defense.

ZIERLER: Now the dissertation committee was made up of professors both from Moscow State University and from Frumkin Institute?

LEIKIN: Only Moscow State University.

ZIERLER: I'm just curious—given this connection, why not just transfer to Moscow State University? Why not just be fully affiliated with them?

LEIKIN: Well, first of all, Moscow State University would not take a Jew in. [laugh]

ZIERLER: So they'll pass a Jew for a dissertation exam but they won't take you as an official student?

LEIKIN: No. No. Dissertation exam is just a dissertation exam. They didn't have to submit the paperwork, how many Jews they have in their department, based on a dissertation.

ZIERLER: So you were an under-the-table Jew.

LEIKIN: Look, it's not that they were anti-Semitic. No. It was not at all by any stretch of imagination. It was the government, always.

ZIERLER: Right. I understand.

LEIKIN: It was the government. The University had to report how many Jews they had.

ZIERLER: Now you said earlier that for your master's degree, you had studiously avoided lab work, right? Had you discovered at the Frumkin Institute that you enjoyed lab work more, or still not? That would come later?

LEIKIN: No, I hadn't started doing lab work myself at all. But, I found for myself that I was really interested in trying to understand and explain results of experiments, more than doing a purely theoretical work. Because there were experimentalists in Chizmadzhev's department, I got exposed to them. I got exposed to how they do their experiments. I got really interested in that. Not to the level yet that I would start doing experiments myself, but to the level that I was interested more in explaining their observations than in working on abstract theories. So my thesis was really trying to explain their observations.

ZIERLER: What was your dissertation thesis? What did you focus on?

LEIKIN: Well, it was role of fluctuations, in particular fluctuations of biological membranes, and their role in different biological phenomena.

ZIERLER: What kind of phenomena?

LEIKIN: Well. For instance, in that lab they would make these artificial membranes called planar lipid bilayer membranes. The lab was studying their electrical properties. They [planar lipid bilayer

membranes] are insulators but they also pass currents through ion channels, or if you apply too much voltage. And I studied, for instance, how fluctuations of these membranes—thermal fluctuations—affect their properties. And I'll give you only two examples. I think I had three chapters in my thesis; all of them were published separately. I'll give you two of them. One, because it's kind of interesting. It was formation of pores in those membranes, reversible formation of pores, not when the membrane completely blows up but when a large pore forms, induced by voltage. Now that paper is very highly cited for a very simple reason, which is that pore formation is these days used for transfecting cells.

ZIERLER: I missed that. It's used for what cells?

LEIKIN: For transfecting cells. If you want to introduce foreign genetic material into a cell, these days it's mostly CRISPR/CAS9. The technique is called electroporation and it's the most commonly used technique these days [for gene editing].

ZIERLER: Did you recognize that at the time, that it would have that technique value to it?

LEIKIN: Not me. It was recognized by others. I think the first who recognized that was a guy with the last name Zimmermann in U.S. I believe he was a pioneer of that. But he actually referred to our work of studying how these pores formed. We were just interested in fundamental aspects of that, back then.

ZIERLER: Again, you're totally aloof from the human health aspects of this research?

LEIKIN: Absolutely. At that time, yes. Absolutely. Now I understand that in fact those early fundamental things, they have major implications in human health issues these days. Back then, I didn't recognize that. No, not at all. And a second out of three parts of my PhD thesis was the role of thermal fluctuations of lipid membranes in interaction between these membranes, and in interactions between cells. And that led to my later connection with Adrian Parsegian. Maybe you know the name.

ZIERLER: Yeah.

LEIKIN: And he was my advisor at NIH. He was the one who invited me to NIH, because he was studying what he called hydration forces back then. And we showed how thermal fluctuations can change properties of different types of interactions, including these forces.

ZIERLER: How did you first connect with him? Did he write you a letter? Did he know about your dissertation?

LEIKIN: No. The way I connected with him was that the Frumkin Institute arranged a symposium, I think it was '87. I believe it was '87.

ZIERLER: The year you defended?

LEIKIN: Yes. And Adrian Parsegian was one of the guys who was invited. And because the symposium was in Russia, essentially what happened is that each of us had to be a guide for all the foreign scientists invited to the U.S.S.R.

ZIERLER: You don't mean a guide; you mean like a minder?

LEIKIN: No. Not really.

ZIERLER: No?

LEIKIN: None of us was a minder. We didn't have to do it—we were not instructed by KGB what to do. Maybe in previous years, we would be minders, but it was already ’87. Or maybe ’88.

ZIERLER: So you felt at this point, glasnost and perestroika, you felt the opening up of Soviet society?

LEIKIN: Oh yes, absolutely. Yes, yes. We felt it. Yes. So we were not minders at all. Again, I can tell you an anecdote from that, which is again a very interesting story.

ZIERLER: I'm always going to say yes, Sergey. You tell me you have an anecdote; I'm always going to say yes. Please share.

LEIKIN: Anyway. I will, in a moment. So I was not a minder, we were more just trying to help our colleagues to understand Russia and just take them around.

ZIERLER: And how was your English at this point? Did you have a translator? Did you speak any English?

LEIKIN: Oh, no, I spoke English pretty well. It’s another anecdote why, but—[laugh]

ZIERLER: [laugh] We'll get to that one later.

LEIKIN: My English was—I mean, heavy accent, but it was OK.

ZIERLER: OK.

LEIKIN: But heavy accent, it’s still there. And it’s still there for a very simple reason. I actually wanted to take an accent reduction class, and it was Adrian Parsegian, who told me, “No way. I will not allow you to do that. The beauty of our country is in its diversity.”

ZIERLER: That’s right. That’s right.

LEIKIN: And he said, “I don’t want you to become like any other American. You want to be an American with an obvious Russian origin.”

ZIERLER: Right. That’s right.

LEIKIN: And I took it to heart. I never tried to get rid of the accent. I tried to speak so that others can understand me. And that was his advice, but not get rid of the accent. Anyway, so I met Adrian there because I was kind of his guy and host. It doesn't mean that I was with him every minute. No, no. He went some places completely on his own. But I would tell him where to go and where not to go so that he wouldn't get into trouble and that kind of stuff. And in some places, I would go with him. And so of course I also had the chance to discuss my science with him. So the first time I met him was back in Russia, and that’s where he told me that he wants to hire me—once all my paperwork settles—and there were also issues with my son, who was born in ’87—and once those issues are settled, then he wants to invite me as a postdoc to the U.S. And eventually I came to U.S. in ’89, as his postdoc, to NIH and then I stayed at NIH. Now the anecdote about minders and stuff. A colleague and friend of Adrian Parsegian, Peter Rand—and that was not during that symposium; that was later—he came to Russia just to visit I believe separately. I don’t remember, it must have been spring of ’89 or maybe it was summer of ’88 —I don’t remember. I don’t remember exactly when it was, when Peter Rand came to visit. By the way, Peter Rand became my lifelong friend. Anyway, he wanted to visit an institute in Dubna, which is

about 50 miles away from Moscow. It was a Nuclear Research Institute. And there was a group in there that was doing membrane biophysics and he wanted to visit them. And they invited him. We had to get permission for him to go there [Dubna] because of the institute itself [nuclear research]. I mean before ’88, he [Peter Rand] wouldn't even be allowed to go there. He was allowed to go, but I had to go with him. And in that case, I was told that, “He cannot go alone. He has to have a person accompanying him, at all times, from your institute.” So I had to be with him, period. When there, we stayed overnight at a guest hotel for the Nuclear Research Institute. After we talked to our biophysics colleagues, the next day we're planning to leave. The guys at the reception desk in the hotel told Peter Rand that they couldn’t give his passport back. We had to turn in our passports for registration. And I saw Peter becoming white in his face. It’s a story with good ending; it’s just a funny story; that’s all. And I'm asking why. They said, “Well, his permission to be here was not entirely appropriate and properly signed”. Or something like that; I don’t remember the exact details. So I asked, “So what do we do?” “Well, you have to go to local KGB department.” They told it to me in Russian. They asked me whether Peter understands Russian, and he didn't, and I said, “He doesn't.” So the conversation was in Russian. And they probably didn't use the word KGB because it would be recognized, or something like that. They probably said something—“Oh, you have to go to such and such person.” Because what I remember is that when we stepped out of that reception area, Peter asked me, “So what’s up?” And I'm telling him, “Well, I have to go to KGB and discuss with them what’s what.” And now he’s stone white. [laugh]

ZIERLER: [laugh]

LEIKIN: “You know, it will be OK.” [laugh] So I went there. He had to—he went with me, but he had to stay outside. And those KGB guys, they just laughed about it with me and they gave me his passport—by that time, it was much more relaxed. And they said there was some misunderstanding someplace. Something wasn’t registered someplace. And they gave me his passport. But I still played a joke I probably wouldn't play now on Peter, because as I stepped out of that office with his passport in my pocket—and he was much younger by then, so he asked me, “What?” I said, “Well, looks like you'll have to stay in Russia forever.”

ZIERLER: [laugh]

LEIKIN: [laugh] And I gave him his passport back.

ZIERLER: [laugh] That’s great.

LEIKIN: Anyway. I mean, these days—I later realized—I mean, I was much younger and stupid. These days, I realize that a joke like that can cause a heart attack.

ZIERLER: [laugh] Right. [laugh]

LEIKIN: I wouldn't do it now, but I was young and stupid, so what do you want?

ZIERLER: Now in 1989, when you got the invitation to come to NIH, did you see this as your ticket out, or at this point were things loosening up in the Soviet Union? Obviously it doesn't collapse until ’91. Are you thinking that you have a future in Russia and NIH is just a postdoc and you're intending to come back home? What are you thinking at this point?

LEIKIN: It was a little bit more complicated. [laugh] My life story is a bit more complicated than it is on surface.

ZIERLER: [laugh]

LEIKIN: Because the first time I came to U.S. was not ’89; it was ’88, actually.

ZIERLER: ’88.

LEIKIN: Yes. And I came to U.S. only for about month and a half, two months. It had nothing to do with my work. And I could have stayed if I wanted to. And it was entirely different, because my older son, who was born in ’87, had craniosynostosis, which is when sutures in the skull close prematurely. And so he was born with a triangular forehead. The scientific term for that is trigonocephaly. It’s actually relevant for where I ended up in my research. And by that time, we were able to find a very talented neurologist in Russia, and he told me that if he [my son] is not operated on, there’s a very high risk of brain damage because the brain is constrained, and some of his neurological symptoms are coming from that. And he said, “Your son must have surgery, but this surgery cannot be done in Russia.” And so then we wrote to some of the colleagues we met while at the Frumkin symposium, and one of them—his name was Art Sowers; I still remember that—he worked in the American Red Cross laboratory, as a scientist. And he just asked his American Red Cross colleagues what they know about it. And somebody happened to know a foundation, the craniofacial foundation in Texas, and he connected me with them. And they invited us for surgery.

ZIERLER: Wow.

LEIKIN: The surgeon was—again, he became my lifelong friend. He retired a couple years ago. The craniofacial surgeon was Dr. Kenneth Salyer.

ZIERLER: I missed the last name. Dr. Kenneth—?

LEIKIN: Salyer. S-A-L-Y-E-R. I believe actually he even mentioned my son in one of his books later on. And so he invited us and said that—because I said, “We can’t pay. We have no money.” He said, “Don’t worry about it. We'll cover everything.”

ZIERLER: Wow.

LEIKIN: And he brought us in. It was very difficult to get permission from Soviets. Even though the country was opening up, but Ministry of Health would not want to give us permission to go abroad for medical treatment. But in the end, they did.

ZIERLER: Like politically they're saying we're good enough you can have the surgery here?

LEIKIN: Exactly. But I was helped by the director of a Neurosurgery Institute in Moscow, who wrote a letter for me saying that they can’t do that. That they’re really just not good enough to do that.

ZIERLER: How rare a condition is this, that your son had? Is that the problem?

LEIKIN: It’s not that rare. I don’t know the exact prevalence of that condition, so I don’t want to misguide you. But anyway, so we came to the U.S. in the Fall of ’88 specifically for that surgery. And it was done in Texas at Humana Hospital in Dallas, Texas. And we stayed for about a month and a half for follow-up after that surgery, and then we went back to Russia. And in fact, I had to promise to the Ministry of Health that we will not stay. And I figured that my mother would pay dearly if I break the promise. And I also felt that it would be unfair to my mother at that point.

ZIERLER: Your father had passed on at this point?

LEIKIN: My father passed away, yeah. My father passed away a long time ago. And my mother and father were divorced. He didn't live with us since I was seven. And he wasn't really in the picture, but he already passed away, yes. So we returned back to Russia in December of '88. But now back in Russia, I had two missions. One, I wanted to set up all this fellowship at NIH. By that time, I was already invited, and all my paperwork was in, and I had an invitation letter from Adrian Parsegian. But I had to delay coming to NIH for a little bit, because I became friends with Dr. Salyer, through all those interactions while we were in Dallas, and he offered that he can help a whole bunch of Russian kids. And so I had my second mission to arrange a visit of Russian kids with severe craniofacial deformities, and the visit of that director of the Neurosurgery Institute in Moscow to Dallas—

ZIERLER: Oh, wow.

LEIKIN: —to establish a collaboration between them. I was kind of a go-between.

ZIERLER: Now Dr. Salyer—why such generosity? Was this just the kind of person he was? Did he have an affinity with the Russian people? What were his motivations?

LEIKIN: Just the person he was. He would always do things like that—and he told me right away that he does a fraction of his surgeries for free. It had nothing to do with Russians. Some American kids who would come for surgery and couldn't pay, he would do it for free. He would charge nothing. And he had an agreement with the hospital that the hospital would charge nothing as well.

ZIERLER: Wow.

LEIKIN: He was just such a guy—you know, he was—that was just the person.

ZIERLER: Special person.

LEIKIN: Yeah, yeah. I love him. And he—I mean, we talked a lot. We talked about medicine in Russia and stuff, and I told him that the surgeons at this institute for neurosurgery in Moscow, they're really good, but they're just not trained in this stuff. And he offered to train them, or at least to show them how these things are done. And so in the end, we did set up this program. And so I had to delay coming to NIH for a little bit. So instead of coming in the Spring of '89, I came in the Fall of '89, because I was trying to help with arranging all of that. And Dr. Salyer came to Moscow in the summer of '89, so that they would select which kids to take for surgery to the U.S. and that kind of stuff. And so he came to Moscow. He gave some lectures at the Neurosurgery Institute. He met with officials at the Ministry of Health. And there, I acted as his translator. Because Ministry of Health wanted to give him an official Soviet translator, probably former KGB or current KGB, whatever. Dr. Salyer totally refused. He said, "No. Sergey will be my translator." So I was his translator. And in the end, we were able to negotiate the visit of a group—I don't remember—ten or 15 Russian kids with fairly severe deformities, to U.S., plus some Russian doctors who observed all of these surgeons and how it's done, while those kids were in U.S. So that was a kind of training, including that director of the Neurosurgery Institute.

ZIERLER: Now is it fair to say at this point that you're starting to think about health science research for your own career?

LEIKIN: Yes, absolutely. Yes.

ZIERLER: I figured.

LEIKIN: Because I got involved with that. That was one of the biggest pushes in my life. It kind of changed my perspective quite a bit on what I want to do for the future.

ZIERLER: So the postdoc at NIH, what exactly was the postdoc? What were you going to be working on?

LEIKIN: Well, I developed a theory for explaining the measurements that were done by Peter Rand, the one I mentioned before, in collaboration with Adrian Parsegian. Adrian was more of a theoretician for these experiments, but I developed a different type of theory for them. And the initial paper was actually published even before I came to the NIH, but then we published a whole bunch of papers together with Adrian Parsegian and with Peter Rand, on that. So the initial idea was that I would come to NIH and continue working on the theory to better explain the forces that Peter Rand and Adrian Parsegian were measuring. And at that point, those were forces between lipid bilayers and forces between DNA molecules. And I actually stopped working on this theory only maybe about six, seven years ago.

ZIERLER: Wow.

LEIKIN: I worked on it [laugh] for over 20 years. It changed quite a bit from the initial ideas. And I stopped working on lipid bilayers somewhere in mid-'90s. After that, it was mostly DNA, and then I progressed to collagen, and then I became a collagen person. Then I became collagen-related diseases person. Then I became bone diseases person.

ZIERLER: Wow.

LEIKIN: That's, in one minute, my life story. But that surgery on my son had yet another effect on my career. It completely changed it. Because what happened—so I came to NIH in '89, and then in 1990, I was at NIH doing my theoretical work, and then in the Fall of 1990, that group of Russian kids is coming, and Dr. Salyer wanted me to help with that. And he said, "And because you'll be coming here anyway, take your son, we will do another CT scan on him, we'll just take a look what's happening with his skull." And so I flew to New York to meet that group of Russian kids to help with their transfer, and then flew to Dallas together with my son and with the group, and I helped with translations. I helped with explaining some of the more complicated things to Russian doctors in Russian, because some of them simply didn't know enough English, and all of that kind of stuff. And also in the process of that, they did another CT scan on my son, and they discovered a huge cyst in the middle of his brain.

ZIERLER: Wow.

LEIKIN: Then they looked back at his initial scan, and they found it actually was there, but it was so tiny the radiologist didn't notice it. So he needed yet another surgery.

LEIKIN: It was benign? It was not cancer?

LEIKIN: It's a cyst. It's not a tumor. A cyst is a sac filled with liquid. Yes, it was benign. But his neurosurgeon—because all of these craniofacial surgeries, they're always done by a team of a craniofacial surgeon and a neurosurgeon. And his neurosurgeon, while we were there, actually—he didn't even tell me that my son had a cyst. He told me—he called me later. When I came back to D.C., he

called me up and said, “We wanted to see what’s happening, so we didn't tell you right away. We had to reexamine all the films.” And all of that stuff. My son had a cyst that developed over the year, in part because of the craniofacial surgery. It was there to begin with, but when they do any craniofacial surgeries, they leave some space [in the reconstructed skull] because there’s always some swelling. They don’t want swelling to push on the brain after the surgery. So they leave some [extra] space [in the skull], but that space also allows a cyst to develop very rapidly instead of slow. In a way, it was a blessing in disguise, because if it would be developing slowly, it would cause symptoms before it was noticed.

ZIERLER: And your son, was he expressing any symptoms at this point, or no?

LEIKIN: No.

ZIERLER: This was a total surprise.

LEIKIN: Total surprise. And so the neurosurgeon told me, “Because the brain is not under pressure even now—right now the cyst is not causing any problems—I want to see for couple of months what’s happening with it. Where is it going? Before I decide what type of surgery I will do.” And so that conversation was in January of ’91, I believe, or something like that. And he said, “We will do the surgery sometime in April or May.” So I had the four months of total uncertainty. I couldn't do any theory. My brain wasn’t functioning. So I come to Adrian Parsegian and say, “Look, I want to learn how to do experiments. My mind is not functioning. I'm not functioning as a theoretician anyway. My hands are!” [laugh] And I wanted to do it, and since being exposed to all of that, I had been thinking about it anyway. That’s how I got into experiments!

ZIERLER: Wow.

LEIKIN: Two years later or three years later, I was doing experiments at least 50, 60% of my time, because I found I enjoy it more. But I was still continuing in theory for a while. And also, I got exposed in conversations with this neurosurgeon to hearing how much scientific thinking determines the health outcome. So that personal story got me into understanding how medicine works. Because my conception of medicine was totally wrong before that.

ZIERLER: How would you characterize your conception of medicine before this?

LEIKIN: Before that? I don’t know if you've read Solzhenitsyn?

ZIERLER: Sure.

LEIKIN: I think there is a scene there, if I'm not confusing, when a patient comes to the doctor and says that he is sick that he has severe headache and stomach problems—I don’t know, was it the GULAG Archipelago or another book. And the doctor gives him aspirin, breaks it in half and gives one half—“This is for headache”—another half—“This is for your stomach.”

ZIERLER: [laugh] That was how you thought of medicine. [laugh]

LEIKIN: Yes.

ZIERLER: So you were probably inspired by the thought process that the neurosurgeon put into this, not just to jump in with surgery right away.

LEIKIN: It's a craniofacial surgeon and neurosurgeon. It's not just neurosurgeon. I was really inspired by how much science and thought process go into that, even after spending half a year or maybe even more than a year at NIH. Initially, because I was just sitting in my office writing equations, I didn't talk to real biologists or someone like them. And so even after a year at NIH, I was still not into it, not really understanding what medicine is.

ZIERLER: You're in a bubble, essentially. You're at NIH, but you're in a theoretical bubble.

LEIKIN: I was in a theoretical bubble, yes. That's fairly accurate description. And it's talking to the craniofacial surgeon and the neurosurgeon. It's observing what they did—when I was helping those Russian kids. Because I had to go into the surgery room and translate the procedures done on some of those kids, and then on other kids. One procedure, which really impressed me the most, was performed by these neurosurgeons not on Russian kids. It was a totally unrelated neurosurgery, which he [my son's neurosurgeon] was mostly occupied with on that particular day. But he was also kind of on a call, helping the craniofacial surgeons as a neurosurgeon as well. It was a patient with some kind of convulsions in lower extremities or just lower extremities seizing up. I don't remember exactly what it was. Apparently some nerve misfired, and the idea was to cut that particular nerve so that it would stop misfiring. Seizures were really dangerous for the patient. And so we observed the surgery. They were testing nerve by nerve in the spinal cord, axon by axon essentially, looking for which one is misfiring. Kind of zooming in. Kind of like in a microscope. I don't remember the exact details. But it was like finding one bad cell in a sea of cells. First it was a low magnification objective, higher and higher and higher, then actually finding it, and then cutting it and completely stopping those lower extremity seizures or something like that. And it was really inspiring. Unbelievable.

ZIERLER: And it dawned on you that this was what you were witnessing. This was real science that was taking place.

LEIKIN: This is real science. That medicine is real science. That good medicine is based on real science. Yes. And it's not that it dawned on me in five minutes. I mean, I was still young and stupid.

ZIERLER: Sure. But it was a breakthrough moment for you.

LEIKIN: It was a gradual transition. It's doing the experiments. It's talking to this neurosurgeon and craniofacial surgeon. It's then talking to some of the physicians at NIH and slowly realizing, boy, with my science, I might be able to make a difference for medicine.

ZIERLER: And given the fact that you're at NIH anyway—I mean, you're well positioned to make this transition.

LEIKIN: Yes. And that's when the transition started, in about '91.

ZIERLER: So what's your first move? What's your first project now that you have this transition in place? What do you start working on?

LEIKIN: So at that point I was working on a theory, trying to understand interactions between DNA molecules, specifically. More than lipid bilayers. I was trying to understand the forces that Peter Rand and Adrian Parsegian were measuring. So I started measuring those forces myself and started doing the experiments. But I also wanted to do something else, because my theory was suggesting that the helical structure of DNA molecules plays a very important role in their interactions. And then I thought of

another molecule with a helical structure that is very relevant for the pathology my son had. And we didn't even know how those molecules interact at all. Nobody had measured forces between them. That molecule is collagen. So I started talking to an experimentalist in Adrian Parsegian's lab. Unfortunately, he died a number of years ago from cancer. His name was Don Rau. He was the one who taught me how to do experiments with DNA, so I asked him to help me to learn whether we can do the same with collagen. Together with Don, we did it. We measured forces between collagen molecules in collagen fibers.

ZIERLER: How did you know to get to collagen? What was the development that made you focus on collagen?

LEIKIN: It was a realization that helical structure of DNA is informing interactions between DNA and thinking that helical structure of collagen may be informing interactions between collagen molecules. And because interactions—OK, interactions between DNA molecules—back then, we didn't know how important they might be. It was totally artificial, the way we were doing it. We didn't know what we learned much later, how much these interactions can be important for things like homologous recombination and really fundamental biological processes.

ZIERLER: So when you say artificial, you mean you didn't even know what you didn't know?

LEIKIN: Yeah. We didn't know what we didn't know. What we used was purified DNA molecules assembled into a liquid crystalline aggregate, which doesn't look at all like chromatin or any other kind of normal physiological DNA structure. We measured interactions in liquid crystals of DNA. OK?

ZIERLER: OK.

LEIKIN: It was too artificial. We didn't know that this is actually very relevant for biology. We didn't know about that. We were more interested in physics of these forces. But I thought about collagen helices, that interactions between them determine the biology of their function. Because it's due to these interactions that collagen molecules assemble into fibers, and it's those fibers that are a functional unit of type I collagen based material. And so I thought that to understand their biological function, we really need to understand the interactions responsible for their assembling into fibers. So I figured here we can start with a biological system, with a collagen fiber, and measure interaction directly in the fiber. And those fibers we took from rat tail tendons. Later on, I did the same with mouse tail tendons. Doesn't really matter. We learned how to measure those interactions, and we were able to understand what they are, and how these interactions might affect fiber assembly, and published a whole bunch of papers on that. Without Don Rau's help, I wouldn't be able to do that, because he taught me all the biology. Then other people taught me more about biological systems and how to work with them. And that's how I got into more biologically relevant things. But theory was still very important for me, because I still needed to understand. The theory is what allowed us to understand what those forces were.

ZIERLER: Now at this point, did you have a sense that what you were doing would ultimately have clinical or therapeutic value?

LEIKIN: No, I didn't, but I wanted to do something that would have clinical and therapeutic value. In mid-'90s, I got in touch with people from NICHD. Back then, I was still not part of NICHD. I was part of a different NIH institute.

ZIERLER: Which one?

LEIKIN: I had kind of a dual appointment. My primary appointment was at what was called Division of Computer Research and Technology. That's where all the theoreticians were back then. And my secondary appointment was at NIDDK. That's where Adrian had a lab—that kind of corresponded to Adrian Parsegian's appointment. And that was still the same as when I was a postdoc. In mid-'90s, I was on tenure track, but I was still in his lab. I was a tenure track scientist but I was still in the lab of Adrian Parsegian.

ZIERLER: I meant to ask—so when exactly did you transition from postdoc to tenure track? When did that happen?

LEIKIN: After three years of being a postdoc, so I think my tenure-track appointment became official, I believe, in '93.

ZIERLER: And it's pretty unique for postdocs to transition internally to tenure track That usually—in your experience, that's a rare thing? Is that fair to say?

LEIKIN: These days. But let's say in '70s and '80s at NIH, it was normal for a postdoc to transition into a permanent position. They were not called tenure track position back then. It was just like—Adrian Parsegian told me about him at NIH. He also came at NIH as a postdoc, I suspect sometime in '60s. I don't remember the exact date. And then he said, "I received a letter in the mail that I was converted from a postdoc to permanent appointment." [laugh] That's how Adrian formulated it. So back then at NIH, that was normal. They didn't have a tenure track system. I was one of the first ten people officially entering into tenure track program at NIH.

ZIERLER: Interesting.

LEIKIN: At entire NIH. It was still kind of—it was very new for NIH to have a tenure track program in the early '90s.

ZIERLER: And what was your employment status at this point? Are you working on a Green Card? What's your status?

LEIKIN: No. When I was a postdoc, I was on a J-1 visa, which had a so-called 2 year physical home presence requirement. But because NIH offered me a tenure track job, NIH applied for a waiver of this requirement for me. It was granted. Once it was granted, I began processing for the Green Card. I was kind of in between with just an employment authorization for about a year or so, and then I received my Green Card. Essentially that's when my tenure track started. More or less at the same time I got the Green Card.

ZIERLER: And were you no longer worried about your mom, now that you were clearly going to become a permanent resident of the United States?

LEIKIN: Unfortunately by that time, my mom died.

ZIERLER: Oh, OK. Would you have been concerned? Had the political situation changed after the end of the Cold War?

LEIKIN: It changed, yeah. I mean, it wouldn't be a concern. No. It really changed.

ZIERLER: So to get back to your quest for clinical and therapeutic value, did you achieve that with your work on collagen? Did you have that satisfaction, that this actually did translate over?

LEIKIN: Yes. It took quite a bit of time. But right now, most of my research is purely translational. I really work on clinical problems. But the transition was long and slow, and I'm glad that it was long and slow. Because I had to learn a lot. As I told you, my knowledge of biology and medicine was zero, to begin with. It took years and years to gain all the knowledge I needed. And it's good that I didn't start working on medical problems right way, and just slowly transitioned into that.

ZIERLER: I wonder if you can talk about the spirit of collaboration at NIH in terms of your capacity to work with scientists across a range of disciplines, and what help that might serve for your own research.

LEIKIN: Well, that's what allowed me to do what I did. Because as I said… For instance, to begin with, I was just working with Don Rau on a problem that was pure physics. We realized how the interactions between collagen triple helices regulate assembly of collagen molecules into fibers. And then, a puzzle came. By that time, I was interested in getting into medical research with the help of Don Rau. I think he suggested this idea—he said, "You know that the triple helix of type I collagen contains three thousand amino acids." It's three chains of one-thousand-plus amino acids each, and a change of just one of the amino acids, just one, in the middle of the triple helix, causes severe disease called osteogenesis imperfecta. It is actually one of the diseases I work on these days.

ZIERLER: This is bones. You're working on bones, at this point?

LEIKIN: Yeah, yeah. Well, no, at that point, I was still working on just collagen. Now, yes. Back then, no. I knew it's important for bones, because bone is essentially mineralized collagen fibers. It's a bit more complicated than that, but for a layperson, you can think of it as mineralized collagen fibers.

ZIERLER: So that's a natural transition, from collagen to osteo issues.

LEIKIN: Yeah. Well, and that's to begin with, because that's one of the reasons why I was interested in collagen and that kind of stuff. Because I knew that craniosynostosis, that disease of my son, is related to collagen.

ZIERLER: So to get back to the question with collagen, when did you first realize that what you were doing did have clinical or therapeutic value?

LEIKIN: So that was the thing. When Don mentioned that it's just a change in just one amino acid out of 3,000, which shouldn't really affect the entire triple helix, somehow it causes bones to become extremely fragile. And he said, "How could it change the interactions between the triple helices so much?"

ZIERLER: Given that it was so small?

LEIKIN: Even though the change is so small, right? It doesn't extend far along the triple helix.

ZIERLER: But it manifests very dramatically, is what you're saying.

LEIKIN: The manifestation is very dramatic. Bones become fragile. Some kids actually, they can't stand. The bones break. They can't ambulate. So, well, being a theoretician by education, I immediately came

up with an explanation for that. [laugh] Theoreticians can explain everything, even if you flip the graph over.

ZIERLER: [laugh]

LEIKIN: They are gonna explain it, right? So the idea was, why don't we check this? Why don't we check experimentally what happens with those interactions [between collagen helices]? So I started talking to people at NICHD who were studying that disease. At that point, they were just developing the first real mouse model of the disease. But before I could put my hands on this model, in mid-'90s when I started working in collagens, there was another mouse model. It is a naturally occurring mutation in mouse, which causes a much bigger change than one amino acid. Type I collagen has two alpha-one chains and one alpha-two chain. In that other mouse model, the alpha-two chain is missing. So instead of two alpha-one chains and one alpha-two chain, it's three alpha-one chains, so-called homotrimers. So, I got my hands on that model, and I found that interactions between homotrimers and normal heterotrimers of type I collagen are quite different. We could even explain some of those differences.

ZIERLER: Theoretically, you could explain it?

LEIKIN: Yeah. And I thought, OK, I really need to look at these single mutations because we have something in there. Maybe it's really all in how these mutations affect interactions and therefore assembly of collagen fibers. That became my hypothesis. And by that time, the group at NICHD developed their new mouse model. I was able to get tail tendons from their mice, because they're easier to work with than bones, and started measuring those interactions. And to my surprise, I found absolutely zero effect of that mutation on the interactions. None.

ZIERLER: Which tells you what?

LEIKIN: None at all. I didn't know what it told me back then. I thought maybe it's different in bones. Maybe it's not interaction of collagen molecules with each other; maybe it's interaction of collagen molecules with something else that's present in collagen fibers. In bone, there is quite a bit of other stuff. Less so in tendon. Tendon is 95% type I collagen. Bone is maybe only about 80% type I collagen. There are quite a few other proteins in there. Still, majority is type I collagen, but quite a few. So I thought maybe it's interaction with other proteins. Maybe we have to look there. But back then, I was still convinced that it's all in those intermolecular interactions, the theory of which I was working on. And so I had to start learning. Well, OK, how can we work on interactions between individual molecules that have different structure, that are not in fibrous aggregates or in liquid crystalline aggregates? These are much more complex interactions to measure. So, I started to think how we can approach that. And to approach that, first I needed to understand collagen itself. Not just interaction between collagen helixes, but rather the molecule itself—how it folds, how it functions, so that I can work with it. And that's where further discoveries started happening. We found that collagen is very unusual in terms of its folding process, that these single amino acid mutations really disrupt that folding process, big time. And eventually over next 20 years, it brought me to realizations that it's not collagen interactions in fibers outside cells that are primarily responsible for pathology; it's the disruption of collagen folding that occurs inside the cell. This causes disruption of endoplasmic reticulum in the cell. It [endoplasmic reticulum] is a master regulator of cell function, so that its disruption causes disruption of the cell function. And it's malfunction of the cells that make bones, which is responsible for most problems. Some problems are due to mutations in secreted collagen molecules outside the cells and their

improper interactions. But what we're finding more and more, it's mostly the cell malfunction that's responsible for the pathology. And so in the last maybe ten or so years, my research has focused really more on what is the cell malfunction in that pathology, how it contributes to pathology, and how can we treat it.

ZIERLER: So what is the connection between discovering—just making these discoveries, and how to treat them?

LEIKIN: Well, I'll give you one example. I still don't know whether it's working or not. So to understand the source of pathology, we created a different mouse model. I helped Dan McBride from the University of Maryland, and together we created a different mouse model. It is a bit easier to work with, but it's still a single amino acid substitution, which truly mimics the disease in humans. And so I made a whole bunch of modifications now in my lab to this mouse model to better understand the pathophysiology of that mutation. We understood quite a bit. And we understood how cells themselves deal with the problem. There's a huge range of phenotypic variation in human population with this disease and in mice with this disease. Really huge. The exact same mutation can lead to very mild symptoms so the person doesn't even know that the person is sick. And exactly the same mutation can cause such severe disease that bones will break on their own all the time.

ZIERLER: Is this happening there because these are problems that are manifesting mostly in children? Is that the idea?

LEIKIN: Yes. That's part of it. It's a developmental disease. Osteogenesis is bone development. Osteogenesis imperfecta is disrupted bone development, if you translate it from Latin to English. It belongs to a category of diseases that are called skeletal dysplasias, which are abnormalities of skeletal formation. It's a developmental disease. It's most severe in children. In many cases, it's perinatal lethal, unfortunately. Some children that are born with this disease die within hours, some [die] within the first year of life. In less severe cases, it [osteogenesis imperfecta] really has—I mean, it has an impact through the entire life of a person, but in some people, it kind of moderates. When they [latter individuals] become adults, they stop fracturing for a while, and they start fracturing again when they're older adults, kind of like osteoporosis. Actually these days—last spring, I was giving a set of lectures at the Hospital for Special Surgery in New York City, and I was sitting together with orthopedic surgeons, and we were discussing symptoms of some of their patients, because they were telling me they have a lot of patients that have recurring fractures in childhood and then nothing, and then again severe, poorly healing, recurring fractures in later years. And having discussed all of those symptoms, we came up with the conclusions that actually most likely they simply have a very mild form of osteogenesis imperfecta, and many of them might have some of the signs. And then, actually at about the same time, Frank Rauch at Shriner's Hospital in Canada, in Montreal, was analyzing databases of normal human DNA—of people who are considered normal, whose whole genome was sequenced. Turns out that some of the mutations are present in people who were never diagnosed with OI [osteogenesis imperfecta]. So we believe that is the case. It hasn't been proven. But it [OI] may be that mild in some of the mutations. The same mutation can be perinatal lethal [in some people] and almost asymptomatic [in other people].

ZIERLER: How much are you looking at the genetic basis of this? Are you doing family histories? Are you looking at the parents? Is that part of your research?

LEIKIN: Well, it's more—it's done by my clinical collaborators a lot. I don't. I do a lot of genetic research these days, but on a different subject. Because my focus really is on understanding the cell biology. Because I told you that we're coming to the conclusion that the most severe symptoms come from abnormal differentiation and function of cells that build bones. These cells are called osteoblasts. And so my primary focus is cell biology of osteoblasts, and what can we do to normalize their function. And there's one very simple idea which I am testing in my lab right now. Unfortunately the testing has been interrupted by COVID-19, but the idea is extremely simple. Because what we discovered is that—The way cells deal with that malfunction is that when the misfolded molecules begin to accumulate in the endoplasmic reticulum and disrupt it, cells degrade them through a particular process. The scientific name for it [this degradation process] is autophagy. Right now it doesn't really matter. But that process of degradation and how efficient it is depends on a whole number of genes in the cell. And one person may have entirely different genetic background from another. In one person, that process may be very active, preventing severe accumulation of misfolded molecules in osteoblasts and normalizing their [osteoblast] function. That would be my explanation for why in that person the disease is mild. And in another person, that process may not be active enough to handle the problem, and the disease is severe. Now, there are actually some drugs that can be used to modulate that process. But not just drugs; diet. So right now, we are testing dietary intervention in our mouse model. We don't know yet whether it's working. It's complicated. The diet that we're testing actually these days is all the buzz. It's called intermittent fasting. You've probably heard that.

ZIERLER: It's all the rage for very many reasons.

LEIKIN: It's all the rage for many different things, and I believe that one of the reasons why it's working in many different things is exactly because it's activating that process of autophagy, which removes all kinds of junk from the cells. And lots of cells and lots of different diseases are impacted by accumulation of junk. Junk can be of all kinds of things. In fact, if we come back to viruses, in many cases, the way cells eliminate viruses from inside the cell is exactly the same process. This is not to say that I would advise intermittent fasting for treating COVID-19!

ZIERLER: [laugh]

LEIKIN: [laugh] Not by any stretch of imagination. We've never tested. And we're focused on a different—I mean, we could probably justify keeping our lab open by testing that, but I don't think it would be fair, because we're really focused in other things, and so we really should do what we are ready to do, not something totally out of the blue. But it's that process of intermittent fasting, which unfortunately is not so simple. Because yes, it definitely activates the autophagy process [of junk degradation]. We have information on that. It definitely improves the function of bone cells. That's all true. It all works. But the other problem is that it's really kids that are growing that need help the most. And intermittent fasting during rapid growth isn't such a great idea in general, because it affects nutrient supply. And so we're trying to find a combination [of treatments] and whether we can find such a combination where this intermittent fasting can be done in such a way that it still provides sufficient nutrients for normal growth—

ZIERLER: Plus you have to tell a small child not to eat for a long period of time. That's no easy task, either.

LEIKIN: Yes. So it's complicated. And I don't know whether it will work or not. But maybe a combination of diet approaches with some of the autophagy-enhancing drugs will work. We're also trying to do clean experiments where we genetically modify the animals to alter the autophagy process. This is one place where we have very clear success—we can definitely explain the mechanism—and we're beginning to write that paper. It's not written yet. We don't even have a full draft. But what we were able to do, very clearly and very easily, is completely disable the autophagy process of removing the junk. Our mouse model of osteogenesis imperfecta is moderately severe. Spontaneous fractures in these mice occur maybe in one or two out of hundred mice or something like that. Normally they don't spontaneously fracture. They're not heavy enough. You have to do biomechanical measurements to see increased bone fragility. When we disabled the process of autophagy, almost every single mouse had a femur broken. It got that bad. Really severe with 50% perinatal mortality, which we never observed in mice without deficiency in autophagy. So we can clearly demonstrate that simply by changing the efficiency of autophagy, without changing the mutation, we can observe a full range of phenotypic variability of the disease.

ZIERLER: So how do you change the efficiency of that process? Is that the fasting?

LEIKIN: We know some of the proteins that are involved in this process, and we can knock them out. And we can knock them out, for example specifically in osteoblasts. Just in osteoblasts.

ZIERLER: Does the word "blast" and "osteo"—does that connote that there is a malignancy, or that's a different concept?

LEIKIN: No, no. Osteoblast is just the cell that makes bones. That's all. Has nothing to do with malignancy. Osteo is bone, and blast typically stand—blasts are cells that produce collagen and produce tissues. Like fibroblasts make skin, make collagen in skin. Or in tendons. Myoblasts make collagen and precursors of muscles and that kind of stuff. And osteoblasts are the cells that build bone. That's all.

ZIERLER: So where would this research lead that would suggest to you that you really have made a significant discovery that can really help patients with these maladies? What would that look like?

LEIKIN: Well, for instance, if we find a combination of dietary approaches and drugs. We are coming to realization—so right now, we are actually getting better ideas of what we need to target by drugs in a cell. Our initial ideas were wrong. If you would ask me about five years ago, I would name an entirely different set of targets. It's just the nature of scientific research. And so the idea is, OK, fine, we'll find the targets, we'll find the drugs that can affect those targets in the cell. We'll normalize cell function, ideally without disrupting anything else. And then, we have a therapeutic approach that can—it will not cure the disease, but at least it can shift the phenotype from severe to mild. Some kids have to spend their life in a wheelchair, cannot walk ever, simply because if you put the kid on his or her feet, the legs will break. The legs will break. That's it! Just like how mice are breaking their femurs. And then you make the disease mild enough that unless kids participate in high-risk sports, they can lead totally normal life. So that's my commitment. It is to find something like that. And once they become adults, they would not need that much of an intervention. The current therapy cannot achieve that—but it's not just this disorder. This disorder is actually a model for much more general problem, the problems that will affect you and me.

ZIERLER: Like osteoporosis, something like that?

LEIKIN: Osteoporosis, exactly. And actually what we do know about osteoporosis is that with age, the same cells, osteoblasts, begin to poorly function. They cannot rebuild bone anymore. Nobody has an answer of why, because a multitude of things happen in cells with age. But one of the processes that is actually known to go down with age the most is the same process of autophagy that removes junk from the cell. In fact, the mechanism of pathophysiology, many of the things that go wrong in osteoblasts in an aging person with osteoporosis and in a young kid with osteogenesis imperfecta may be exactly the same, accumulation of junk in endoplasmic reticulum.

ZIERLER: So amazingly, your research on children might actually help the scourge of old people breaking their hips and the problems that that causes. Theoretically.

LEIKIN: I surely hope so. That is also one of the things I keep in the back of my mind always. And I do some experiments on the side to check and see that it might be the case. We don't have a proof now. Not yet. These things don't happen that fast. [laugh]

ZIERLER: But you're thinking ahead. You're thinking ahead.

LEIKIN: Yeah. It's a slow, painful process. But right now, the treatment for young kids with osteogenesis imperfecta is exactly the same as for old people with osteoporosis. Actually, if you do histology of bone, they look very similar. It's just the bone of these young kids looks like osteoporotic bone in many ways. So the treatment is the same, using the drugs called bisphosphonates. And what these drugs do, they kill cells that are called osteoclasts, and these cells resorb bone. Bone is a complex organ. The cells that build it, osteoblasts, the cells that get embedded inside bone—they're called osteocytes—they act as mechanosensors. They actually form from osteoblasts. Osteoblasts eventually differentiate into these osteocytes and get embedded into the bone. Osteoclasts are the third major class of bone cells—there are many more, but these are three main cell types that are responsible for bone buildup and recycling. And bone is constantly being remodeled. It is osteoclasts that resorb bone. And it's very important to have osteoclasts, because with age all long-living species like us accumulate defects in bone, micro-cracks and that kind of stuff. If you don't remove these defects, the bones will become fragile real fast. So bone has to be constantly remodeled, disassembled and reassembled. So it's disassembled by osteoclasts, reassembled by osteoblasts. So the current therapeutic treatment, the primary one—there are several ones, and we don't have time to discuss them all—but the primary one is to kill osteoclasts. These drugs, bisphosphonates, that's what they do. They are the main drugs of choice for treating age-related osteoporosis and for treating osteogenesis imperfecta. So what happens? It does not improve bone, at all. What it does, it prevents resorption of bone so that you accumulate more bone because cells that build it, they still build it. They build poor bone, but they still build it. And cells that resorb it, they get killed, so they don't resorb it enough, so you have more poor quality bone. Which is far from ideal solution.

ZIERLER: Well, this is a remarkable intellectual transition from where you were working on theory as a graduate student, right? [laugh]

LEIKIN: Yes. And I realized, about maybe ten years ago, that once we got into cell biology, into what I describe you now, I really need full-time commitment to that. I can't continue doing theory and this stuff [at the same time]. And this is not only because it's fascinating studies. I love working with my hands. I am—it's me, not my fellows—I am the mouse mom in my lab.

ZIERLER: [laugh]

LEIKIN: I go inject mice. I go set up breeding cases. When we finish talking, about half an hour after that, I have to go back to NIH because I need to finish rearranging our mouse colony so that it can be preserved during this time. Because there's a high risk that mouse care technicians can get infected, and their staff can be reduced by a factor of two, three, or even four, and we don't want to lose all those unique mouse lines. So I have to reduce—unfortunately I have to reduce the size of the colony and rearrange it in such a way that it requires only minimal maintenance. So I am allowed to be at NIH from about 2:00 p.m. to 7:00 p.m. to do that.

ZIERLER: Well, on that note, I think as we reach the end of our wonderful discussion, I'd like to ask you a few questions for you to reflect on your career. The first is, this remarkable transition from pure theoretical physics to the most hands-on biological work that you could conceive of—I wonder if you could talk a little bit about, what are some of the fundamental concepts in physics that stay with you, day to day? That you bring with you to your work? That are always close to you that you rely on to make the discoveries that you're making, as a physicist, working in a biological context?

LEIKIN: [laugh] The most fundamental concept, as I always tell in my lectures, is first Murphy's Law.

ZIERLER: [laugh] I didn't realize Murphy was a physicist, but OK! [laugh]

LEIKIN: But if something can go wrong, it will. If nothing can go wrong, it will go wrong anyway.

ZIERLER: [laugh]

LEIKIN: And I think it's the most fundamental concept of them all! But to be a little bit more serious—I just can't be serious all the time. I'm sorry.

ZIERLER: [laugh] That's great.

LEIKIN: Particularly in these times. But a lot of it. Actually, I can't even separate which one. Some of the most useful ones are the laws of thermodynamics. And unfortunately, many biologists, they don't have good training in that. For instance, it is particularly difficult for them to understand the following concept. Let's say we have a very unstable protein that tends to misfold, and another protein binds to it. And if that other protein preferentially binds to unfolded conformation of the first protein, then the laws of thermodynamics say that it will stabilize unfolded and destabilize the folded conformation. You would be surprised how few pure biologists have a grasp of that concept, how many of them make this mistake all the time. They don't understand the classical chaperones that function in endoplasmic reticulum, which preferentially bind to unfolded protein chains. These chaperones do not stabilize the native protein conformation, they actually destabilize it.

ZIERLER: So your suggestion would be that you should go to graduate school for physics and you should learn biology on the job. That's your prescription.

LEIKIN: No, no. My suggestion is—don't drop physics courses.

ZIERLER: [laugh]

LEIKIN: In university or graduate school, they [physics courses] are incredibly important. And I had a few students who were purely biologists, molecular biologists, who didn't have physics or were not required

to take physics. And I had to teach them physics. And then they told me later that that's why they were eventually successful. Because some of these concepts of how do you alter a system, these thermodynamic concepts, they apply not only to what happens to protein in endoplasmic reticulum, but they apply also to human interactions. One of my former graduate students eventually went to University of Pittsburgh working on interventions into drug-related issues. And then she developed some programs on how to prevent those drug overdoses, how to address this terrible problem for the society. And right now, she is a consultant working in D.C., sometimes sitting on task forces in the White House. And some of the concepts she used to develop those ideas are essentially the same as simple concepts of thermodynamics. If you want to stabilize certain state of a system, you want to find the preferential interactions for that state.

ZIERLER: And you can't do that if you drop those physics courses, at the end of the day?

LEIKIN: Well, I mean, if you get a good teacher, somebody who can teach you those things, you probably can. But I had to work a lot with that graduate student to teach her these basic concepts. If there is a preferential interaction, it will always stabilize the state in which it occurs. Not any other state, but that particular state. That's one of the basic principles of thermodynamics that applies everywhere. Sometimes in non-equilibrium system as well. [laugh] And that's one of the main ones. But there's a lot of other things. A lot of what we do when we want to see what happens in a live cell, we use fluorescence microscopy. It's pure physics. All the principles behind it—how you do super-resolution microscopy. We use a lot of spectroscopy and spectroscopic techniques, simply as techniques to answer our questions. But it's again the same concept of physics. We now in my lab developed a technology for RNA based histology. So essentially what we do, we take a histological slide, and instead of using standard labeling techniques like histologists use, what we do, we conjugate fluorophores, which are commercially available, to messenger RNA, and then image it. And so we can look at expression of different genes in tissue with subcellular resolution. Many people are developing these kinds of technologies. But the step which we made is to understand how to stabilize the tissue so that we can make those tissue sections, and they will not fall apart when we try to label that RNA. Now we can cut fully mineralized bone to do that. Now we can make it stable during imaging and processing. Now can we remove all autofluorescence. And all of that is crucially important—and so we developed that technique. So now the company, which developed the commercial assay for revealing these messenger RNA molecules in tissues, they send people to us to learn how to do these processes. They simply refer people to us, and we often send protocols all over the U.S. universities, other national labs, and that kind of stuff. But that's all based on physics. Just simple physics concepts—how you do that. So to remove autofluorescence, you need to understand what autofluorescence is and where it's coming from. What do you need to do to remove it? That kind of stuff.

ZIERLER: Well, Dr. Leikin, it has been an absolute pleasure talking with you today. I really appreciate your time. And for the sake of all of the people who have ailments in the field that you work on, I want to wish you the best of luck in your future research endeavors.

LEIKIN: Thank you.

ZIERLER: OK. Thank you so much.

LEIKIN: You're very welcome. If you have any further questions, you can just email me. So I promised to send you my first paper. Do you still want it?

ZIERLER: Absolutely.

LEIKIN: That was essentially the basis of my master.

ZIERLER: That would be wonderful.

LEIKIN: That, I can absolutely do. I'll email it to you.

[End]