

CHEMICAL HERITAGE FOUNDATION

ROBERT P. GOLDSTEIN

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

David J. Caruso

at

The University of North Carolina, Chapel Hill
Chapel Hill, North Carolina

on

24 and 25 April 2008

(With Subsequent Corrections and Additions)

ACKNOWLEDGEMENT

This oral history is part of a series supported by a grant from the Pew Charitable Trusts based on the Pew Scholars Program in the Biomedical Sciences. This collection is an important resource for the history of biomedicine, recording the life and careers of young, distinguished biomedical scientists and of Pew Scholars Program in the Biomedical Sciences Advisory Committee members.

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Robert P. Goldstein, interview by David J. Caruso at the University of North Carolina, Chapel Hill, Chapel Hill, North Carolina, 24-25 April 2008
(Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0417).



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ROBERT P. GOLDSTEIN

1967 Born in Oceanside, New York, on 2 October

Education

1988 B.A., Biology, Union College
1992 Ph.D., Zoology University of Texas at Austin

Professional Experience

1992-1993 MRC Laboratory of Molecular Biology, Cambridge, England
Postdoctorate, under John White
1993-1996 Postdoctorate, Independent

1996-1999 University of California, Berkeley
Postdoctorate, Molecular and Cell Biology under
David A. Weisblat

1999-2005 University of North Carolina, Chapel Hill
Assistant Professor, Biology
2005-present Associate Professor, Biology
2010-present Full Professor, Biology

Honors

1993 Outstanding Doctoral Dissertation, University of Texas at Austin
1993-1994 American Cancer Society Postdoctoral Fellow
1994-1996 Human Frontiers Science Program Postdoctoral Fellow
1995 Development Traveling Fellow
1996 Medical Research Council Postdoctoral Fellow, Cambridge, England
1996-1998 Miller Institute Research Fellow, University of California, Berkeley
2000-2002 March of Dimes Basil O'Connor Starter Scholar
2000-2004 Pew Scholar in the Biomedical Sciences
2005 Phillip and Ruth Hettleman Prize for Artistic and Scholarly Achievement
by Young Faculty, University of North Carolina, Chapel Hill
2007 Visiting Fellow, Clare Hall, Cambridge University
2007 Guggenheim Fellow

ABSTRACT

Robert P. Goldstein (Bob Goldstein) grew up in Massapequa, New York, the second of three boys. His father was both a lineman for the telephone company and a bus driver. His mother was a nurse. He attended public schools until high school, when he went to a Roman Catholic school. He did well in his classes, even obtaining a year's worth of college credit, but he had not yet displayed a special interest in science. He held jobs as a hotdog seller and a stockboy when he was in high school.

He decided to enroll in Union College, originally thinking he would go to medical school. He liked Union and college life; he rediscovered his childhood guitar and his interest in music, and learned to play the carillon there. For a while he thought about a philosophy major, but a class in symbolic logic, taught by Jan Ludwig, and a class in embryology, taught by Ray Rappaport, persuaded him to use his biology major in research. While working in Michael Frohlich's lab, Goldstein was also manager of the campus radio station and worked in campus security for spending money.

When Goldstein decided that he wanted to study embryology, Ray Rappaport recommended Gary Freeman's lab at the University of Texas for graduate school. Prior to matriculating at Texas, Goldstein spent the summer with Freeman at Friday Harbor Laboratories in Seattle, Washington, conducting research during the day and camping out at night—he continued this tradition at Friday Harbor in subsequent summers. His first two years in Texas produced nothing substantive, and so he switched from ascidian and snail embryos to *C. elegans* and began to see results. His data differed from the accepted scientific findings, and so his first talk caused him some anxiety. Goldstein went on to win the year's Outstanding Doctoral Dissertation award.

For a postdoc Goldstein chose John White's lab at the Laboratory of Molecular Biology of the Medical Research Council in Cambridge, England. No sooner had Goldstein arrived than White left for Wisconsin, but he left behind marvelous equipment, including the original confocal microscope. Goldstein also shared a 4D microscope with Steven Hird, who had independently developed a similar project on axis specification in *C. elegans*. His love of scientific discovery and enjoyment of his postdoc years led Goldstein to another postdoc at the University of California, Berkeley, in David Weisblat's lab. Working on evolution of development, Goldstein and his collection of snails, worms and leeches met his future wife in a lab across the hall. They married after their postdocs, spent their honeymoon in Hawaii, and set off on a road trip to North Carolina, where Goldstein had accepted an assistant professorship.

At the end of the interview Goldstein talks about his parents; his brothers' careers; his first postdoc, Jean-Claude Labbé; and music in Chapel Hill, North Carolina. He describes his lab set-up and management (including a story about gluing his sock to his foot) and the way his lab writes papers. He explains his administrative responsibilities and his need for independence in his work, and the role that the Pew Scholars Program in the Biomedical Sciences award played in his research. He discusses his grants, and he compares those from the National Institutes of Health with those of the National Science Foundation; he then goes on to compare funding in the United States with funding in England. He gives his definition of biomedicine, his opinion about the role of politics in science, and his praise of cultural diversity at the University of North Carolina.

INTERVIEWER

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

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INTERVIEWEE: Robert P. Goldstein

INTERVIEWER: David J. Caruso

LOCATION: University of North Carolina
Chapel Hill, North Carolina

DATE: 24 April 2008

CARUSO: We are interviewing here at Bob's house, just outside of Chapel Hill [North Carolina]. Thank you very much for meeting with me. And if you don't mind, I think I'd like just to start with [your childhood]. So if you could tell me a little bit about growing up in 1967, Long Island...Oceanside, New York.

GOLDSTEIN: I was born in Oceanside, but we lived, at the time, in East Rockaway [New York]. At the age of two, we moved to Massapequa [New York], so I don't remember anything before Massapequa...I don't know what my earliest memories are now.

CARUSO: Do you have siblings?

GOLDSTEIN: Yes.

CARUSO: How many?

GOLDSTEIN: I have an older brother, Jeff, who's almost two years older than me, and a younger brother, Pete, who's nine years younger than me.

CARUSO: What did your parents do?

GOLDSTEIN: My father, at the time, had a few different jobs. Around the time [...] I was born, my father had two jobs [that he held] for a while. I know he was driving a bus as a second job and...I forget what, at the time, his first job was, but he eventually was working for the telephone company—for AT&T—in New York climbing poles and fixing wires and that sort of thing.

My mother moved from Ireland when she was seventeen [...]. She moved in with an aunt of hers who lived in Lynbrook, [New York]. Her brother and a sister—one brother [Patrick Gallagher, Navy Cross recipient, died in Viet Nam in 1967] and one sister—had moved before her to that same aunt[‘s house]. And I think they each [lived with their] aunt and then went to a house that they all lived in together. My mother was working in a bakery and my father liked baked goods, and they met in a bakery in Baldwin, [New York]. My mother later retrained as a nurse.

CARUSO: Oh, she did? How old were you?

GOLDSTEIN: I must have been about five or six then. I remember going to classes with her and sitting and coloring while she listened to the lectures [at State University of New York, Farmingdale].

CARUSO: And so, she started that immediately once she completed the program? She started nursing?

GOLDSTEIN: She started nursing...yes, yes.

CARUSO: In hospitals?

GOLDSTEIN: In hospitals, and then later home healthcare. And [after that] she owned a small home healthcare company [called Total Care].

CARUSO: So what was the family lifestyle like in regard to...what did you do on a daily basis, sort of, as a young child? Were you outdoors playing? Were you inside reading?

GOLDSTEIN: My mother always teased me that I didn’t like to get dirty. [laughter] My memories are of...we had a school that was right down the street from us (we lived on Cedar Place; we were on one end of it, [and] on the other end of it was the school we went to). And so we could walk down the street—it was five or six houses down the street—to a big schoolyard. We’d play there often. And then, when we were old enough, we’d play in the street...[we played] kickball in the street all summer, and often in the afternoons after school, and sometimes played other sports. But I remember kickball an awful lot...I’m sorry, what did you ask again?

CARUSO: Just what you did as a child. Were you outdoors playing...?

GOLDSTEIN: Let me think...what else we'd do a lot? I don't remember this, but my mother would tell me often how I just didn't like to get dirty. If there was sand and there was some concrete, I would be sitting on the concrete on the edge of the sand, but afraid to touch the sand. I don't know if this is a common story among scientists; it's kind of embarrassing in hindsight. My kids are not really like that, which is nice to see.

In the winters, we'd play in the snow. I remember clearly, one time, going...when I was in preschool...one of my few memories before school [was] coming back from preschool one day and my brother and bunch of friends had built a chair out of snow in the middle of the lawn and told me it was for me. I was very excited about it, and I can still picture this little chair. The other memory I have from that time is, one time, getting on the bus for preschool in the morning—and I think we probably only went for one year; my mom raised us at home until we were at school, except for, I think, the one year of preschool—so, one morning, I got on the bus and my mom had given me two cookies. I remember clearly they were NILLA Wafers. I had these cookies, and I got on the bus and sat next to some kid in the back on the bus who decided he wanted those cookies and took them right out of my hand and ate them immediately. She could see my crying, and she came on the bus and gave every child two NILLA Wafers. I think there were a lot of kids. She must have emptied the whole box.

CARUSO: Oh, wow.

GOLDSTEIN: But I remember this clearly for some reason. I don't remember a lot of other things from that time.

CARUSO: And what was it like around the house in the evenings? Were your parents very set on, "Do your homework and go to bed. Brush your teeth," things like that?

GOLDSTEIN: For years, of course, it was me and Jeff, and Pete was born much later. Both of us were good students and we both worked pretty hard. And then I think we sort of [diverged] and I continued to just be really interested in...I don't know if I was really interested or just sort of trying to please my parents, but I would be keen to do my homework and to get it done and do well. And [Jeff] was a little sharper than I was in that he would try to get out of it in clever ways.

CARUSO: And around the dinner table, what were the general sort of topics of discussion? Did your parents just ask you about how your school went that day or were there talks about your father's job, your mother's job, politics, religion?

GOLDSTEIN: I'm not sure I remember. I'm sure we weren't talking politics much. My father was very conservative and my mother was not—[she] was quite liberal—but I don't remember that being clear at that age at all.

CARUSO: What about as you grew up? Was there anything that sort of started to stick out about that?

GOLDSTEIN: My mother was an Irish citizen until just a couple years before she died (and she couldn't vote in [U.S.] elections until then), but she became a citizen not long before. My parents got divorced in, about, 1993 and then she, soon after that, had to become a citizen for... I forget exactly what the reason was, but then she voted in her first election. It was when Al [Albert Arnold] Gore [Jr.] was waiting for ages and then didn't become president, right? But the night before, when the returns were coming in, I remember her calling on the phone—we must have had thirty phone calls in the one night—[her] saying, “We have Iowa,” or, “We have...” she called for each state. I clearly remember her calling and saying, “We have Florida,” and then we didn't have Florida. So it was exciting [for us both] to follow this.

With my dad, for a long time, I had a lot of disagreements with him about these sort of [issues]... he grew up on Long Island in a town [Baldwin] that was very much white. The town we grew up in [Massapequa] was almost exclusively white, and yet it was right next to a town [Amityville] that was mixed race, and we disagreed about [issues related to this] a lot. I realized when I was a kid—or really when I was a teenager, sort of high school age—I thought of him as a racist in the worst possible way. In hindsight, I think, although there's no excuse for being racist, I do realize that he grew up in a different situation, and then he worked for the phone company fixing lines in places where he might not have been the most welcome person in neighborhood. He might have had experiences that led him to feel this way. [In my mind this didn't excuse this kind of attitude, but it did] sort of explain it a little bit.

CARUSO: Yeah. My grandfather definitely has his own worldviews about things, and it's clear that it's from his experiences when younger. Which, again, of course, not a justification, but, sort of, something you can kind of understand. I would say that's true of my parents as well.

GOLDSTEIN: But I know through high school, I found it so inexcusable that [between this and typical teenage rebellion], I really didn't like him.

CARUSO: You mentioned going to nursing classes with your mother. Did you ever go to work with her or did you ever go to work with your father?

GOLDSTEIN: I never went with my father; my mother: for a while. Before she was nursing, I remember she was cleaning houses for a little while. She probably wasn't doing it full-time because she was taking care of us, but I remember clearly, a few times, going to houses or waiting in the car when she ran into one for a little bit. I don't think I ever went to any hospitals she worked in. When she was doing home healthcare I met some of her patients, but I'm not sure I ever went while she was working.

CARUSO: You played outside a bit. You played with your brothers' friends. Did you have any hobbies as a child? A lot of people mentioned, for example, having a chemistry kit and liking to blow things up.

GOLDSTEIN: I did not. A lot of scientists have these stories where they could tell they were going to be a scientist from a very early age. I'm reading a Dorothy [Crowfoot] Hodgkin biography now and she starts off saying that she was fascinated by crystals, and, of course, she became a famous crystallographer.¹ She must have been like seven or something when she became fascinated by crystals and watched crystals grow. I don't have any story like that at all.

I was encouraged to do well in school and I think I liked the encouragement and I think I tried to do well, probably in large part to please my parents, but out of [my own] interests somewhat, too. I don't know how this came about, but at some point...when I was a kid, I remember wanting to be a psychologist for some reason. And I'm not sure I even knew what a psychologist was. Maybe I just liked the idea of talking with people. And then, little by little, I remember my mother, and maybe some other relatives, saying, "No, no. You don't want to be psychologist. You need to be a psychiatrist because that's the medical line that gets a lot of respect." So, little by little, I thought I'd do medicine, which, I think, a lot of kids now grow up with this. They see it as a respected profession and maybe don't give it much thought.

And then it wasn't until when I was in university as a biology major and learning...unfortunately, a lot of biology classes are taught everywhere as, sort of, a compilation of facts, and I [didn't] like facts. [laughter] I [didn't] like too many of them. I [liked] to learn facts as needed. So it wasn't until then that, really, I started to make conscious decisions, I think, about what I wanted to do. And I remember at one point dropping my biology major and becoming a philosophy major—at least in my mind; I'm not sure it was on paper yet—and then realizing I really enjoyed the philosophy of logic, and I took a [great] class in symbolic logic [taught by Jan Ludwig at Union College...]. I just loved the idea of doing math with logical terms that could [...] explain something. [I] then came back to biology through an interest in research...through that, I think.

¹ Georgina Ferry, *Dorothy Hodgkin: A Life* (Cold Spring Harbor: Cold Spring Harbor Laboratory Press, 2000).

CARUSO: So, in high school, did you have any favorite classes? Were there some subjects that you were just in love with, or was it just everything is sort of...?

GOLDSTEIN: So earlier than that, I remember I really enjoyed math. And I do remember...the one clear nerd experience I remember that's akin to the chemistry kits, [is that] I had some sort of math workbook at home, and I would, in my spare time, go through it and try to solve problems, which seems kind of funny in hindsight.

CARUSO: I was actually on math team in junior high school, which...

GOLDSTEIN: So, I was a mathlete! [laughter] [...]. When we cleaned out my mom's house after she died, we collected a lot of old things, and somewhere I found a little mathlete award...[I was] still in high school when I did this.

One strange thing is that, although I'm a biologist now, my history's a little unusual in that I worked in the part of biology—molecular cell/developmental biology—where people tend to work in teams and [your] advisor was always [an author] on [a] paper. I was in a really unusual situation in that they weren't...and I published—[when I was] quite young—a paper on my own.² The time between...from that [time] back to when I first knew what a cell was, because I was taking a biology class, was actually quite short. I realized at one point in grad school that there were people who'd been in grad school [with me] since before [I knew what a cell was] and were still in grad school after I left. [...] They had trouble pushing people out in time...[well,] I think, some people, out in time [...]. Most of my friends and neighbors were taking biology classes in seventh and eighth grade middle school and I was in one of these accelerated programs where they'd give us different material. And, for whatever reason, we were taking, I think, earth science and something else, so I didn't actually have a biology class until I got to tenth grade. And I certainly remember sitting in that class and realizing, "Something's wrong. Everyone knows what's going on and I have no idea what they're talking about."

So at some point in the class, I remember the teacher, [named] Mr. Hock, talking about cells and I had no idea what these things he was talking about were. And I remember raising my hand and just asking, "What's a cell?" [I wondered where] would I find one of these things? I had no idea that...I suppose I should have learned that earlier at some point, but somehow I had missed it until quite late.

² B. Goldstein, "Induction of gut in *C. elegans* embryos," *Nature* 357 (1992): 255.

CARUSO: Any other interesting happenings in terms of science in high school, classes that took you by surprise? Inspirational teachers, maybe?

GOLDSTEIN: The teachers I remember, actually, are not so much the science teachers. I went to a Catholic high school, which is unusual for someone named Goldstein. My brothers and I all went to Catholic high school, and we ended up, actually, going to three different Catholic high schools, and in each [one] they were surprised to find another Goldstein.

So, I guess I [should] back up. In junior high school, both my brother, Jeff, and I had become, sort of, discipline problems. We were getting in trouble now and then, and my mother decided we should go to Catholic school (we were in public schools until then) [...]. She took my brother around to a few high schools to look at them and, at the time, I think you had to actually interview at these places. And the first one we went to was Chaminade High School [in Mineola, New York]—the high school I ended up going to—which is an all-boys Catholic high school. I remember standing outside the place and seeing...they have, I think, four big columns out the front, and to me it looked like a university and that excited me. The three of us walked inside, [Jeff] and my mother and me, and [Jeff] looks on the walls and sees the pictures of the graduates and he says, “Where are the girls?” So my mother had never mentioned that there were only boys at this school, and my mother explained to him. He said, “Come on, we’re going,” and that was it. I think we spent two minutes inside this place. And I remember leaving thinking, “Wow, those are really nice columns.” [laughter]

I discovered girls a lot later than he did. My brothers and I are, sort of...I think we’re equally bright, but we took very different paths. And it’s sort of funny to think about these quirks that might have led us on very different paths, that if I’d discovered girls a year earlier, I might have a different career, right?

CARUSO: Just a clarification question. I actually went to a Catholic high school in New York City [New York], and you did have to be a confirmed Catholic to go there. Was there a religious...?

GOLDSTEIN: We were baptized. So, the way I understood it from my parents was that according to the Jewish faith, the mother does the spiritual raising of the children. [And] according to the Jewish faith, [therefore], we should be Catholics, which, I’m sure, contradicts something else in Jewish laws.

CARUSO: Okay. So you were...

GOLDSTEIN: So, yes, we were baptized. We were not especially religious growing up. Both my mother and my father came from very religious families. My mother believed in God, but was not overtly religious in that she wasn't going to church every week.

CARUSO: More of a holiday Catholic? We call them holiday Catholics.

GOLDSTEIN: Yes.

CARUSO: Okay.

GOLDSTEIN: I mean she had a very religious sense of charity. She was, I guess, the most charitable person I know, in some ways.

CARUSO: Okay. So you mentioned that although you may not have had inspirational science teachers, you did have some influential teachers in high school?

GOLDSTEIN: Yes, yes.

CARUSO: In what way? Who were they? In what ways were they...?

GOLDSTEIN: So [I] remember clearly an English teacher who I absolutely hated, and, in hindsight, I appreciate a lot, named Brother Lahey [(most of the teachers at the high school were religious, Marianist Brothers)], who, [...], I think taught English really very well, both composition and appreciation of literature. I never liked reading anything longer than a short poem, so I always struggled through reading full books and...we were actually about a fifteen minute drive away from the high school, but I was the first one picked up and the last one dropped off (or almost [first and last]), and so it was an hour trip each way. And so I remember reading on the way to school on a bumpy bus trying to get through to the end of the chapter well enough to be able to answer some questions. But still, some of the poems we read, I remember quite clearly now...and the writing: I think he taught rules of writing really well, rules of style and grammar. I don't know why I remember that. I guess I do a lot of writing now, but not that sort of writing.

CARUSO: Anyone else?

GOLDSTEIN: I remember a geometry teacher, Brother Sylvester—so almost all these are Brothers...I have a fascination for logic and I liked geometry, that it followed strict rules. It's a lot like the symbolic logic class. You could come out with a very clear answer at the end after doing the math and forgetting about what the problem was in a sense, but, sort of, working it out on paper and coming back then to what the original question was...

I do remember clearly there were very few female teachers in the school, which, in hindsight, seems like a very strange thing to me. To take kids at the age where they should be developing socially, separate them from girls, have almost no female teachers and have religious brothers teaching them all...I definitely missed a part of my development that I had some remedial work on later.

CARUSO: Yes. [laughter]

CARUSO: But there were very few female teachers. I think there were two sisters—two nuns—who were working in the school at the time, and then there was one female art teacher who was very attractive. And there are about two-thousand boys all taking art classes from this one poor woman. I'm trying to think of other teachers.

CARUSO: Did you have laboratory classes for your science?

GOLDSTEIN: I remember biology classes that smelled of formaldehyde, where we did dissections and stuff. I think we did either fetal pig or rat dissections. I remember chemistry labs. Oh, we did have physics labs, too. But I don't remember [the labs] really getting me excited, at least not in a way that stands out now.

CARUSO: Was it just assumed that you were going to go to college? I mean, was it an expectation from your family?

GOLDSTEIN: Yes.

CARUSO: What were you thinking about in terms of going to college? Obviously, you were expected to go, but did you have some other reason? Did you want to go?

GOLDSTEIN: I was excited about getting away and seeing a new place and learning new things. But I think, in honesty (it's embarrassing), but I think I went to college because high

school was over. It was the next thing to do. And it wasn't until I got to college that I was really...I got very excited about what was going on...

CARUSO: Do you remember how many you applied to?

GOLDSTEIN: I think I applied to about five or six. I do remember my top choice was Williams College, and I haven't yet heard from them. [laughter] I don't check the mail every day, but...for some reason I never got an answer from them. But I think the high school also had information on who got into where, and from them...I'm not absolutely sure that Williams got my application, in hindsight, but at the time I believed that I didn't get in. The two I was interested in were Union College and Bucknell College. We visited both of them quite late. I remember we paid the deposit at both of them not realizing that they would discover this. I think there was only about a one-hundred dollar deposit, so before we visited them, we just paid them both thinking we could decide this later. And then I went to visit both of them. Bucknell seemed like a beautiful place, but they both seemed equivalent in a lot of ways. In New York, by being in-state, it would cost a little bit less because I qualified for some—I forget—some funding that defrays some of the costs. And they were both quite expensive schools, so this ended up what made the difference.

CARUSO: I'm trying to remember. I think it's the TAP Loan [New York State Tuition Assistance Program] in New York. I could be wrong. But in-state always winds up saving you a little bit of money. Why were you interested in Williams?

GOLDSTEIN: I remember I was an ambitious student earlier on, or at least I thought I was an ambitious student. I'm not sure I always worked as hard as I should have. But I just thought, "I'd like to do the best," and I thought I'd go to Harvard [University]. Then when I got to high school, I realized there were a lot of other bright kids and I was not the smartest. I was always a good student. I think I was an A student. But our high school, when you walked in past those columns, right inside the door there were four boards and they had the [grade point averages] of the honor roll students (the average number score). And I think it was down to one decimal point, so you could see who got 99.9 [percent] average on all of their classes, down to about 90 [percent]...

CARUSO: Oh, wow.

GOLDSTEIN: ...which, in hindsight, seems bizarre. But this was fairly motivating. I remember I was always down near the bottom of that, at 92 [percent] or 93 [percent]. It was a very good high school. I think it was one of the best high schools in the area, and I felt like I

was doing well, but I realized I was not a Harvard student. And so, just below the Ivy Leagues, Williams [College] was, sort of, an obvious choice...

CARUSO: Did you have any idea of what you would want to study other than just a broad curriculum?

GOLDSTEIN: I was pre-medicine and that was it. Then when I arrived at college and saw that people were actually interested in things, [that] people my age had interests that were not all how to figure out how to get beer on the weekend without your parents figuring out and this sort of thing, I got very excited to see that people would cultivate their interests and take classes solely out of interest. I think it turned my head really fast. I roomed my first year with three other guys, one of which was in the Army Reserves [(Bill Hardy)]. I never completely understood [him], though he was a nice guy. Another, [who] seemed like a very nice guy, [...] he disappeared halfway through the year [when police came to recover some stolen possessions that his friends had sold him].

But then I have this friend, who I'm still friends with, Dave [David Calvin] Greenlaw, who was interested in physics. This kid came in at eighteen years old absolutely in love with physics, and I'd never heard of anything like this. [Before college, friends and I] would discuss classes in high school and be vaguely interested in them and we took classes that bordered on philosophy/psychology/religion, which would encourage a lot of discussion, but there was no one I'd ever met, before then, who was just absolutely in love with an academic subject.

CARUSO: And was it just that he talked about it all the time? Was it just he was a physics major through and through?

GOLDSTEIN: He had other interests as well. He had a nice record collection when he came down and it was a lot of stuff from the 1960s that...I think he'd taken some of his parents' records with him to college. And so, he had other interests, and we'd sit around and talk about life. And your first year in college, suddenly away from your parents, that's an exciting time to stay up until all hours in the morning and talk about things that you may not have before. But I remember physics just drove him. He said if he had to live out of a shoebox so that he could be a physicist and study physics, he would. He now builds chips for AMD [Advanced Micro Devices], one of the big chip companies, and makes a lot of money.

CARUSO: You started college in 1985?

GOLDSTEIN: Yes, although my last year in high school I was in a program that about a quarter of the high school did, where instead of taking senior classes, we took a year of college

classes with college professors from Long Island University, C.W. Post campus. So, they would come to the high school and teach us classes. I think probably everyone who was an A student, and maybe even a little below, was in this program. And the freshmen classes at C.W. Post were actually no harder than the senior classes in our high school, so I'm not sure it was any more challenging...so, I came in with a year of credit.

CARUSO: Yeah. I was going to ask. Okay. Because you graduated in 1988 from...so, that's why it took you a little less time, because you had the year of credit?

GOLDSTEIN: In college, at one point, I really wanted to stay on for a fourth year. I remember clearly writing a letter to my mother expressing this and her phoning me the moment she got the letter explaining how much money it cost to go each year and how I better get my ass in gear and cut the crap.

CARUSO: [laughter] So, the 1970s and 1980s, more generally, were interesting times in terms of broader social/political/cultural issues. Did those ever play a role in your intellectual formation or anything along those lines: the [Ronald W.] Reagan presidency, or HIV [Human immunodeficiency virus], or wars or anything like that? Were you aware of those in the sense of actively thinking about those sorts of topics, or was it just something that was happening in the background through high school and college and stuff like that?

GOLDSTEIN: I mean, in high school I don't think I was so [aware]...once I was in college for a while, I did become very aware, and I think I became very liberal in college. I had a good friend—well, not a very close friend, but someone who I sort of admired and who I'd talk with often—Daniel [J] Keniry, who actually became a special assistant to President [George W.] Bush, who was one of these sort of young republicans in college, although I don't think, at the time, we had a young republican's group. I had a close friend who was a roommate, Bill [William Gilbert] Boyd, who helped start a group called Students for Political Awareness and Activism. He was really disappointed that at our conservative college there was very little discussion of political activism and what was going on in the world around us. He got me very interested in this.

I remember Dan Keniry would often help when I was having trouble researching something that we wanted to write something about or have a discussion about or invite a speaker about. He would let me know when I wasn't thinking straight and where I could find information and that sort of thing. Now, seeing how I just assume most people who work in the White House are in some senses political hacks, sometimes they grow up through a system that they tend [to be] sort of fascinated with Watergate-[style] dirty tricks instead of having an honest discussion of ideas. And so it's refreshing to meet people like him who do that sort of thing...

CARUSO: So, what were your interests? I mean you mentioned biology. You mentioned philosophy, although not necessarily switching up to the major. What were the courses that you were interested in taking? Was there a set curriculum that you had to follow?

GOLDSTEIN: In university?

CARUSO: Yes.

GOLDSTEIN: I was a biology major and I had to take certain biology classes for that and chemistry and physics. And then my electives: I ended up taking a lot of philosophy classes and some psychology classes. I guess probably through staying up in the middle of the night having discussions with people, I got really interested in philosophy. I'm trying to think what else.

At one point I took a jazz dance class, which I regret. [laughter] My roommate [Bill Hardy], who was in the Army Reserve, was the only other male in the class. I was very interested in music. I took guitar lessons from third to sixth grade and then forgot about [making] music for a long time. And then when I came to college, Dave Greenlaw, this guy I was talking about, took guitar lessons in town [at Hermie's Music Store, Schenectady, New York], and he would come back and teach me what he'd learned. So, I found my old guitar from when I was ten years old, which, of course, was way too small. By this time I was almost six feet tall and had this tiny kid's guitar. But he would teach me what he'd learned. And so I, sort of, took guitar lessons by proxy this way.

My last year in college, I played the bells on top of...a carillon on top of a chapel on campus, which was funny because there was an old psychology professor [Charles William Huntley] who—he must have been in his seventies or eighties when he taught me; he was a pretty old man. For whatever reason, he was the person who took care of the [carillon] bells and found someone to play them. I noticed I hadn't heard them for a long time and I heard from talking to people that he was the person to talk to. And so, I went to him and asked if I could play the bells. I said, "I'd be happy to do this if you don't have anyone." He said, "Well, have you ever played them before?" and I said, "No." He goes, "Do you play piano?" and I said, "No." He said, "Do you play any instrument that's laid out sort of left-to-right like this?" I said, "No. I only play guitar." He said, "Well, we don't have anyone else. Okay." [laughter] And it was very exciting because it was a beautiful old chapel on campus. I realize this has nothing to do with science, but I guess that's okay? [Caruso nods his head.] Okay. So, each [day] I'd have to call campus security and they'd come open the door and then I had a key for inside doors. It was an exciting climb to where I had to be to play those bells. So, you'd go through a vary narrow stairway, and then another narrow stairway, and across between the roof and the ceiling there was a space where you could see a lot of insulation in there and then a little path that you could walk in. And then through a hatch and eventually up into a space that was just a beautiful space, and you could open up the hatch to the bells so you could hear the bells

even louder than you would otherwise.

And at first I had no idea what I was doing and I would hit a lot of bad notes. When you're playing bells that are—of course, you can hear all over the campus, but where I was it was the loudest thing I probably had ever heard, just about. And when you hit a wrong note, it was very funny. And so, for the first few weeks I didn't tell anyone at all that I was playing these bells because I was so embarrassed how bad they were. I actually remember overhearing people saying, "Who on earth is playing those bells? It's terrible." But it was fun after a while because there were some songs there that were written out and I'd found...they were very old transcriptions of old sort of 1960s protest songs. I remember *We Shall Overcome* was in there. It's a very simple tune that actually lends itself to bells quite well because the chime lasts so long and if you're playing anything that's sort of fast and notes close to each other it becomes mud quickly. So these sorts of things worked well. And then I'd transcribed a Bob Marley song [Redemption Song] for it. It was fun. You were asking about other interests. Music was another interest. I guess music became [even] more of [an] interest in grad school than in college...

CARUSO: Did you have jobs while you were in college?

GOLDSTEIN: Yes. Before then I worked in a shopping mall in Massapequa. I worked in the Sunrise Mall [now the Westfield Sunrise Shopping Center].

CARUSO: Doing?

GOLDSTEIN: My first job was in a place called Snnacks—with three Ns—and it was a place that sold hot dogs and sodas and stuff, and it was wedged underneath a stairway. I remember, in order to get that job, which, I know, doesn't sound like a great job, I ended up lying about my background. I was in my senior year and I was taking classes through Long Island University professors. And so, I just told them I was a Long Island University student, which I guess was technically true, but I did, sort of, pretend to be a college student already, thinking that would give me a better chance because I went for weeks, going to almost every store in the mall, filling out applications and getting nowhere. So then, after working that hard, I got my hot dog-selling job. [laughter]

I had a few jobs in that mall. I had a job just across from there. There was a [Hallmark] card shop and it was a family owned—a father and son [Simon and Marvin Goldfarb] owned it. They owned five or six stores in that mall, and they had the one stock room for it, and I worked stock in there. But when I first was hired to do that, they [had decided] their stock room was too small, but it was tall enough to build a loft in to expand the storage space. And I spent a week at a job trying to help a guy build this loft space and I could not hammer a nail, so I got fired from the job after a week. They said, "You seem like a nice guy but you can't hammer a nail. Every

nail goes sideways. We pull it out.” I’m sure I was a headache.

About a year later, I got hired back at that same place to do stock and worked very hard and did well. In fact, I remember after a week, instead of getting fired, I went to them and asked for a raise because I realized that the other stock boy would go to the dumpsters and smoke pot and not do much and I was just...I didn’t like watching the clock, so I would just work hard...

So then in college, I had jobs. I ended up getting jobs in campus security, but just one of them was...there was an all-girls dorm on campus [...]. One person would sit down where they would exit and enter just to make sure, I guess, no one was going in who shouldn’t. I think they were allowed to bring anyone they want, but if anyone came and tried to sneak in...

CARUSO: Just [tried to] go in...

GOLDSTEIN: Yes. We didn’t have weapons or anything, but we had a phone we knew how to use! And I’d sit there and do homework. It was either Friday or Saturday nights, I forget which, from midnight until 8:00 a.m. I would do homework for the first few hours and then, sort of, fall asleep. Once it got quite late, you could fall asleep. The door was locked and if someone came in, you’d hear it.

And then, I had job for a while driving one of the security...there was a security van on campus that they decided that people, I guess women especially, should be able to call and get a ride late at night instead of walking to places where it may or may not be safe. I didn’t know how to drive very well. I took Driver’s Ed in high school, not through the high school, but locally, near home. And I remember the Driver’s Ed teacher called me "Crash". So, there were four of us taking this at the same time. And so you’d have one drive and the other three would sit in the back seat. When it was my turn, I could tell the guy was getting nervous. Then, one time, I remember taking a right turn and he said, “You almost took the pin striping off that Honda!” [laughter] because I really was as close as can be to it. There was another time when he slammed his foot on the brake because I was doing something—I forget what the obstacle was, but there was an obstacle—and I, out of reflex, went to slam my foot on the brake, too, but hit the accelerator and the car sat there and made loud noise and a lot of smoke for a few seconds. So, by the time I got this job, I actually...I didn’t have a car and I didn’t have much experience driving. I remember it probably wasn’t a good idea to take this job.

I do remember a few times...it was a small campus and there was me and maybe two security cars going around campus and there were very few roads on the campus. It’s mostly a walking campus, Union College. I remember a few times—they wouldn’t refer to each other by name, which seems funny because there were only a few of them—they would say, “Unit One to Unit Seven.” So a few times I’d hear, “Unit Two to Unit Seven. You need to turn on your lights.”

CARUSO: [laughter] So, why were you doing these jobs? Was it just a little extra pocket cash?

GOLDSTEIN: It was for spending money...

CARUSO: So you came in as a pre-med.

GOLDSTEIN: Uh-huh. I said that was my first job in the Snack Bar. I had paper routes when I was a kid, too. My brother had paper routes.

CARUSO: You came in as a pre-med student.

GOLDSTEIN: Yes.

CARUSO: At what point did you stop being a pre-med?

GOLDSTEIN: I was pre-med, and we were declared as biology majors. I don't think anywhere was it written down that we were pre-med.

CARUSO: Okay. So there wasn't a pre-med major, *per se*. It was just...

GOLDSTEIN: Yes. And I wouldn't be surprised if, on paper—it's hard to remember, but I think it's possible I was a biology major continuously through college. In my head, I was a pre-med for, it must have been, about a year and a half. And then I was considering being a Philosophy major. I remember talking to my parents about it and thinking my father, who was very conservative and practical, and my mother, who was not...I had assumed that my mother would say, "You can do anything with your life," and would be supportive, and my father would say that that's crap. And it turned out to be just the opposite way. But I realized my parents were making an investment, in some ways, and they probably didn't want to see me making a bad choice. I'm not sure what...if you were a philosophy major your choice of jobs—a lot of philosophy majors go on to grad school or to law or something like this, right? I knew I didn't want to be a lawyer. I wanted to be a philosopher for a year or two. So then, at one point, I remember there was a class I really wanted to take and I think it may have been the symbolic logic class, where the class was getting quite full and the professor said, "I'm only going to take philosophy majors now because we don't have room." And so I explained to him my interest in becoming a philosophy major. I think I believed it at time, too. And then, like I said, symbolic

logic really I got excited about, I guess, thinking seriously about logic that applies to something interesting. That's what got me really interested in research. I did have one absolutely outstanding professor that I think was really influential in this.

CARUSO: Who was that?

GOLDSTEIN: It was Ray Rappaport. He's well-known for studies of cytokinesis—the physical process of how cells divide. I guess he and one other professor were really influential [to me], Michael [W.] Frohlich, who is a botanist, but did some developmental biology of plants.

Most of the classes [in Biology] I, sort of, saw as, “There are a lot of facts and I need to know them.” There was one class in invertebrate zoology taught by Barbara Boyer that I remember getting, sort of, turned on by the diversity of things we were seeing. And then, at the end of the course, she had a dinner at her house for all the students, though I think there were only about ten or fifteen students in the class. And we had, I think she called it, “a six phylum dinner” or something like that: we had clams from the mollusks; we had shrimp from the arthropods; we had, sort of, one or two representatives of six different phyla. I remember going to her house—her husband was a professor, too—we went to their house and they were obviously interested in biology and in teaching. It, sort of, opened my eye as all this being more than just something you do because classes exist, right?

And then, Michael [W.] Frohlich, I ended up doing research with. I wanted to do research with either Barbara Boyer or Ray Rappaport. And they both worked with animal cells and they both used their hands doing physical manipulations with animal cells, which now is very unusual, and even at the time was somewhat unusual, right? And I was impressed that you could dissect the logic of how things worked by physical manipulations of cells. So, Boyer did her research in Woods Hole [Marine Biological Laboratory] in the summers. And, I remember, I couldn't work with her in Woods Hole in the summer and, I think, either because she already had someone or she wasn't going the year that I wanted to go.

Rappaport didn't take undergraduates to work with him. He's famous for having worked for about four decades on his own or with his wife, doing physical manipulations of cells to study how cells divide. And almost all the experiments involved sort of changing the shape of a cell or removing the division machinery at specific times and this sort of thing.

Rappaport taught a class in embryology, and for the entire class, the class went like this. He'd start by talking about...giving the background of an interesting problem. And by the end of this I knew what the question was and I still have the notebook—it's sitting at work—I'd write, “Q,” and then “this is the question.” Then I'd write, “Experiments,” and then I would write out the experiment. It was always interesting [to see exactly] how someone had devised an experiment to test something. To go from a question to an experiment wasn't always an obvious process. Sometimes people were clever at that stage. And so, that's one of the stages I

got excited: going from seeing biology as a compilation of facts to seeing it as something where people were doing—there was a creative activity—really turned my head.

So, they'd design an experiment. We'd get the results from the experiment. And then there'd be a conclusion. And, I think, almost my entire notebook is: question, experiment, results, conclusion. The conclusion would often lead to another question, and it would continue like that. Sometimes the results were...it was such a well-designed experiment that the result...you wouldn't even need to write down what the conclusion was. You could tell, immediately, what they'd learned from it. This got me really excited.

He taught his own experiments, which were very influential in his field, for about two or three weeks of class and never mentioned that they were his own experiments. So, we had no idea he was talking about his work and that he was famous for this work. And then, he talked about a lot of other stuff, too, in embryology. So, I couldn't do research with him.

Michael [W.] Frohlich was the guy who I found very funny. He was a funny guy and he could be the textbook definition of a plant nerd, and I don't think he'd mind me saying that. I remember him saying proudly that he had his plant import license before he had his driver's license, when he was a high school student. So, hearing stories like this, I never really related to this—people who were completely turned on by what became their career very early on. He was kind of a strange guy in some ways. I don't know quite how to explain how. He was very much excited about what he was studying and the things he was talking about. He would speak his mind. I think he'd rarely talk about political things, but when he did, he would say it quite clearly. He treated students as people to have discussions with and not just...he needed to unload these facts and get out.

And then I did research with him. I think his style of having undergraduates do research affected me very deeply in that he had a small room, maybe 10x12 feet, something like this. There were some plants in it. There was some equipment. It was actually right next door to Ray Rappaport's lab, which was a similar size, which seems strange, in hindsight, because Rappaport is an admired...his experiments were admired by a lot of people, and I had a little room next to him and I was the only person in that room, most of the time, when I worked. So, Frohlich would discuss an idea for an experiment and he would say, "I think you should do this," and he'd show me how to do it, and then he would leave and I would be alone in a small room working, for a long time. It's not like today's labs, that you see usually, where there's bay after bay after bay and you have a lot of other people to talk to and you ask how they're doing things and they give you input on what you're doing. I was alone in this tiny room with some organic solvents and bad smells and some plants and trying to figure some things out. It was exciting just to be left alone. It was like a playground, in a way. It was a very difficult playground in that I was...to answer the questions we wanted to answer, I was sectioning through centimeters of root every...I forget how thick the sections were, but they must have been 10 to 20 micron sections or something. I had paraffin sections laid out and I couldn't sneeze or breathe on them. I'd often mess up, and so it made me a little bit tense. But, in some ways, it was very exciting that I could do this on my own time. I could go in on nights and

weekends, and I often did. I'd go in between classes and get things done. It was great to have a project of my own that I could try to push forward on my own.

CARUSO: You mentioned that he did give you a couple of things to pursue. What were the areas that you were looking into?

GOLDSTEIN: Before I got there, another undergraduate was looking at the roots of plants that Frohlich worked on a lot, *Heliotropium*, and had noticed that where they form xylem rays, the xylem rays are very wide. Typically plants' roots are defined by not having differences along the length of the root, except root [branches] or adventitious stems can grow out of them. The core of the root—at least my understanding was at the time—was that it's pretty homogeneous in the sense that you find the same sort of elements as you go through. Then, when they found these wide xylem rays, they wanted to know: Do these form where other roots or adventitious stems—or stems that grow off of roots in some kinds of plants—do they only form where they are? Do they form before or after these different kinds of side branches can form? Does one cause the other [...] We had no way of asking [this], but we could, at least, ask the temporal sequence: What happened first?

The answer turned out to be both in that we could see side roots forming off that would have wide xylem [rays]. I think all the side branches of any kind had wide xylem rays near them. Sometimes you would see roots branching off where the rays were too small to even be defined as wide or not, and so, we knew that a xylem ray becoming wide could follow where a branch had formed earlier. On the other hand, when adventitious stems formed they would often form where these wide xylem rays had been. And this I only found, I think, a day or two before graduation, and, I think, told Frohlich after collecting my degree, while still wearing my cap and gown, walking back to my chair during graduation. I explained to him the results, at least, to him and me were very exciting. But I don't know if they were to others. And I remember him being very excited about it and then asking, "Did you leave the undergraduate thesis?" I said, "Yes. I left it in the room there for you," because he had already approved it and I'm not sure he'd seen the final copy yet.

CARUSO: So you actually had to write...was that thesis part of your degree, or was it...?

GOLDSTEIN: I forget if there was an honors associated with it, but I could do research and then the plan was to write it up.

CARUSO: Now you mentioned running into some difficulties with doing the experiments; breathing too hard could be a difficulty.

GOLDSTEIN: Yes.

CARUSO: You also mentioned that you weren't necessarily that successful at using a hammer and nail. Did that translate into being at the bench as well? Did you find it difficult to manipulate things using your hands or did that actually come more easily to you?

GOLDSTEIN: No, not especially. Since then...the work that I've done since then, the stuff that's gone well, is defined by being by hand. And it's unusually "by hand" for the field that I work in. It's much more craft-like than a lot of areas of modern biology. I don't have very steady hands and my family has a family history of multiple sclerosis, and I do occasionally worry that my shaky hands are because...I worry that I've got early symptoms of something. But they've been similarly shaky for years, so it's probably not.

People in my lab, who want to learn how to do direct manipulations of cells are often encouraged to see that I don't have very steady hands and I can do it anyway. I don't think I was especially clumsy. My mother used to tease me that I was very forgetful. My younger brother was born when I was nine years old, and I remember changing his diapers and pushing him in the stroller. And she often told the story—well, a couple of stories—one where we had a dog, and I'd leave to walk the dog without the dog. I'd just have the leash in my hands. And I know...I see one of my sons doing this sometimes, similar things, where he's obviously thinking about something else while doing something. The other story she would tell often is that I pushed my brother to the schoolyard and then my friends were playing kickball there. She claimed that I left him at second base. But I maintain that I left him *as* second base. [laughter] I didn't leave him because they still needed a second base. I think I was walking the dog and my brother, and I came home with the dog and had to go back for my brother. So, I don't know if I was especially clumsy, but I was forgetful.

CARUSO: At what point during your college career did you think, "I want to go to grad school. I want to continue on pursuing this biology stuff"?

GOLDSTEIN: It was, at least, by the beginning of my last year. It's hard to remember exactly when. So, I do remember when I applied to grad school, I was not committed to being a scientist and I was not committed to staying in grad school. I was thinking, "This is a no-cost thing that I can try out." People TA or they get paid just to do research. The place I ended up going, the University of Texas at Austin, at the time, really underpaid their students. We got six-thousand dollars a year and I remember having a check for...something...I remember holding a check. For some reason, I remember the amount of five-hundred and fifty-seven dollars and that was my month's spending. I managed to find an apartment that was cheap enough to just barely get by. I didn't get a phone [at first]. I didn't get a car [either] when I first got there, because I wasn't sure I could afford these things. But I knew from when I was in college that I could go and it wouldn't necessarily cost me anything. It would allow me—my

parents were paying my tuition up until then and tuition at Union College was expensive then. And I was excited about trying to see if I could survive on some money with a little more independence and a little bit further away geographically from my parents. But I knew I could try it [grad school] at essentially no cost.

I went to Barbara Boyer and Ray Rappaport and asked them...I knew I didn't want to be a botanist. I didn't really like plants that much. And so, I'm not sure if I asked Michael Frohlich for advice, specific advice anyway, about where to go...I went to Barbara Boyer and she gave me some advice about what kinds of schools to apply to. I remember telling both Boyer and Rappaport that, "I'd like to do research in biology. I'm not sure what area. I know some areas I don't like. And I don't want to have to deal with molecules at all." So, I knew that I didn't want to do molecular biology or biochemistry. And so Barbara Boyer recommended some schools. Ray Rappaport said, "Look. You can't be a biologist without thinking about molecules"—which...he succeeded at being a very successful biologist without thinking about molecules, or without, at least, doing experiments with them, but I think he was one of the last of that kind of biologist anyway—he said, "You can't do that." He goes, "But if you want to start doing something different," he goes, "why don't you tell me what sort of fields you're interested in?" And I remember telling him that I just didn't have a clue what sort of fields I was interested in. He says, "[...] Go write a list of all the things you don't want to do, and then look at what's left and see what you like then." I remember clearly this [seeming like] a bad way to make a decision, but in a way it led me to remember what it was I did like and started to think about what I did like. So, I knew I really enjoyed his course in embryology and I thought, "Well, I'll try this."

When I was applying to grad school, I was applying to biology and zoology programs, so I didn't necessarily have to decide a subfield within those. But he convinced me that it would help on an application to indicate a subfield and then you can decide later if that's that or not. So, when I told them both, at some point, that I wanted to do embryology or developmental biology, but not think about molecules in the beginning, they both recommended one person, Gary Freeman at the University of Texas.

Actually, Ray Rappaport also recommended one other person, Albert [K.] Harris at UNC Chapel Hill [University of North Carolina at Chapel Hill], who's now a colleague in the department I'm in. I applied to both places, and then I think I applied to a few other places. I applied to Duke [University], and I think I got in, but without any funding, so that was useless to me. And then I got into Texas. When I was in college, I worked in the campus radio station. I was briefly the manager of the campus radio station, and [in college radio,] Austin [Texas] was on our map the way that New York and Tokyo [Japan] or places like this are on most people's maps. Austin, there was great music coming out of Austin and it seemed like an exciting place and I knew a lot of young people were living there.

When I got an interview at Austin, I was just excited as can be. And then, after going there, I was completely sold. It was very exciting to see a place where...growing up on Long Island, Long island has a culture of its own. It's an unusual one in some ways, but it's a little different than going to somewhere like Texas where people are friendlier. They're proud to be

from there. There are real regional differences. A lot of where we grew up, what made the place unique [...] was [actually shared by] a lot of the suburban places (as opposed to non-suburban places)...whereas in Texas, it was exciting to see—we could drive a mile out of the center of Austin and see places where people would go two-stepping on sand-covered floors to country bands. It was exciting to see. Now I forget what your question was. It probably had nothing to do with that.

CARUSO: No, no, no. It was: what turned you on to going to grad school and the process? Before leaving college, or before moving on to the topic of graduate school...I don't know the best way to ask it, but it sounds like you were quite busy working in the lab...classes. You mentioned having several friends. But did you have much of a social life outside of the academic realm?

GOLDSTEIN: Yes. The radio station, we spent a lot of time working and I had a lot of friends who worked in the radio station as well and made friends through that. And then my roommate, Bill Boyd, my last year, was music director while I was manager of the radio station. I do remember my last year running around. I think it was the first time I used a calendar in the way that people should use calendars, in that I would take a day and have things written down for things to do throughout the day and things where I'd have to run from one to another to get everything done, plus doing the class work and everything.

There was the political awareness and activism group. There was the radio station. At one point, the university decided our graduation speaker should be [J. Peter] Grace from W.R. Grace & Company. And it was not long after either *60 Minutes* or *20/20* had done an expose on a problem downstream [of] one of their plants where a lot of people had gotten leukemia. And this seemed like the worst possible choice to a lot of us. We spent a lot of time—we actually, at one point, met with a representative from W.R. Grace & Company to try to smooth things over and not have the students protest and get something in the news. So, we ended up at the graduation putting...we decided to do something that would express our displeasure with this without being disruptive. We ended up putting little notes on every seat explaining our view of this. I forget if there was anything else we had done as well.

But between research and classes and the radio station and the political awareness activism stuff, and then I did hang out with friends and drink beer and go to parties. I mean, when I got to college, of course, that was one of the most exciting things as well as staying up late talking philosophy. It was no longer a struggle to get a 12-pack of Budweiser and drink in my friend Vinnie's [Vincent R. Olson] basement.[laughter] It was a very positive thing at the beginning.

CARUSO: And what did your parents think about your decision to, at least possibly, pursue a graduate degree?

GOLDSTEIN: I'm not sure if they were especially in favor or not in favor. My mother, who I was closer with, I think wasn't too keen to see me move that far away, to Texas. They always seemed very proud that I did well, and, I guess, they saw this as a product of doing well, so, in that sense, I think they were proud.

CARUSO: Because you also mentioned the notion of practicality, right?

GOLDSTEIN: Yes.

CARUSO: Being a philosophy major, what are you going to do?

GOLDSTEIN: Right.

CARUSO: Being a biology major, though you weren't necessarily committed to pursuing an academic career, someone might ask, "Well, what are you going to do with that degree?" Was there ever any sort of sense...?

GOLDSTEIN: No. I suspect the worry was less than it was for philosophy. I think that my mother, who had expressed these kinds of concerns more, I think became less concerned over time. I'm not sure why. I mean, I don't know if it's because she had other things she had to worry about or she just had less worry overall.

CARUSO: My mother, interestingly enough, contacted my undergraduate institution pretending to be someone considering going to graduate school just to find out...because I had told her that, yes, they actually pay you to go to grad school and she didn't believe me. [laughter] So she spoke with the department chair, pretending to be a potential grad student, trying to find out whether or not it was true that you actually paid people to go to graduate school because it was something that she just didn't believe. She was like, "Well, you're not going to make money doing this. Why are you pursuing it?" So, I was just curious if your family had felt the same way. So you moved out to Austin and weren't necessarily receiving a whole lot of money. Did you also have a job while you were doing graduate school?

GOLDSTEIN: No, no. See, you couldn't...we were paid to put our full effort into research and classes and we were discouraged from having—I mean, probably, not supposed to at all take any other source of income, any other kind of job. So, no.

CARUSO: So what was graduate school—how was it structured? Was it coursework and lab work at the same time?

GOLDSTEIN: I remember when I arrived, it was August, in the middle of Texas, and it was not a good time to be introduced to a new place. Plus, I didn't have a place to live at the beginning and I stayed in the house of someone [Bob Srygley] who became a good friend later, but he was away, I was taking his room. And there were these giant Texas cockroaches. I knew no one and I was very upset about losing all my friends and going to a place where I knew no one. I remember not being able to relate well with the students at the beginning, which completely disappeared after the first few months or something. But I found it a very difficult transition. And, at one point I remember, I went to the radio station and volunteered to do some work in the radio station, but just it would be like an hour every few weeks or something like this, and made [...] friends—[Koan Jean Davis, Laura Martz, Jarrett Michael Paschel]—through that, and then later came to enjoy spending time with the biology students as well. But at the beginning, I found it a very foreign experience and difficult, a really difficult transition.

CARUSO: In what ways?

GOLDSTEIN: In that I wasn't around the people that I knew well. I was living alone in an apartment, which I was excited about—I felt like I was making it on my own, even though I was supported by an academic program. I remember I just never had the experience of being alone before like that. I do remember a few times I'd set pens on end before I'd go to work in the morning and then come back in the evening and be amused that they'd still be standing... [laughter]...that really there was nothing going on there when I was away. I have a very strange memory where I was making, for some reason, peanut butter and jelly sandwiches almost the whole way through graduate school for lunch. And, at one point, when I worked at a marine lab for a week and it was hard to get to supermarkets, I ate peanut butter and jelly sandwiches for a week for every meal. But I remember once, when I was first on my own in this apartment, scooping out some peanut butter and the knife flicked and the peanut butter went flying in the air and landed in a pot of water and made a funny sound and just laughing very hard at this and finding it strange that I'm not sure I'd ever laughed alone. I must have laughed alone before, but maybe not that hard. In hindsight, it seemed like a strange experience.

So then, I was taking classes my first year. I rotated in three labs [including] with my advisor, who I went in intending to work with this guy and then I did rotations with the intention of coming back to—it was Gary Freeman—coming back to [his lab]. I rotated with Wes [Wesley J.] Thompson. It involved, mostly, sectioning muscles from...I think it was rats and staining them. The most fun to me was first we were using the cryotome, so doing frozen sections. Actually, with a cryotome, you have to be very careful with what you do with water anywhere near it because it becomes solid in everything you're working with. It was very tricky to me, but I had done paraffin sectioning before, so I got the hang of it. And then there was a

darkroom for making the pictures, and I thought it was fun to work alone in a darkroom and develop pictures.

And then I worked in another lab, Bill [William R.] Jeffrey's lab, and did experiments that again I was—although it was a lab with a lot of people—I was doing, really, my own experiments separate from other people. I do remember, for a while, doing the experiment completely wrong where I was treating cells with cytochalasin to, basically, take apart the actin cytoskeleton and then fixing them and staining them for something later. And, for a little while, I know I was doing it backwards where I was first fixing and staining them, and then treating with something that, of course, is completely irrelevant once you've fixed and cross-linked everything in these cells. And when I discovered my mistake, I thought, "Boy, maybe I'm not cut out for this." There were several times I was convinced I wasn't cut out for it. I went through my first two years of graduate school without a single experiment working. And when I tell this to students now, I think they often misunderstand and think nothing worked well, and what I mean is, not a single day did I go home thinking I'd done something that worked. I think that's probably just about true. There may have been days when I got something to stain that other people had before, but, really, it was an unmitigated failure for two years.

I was taking classes for the first year and doing research, and then the second year I was just doing research. And I was trying three different kinds of experiments. One was in mollusk embryos. There was a little clump of protein and RNA [Ribonucleic Acid] on one end of the embryo that got segregated into specific cells and the function of it wasn't completely clear. And I thought it would be interesting to study the function of that. All I ever did was stain for it so I could see it and never took it any further.

The second was in ascidian embryos. So, ascidian embryos are a little like *C. elegans* embryos in that they go through rapid divisions. And then the time at which you can start to see that cells are behaving different from each other, starting to really differentiate from each other, is only a short time after the cells are born and separated from cells of other cell types. And it's such a short time that I wondered how that was timed. And so, I was doing experiments to try to test the hypothesis—which really was my advisor's hypothesis—that it was the ratio of the nucleus to cytoplasm [that acted as a timer]. You start with a certain amount of cytoplasm, and in most invertebrate embryos, the embryo doesn't grow at all but the cell divisions go on. You have twice as much DNA [deoxyribonucleic acid] every round of divisions. This ratio of nucleus to cytoplasm changes rapidly. The idea was maybe, somehow, nucleus to cytoplasmic ratio was being measured and there was some precedence for this, for timing other kinds of events in other embryos. I was trying to test that a little bit in Texas, and some in—I spent summers in Friday Harbor [Laboratories], University of Washington Marine Lab—and there, too, I ended up introducing a lot of DNA into embryos and killing them in loads of different ways and never learning, really, anything. And then I also tried experiments in *C. elegans*.

Gary Freeman's lab was a really unusual place in that [...] it was a really unusual place in that, when I arrived in the lab, there was not a study organism for me and there was not a topic. And this is absolutely unheard of, certainly in molecular cell developmental biology, but to some extent, in biology in general. When I got to the lab, there were two other grad students

in there. One was just finishing. This was, probably, the most crowded the lab had ever been, and there were three of us there at the same time. And there was a technician woman, Judy Lundelius who was their technician, but more doing some literature research with our advisor part-time.

So these two other students...Andy Ransick was doing experiments with volvox, an alga—a plant, not even an animal; Elizabeth [R.] McCain, who was doing experiments with Ilyanassa embryos—mud snail embryos—but both of them were doing experiments asking about how cell fates are specified and using physical manipulations to test questions about how cell fates are specified, how one cell becomes a gut cell and another a muscle cell and another a neuron. When I came, Gary...Actually, when I first came, Gary asked me if I wanted to spend the first summer before grad school in Friday Harbor, where he was doing research. So, he would go every summer to this marine lab to do research. And I said yes. So a week after I graduated, I started in a small lab with him in Friday Harbor.

CARUSO: Oh, okay.

GOLDSTEIN: And it was the two of us. The day I arrived he said he was leaving—the next day or the day after—for a week to go teach in the Woods Hole embryology course—this famous embryology course that had been taught for one-hundred years—and that I should try to do some experiments while he's away. [laughter] There it was nice because there were tons of study organisms you could use and he showed me how to get some embryos, I think, from ctenophores and from some jellyfish. He said, “Try to do experiments and test a question you're interested in,” and left. This, plus the way I worked in Michael Frohlich's lab, I think, had a profound influence on just thinking you could. Of course, I failed miserably this time. He left and the one question I was really interested in is...I remember these old embryology experiments where embryologists had taken frog embryos at the two-cell stage, and either separated the two cells from each other and asked how they developed, or killed one of the two cells and asked how the remaining one develops. When you kill one cell, the other cell will develop as, basically, half a tadpole. When you separate the two cells, you get two complete tadpole larvae. So, this suggests something going on in that dead cell is affecting how the live cell will develop. And I wondered if it could be just a physical...it could be something completely physical. So, I thought, I'll try this experiment with...I think I did it with ctenophore embryos, in which the same phenomenon wasn't known, so that was my first mistake. My next mistake was much more serious, which was I thought, “How do I introduce a physical obstruction? I know what I'll do. I'll take glass tubes and put them in them and they'll be small enough that it'll squash the cells a little bit. And then, I'll seal them and put them in the fridge overnight and see how they do at sea water temperature.” Of course, there's no gas exchange and they're sealed in glass and they died very quickly. But, I think my...I tended, for a long time, to only learn facts as I needed to know about them and any ideas about how gas exchange would be necessary had escaped me, probably for that reason. So, he came back and did not laugh at me, but instead said, “Okay. That's an interesting idea, but it's not going to work for this reason.” He was very clear about why it wouldn't work, but was encouraging

about testing one's own ideas and this is the way it went on in grad school the whole time with him.

He would not give us a project. We had lab meetings...the way he did his lab meetings I guess is unusual and it's the way I do my lab meetings now in my lab. So, one week he would pick a pair of papers, usually they'd be related to each other. Sometimes they would be two papers that had similar things. Sometimes they'd [be] sort of one development and the next development along the same line. Sometimes there'd be papers that said the exact opposite of each other, which I think is a very interesting...it's an interesting test to see...with students now if you give them two papers that say the exact opposite of each other and you ask them what they think, some students will summarize the first paper and summarize the second paper. Other students will discuss the differences and what they think is going on and why there is a difference. And, boy, you can really tell someone who's thinking from someone who's not from an exercise like that. So, he would pick a pair of papers, and we would sit and discuss them. I like to say it was like a journal club in that...people are familiar with this term. Journal club is used a lot of places. Except in journal clubs typically what happens is very few people read the paper and then most of the time is spent just getting the facts out. I say it's like a journal club except we all actually read the papers. We would rotate through the lab picking the papers. He would pick them one week, I would pick them the next week, and at times when there was a third person in the lab, they would pick them as well. He would call on us to present them, seemingly, at random. So, we'd always have to be ready to present. I liken this now to in Cambridge [England], on Christmas Eve, the King's College Choir sings and there's a solo that they do and the story goes that there are something like five or six kids who might be doing the solo and they all prepare the solo. And, at the moment when the first note is about to begin, the conductor points to...so they separate them out well enough [and] the conductor points to one of them and they starting singing that first note and they sing the entire solo. But they don't know who it's going to be until it's about to start, which I realize can be scary. But these kinds of discussions only work well when everyone's prepared to get the facts out and then move beyond the basic facts to discuss what's really interesting and what you would do next, whether or not you believe it, why you do or don't believe it, that sort of thing. So, although he didn't assign projects, by doing this kind of lab meeting, we were talking about interesting issues all the time in various organisms. And then the projects would often jump off from those. I suspect, at times, he was planting ideas that he already had when doing that. The ascidian project I did was clearly his idea and I remember resisting it for a little while because he was assigning an idea and it wasn't my own. Which now, working on molecular cell development in a lab, no one comes in starting by testing their own ideas. A student resisting this in a typical lab would be looked at like they were crazy.

CARUSO: Yeah. How else did he run the lab while you were there? Was he at the bench as well?

GOLDSTEIN: He did experiments, too. He did most of the experiments in the summers, in Friday Harbor [Labs], but he did some at Texas as well. He had, I think, a very regimented life

in that he would come to work all week, and then on Saturday he would work until NPR [National Public Radio] stopped playing the opera in the afternoon. And he would often do experiments on Saturdays as well. He was open with us and explained that he and his wife had an unusual arrangement where they had a complete separation of responsibilities where he would go to work. He'd ride his bicycle to work every day. Once a week he would stop at a specific bakery to pick up some baked goods for our lab meeting—which is something I still do for my lab meetings now, but I don't ride my bike for it—and then he would be in on a Saturday and his wife raised the kids and listened to NPR and brought in all of the interesting non-scientific ideas through listening to NPR. Gary was very interested in opera and modern art. He had a lot of interests, but I suspect they all came in through his wife listening to the radio. I remember, one weekend, someone telling me, "I saw your advisor in the mall," and I said, "That wasn't him. There's no possibility that that was him." [Sure enough, it wasn't.]

Sometimes his limited experience became really clear. So, in the first Gulf War, when I was a graduate student, he came in once and said that instead of watching *McNeil/Lehrer News Hour* on PBS [Public Broadcasting Service] one night, he decided to watch a network newscast. And he described to us step by step, he says, "I turned on the TV at ten o'clock. The news was supposed to start at ten o'clock." He said, "There was an advertisement for a show called *Friends*." He goes, "I don't even watch *Friends*." He couldn't understand why they were showing him an advertisement. And then he went through and described, minute-by-minute, how, "at thirteen minutes after, there was yet another commercial. When they came back, there was nothing but the sports and weather," and told all this in this incredulous face as if this has never been seen before. [laughter]

Another time when we were out in Friday Harbor, I drove him to an opera in Seattle [Washington]. He bought two tickets for the first night of *The Ring* [*Der Ring des Nibelungen*] opera and gave me one in exchange for the ride, which I was excited to go and see some music and it was fun to go for a trip with him. We got into Seattle and there was typical rush-hour traffic. I remember him looking out and saying, [incredulous], "Have you ever seen traffic anything like this?" I said, "Yes, I have."

CARUSO: So, you went out with him regularly for the summers?

GOLDSTEIN: Yes. I went every summer, except one summer I started off out there and went to Woods Hole to take the embryology course, and then went back to Friday Harbor before going back [to Texas].

CARUSO: And was it, essentially, just the two of you out there?

GOLDSTEIN: Most of the time it was just the two of us. At times there were other students. I'm trying to think who else was out there regularly when we were there. Maybe no one was

there regularly. It must have been my last...no, not my last year, because another student started...for a while I was the only student in the lab. There was a time when he went away and I was the lab. In fact, around the time I was finishing [my PhD] this happened. There were a lot of times when I really felt out on my own in some respects in that he was very critical about the science and would discuss the science and would think carefully about it and have intense discussions about it, but he had very little patience for thinking about trying to submit to higher-profile journals and that sort of thing. So, my first paper, we submitted it to *Nature* and he agreed that would be okay, but didn't necessarily encourage it. I dealt directly with the editors, which a student almost never does now. So, in the correspondence I have...I have all the letters and I can see silly mistakes that I made, that a twenty-three or twenty-four year-old grad student would make, that I cringe looking back at.

CARUSO: How did the writing process work? I know some PIs [Principle Investigators] tell students, "All right. We'll write this together"; some write the paper for them; some get to do the first draft and then the PI comes in and says, "Okay. This is what we need to change." What was his style?

GOLDSTEIN: We [grad students] wrote drafts and he would correct them. A similar thing came up when we were discussing when we'd give a practice talk for a talk we were going to give and he would give comments on that. But there he would give much more directed comments. When we were really screwing up, he...or when I was...he would say, "You need to stop. You need to have a slide that says this, this, and this," and you could see in his face how frustrated he was, sometimes, that we hadn't seen this for ourselves. He would give very directed advice at times, but he did not write the paper. He really didn't take part in writing the paper. He gave us comments on our paper. He didn't put his name on as an author, too, which is unheard of in this field of biology.

CARUSO: And did you have any sense of the broader aspects of a scientific career from him, the politics...maybe, the departmental politics, grant-writing processes? Did he include you in that stuff as well? Did he try to shield you from...?

GOLDSTEIN: I never knew when he was writing a grant, which seems strange in hindsight. He would talk about the department politics. He was very openly critical of other people and, I think, got himself into trouble a lot of times in the department because of it, because he would blurt out something that was sometimes appropriately critical and sometimes completely inappropriate. He was famous in the department for this. He didn't include us in grant writing. He did include us...when he wrote a paper, he would have us read a draft and give comments. I'm not sure I was aware when funding came in and for what projects. I met someone years ago who told me that they sat on a panel that reviewed one of his grants. And, at a point during a discussion of whether it should be funded or not, someone said, "Oh, God. Look how little he's asking for? Let's just give it to him." He always did good science and was well-respected for

science, but he did it with so little resources that...I'm not sure, exactly, how his grant writing experiences went because I didn't get in on them. But it's funny to hear, in hindsight, how people treated them on the other side.

CARUSO: During the summers...?

GOLDSTEIN: Some of the issues I think about now, the social issues related to science, like issues of women in science, minorities in science, and so forth, these sorts of things, he was willfully ignorant about because he just believed that it was a non-issue. He said, "You are judged solely for your science, and there are no other issues." And I bought that for a while. And I remembered cracks in that belief appearing in...we were in Texas, and there were a lot of the things about the department that were Texan. Although there were a lot of young people that thought in more modern ways, there was an Old Boy's network in the department in some ways.

I remember we reviewed a fantastic...the department interviewed a fantastic fly developmental biologist, Janice [A.] Fisher, who had come from Gerry [Gerald M.] Rubin's lab. When she interviewed, she must have been about eight months pregnant. I remember seeing her and seeing...I think she wore a dress to her interview, and I hadn't seen many women in science. I certainly hadn't seen young ones who were at the age where they'd be pregnant. I remember sitting and thinking about, "well, she had to make a decision about what to wear." It was either her or someone else who I remember seeing in a floral print dress that looked very feminine, and I remember it striking me as...I noticed it, right? And I wouldn't have had to worry about that, right? I could show up in a shirt and tie for a job interview and I would have very little worry about how I was perceived because of what I wearing.

CARUSO: So, what I was going to ask, with regard to the summers, it was essentially the two of you out there. Was it all science? I know you mentioned that there was the opera, but was it essentially all science all the time?

GOLDSTEIN: No. Friday Harbor in some ways is like a summer camp. Everyone who goes out there goes from somewhere else. That's not completely true: there are now year 'round people there as well. But, at the time, the number of year 'round people was very small, and almost everyone was there just for the summer. And so, everyone would put away their home lives and the people they knew in other places and come out to this place. You'd make friends very quickly because of this.

Most of the summers I was there, I spent the whole summer sleeping outside in a sleeping bag under the stars, which was really a very pleasant experience. At some point at night, I'd get my sleeping bag and walk through the woods. There was a path through the

woods and you would come out back on...so that Marine Lab was right on the coast, and then there was a path through the woods where you would come back out on the coast again. We called it a bed of moss because it was, literally, our bed of moss. And sometimes a few of us would go out there; sometimes I'd be out there on my own and then sleep there. And in the morning I'd wake up, usually it would be when the sun warmed my sleeping bag enough that I was starting to toast. On cloudy days, I'd get to the lab a little bit later. And Gary would poke fun at this. He said, "It's cloudy this morning. I knew you'd be a little bit late." And then we played music with friends a lot out there. We would have rowboats you can row into town, and there were a few bars in town. There's a couple of supermarkets there. You could walk into town, also, but it was actually a much longer walk than it was a row because it was a row right across the harbor. And so, it was fun rowing across the harbor. I forget...

CARUSO: Was there a lot of collaborative research going on there, or was it just like...?

GOLDSTEIN: Gary actually was doing a project with a guy named Ellis [B.] Ridgway looking at calcium imaging cells. There are dyes that you can put into cells to see the calcium bursts or calcium-sensitive photoproteins that'll emit photons when calcium binds. These were found first in jellyfish. And so, what they were doing were looking directly at the jellyfish that already had these things in them, so they didn't have to inject anything special and they could just do the imaging on them.

They were a very funny pair. Ridgway was very conservative, from Virginia and a very different kind of character than Gary was. I remember, at one point, there was a guy at the lab selling Jesse Jackson T-shirts when Jesse Jackson was running for president. And Ridgway bought one from him and I was shocked to see that he was buying one, because it seemed he would never support...it was the exact opposite of his political leanings. He did it as a joke to plug up a little hole in his light apparatus [laughter] and to say that he had done that. So, you were asking other things. Oh, was it collaborative.

CARUSO: Were you working with anyone?

GOLDSTEIN: No. And Gary was working right next to me on a separate project. Did I ever work with anyone? I think I got technical help from people occasionally for something I was doing that I didn't know how to do. But, no, I don't think I ever worked with anyone out there.

CARUSO: What about back at Austin? Were there other labs nearby that you'd go spend some time in just to learn techniques?

GOLDSTEIN: No. At one point, when I was trying to load ascidian embryos with DNA to test his hypothesis that the DNA...the [nuclear-to-]cytoplasmic ratio made a difference for timing of differentiation, I got some DNA from another faculty. Paul [A.] Krieg gave me some plasmid DNA that was...I can't remember. Unless I'm blanking on something, I can't remember another collaboration.

CARUSO: So, you were essentially an independent researcher in college and in your graduate school.

GOLDSTEIN: Yes. And in grad school, at least in Gary's lab, this is the way everyone worked. This wasn't unusual there. In his career, he only had about twelve or thirteen grad students. They all did independent projects. Most of them got faculty positions. So, although he trained very few, they were incredibly successful in the kind of positions they got and being able to do exactly what they wanted afterwards.

CARUSO: You also mentioned that, pretty much, for the first two years during grad school, your experiments...nothing came about.

GOLDSTEIN: Yes.

CARUSO: Did you ever think to yourself, near that end of the first two years, "I should just move on"?

GOLDSTEIN: Almost every day.

CARUSO: So what kept you going there?

GOLDSTEIN: At first when I went, I thought, "If I wake up one day and I don't like this, I'll quit." And then, after a short time, I realized, "I can't have that attitude. I have to be ready to invest more than one day at a time" because it does take some work. It didn't take long to figure out that you have to put in some grunt work to get a return from it. And so, I was willing to do that for a while. Of course, that wasn't going well either. I did spend a lot of time exploring other interests. I was happy in that I had other interests that I was enthusiastic about and actively trying to learn about. I wonder if I didn't have other interests and I was still sticking with it if it would have been a lot more depressing for me.

In the summers, in Friday Harbor, there was a small library there that it was just a biology library, but you could get books from the main campus. Once a week they would take orders for books from the main campus and someone would go pick them up and bring them back. I remember getting *The Montessori Method* by Maria Montessori³ and books on child development by [Jean] Piaget. I was really interested in preschool education. I mean, some of it may have been sparked by being in grad school and thinking about how people learn. I was interested in theories about how people learn and different sorts of ideas about this. I was going to be a preschool teacher for a while, and I was ready to quit and do that for a while. I'm really glad I didn't because, with my kids now, I see very good preschool teachers, and I can see that that's not me. I don't think I would do well at it, nor would I be as excited as they are.

When I was in Austin, I played music a lot with friends. I played guitar in graduate school, and then, for a while, any time I would find a cheap musical instrument, and usually one with strings, I would go ahead and buy it...they're scattered around the house here. There are about twenty instruments all over, hidden in corners and everything, which is really fun with the kids now. The guitar is the only one I really knew how to play. And then, I picked up a banjo, a mandolin, a ukulele. There's just loads of these around now. I would play music with people. And then I'd found a bunch of people in Austin who had day jobs but they were...some of them were very interested in what they were doing for their day jobs, and [I suppose] some were not necessarily. They would get together in the evening and play music. You could go every night of the week and find people to play music with, even if you didn't have friends who played music. So, there'd be an Irish session one night, and a bluegrass session another night in a different place. There'd be a contra dance once night with a pickup band where anyone could show up and join in and play. I did a lot of it. I mean, I didn't do it every night because I was working hard in grad school, too, but I did a lot of this and met some people, who I admired, who did their job during the day and went around...there was one guy who I would see at the Irish Night, the Bluegrass Night, [and others]. He'd be at all of these things. Whenever I went to any of them, there he was. He was actually a single dad raising two kids, but managed to do this, to get out and do what he loved. And so, for a while I thought, "I'll go get whatever kind of job and play music in the evenings all the time." In hindsight, I'm really happy with the fact that things did work out and I did stick with it because I'm not sure I would have [remained] happy with many of these other things.

CARUSO: So, what did keep you going in the lab?

GOLDSTEIN: Well, I guess I just decided I needed to try it out fully before making a decision. Eventually, something worked and that made a world of difference. I got a lot confidence from it. I really didn't have a lot confidence before, and it was dwindling fast as things weren't working for so long. But when something worked, it really worked. It worked really well. And it worked in an organism...worked in *C. elegans*, an organism that I didn't

³ Maria Montessori, *The Montessori Method* (New York: Schocken Books, 1964).

really appreciate when I started working on it... what an audience there would be—an audience where almost everyone who worked in the field were trained as geneticists. And it's an unusual field in that there was a founder of all of the modern *C. elegans* research, Sydney Brenner. Almost everyone who works on *C. elegans* was trained either by Sydney or by someone who worked with Sydney or by someone who worked with someone who worked with Sydney. So, there's a real lineage of scientists who work with *C. elegans*. The first meeting I went to, there were five-hundred people. After working with snails and ascidians—ascidians are actually a fairly popular model now, but there still aren't five-hundred people at their meetings. To see five-hundred people talking about a single organism, an organism that only had nine-hundred and fifty nine cells... There was one person for every two cells. I'm not sure that's the appropriate way to look at it, but it shocked me at the time. It was exciting to dive into this area where there a lot of people who are very interested, and I could see how... I didn't see *C. elegans* as being any better a study organism than any of these others I was thinking about. But, in hindsight, the things that you can do with *C. elegans* that you can't with a lot of these others made a world of difference. A lot of the experiments I was doing early on would have gone one step and stopped with these other organisms.

CARUSO: So you actually—I assume—picked up your dissertation project and finished it within about two years? I mean you finished your Ph.D. in 1992. You started in 1988, and with two years of going nowhere.

GOLDSTEIN: Yes.

CARUSO: Now, if I understand it correctly—and please correct me if I have this story wrong.; I'll probably ask you just to give it in your own words—but your dissertation project was, essentially, developed from your reading of some papers about gut specification during embryogenesis; the fact that I think the previous literature mentioned that it was a cell autonomous process.

GOLDSTEIN: Yes.

CARUSO: And you found logical flaws...

GOLDSTEIN: You do a lot of homework. [laughter]

CARUSO: ...in terms of what these papers were saying. And that's where the dissertation project came from. Is that...?

GOLDSTEIN: So, actually, where it came from was, when I was working with ascidian embryos, we were discussing these experiments where you could see how cells differentiated and when they differentiated. And I was studying this process of how differentiation is carefully timed so soon after the cells acquire their fate. I realized there was a parallel literature in *C. elegans* where people had done almost the exact same experiments. Bill Jeffrey—who I had done a rotation with—I remember running into him once in the mail room when I had this notion of trying experiments in *C. elegans* and trying to do the kind of experiments that my advisor and his group were famous for: separating cells, doing direct manipulation of cells, to ask how cell fates were specified. I went to him and I said, “Have you ever heard of this organism *C. elegans*?” Bill...I remember him looking at me like was an idiot, but he never actually said it. It turns out he was the person, I think, who suggested some of the experiments to the *C. elegans* people that were similar to the ascidian [experiments]. So, not only had he heard of the organism, he was the reason [indirectly, that] I was interested in this organism. He was the person who sparked the experiments that led me into it.

I remember one day just saying to Gary, “I want to get some *C. elegans* and see if I can do embryology experiments,” because there was this claim that there weren’t many cell interactions, and yet there wasn’t a history of [experimental] embryology in that field. There actually were a few people who were doing manipulations, but it was all...they would eliminate cells rather than put them back in new combinations. Often, when they eliminated cells, there were problems about whether they were getting entire cells out and there was this classic experiment—like I said in frogs—where if you kill one cell at the two-cell stage, you get one result. But if you completely separate it off you get a different result. And so, if you really want to know what a cell does on its own, in my mind, you want to completely get rid of the other cells. And so, there was no one, really, who was doing that approach of completely separating the cells from each other cleanly. I said to Gary, “I’d like to get some *C. elegans* to see if I can do this.” I may have only proposed it as a theoretical project, but he said, “Go get some and do it then.” There was one graduate student in our department...there was no one in Austin who was working with *C. elegans* except for this one graduate student in ecology and evolution. I guess I should say, the department we were in was not especially strong in cell and developmental biology. The part of cell and developmental biology where it was strong was it had some very good embryologists. It had Gary Freeman and Antone [G.] Jacobson, who’d done a lot of embryology experiments in amphibian embryos. It had Klaus Kalthoff, who’d done physical manipulations in insect embryos that led to the classic fly work that’s known now, but it’s work that’s not...it’s hardly ever cited now I think as being a predecessor for it. So, there were a few people who had done these sorts of manipulations, but there weren’t many people, at least when I got there, who were doing modern cell and molecular biology of development.

If you wanted to hear really good science in the rest of the department, you’d go to the ecology and evolution seminars. I had a lot of friends in ecology and evolution, and I loved that the graduate students would work more independently in that field. So, every—I think it was on Mondays—they had their talk at lunchtime, and so I would just have my lunch and listen to their

talks. And you'd hear great science. There were several people there who were doing fantastic experiments, at the time, that are now famous experiments in those fields.

CARUSO: Were these faculty members giving talks?

GOLDSTEIN: Faculty members, students, postdocs. And in ecology and evolution, there's more of a tradition of grad students and postdocs doing independent projects and being treated as colleagues from very early on, rather than being handed projects. What was your...?

CARUSO: We were talking about the origins of your project.

GOLDSTEIN: Right. Oh, okay. So there was one student, David [M.] Barker was his name, in Mark Kirkpatrick's lab. And David had some *C. elegans*, so he was studying the function of the mating plug in *C. elegans*, but sort of from a...studying the evolutionary relevance of this. There were some populations where the male leaves the mating plug that...I think...he was testing whether it really prevented mating with another male or slowed it down and this sort of thing. He had some worms, and so he agreed to give me some. I took them downstairs and started making some plates of agar.

I had taken the Woods Hole embryology course in 1989, and this must have been in 1990...it probably was about the fall of 1990, but I'm not sure. And when I took the embryology course, Paul Sternberg—a *C. elegans* scientist—had taught in it. He and a nice guy who was acting as a TA for him, Raffi [V.] Aroian, who was a postdoc in his lab, came out and taught about *C. elegans*. We had plates. We all brought dirt with us to the summer course, at his request, from different places and we'd put them on plates and watch worms crawl out and started looking at diverse worms, which Paul's lab actually now has. One part of the lab has been studying evolution of development and he's had some terrific people come out of there, studying evolution of development. And, I suspect, this was the beginning of his interest in this sort of thing. So, we treated these wild worms as if they were *C. elegans*, and looked at cell divisions and that sort of thing. I had seen worms before: we had done laser ablations in this course in Woods Hole, ablating single cells with a laser focused through the microscope. And then I hadn't thought about them for a while and then I came back to them in Austin. So, I remember when I started making plates, I had that sense that things were going right when I smelled the plates after making them up and it brought me right back to Woods Hole, and I thought, "This must mean I haven't screwed this up, at least not so badly that it smells completely different."

And so I had glass plates—which no one uses in *C. elegans* now—big, 10-centimeter [diameter] glass plates, and had worms on them. I got some bacteria [with] the worms from David and started growing them. I do remember, after working with them for months, these glass plates were...it became a lot of work to continually make up agar in these glass plates and

then clean the glass plate and run out of...we only had about 20 in the lab. So, at one point I remember going to Gary and said, "I'd like to switch to using plastic plates." He did not have tons of funding, and so we didn't rip through supplies like some labs would now in a way that seems, actually, efficient. He listened to the argument and he agreed to let me start buying plastic plates—which to *C. elegans* people now is hilarious because everyone uses plastic plates.

I got the worms and I started trying to do embryology experiments on my own. I looked in the literature and found experiments by Jim [James R.] Priess where he had put holes in the egg shell and pushed cells out and made up the medium that he had used, and then tried putting embryos down on a slide and then using a needle controlled by a micro manipulator on a microscope to hack away parts of the egg shell. And, after bludgeoning a lot of embryos, found that I could actually make holes. I could get cells out. The cells inside would continue dividing, but they'd divide once or twice more and then quit. The ones on the outside, I think, probably did even worse. (I've got my old notebooks on this still, at work.) I did this for a while, and then I remembered putting together a table of every variable that was present in the...there was the slides. I wasn't sure I was washing the slides well enough. Maybe there was some contaminant on them that was making the embryos sick. The medium may not have been good enough. The needle might have had something...So, I put together a table of all these things that I could change, and started changing one at a time, and then in different combinations. At one point Gary said, "I think you're going about this all wrong." I couldn't imagine how I was going about it all wrong because I was doing it as systematically as possible and I was sure that at some point I would get this right. He goes, "Why don't you just call someone who can do it?" [laughter] I felt so stupid. I called Jim Priess, who had done these things, and he recommended Lois [G.] Edgar.

When I see Lois, I always am tempted to get down on my knees and thank her for giving me a career. Lois, at the time, she was working in Bill [William B.] Wood's lab. But she's got a very interesting story. She was a technician for Sydney Brenner when her husband, Robert [S.] Edgar, was working on phage assembly. And then later she got her Ph.D., and she must have been in her late 40s, early 50s. I mean, she got her Ph.D., I think, around the same time as her son did. Her son, Bruce [A.] Edgar, is a famous *Drosophila* cell and developmental biologist. He works on cell cycle. She got it in Calgary, [Canada] with Jim [James D.] McGhee. And part of what she did then was study gut development and did experiments that suggested there weren't any cell interactions involved. So, what she would do is taking embryos of early stages, squash them between a slide and a cover slip and get it to the point that some of the embryos were killed and some were not. Then she would pick out the ones where only certain cells had died and use those as experiments where she had killed those specific cells, and then asked how the other cells developed in the absence of those cells. The idea was, you could find interactions by doing this if you eliminate a source of interactions. It was a low-tech way of doing it, but it was a clever trick for doing manipulations where it was hard otherwise because there was a thick eggshell on the embryos. But, while she was doing these experiments, which suggested there weren't any interactions, or at least she couldn't find any, she also developed a culture medium for the isolated cells. What she did was, she's told me, she started with other peoples' culture media for insect cells and other kinds of cells and started making adjustments to them. And she would adjust osmolarity to get it right, and then take

eggshells off embryos. So, she came up with tricks for enzymatically and then physically removing eggshells, put them in the medium, and then let them develop for a while and then fix them and stain them for the nuclei and count how many cells there were. If she added something in and there were more cells, she would leave it in. If she added something and there were fewer cells, she would take it back out and then she would address the concentration of each of these things as well. She must have spent an awful lot of time making [this medium].

CARUSO: It sounds like it.

GOLDSTEIN: It has a ridiculous number of components in it, and the first time I made it up it took me two months just to get everything into the lab and make it up. So, she made this up, but then she didn't use it for...she used it for certain kinds of experiments, but not the classic embryology experiments. When I talked to Jim and asked him about this, he told me about Lois' medium. And so, I talked to Lois and I wrote a letter to her and asked her if I could visit her lab and learn how to do this. She was working in Bill Wood's lab in Boulder [Colorado] and I was in Friday Harbor one summer, and then in August, when it was time to go back to Texas, I drove down to Boulder and met her there. She was very nice and very generous with her methods. I remember on this trip, I took a friend from Friday Harbor to Sea-Tac [Seattle-Tacoma International] Airport in Seattle. And on the way, I think there was some smoking coming from under the hood of a car—it was a 1978 Buick Regal with a giant hood—and I was way out by the end, near the battery, and the hood came down on my head.

CARUSO: Oh.

GOLDSTEIN: And I got a bad cut in the back of my head, and in one of my eyebrows. I remember going into a hospital and them immediately asking for my insurance information. And I said, "Aren't you surprised I can speak. I have holes on both sides of my head." So, I got stitched up and then, when I got to Lois' lab...I was there for two days and I was camping in Golden [Colorado], which in hindsight, was really quite far...much farther than I needed to be, but I didn't have a [detailed] map and I saw a state park and thought, "I'll camp there. That'll be cheap." I went in for, I think it was two days, maybe three days, and she showed me how she did things for an hour or two each day. And then I talked to some people in the lab and met Bill Wood, who's a fascinating guy. He's one of the people I really admire in science in that he succeeded in multiple areas. He succeeded in studying *C. elegans*' development, sex determination, phage assembly. He studied phage assembly when he was young and he was a member of the National Academy [of Sciences], I think, at thirty-three. But before then, he sang and played guitar on Joan Baez's first album.

CARUSO: Oh, really?

GOLDSTEIN: Yes, which is very strange because, when you talk to Bill now, it's hard to get very much out of him. He tends to answer in one word responses. But he's got an absolutely fascinating life. And I really admire the people who can avidly pursue multiple things like this.

So anyway, I visited Lois. She showed me how she did this. And then a guy who was working in Bill Wood's lab as an M.D./Ph.D. student, Mark [D. Yandell]—I can't remember his last name right now, but I can get it if you want—he was an M.D./Ph.D. student and he just learned how to take out stitches, and so he agreed to take out my stitches. So, in the lab with the forceps, he took the stitches out for me. I connected with him again recently. He's now a bioinformatician. He didn't end up doing medicine afterwards. He does bioinformatics with an organism, not *C. elegans*, but this other organism he adopted—it's about to have its genome sequenced—and he's got funding to do bioinformatics on these sorts of new organisms. It was funny to reconnect and say, "Are you the guy who took my stitches out?" almost two decades ago.

Lois was very generous teaching what she knew. And I went back and started doing experiments and then things flew. They really just flew. So, I started off... what I wanted to do was... we knew the endoderm (the gut) developed from one cell of the eight-cell stage based on old lineage work. So, at this stage, the complete lineage was known based on the work of, mostly, John [E.] Sulston and some other people. We knew the endoderm developed from one cell of the eight-cell stage. I did not care which tissue I worked on, whether it was endoderm or muscle.... I wanted to study how cell fates were specified in general. But the endoderm was the first to be set aside like this. So, at that stage, all the other cells are going to contribute to multiple tissues still. There was a really easy marker for endoderm where, basically, if you did an experiment and you let the embryo develop overnight, you could check the next day. Just change the optics on the microscope, and see whether or not endoderm had developed. The endoderm in *C. elegans* developed birefringent granules that under polarized light are really obvious—they light up. So, I thought, "This is something I can do. I can do the manipulations and not have to go through immunostaining the next day and lose the embryos." Eventually I did the immunostaining, but it turned out to be tricky to get it to work with small numbers of embryos that weren't attached to anything.

I did this. At first... I remember when I'd isolate... so, I was going to try isolating this E cell, this endoderm precursor from the eight-cell stage, but I thought it was going to be easier to start with experiments at the two- and four-cell stage where it's easier to identify the cells. I noticed when I'd isolated the endoderm precursor from the four-cell stage, sometimes it'd make endoderm, and sometimes it wouldn't. For a time I thought that's going to be this story, right? Then I started to look at exactly... so I was writing down exactly when I did it and when I saw divisions. I noticed that there was sort of a trend where, when I was isolating the cell early enough, it would never form endoderm. When I was isolating it later, it would often form endoderm. The ones I was isolating really early didn't appear to be to be damaged when the divisions were going on. So then I thought maybe there was something interesting here.

I'd actually taken a class specifically on embryonic induction—on the kind of cell-cell interactions that specify fates, taught by Antone [G.] Jacobson—and I'd learned about inductions and there's a lot of really interesting phenomena when cells interact with other cells to specify fate, especially in vertebrate embryos, [phenomena] that are still, I think, not well understood by the molecular explanations where, you know, ligand and receptor and signal transduction pathways...And so, I was really fascinated by this stuff and I knew from what he was teaching us and from reading the papers, that inductions normally take hours or maybe days. The fact that these things didn't make gut when isolated early in the cell cycle, but did later, suggested the possibility that there was an interaction occurring, very quickly, right then. But to me, it seemed unlikely because these things took a long time.

But then...almost all that work had been done in vertebrate embryos where people had actually done experiments to ask: "How long does an interaction take if you take off the signaling cell, put it back on at certain times? What's the time window when a tissue can respond and that sort of thing?" So, I started timing them. I still have the notes at work on putting them in order of the time that they'd been isolated and looking at whether or not gut developed and started to notice this trend and started doing more to test the hypothesis that first, simply, is this really true that if I isolate them early they never form gut, and if I isolate them late, they usually do. And it became really clear that this was standing up.

Then the hypothesis was: when this cell is isolated early, it's missing an interaction with a cell. And so then I just started putting this one cell back together with each of the other three cells of the four-cell stage and found, sure enough, there was one that could rescue gut development, and it rescued it every time. In every case when you isolate the cells...they were named by Germans one-hundred years ago, and the names for the most part don't make sense to us...

CARUSO: [laughter]

GOLDSTEIN: ...in some ways they do, but maybe it's not worth going through all that. There was one cell called P2—it was the smallest cell. There were four cells and one was smaller than the others, one was medium-sized, two were larger. The smaller one would signal to the medium-sized one, P2 would signal to the EMS, to produce the gut. This was exciting. To me it was very exciting because I'd read a lot of papers on cell interactions. I knew, especially in *Xenopus* embryos, there was a lot of work on molecular basis of cell interactions. I thought just finding a new cell interaction that specifies a fate in an organism...it was something I felt I could stand on, right? I knew I'd found something that, at least to me, would feel like I'd ratcheted to the point where I'd found something that would stand, right?

CARUSO: And how did Gary Freeman feel about this as the project was going on?

GOLDSTEIN: Well, Gary was positive about it, but he never really was effusive about it. I mean, up to the point where...I remember when my paper on this—when I'd finally done the experiments and my paper on this got accepted in *Nature*⁴—I remember going out to drink with a friend [Aaron M. Zorn] and his advisor [Paul Krieg] and not my own. [Gary] was very positive and encouraging, but I guess in a way...with my own students, when something goes really well, we have champagne or we go out for a beer. We celebrate it in a way that they remember that we celebrated it. I have a hard time remembering if we did anything. He maintained some skepticism for a while, that it was possible that when I isolated the cell early, I was just damaging it. Then when I put a cell back on and rescued it, it suggested it probably wasn't damaged, but it didn't completely rule that out yet. Eventually, I remember the experiments had gotten to the point where I could see that this one cell, the small cell, could rescue gut development in the medium-size cell, but neither of the larger ones could. So, now we started to think, "Okay. If it's just damaged and having other cells around helps, it doesn't look like that's the case. It looks like a specific cell's doing it." And it made sense that the medium-size cell would form gut from one side and other tissues from the other side. And the cell that was inducing was on the side where gut was going to come from.

At some point, he suggested, he said, "Well, why don't you go to the *C. elegans* meeting and describe this and explain it to people?" It was a really exciting time for me. So, it was 1991, the summer of 1991. I remember I was living in a place that I moved out of just before, because I knew I was going to be gone for the summer, and stayed with a good friend mine, Koan Davis, who...she's not a scientist and never studied science, but was always really interested in hearing about what was going on in the lab. She's still is a fan of...she'll ask about experiments. And I think it's always been a great exercise for me. I've always had friends, who were really intellectually curious but not necessarily scientists, who would ask questions about what was going on and I'd be forced to explain it in terms that intelligent [people], but non-scientists could understand.

And I remember I was sleeping on her floor. She had a studio apartment and I was sleeping on her floor, for about a week I think, before the meeting, and then a couple days afterwards before I went up to Friday Harbor for another summer. I went to this meeting and when I came back, she said, "How did it go?" I said, "Boy, it couldn't have gone better." I was speaking in an embryology session and I remember Bill Wood was speaking in the same session. While at the meeting, I heard some of the stories about Bill Wood and his musical past as well and I was very excited to hear about this. I was really impressed that he was, probably, the only professor who spoke at the whole conference. So, the tradition at the *C. elegans* conference is that the students and postdocs who were doing the work are the people who gave the talks. And so it was really exciting to be speaking next to this guy. I felt sort of humbled by, "Should I really be up here?" I didn't realize he was in the National Academy at about age thirty-three, or even what that meant at the time. But still, I knew he'd done some really cool experiments around the same time, too, that I really enjoyed. So, I gave my talk. At the time, I was staying with a friend, Bill Boyd, who was my roommate my last year in college who was

⁴ Goldstein, "Induction of Gut in *C. Elegans* Embryos."

then living in Madison [Wisconsin], and I stayed on his porch and slept. This wasn't completely outside. It was a screened-in porch. [laughter] I wasn't always sleeping outside. I stayed on his porch. It was kind of funny because I was separated from the meeting a bit in that I was staying on my friend's porch, rather than where everyone else was staying. And then, I knew no one who worked on *C. elegans*. David Barker, who had given me the worms didn't go to this meeting. No one else in Austin worked on *C. elegans*, and I really didn't know anyone, except I visited Lois and had met Bill Wood before on that one trip. I felt very much like an outsider coming in.

The first session I went into, I sat down and I sat next to a guy named Paolo Bazzicalupo, and Paolo had done experiments like Lois' experiments—asking whether cells required cell interactions in the early embryo and had done experiments suggesting they hadn't. I didn't realize who I was sitting next to at first. When I looked at his nametag, I said, “Oh crap.” I said, “I'm afraid I'm about to talk about something that counters something you've done,” and he was very positive about this. I was afraid someone would be offended. I'd never experienced this before. And, of course, for someone who's friendly and open-minded, there's no offense taken for that sort of thing. Although, probably, some people personally would feel some offense. But he was very kind about it, which really started me off on a good foot.

I was staying on my friend's porch, and then I went in and spoke. I remember being very nervous about getting up and speaking to five-hundred people. I had trouble speaking. I was always a very shy kid and I was starting to get some confidence, I think mostly from having some success with doing something on my own. But I still, of course, was very nervous about this. I described the experiments and I made a terrible mistake, which was I made no mention of Lois Edgar's development of these techniques. In hindsight, I realize people were interested in those experiments and—I think it was published in *Nature*—not just because I'd found an interaction that wasn't known before in a system where there weren't many interactions known, but also because it introduced a new technique that could work synergistically with other techniques already in *C. elegans*. And that was not my contribution. That was Lois', right? So I gave the talk without ever mentioning how I did the experiments. I just said, “I isolated this cell and this is what I found, and then I did this.” And then, at the end, I talked about experiments I did after submitting the abstract, but before the meeting, where I'd asked: “When do the cells have to be in contact to get a successful interaction?” And it suggested, already, that this was a very quick interaction.

Someone actually asked in the questions...one of the questions was, someone raised their hand and said, “How did you do that?,” which was a great question, and so I, nervous, stood up and explained how I did it, and again, never mentioned Lois. I feel awful about it still. When I see Lois at meetings...the last meeting I saw her at, she says, “Oh, no. I don't have a pen.” We were sitting down as the session was about to start. I said, “I have a pen. I'll give it to you, Lois.” She says, “This is a nice pen. I'll give it back later.” And I said, “Lois, please, keep the pen. You gave me a career. I'll give you a pen.” She said, “Stop saying that.” She's very modest and a little shy. So, I felt bad about that, but I was very happy otherwise with how the talk went. I remember being very nerv...this was in the day when people used actual slides. I was very nervous about the slides getting broken or not getting there or getting damaged or

something, so I took an entire carousel with me for about eight slides, and then went back to my friend Bill's house in the evening and stayed up late talking to him about how it went.

It turns out he had showed up for the talk and was there and I didn't know at the time. So, that was sort of fun. He's not a scientist. This was a really exciting time. And it was fun. A couple years ago I got to go back to a *C. elegans* meeting and give a keynote talk on this area of development, early development. It was supposed to be partially historical, so I talked about historical stories I enjoyed, like the stories about Bill Wood and stories about Jim Priess—who had done some really nice experiments at the time—and got to talk about my experience of first going to the meeting. It's nice. Sometimes people tell me, "Oh, I remember that first meeting." I guess it was unusual for an outsider to come in and do something very different.

CARUSO: And so, you'd say the community received what you were doing pretty well, even though you were going against some of the traditional...?

GOLDSTEIN: For the most part, really, very well. There were some really big exceptions, but for the most part, really, very well.

CARUSO: Were those big exceptions some of the people that were advancing the original theory, or...?

GOLDSTEIN: No, actually... Jim Priess was a holdout for a long time. So, Jim's probably one of the best developmental biologists in the *C. elegans* [field] and is a really clever guy. Jim's got an interesting story that he, actually, was invited to join the National Academy and said, "No, thank you," because he likes to do experiments and the story, I've heard anyway, is the reason is that he likes to do experiments and you have to deal with PNAS and other National Academy duties. And he just does not want to be piled on with more duties that'll stop him from doing what he loves. Jim was a holdout for a long time. At the meeting itself, people were very nice about it. I remember sitting down, after the talk, having a meal with Judith Kimble and Bill Wood. I felt lucky to be in... I was twenty-three years old and was sitting down with people who... I'd read their papers and had never met them before and they were terrific scientists. I felt lucky to be there. And they were very kind with advice. Judith, I remember, being very clear about saying, "You should publish this right away." And I said, "Well, I'm going off for the summer, back to Friday Harbor, to try some of the ascidian experiments that I wanted to continue. And she looked at me and she [repeated], "You should publish this right away." I think she was being clear that this was a competitive field. Although people were friendly, for the most part, it could be competitive and there was a chance that I would lose the ability to announce this result if someone else ran over it. Which was kind of her, to take the time to explain this to me.

I remember Bob [H. Robert] Horvitz—who is now a Nobel Prize winner [2002 Nobel Prize in Physiology and Medicine]—coming up to me and asking me all sorts of questions and saying he enjoyed it. He didn't have a name tag on, I think, because everyone in that field knows Bob Horvitz. At the end of the discussion, I asked him who he was because I didn't know who he was, which seems funny now but some of the students and postdocs there... I told them that story then. At the time they thought it was very funny. So, people, for the most part, were very positive about it, at least the people I spoke to, which may have been a biased sample. Jim didn't believe it for a while. And we've discussed why he didn't believe it at various times in my career... He was one of the two reviewers on the paper.

I went back at the end of the summer and did a few more experiments, but mostly wrote up what I'd already had. Then, at the time, I was applying for postdoc positions. I wanted to go to a place where I could do what I wanted on my own again. This was unusual, right? So, Julie Ahringer, who is now faculty in Cambridge, who has her own lab in Cambridge, was a postdoc in John [G.] White's lab and told me, "John White's lab is a place you can go and do what you want." And so, at one point I needed letters of recommendation. I applied to John White, I applied to Jim Priess, and I applied to Bill Wood. But I knew that John's lab was the place I wanted to go to most because my initial discussions with Jim and with Bill suggested I really couldn't do, completely, what I wanted. Although, knowing what they're like, I bet they would have encouraged it once I was there. They weren't as positive about it before. What was I going to say? Oh, so, at one point I needed letters of recommendation and I could see the letters of recommendation that people were writing for me in Texas because some of them shared them. And they would say, "He's good with finicky techniques and can get them to work." And I thought, "What I really need is someone who'll say the importance of this in the field." So, I thought, "I'll write to Jim to ask if he can write a letter for me." Jim agreed to write a letter for me and then later changed his mind. So, actually, I think I applied for six postdoc fellowships. He wrote for the first three but not the last three, I think. And when he changed his mind, he wrote back and said, "Look. I don't know you as well as I know the people who work in my own lab. The people in my own lab are very competitive and I feel I can't write you as strong a letter as I can for them." The people in his own lab at the time he was talking about it were Craig [C.] Mello, who went on to win the Nobel Prize [2006 Nobel Prize in Physiology or Medicine, Class of 1995 Pew Scholar], and Bruce [A.] Bowerman, who's at least as good a scientist. He's a fantastic scientist and quite famous for work on *C. elegans* development and cell biology. And now I understand why he couldn't write me as strong a letter. But also, he just didn't know me that well. And if he was skeptical about the experiments, I imagine it would be difficult to write a good letter. What he did was, he eventually wrote back to me and said, "I don't feel comfortable writing the letter for these reasons," and really took time to explain what his problem was with it.

When I got this letter, I looked at it and I thought, "That's a funny font I've never seen before. The letters looked really separated and the paragraphs started pretty [far] from the left side. Now, I don't know why I noticed this, but, when I got my reviews for my paper soon after that, one of the... This was at a time when they were not electronic. You'd get something faxed and they'd just cut off the name. I thought, "That's a funny font with the letters pretty separated and the paragraphs started pretty far out. Actually, I have the papers here. I can show you. I

took them and held them up to the light and could see they matched up exactly. And so, I knew this review was from Jim. I feel very stupid about this because I believe in anonymous peer review. I think there's a very good reason for it to be anonymous and I don't like playing games with this, but when I knew the answer was sitting right in front of me, I couldn't help but check: did they line up perfectly? And they did.

The other reviewer I found out, very soon afterwards, was Iva Greenwald, who's at Columbia [University], because, around the time the paper was accepted, she phoned me and said, "I was the other reviewer," [laughter] because she wanted to use the paper in a class she was teaching or something like that. So, it was strange. I knew who both reviewers were pretty early on. Iva was positive as can be, and Jim was not.

And Jim's concerns had to do with...the main substantive concern, I think, was that when you isolate the cell and it doesn't develop to produce gut, what does it do? And his concern was either it dies or it doesn't develop quite far enough, and so you don't...although it would form gut if it would develop long enough, it hasn't developed quite that long. I had found that the timing of divisions that the cell would take on was...it was exactly as its sister cell would take on. So, it looked like, when it was uninduced, it was acting like its sister cell. But at the time, I couldn't follow differentiation except for the gut and these isolates. Later, I figured out how to do that and confirmed this. But at the time I submitted the paper, I did not know this. And so, he wanted to know what these cells form when they don't form gut. Again, I have the reviews. This held it up for a while.

So, it went through three rounds of review. One round I got a really positive review from Iva; a negative one from Jim, with these concerns. I responded to them. At the time I remember being very angry and thinking someone wasn't playing fair. Now when I look back at them, I don't think that was the case. I think he had an honest difference of opinion.

CARUSO: Right. But it is also your first paper. So responding...

GOLDSTEIN: Yes. Although, in hindsight, I think his request for a burden of proof was higher than, I'd like to believe, I would ask for now of someone for similar kinds of experiments, but...at least for similar kinds of experiments at the time when they were more difficult to do. Then it went through a second round. I responded to the editor, went through a second round of review, and I got back the shortest review I've ever heard of from Iva. It said, "I liked it the first time and I like it this time." [laughter] And I got, essentially, the same review, similar concerns, from Jim, just laid out in more detail. I went back to the editor...I wrote a letter explaining why I thought the reviewer, who turned out to be Jim, was not being fair and asked for new reviewers. And, I realize now, it's rare...usually they [editors] lose patience for you pretty quickly. But luckily they didn't this time. So, they sent it to two new reviewers and sent everything—the paper and all the reviews up to that point—and both the new reviewers were very positive and so it got in.

CARUSO: I'm guessing you don't know who the two...

GOLDSTEIN: I don't. No. I haven't done any font analysis.

CARUSO: [laughter] And no one called you up and said...

GOLDSTEIN: No one told me, no.

CARUSO: ...“I want to use your paper.”

GOLDSTEIN: No.

CARUSO: All right. Well that seems like a very excellent start to your career. And this is, pretty much I guess, while you were...were you writing your dissertation at the same time? Was your dissertation just a collection of papers, or was it something independent?

GOLDSTEIN: Yes. I'd done this, and then I'd done some other embryology experiments that led to the second paper.⁵ And then I'd done some others that led to part of a third paper,⁶ but the rest were written...I was applying for postdoc [positions]. I was on my way out as this paper was getting published.

CARUSO: You also received the award for Outstanding Doctoral Dissertation in 1993?

GOLDSTEIN: Uh-huh.

CARUSO: Was it science-specific, or was it about...what is that award about [...]?

⁵ B. Goldstein, “Establishment of Gut Fate in the E Lineage of *C. Elegans*: the Roles of Lineage-Dependent Mechanisms and Cell Interactions,” *Development* 118 (1993): 1267.

⁶ B. Goldstein, “An analysis of the response to gut induction in the *C. elegans* embryo,” *Development* 121 (1995): 1227-36.

GOLDSTEIN: I got two awards when I graduated. One was this one, and the other was I was the five-hundredth Ph.D. recipient in the zoology department.

CARUSO: Oh.

GOLDSTEIN: It was very strange after all this hard work to then get a turnstile prize. The president of the graduate school showed up to the party after my defense because they decided to make a big deal of this five-hundredth. So I have—we took it down off the wall in my mom’s house—we had the five-hundredth Ph.D. thing framed but I don’t think I’ve ever had the other framed. [laughter] The outstanding dissertation prize, it’s given to, I think at the time, it was three students each year in the university, and it was dissertations that they thought were good. Someone would nominate them for this and then it came with some money.

CARUSO: Okay.

GOLDSTEIN: What was I going to say about it? I think some people on my committee wrote letters for it, but I don’t know which ones, and so I’ve thanked some of them saying, “I’m not sure if you wrote a letter, but, if you did, thanks.” It came with some money and I found out about it after I was already in England. I did write back and thank them. The notice that I was going to get this said that it would be presented at graduation, which...I was in England. I wasn’t going to be back for...I left as soon as things were done, as soon as I defended...pretty soon after that. It came with money, and I was annoyed to see that it was the president of the grad school who was going to do this because this guy I was, again, sort of vaguely politically active in grad school, but with graduate student issues. Actually, I was more active...the first Gulf War was going on and I helped organize protests in Austin. We protested. Other people were organizing and I put in some help. But we got paid way less than almost anywhere else when I started off. At one point, they were going to take away our health insurance—saying we weren’t real state employees, we were students—and someone was blind to the fact of how little we were getting paid and how much health insurance would cost and the graduate student population would have been decimated. It was, just, a blind mistake. They were going to double our tuition at some point. I was active in a group that they came up with a terrific way to deal with this which was to show how much the graduate students did by teaching all their classes in front of the main administration building for a week or a few days. I think when the health insurance was going away, they did this. It was the trustees of the university had a lot of power, but the trustees were mostly west Texas oilmen. They weren’t even in Austin, most of them. So, the trick was you had to do something that would also get you on the news so that they would watch the news and...

CARUSO: Right. And see...

GOLDSTEIN: “What the hell’s going on in Austin?” So, they did a fantastic job. They gridded out this huge concrete area. And if you needed a blackboard, if you really, really needed one then you’d sign up for one. Then they’d come and it would get wheeled to your square at the time your class started. We’d teach out there. The students would say, “What’s going on?” We’d explain and then teach our courses. It was incredible. How did this lead me to this? What was your question again?

CARUSO: I was...I don’t actually remember what the question was.

GOLDSTEIN: You’re not sure either? [laughter] Let me think here.

CARUSO: Oh, yeah. We were talking about the award.

GOLDSTEIN: Oh, so I dealt with this—[William S.] Livingston was his name. I dealt with him a few times before trying to get to meet with him about these things. He had an office at the back of an array of secretaries’ offices, where you had to get past the first one to get to the second, and past the second one to get to the third one. And if you got very close, you to go his secretary and you knew you were important at that point, right? But meeting him was very difficult. At one point, I and some other students had put together a list of what grad students get paid at various universities—what their tuition was, whether they pay health insurance—and it showed us near the bottom of the list. I think people sometimes respond, “Well...” If they’re told we’re terrible compared to others, they’re concerned.

So, I remember getting to the last secretary and then hearing his booming voice when he overheard what was going on outside. He said, “Goldstein!” and called me in. He was, actually...at the time there was a phone when you’d register for your classes in Texas, there was a phone system. And the voice on the phone, they gave it sort of a character, I guess, to make it friendly to the students. It was Tex. And Tex, at the end of the phone call, when you’d gotten all your classes set up by phone would go, “Goodbye...and good luck!” in a booming voice, and supposedly, it was his voice because he had this...so I recognized this “Goldstein!”

He was the one who showed up for the party after my defense. My graduate advisor told me, afterwards, that it was ungracious for me to attack him so much at the party. It was hard to get a meeting with him. The only meeting I got was the time he was shouting, “Goldstein.” And there were serious concerns—not that I was bad—that he wouldn’t even meet with people, not just me, but with other people who were involved. There was a secretary, at the time, that often would give us information. So, you could get things from public records. If you knew that a meeting had happened, you could get the minutes from it, or something, through [The Texas] Public Information Act. She would tell us when these meetings happened. But she

would do something funny with her phone each time and I wonder if she worried that her phone—it seems so silly...

CARUSO: That it was tapped...

GOLDSTEIN: Right.

CARUSO: Yeah. Bugged somehow.

GOLDSTEIN: So, she was our deep throat [...]. It was very strange. When I got the award, it said it was going to come from this guy. And so, I wrote, again, perhaps a very ungracious letter and said, "I'm very pleased that Dean Livingston is going to give the award. I've actually had several chances to interact with him before," and I described the interactions and they were not positive. And I said, "I'm not coming back for the graduation and I'm going to use the money and buy a banjo." [laughter] He read out the letter at the graduation.

CARUSO: Oh, really?

GOLDSTEIN: Or, at least, parts of it. I found out through friends.

CARUSO: So, were you accepted to other postdoc positions than John White's or...?

GOLDSTEIN: I talked with Jim Priess and I talked to Bill Wood, but I don't think I ever actually wrote them a letter to formally apply. I wrote to John and he was positive.

CARUSO: You wanted to go mostly because of independence, right? You wanted to pursue your own projects. And, from what I understand, shortly after starting you were completely independent because he, John White, moved out to Wisconsin.

GOLDSTEIN: Yes.

CARUSO: How far into your postdoc was that?

GOLDSTEIN: It was about fifteen minutes. [laughter] Actually, he was there for the first six months. It was about fifteen minutes into it when he told me this. This is a funny story. First, I was due to arrive 1 November 1992. I remember this really clearly because he told me...he said...actually, I saw him at a meeting the summer before this fall. He said, “No postdoc shows up the date they’re going to say. They’re always months or up to a year late.” He says, “Don’t worry about this. We can work that out.” I said, “Okay.” I said, “But I really plan on coming 1 November 1992.” He joked later that he was right. I arrived the morning of 2 November 1992. I flew on November 1st. I flew to London [England] and took the bus up to Cambridge, and then I got off at the bus station in Cambridge, and he had agreed to come meet me and take me to the lab, which was just a mile and a half away. He drove me to the lab. I was impressed, right away, with his driving style. I thought I was going to die. He drove like a New York City [New York] taxicab driver. Then we got into the lab and we went to his office and he said, “So, what are you going to do while you’re here?” and that was how he ran the lab. He didn’t tell people what to do. He asked them what they were going to do and gave input. When he wrote me an offer letter, he said, “I’m pleased to be able to offer you a position in the lab.” He says, “Unfortunately, that’s all I can offer.” He says, “You need to get your own funding.” It’s difficult, of course, to get funding in advance. You need to be applying well enough in advance, but, luckily, I was at the time.

I try to do a similar thing with my own postdocs now. And, of course, very few people apply long enough in advance, with a clear plan from the beginning, that they can apply for funding and get it in time. So, luckily, this worked out there. He said, “What are you going to do?” and I started explaining it and about halfway through, he interrupted me and he said, “I think I should tell you, I might be leaving soon.” I never actually finished telling him what I was going to do. I never got to the second half.

Then he took me to the lab. It was a small room. Among *C. elegans* biologists, it’s a famous room, in that a lot of the early work went on in there. I think I had the same bench that Jim Priess had when he was a student there. John Sulston did the lineage in there. It was Sydney Brenner’s space for his students and postdocs for a while. So, I got to this room and there was about...he showed me a bench that was about four or five feet long and there was a wooden stool, and that was my desk, my bench, and everything. But the first really strange thing was he says, “This will be your bench.” And there was clearly a man standing at it. [laughter] There was a guy from Japan, who was standing there working, who looked up with a surprised look. John looked at him and he said, “You have to go now.” So, the story was, that I’d heard—I’m not absolutely sure that it’s true—but the story I’d heard was this guy had written to John and said, “I’d like to come do some work in your lab.” And John wrote back and said, no, that he didn’t have space, and however, John probably gave a very British “no,” and this guy showed up one day, misunderstood the response and arrived, and so he was told, “Okay, you can work here, but just until the next postdoc comes. Don’t worry. He says he’s coming in November, but it won’t be for a while probably,” and then I appeared.

CARUSO: Wow.

GOLDSTEIN: This style of having four or five feet of bench and no desk was Sydney Brenner's. Sydney used to say that desks encourage time-wasting activities. When we were writing a paper, it was difficult. I remember having an Apple IIe, an old computer, sitting next to the dissecting scope while I was writing a paper and trying to do experiments in the same space. I know some people would bunk their activities. They would sit down to do experiments and stand up and use the first shelf to do their writing and reading and stuff.

CARUSO: Wow. Interesting workspace. And, of course, the guy you show up to work with is leaving immediately.

GOLDSTEIN: Yes.

CARUSO: So, what projects did you wind up pursuing?

GOLDSTEIN: [Can we stop for a break?]

CARUSO: Okay. Sure.

GOLDSTEIN: Okay.

[END OF AUDIO, FILE 1.1]

CARUSO: This is the second session of the interview with Bob Goldstein taking place on 24 April. So, I believe we left off with talking about, you arrived in the United Kingdom, John White told you that he was going to be leaving, which I guess in terms of your overall plans, that didn't necessarily matter much because you wanted to work relatively independently. And I was asking...

GOLDSTEIN: He left the equipment behind, which was absolutely critical.

CARUSO: Oh, perfect, perfect.

GOLDSTEIN: There were four of us working in the lab, and all four of us stayed behind and all the equipment stayed behind. John develops equipment...he was trained as a physicist and moved into biology afterwards. And he's one of the people who developed the confocal microscope. We had *the* original confocal microscope [used for biological research] in the lab, so he didn't take that with him. He had developed a bunch of other technologies. Luckily, they stayed behind.

CARUSO: Wow. That's interesting. I mean, were you at all nervous using those since the confocal was the original? Were you nervous that you might snap something?

GOLDSTEIN: I didn't realize it was the original one at first. And by [that] time they'd licensed it to Bio-Rad [Laboratories] and Bio-Rad was selling them all over the world...But when I discovered it was the original was when someone came—it was a Japanese scientist who came with a camera to take a picture of it—I thought, “Why are they taking a picture of our confocal?” Steve [Steven N.] Hird, who was a grad student in the lab, who I worked together with a bunch, we actually approached a problem from opposite sides and [for a while] didn't realize until we were both working on it and ended up working together. He had covered the thing in stickers from his motorcycle magazine, so it was covered with motorcycle stickers. [laughter] And it was this historical piece of equipment. So, I guess I was a little nervous at first because I didn't...Gary Freeman's lab had, essentially, no equipment. We had dissecting scopes. We pulled glass needles over flames most of the time and that was our most important tool. And then we had one compound scope that we used for looking at everything else. There was one other piece of equipment in the lab. It was a needle puller which worked by gravity. It was an old-fashioned needle puller. We'd occasionally use that when we needed to make precise kinds of needles. But pulling glass needles over a flame was almost the only thing we were using. My Ph.D. was only four years, but in part, just because there was a limit to how much you could do there. No one, I think, actually has done a five-year Ph.D. in Gary's lab. I think everyone did four to four and a half years.

CARUSO: Oh, really?

GOLDSTEIN: I mean, partially, some people did very well and got things done quickly, and part...Gary encouraged people to leave earlier than five years. He felt the learning curve really flattened out by five years, which, I think, is probably true. But the productivity curve continues to go up. In fact, it's often just going up around that time. So, I went from a lab with essentially no equipment to one where we really had state-of-the-art stuff that, it was terrific what could be done.

CARUSO: So, how were things arranged with White leaving? Was it still his lab even though he had left, or did it revert to someone else?

GOLDSTEIN: I'm not sure. We, literally, didn't have an advisor. I think we called it the White lab. I'm not sure. But there were four of us in there, [Julie Ahringer, Steve Hird, Benjamin Podbilewicz and me], and we all continued to do our experiments after he left. We were all doing independent work. This... the LMB [Medical Research Council Laboratory of Molecular Biology] in Cambridge had a history of *C. elegans* postdocs, mostly American, but some not, coming to do independent work and, really, doing their own thing and then going back and starting a lab. And a lot of the people who did are now famous biologists like Bob Horvitz and Cynthia [J.] Kenyon and Judith Kimble and all these people. So, there was this long tradition of people working independently. And then Jonathan Hodgkin's lab was still there, and he had some postdocs who worked pretty independently. John Sulston was there, but while I was there he transitioned to the Sanger Center [Wellcome Trust Sanger Institute]—the new institute they built for [genome] sequencing. There were a few groups with independent postdocs. And interaction with other postdocs...these were some of the most valuable interactions we had. It was a great environment. People would challenge each other constantly. You couldn't get away with working on crap there because another postdoc would tell you [that you] were working on crap. Even if you weren't, they would tell you that and you'd have to defend yourself. Mostly in a friendly manner, this went on, but it was a great environment for that. People were not sitting around doing what they were told; they were doing something they were driven to do. I think a lot of people who worked at the LMB, at this time and earlier, the way they do science and the way they think about science was really shaped by what was going on then and the way people thought and the way people encouraged people to think independently and all this. I think I was really affected by that.

CARUSO: Were there lab meetings?

GOLDSTEIN: I think, once, Julie Ahringer decided we should have lab meetings and, I think, we had one lab meeting. Every Friday we had worm group meetings. So, someone from the *C. elegans*, one of the three or four *C. elegans* labs, would give a talk. [White, Sulston, Hodgkin], Donna [G.] Albertson was there too, and had people working with her. Someone from these groups would give a talk on a Friday afternoon, and there'd be snacks and a talk and people would challenge each other. They were always really interesting to listen to because, if there were fifteen postdocs and five or ten grad students, there were twenty to twenty-five different projects that—they really were almost completely independent projects and the people would have to explain it from square one. It was really nice that way. And then afterwards we would all go to the local bar.

There's a bar on the campus of...it's on a hospital complex. So, there was the Frank Lee Centre, the local bar. And we'd go there and John Sulston would go and Jonathan Hodgkin and some other people, so most of the grad students and postdocs. John Sulston was always very nice in that he bought us beers. He would always get a tray of pints the way people would buy a pitcher in the U.S. They'd have a tray of pints, and they were very good at pouring the pints

into other pints by doing it very quickly. It was great being able to sit and talk with these people and they...from science to social life, it was seamless.

CARUSO: How did your funding actually work at the time, from the basic of you getting paid to requesting equipment when you needed it, or supplies?

GOLDSTEIN: The system at the LMB is unusual in that, we like to call it, the system was “ask and you shall receive.” They were funded directly, as far as we could tell, from the Medical Research Council. And when labs wanted equipment, a clipboard would go around with an empty list and people would write the equipment they wanted to buy. Once I saw one of these lists, and there was dissecting scope, three-thousand pounds, something else. And occasionally you’d see a whole microscope there for twenty-thousand pounds to thirty-thousand pounds. And then, on one of these lists, it said a single mode-lock, some specialized sort of laser that John and Brad Amos—the other person who helped develop the confocal—that they wanted for some imaging experiments they were doing and it was, like, a one-million pound item, and it was sitting on this clipboard list. This was how it worked. I’m not sure everyone would have gotten away with that. Them developing the confocal actually brought a lot of money in, and there have been a lot of projects that have brought money in to this, so the place wasn’t actually hemorrhaging cash. They were bringing a lot of money in by some of the technologies they had developed. So equipment...we were well-equipped. I’m not sure we bought any significant pieces of equipment the whole time I was there, because we were very well-equipped when John left.

For supplies, there was a storeroom there that operated like a storeroom [...]. They had a really well-equipped storeroom that had enzymes and everything, down to stuff that you wouldn’t normally have in a storeroom. And then we all had independent funding. I guess, Steve Hird was a grad student at the beginning of this and then for a year stayed on as a postdoc funded by the MRC. But, at one point, all three postdocs in the lab—me, Benjamin Podbilewicz and Julie Ahringer—had funding from Human Frontier Science Program, which gave a nice stipend and an extra...I think it was ten-thousand dollars in supply money. But we got all our supplies for nothing, so we had this extra [money] that we weren’t sure what to do with, for a while. Now, because some of us were publishing without any advisors, sometimes we would get letters from people applying to be a technician or a postdoc or something like that, assuming we were already a PI. And, at one point, we had this notion that we’d get the three packs of ten-thousand dollars together, hire a technician, and hide them in one of the back rooms and no one would notice. We never actually did it. So, somehow it worked out just fine. Not having an advisor, not really having...we didn’t have to worry about funding. It’s strange. It’s hard to imagine how a headless lab would work now in most places.

CARUSO: Yeah, definitely. I also noticed you had the American Cancer Society Postdoctoral Fellowship from 1993 to 1994, which preceded the Human Frontiers Fellowship.

GOLDSTEIN: Right.

CARUSO: How did you find out about those fellowships? Jack [D.] Keene [Pew Scholar, Class of 1985, Pew Scholars Program in the Biomedical Sciences Advisory Member] was mentioning the other day that he had advisors who essentially...PIs who came down into the hallway and said, "Apply for this. Apply for that." Was this something that you were searching out on your own? Did other people recommend these to you?

GOLDSTEIN: I learned, maybe in part because of my bad experiments with trying to develop a culture medium and learning that the best thing to do was get on the phone, that I knew a lot of people had just gone through this. I contacted a whole bunch of people who were new postdocs, asked them what they applied for, and it's the same strategy we use in mutagenesis when we do genetics. Once you hit things over and over again and you're not finding new things, you know you've saturated. So, there were about six places that I knew I could apply for. Julie Ahringer was one of the people. She gave me her list.

CARUSO: You also have stressed, a couple times, wanting to work independent or on your own project. For you, did this also mean not collaborating with people on projects when it looked...when we started, you had mentioned that someone else in the lab was coming at the same project from a different angle. Were you against collaboration generally, or it just something that hadn't...?

GOLDSTEIN: No. I remember at one point, when I was a graduate student, my Ph.D. advisor asking...so, this guy, Dave Greenlaw, who I knew in college, went to graduate school in physics in Austin. And I remember my advisor asking him once when he met him, he said, "In your field, can one person make a difference? Can a single person, working on their own, make a contribution to the field?" I never even thought of that as a question before, I think. It became of interest to me that a lot of the people whose work I admired were people who could, on their own, have an idea, go out and test it on their own and get an answer on their own. And it meant you'd have a lot more freedom to do and think what you want, rather than being slotted into a giant program and making a contribution that doesn't necessarily involve creative thought.

I've always been driven, since then, to do the kind of science where one person can make a good contribution. I tend to steer clear of areas where it will take a huge team working on something. Now that I've got my own lab, I can do a little bit more of that, but I really encourage people in my own lab to work independently. So, it's only now that there are a few people working on related projects that do mesh with each other. The funding system in the U.S...It's hard to avoid that, but luckily it's worked organically, people have the interests, that it's worked out okay there.

So, no, I didn't avoid collaborations. At one point, when I was in England, I had a notion that I'd move to Dublin [Ireland] and become a professor there. There was one department in Dublin, the genetics department—it was Trinity College [Dublin]—that had a disproportionate amount of the science funding in Ireland. And it seemed like the only place where I thought I could...if I could get a job there, I could be successful and continue to do science on an international level. So, I managed to go visit there. The head of the department at the time sat me down and said...he looked at all these single-author papers and took it as a minus rather than a plus, which surprised me, and said, "What's wrong? Don't you like working with people?" I realized then that...I don't think I have a problem. I still don't think I do, but not everyone takes it that way.

What was I going to say? There are cases where I have interacted with people and collaborated with people. The case with Steve Hird, where we came at the same problem from different ends, we didn't know we were doing the same experiment. There was one...John had designed something that they called the 4D microscope, it would take recordings of multiple focal planes over time. Before this, at least for me, when I thought about developments, everything you recorded was...time was always moving forward and either you caught it or missed it. And if you're looking at something in one part of the embryo, you don't necessarily see what's happening on another part. With this thing, you could basically get an archive of development that you could play forward and backwards and up and down in focal planes to really get detailed views over time. We did do some time lapse recording before this, but it never worked nearly as well as when you could see all focal planes in a nice clear embryo. So, he had this 4D microscope, and there was [just] one in the lab at the time, and Steve and I were alternating days using it: he'd use it Monday, I'd use it Tuesday, he'd use it Wednesday, and so on. For the most part, we would talk about the experiments we were doing. But sometimes we'd act like art school students and say, "You can't see it until it's finished." [laughter] And I actually encourage my own students, I say, "if I you have an idea for an experiment and you don't want to tell people and or you tell people and they think it's a bad idea, if you still think it's a good idea, do it in secret," as long as it doesn't take too much time and resources, to the point where they're really wasting things. But I think having that freedom to do things in secret is important, right, to be able to test your ideas, even if they're stupid ideas. Because some of the ones that you think are stupid ideas, that you have some confidence in for one reason or another, turn out to be the really important ones, occasionally. Steve and I were working on the same experiment from different angles and we didn't realize it until we sat down and talked. I forget which one of us told the other, but the other one said something like, "I'm doing the exact same experiment." So then we started doing the experiment together. The experiment was...the idea to work on this came from my graduate advisor, near the end of my Ph.D. So, one of the things Gary Freeman was famous for was studying how axis specification works, how the initial differences between one side of an embryo and another first appear. If you trace back from forming multiple tissues—like muscle and neurons and so on—back to where you see the initial differences in the embryo that lead to these, then you've got an embryo that has a few different regions, and then the question is: How do these different regions get set up? The initial—if you trace this all the way back, the first question is: How do you initially make one part of an embryo different than any other? And so, this is the question of axis specification. How do you first set up an axis of polarity that'll end up having something to do with how the

animal will develop? And no one knew how the initial axis, the anteroposterior axis, developed in *C. elegans*, and yet it was a popular genetic model. In *Drosophila*, this question had been approached really effectively, in part because you'd make mutants. The genetic systems like *C. elegans* and *Drosophila*, the way it works is, if you want to study something, the first thing you do is screw it up, which, in some ways, is very counterintuitive, right? When I teach this, I explain it would be like, if you wanted to understand how a car worked, you'd line up one thousand cars or a million cars, throw a wrench under the hood of each one and then try to start all the cars. And the ones that don't start, you know you've hit something that's required for starting. And then you could try to figure out, where did the wrench hit underneath to figure which parts are required for starting a car. And then you'd find the starter and the battery, right?

CARUSO: Mm-hmm.

GOLDSTEIN: You could define parts that—this is way genetics works. Genetics in *Drosophila* worked really well for studying anteroposterior axis specification. They were mutants that clearly had defects in setting up when under the other. In *C. elegans*, when you made mutants like this, there wasn't a clear readout. In *Drosophila*, people use cuticle patterns to get a readout of what polarity looked like. In *C. elegans*, most of the mutants that affected processes like this, ended up in a pile of cells that didn't look like a worm. And one pile of cells that didn't look like a worm, looked very much like another pile of cells that didn't look like a worm. So, picking out the important ones was really hard. There were some people who were doing very well at this, Jim Priess and [...], some other people at the time. But there was nothing that really...we didn't have the sort of phenotypes they had in *Drosophila*, double anterior or double posterior or things like that. At least, it wasn't obvious that we had things like that.

So my advisor said, "Why don't you study how the anteroposterior axis is specified." It was just an idea I put away in my head for a while, until I was a postdoc and really started to believe that this was an important unanswered question. This gets to the experiment I was doing with Steve Hird. I'm almost back. [laughter] The egg of *C. elegans* we knew had some asymmetries in it. If you think about, where does asymmetry come from? It could work, as in some other systems, where the egg is constructed with an asymmetry. Their RNAs or proteins, that are very important, are stuck down on one side as the egg's being made. Another possibility is that it uses some external cue to do this. So, it's initially symmetrical. One possible external cue is the place the sperm enters the egg, in some systems, is important. And then there are all sorts of crazy possibilities. In some systems, it depends on gravity and things like this. I thought if you could just guess what the cues are and then reposition them, you could address this.

I was doing similar experiments with this induction at the four-cell stage. If you take the inducing cell off and put it on the opposite side of the responding cell, you reverse the polarity of the responding cell, which tells you that it's not just required to get this response, but its position is important. I just thought I'd try something similar at the one-cell stage with the

initial polarity. Like I said, we knew at the time that the egg had an asymmetry. We just didn't know if it was a developmentally important asymmetry. And that's that the egg nucleus moves down to one side of the embryo just before fertilization. My presumption, actually, was that that would be a sign that there was an important asymmetry already, and that turned out not to be the case. So, what I did was I tried to test, if you alter the point that the sperm enters the egg does that alter the polarity? Is the sperm bringing in something that's important for this? I tried a whole bunch of ways of testing it. It was really interesting, actually, because a lot of people who used to work on *C. elegans* and who used to work in Cambridge and some people who haven't worked in Cambridge, would come back to give talks at the LMB and they'd go around to all the postdocs and ask what they were doing and talk about experiments. And almost every time I'd talk about studying the sperm and egg interaction, people would have stories about experiments they'd tried that had failed. My favorite was, at one point I was trying dissecting out eggs and sperm and just mixing them and trying—like you can with a lot of different systems—just trying to get fertilizations *in vitro*. And it just doesn't work in *C. elegans*. For whatever reason, the tissues around them are important for normal fertilization, but I would try taking sperm still in the tissue that's around them and try putting them up onto eggs, and nothing would happen. And so Gary Ruvkun, who's a *C. elegans* biologist, came once and said, "Oh, yeah." He goes, "I tried to get *in vitro* fertilization to work." And my favorite thing he did was, he took eggs and sperm out, put them together in a tube, and then centrifuged to push them against each other as hard as he could. He said that also failed.

I came up with a trick to alter the sperm entry point, which is probably more complicated than it's worth going into. And then [there was] a complicated prediction, where if the sperm entry point was altered and it specified the axis, then I would see something that I wouldn't have expected to see if I looked at just the right thing, and it's something that I would have overlooked if I didn't have that specific prediction. We found that it required acrobatic predictions that bore out. I'd found that it was the position of the sperm that makes the difference. This was a real surprise to me, in part because I knew that there were other nematodes closely related to *C. elegans* that don't have sperm. And so, immediately I thought, "Finally, I'm working on something where I can study the evolution of it as well; where there's... something interesting has gone on evolutionarily because, clearly, the ones without sperm aren't doing it the same way."

I studied these two things separately. One was how did this mechanism evolve. It's interesting to me because it's one of the—it's how you initially break symmetry. You'd think once there was a good mechanism for doing it, the worms would stick with it, rather than swap out the mechanism. There appears to be another mechanism used in related nematodes. And the other thing I studied was: how is it that the sperm makes a difference? What happens when a sperm enters an egg? How does that set off the polarity? And that was where I bumped into Steve.

So, I was doing experiments where I was setting up these cases where the sperm would enter in a different place, and look at the effect on movements of material inside the egg that we knew were important... we did not know at the time, but we thought may be important for moving determinants to one side in the embryo, which turned out to be the case. It turns out to

be important for that. He, at the same time, was interested in the cell biology of these movements. And I really did not think we could possibly be working on the same thing because he was a cell biologist and I was a developmental biologist and we used the same embryos, but otherwise, we were thinking about very different problems. And all of a sudden, we realized, one day, we were doing the exact same experiment. He was using natural variation in exactly where the sperm would start off, and I was trying to manipulate it. But then, the response of this we were looking at was the same. And so, then it was really fun. This was my first collaboration. It was my first experience actually working with someone. And it was fun, first because Steve's a funny character. He's now a patent lawyer in Boulder, Colorado. He did a postdoc and then decided to go into patent law. It actually suits him really well because he's really interested in technology. He was the one who would open *Nature* or *Science* each week when it came and look immediately for the new technologies rather than the new science, right?

One of us would set up the embryos and the other would set up the films and we'd do it in, sort of...almost an assembly line in a way that made it go much, much more quickly than twice as fast. Together we were a lot more efficient. And it was fun. We would work together and go have lunch or go have coffee and come back and work together. The LMB has this nice tradition of...when Max [F.] Perutz set up the place, he set up a canteen on the top floor where you can see for miles around. And scientists go up there and talk. He set it up with a rule that the people who run the canteen must not ask scientists to leave so that they can clean up, so that if a conversation continues from coffee in the morning until they're closing at night, it can continue like that. So be it, right? So it was great going and having conversations and then coming back down and working hard on this together.

CARUSO: And so how long did that project wind up?

GOLDSTEIN: We were probably only working together for about a month or something, directly one-on-one. But then we wrote the paper. I think, I probably wrote the first draft, and then, by then, he may have been a postdoc in Boulder already and sent it to him. I think this is how it [worked]. I should look back and see if that's right.

CARUSO: So, with your time coming to an end at this first postdoc...I mean, I notice that you went to Miller Institute as a research fellow from 1996 to 1999.

GOLDSTEIN: It was just UC [University of California], Berkeley. The Miller Institute was what funded it. It was just a group at Berkeley.

CARUSO: Okay, okay. But did you want to continue on doing another postdoc-like position?

GOLDSTEIN: At that point, I was doing postdocs where I was doing what I want and people would leave me alone to do what I want. I mean, I wasn't in isolation. I don't mean they would leave me alone...

CARUSO: Right, right.

GOLDSTEIN: There were terrific people to talk with at the LMB. But I was in a position where I got enough money to live and I was doing what I want. And I thought this was the absolute ideal situation. I would have been a postdoc forever if I could have. I was in no rush to take on responsibility and teaching and all sorts of other things—some of which I very much enjoy now. But I guess, probably like a lot of scientists—at least a lot of scientists say—they miss when they were a postdoc and they did experiments all the time. I actually still do experiments and I really believe that I really miss it.

CARUSO: So, how did you come to Berkeley?

GOLDSTEIN: I was interested in evolution of development, and I think it came, in part, from all the evolutionary colleagues in Texas, that...Monday lunchtimes going and hearing them talk about really interesting science and very different ideas. My advisor was also interested in the evolution of development. Evolution of development is a fast-growing field now that's now...now there are a lot of people moving into it. There's a few things written up in the *The New York Times* about it every year, a new book about it, things like this. Now it's hip. Back then, it was, maybe, just becoming hip. And there were some really nice classic studies before then, but it was very much a new field.

I always thought it would be neat to study the evolution of something that I would be well-equipped to study, which was developmental and [yet] might shed some light on how development evolves. So, in my mind, and I think in the field in general of evolution of development—which I should say is only a small part of what my lab work's on, it's sort of our side project—there's one major question and that is: How do you explain the diversity of animals we find out in nature, by changes that happened in development? Evolutionary changes to developmental programs. The idea is a squirrel looks different than a dog because something has changed in the developmental program that makes the nose a little longer and the tail a little less bushy and the whole body a little bit bigger. I don't actually know the anatomy of squirrels and dogs well enough to continue any further than that.

CARUSO: [laughter] And [with] some dogs even saying a little bigger [than] the squirrels...

GOLDSTEIN: Yes. But it should be that the changes in morphology you see, that [they] really account for the diversity of life in some ways. [This is] one of the big interesting questions. We are controlled in part by changes to developmental programs. And evolutionary biology, for the most part, has treated this part of evolution as a black box. They say you get mutations, and then there's a lot of people who study, very effectively, how a mutation that changes fitness by X percent can spread through a population or not spread through a population to be more or less represented in future generations. They study that part of it, or they can study how changes in phenotype and morphology, mostly, can affect the fitness. But, in between—mutation happens and there was a change in morphology—is the black box and that's where studying evolution of development can make an impact. And that's where, I think...there are a few books out that are textbooks of evolution of development, but none of them, yet, have, "These are the general rules by which development can evolve to change morphology," because we don't know what the general rules are. People have taken a stab at what the general rules might be, but I think it's way too early to know yet. There's not enough case studies of how development has evolved to know yet.

So, I was interested in studying this from...I had ideas about it when I was a graduate student, but nothing that would be productive. And then, when I was a postdoc, there was a book [*Nematodes: Structure, Development, Classification, and Phylogeny*] written by a guy named [Vladimir] Malakhov,⁷ a Russian nematologist who studied development, who was looking at developments in lots of different organisms. It was published ten years earlier in the Soviet Union and then didn't come out to Westerners until, I think, it was 1996 [in English], and 1986 in Russian. And when it came out it was like...often, when I read a new paper and get excited—get one more quantum of information, that's exciting. This was like someone dropped a bucket load, all at once. So, it was looking at developments in lots of different organisms. I thought, "I'll look at the things I study and see if there's anything that's different there." At the time, all I'd really studied was this interaction at the four-cell stage, but I was excited [...] I looked at all his embryos of different kinds of nematodes and every one of them had a cell like the signaling cell sitting next to a cell like the responding cell. When I say like...I mean like in terms of the fates that they were going to later produce right next to each other at just the right time. And I thought, "This is probably something that happens in all nematodes." It would be hard to actually test that, and it would be nice to know that, but it would be sort of a boring answer if that's the answer. So, I didn't pursue studying evolution of that.

Then when I found the sperm entry alters the...I'm sorry, changing the point of sperm entry changes the polarity of the embryo, I thought, "Oh, the sperm is bringing in a cue or multiple cues for the polarity and this is something that must be different in other nematodes because some nematodes don't have sperm." I thought, "I'll study the evolution of this." This was something I did before, so this is still before making the decision to go to the second postdoc.

⁷ Vladimir Vasil'evich Malakhov, *Nematodes: Structure, Development, Classification, and Phylogeny* (Washington: Smithsonian Institution Press, 1994).

And the other reason I wanted to study this was I knew it could be studied in large part by just making films. And for the *C. elegans* experiments that were going on in the lab, people were using this 4D scope to make the films. No *C. elegans* experiment took more than an hour or two. And so, the equipment sat unused overnight almost every night. And I thought, “If I just set up films at night when I leave and check them in the morning, I might be able to collect a lot of data with essentially no work.” The analogy I like, which someone told me once in Friday Harbor when I was out at a beach looking for whales, but explained to them that I actually was doing an experiment because a recording was going, he said to me, “Oh, I’m cleaning my oven.” I said, “What are you talking about?” Do you know these old commercials?

CARUSO: No.

GOLDSTEIN: They were old ads, apparently, of a woman lying on the beach and someone said, “What are you doing?” “I’m cleaning my oven,” and it was these oven cleaners that would run on their own.

CARUSO: Oh, yeah, yeah.

GOLDSTEIN: So, when we’re doing a recording but we don’t look like we’re working, we now say, “I’m cleaning my oven.”

CARUSO: [laughter]

GOLDSTEIN: It was a great experiment in that I could...great in that it took very little work and yet I could learn something. I got about thirty species of nematodes. I used to say you could keep thirty species in something the size of a breadbox, because it was literally a breadbox that we kept them in. [laughter] If you’re doing experiments with vertebrates, or even insects, every one needs different culturing conditions and space and all this. It’s very hard to do something like this. I got most of these by mail from other nematologists, and I studied how these things varied. As I was doing these experiments, someone else was doing a molecular phylogeny of the nematodes, which changed the way we think about how nematode evolution worked. We used to bunch groups together that had similar lifestyles because they looked similar. It turns out, a lot of them probably just looked similar because they had similar lifestyles. So, as they were changing that, it led to testing more hypotheses about how this mechanism of axis specification could evolve. Most of the species I could keep in this little breadbox. There were two exceptions, one of which was a plant parasite. That one was actually easy to keep because I’d just grow a plant on a plate and put worms in with it and I could get those. The last one was a sheep parasite.

CARUSO: You couldn't really keep sheep in the lab.

GOLDSTEIN: You can keep them on plates, but only if you have four [plates] positioned perfectly. So, no, we couldn't. There was a lab in Babraham [England], about ten miles south of Cambridge, that was doing a vaccine experiment and I knew a guy named Ed [Edward A.] Munn there. Ed told me they were going to get the results of a vaccine experiment soon with a sheep parasite and that they had some control experiments, where he knew they would be getting in sheep stomachs that were filled with nematodes. This is not pretty. They would be getting sheep stomachs filled with nematodes where, once they take them out of the stomachs, they'll stop fertilizing new eggs. But he knew, at that stage, they would have eggs in them and he said I could have them.

So, for I think it was two or three days, I got a special parking spot at the LMB in Cambridge and drove down with a thermos the temperature of a sheep stomach—which is a little warmer than ours—and went down to there and then waited in a room. It wasn't pretty. About every 20 minutes someone would walk in with another sheep stomach from the vaccine [experiment]. So, they were trying to develop vaccines to help the sheep. But, of course, in the experiments they had to sacrifice some to do it. They'd walk in with these things. The vaccine experiment failed, at least this particular one failed. And so, there were a lot of nematodes, not just the controls, but a lot of them. They would take the nematodes out, I would get them and I'd know they had fertilized the last egg by then. What I wanted to film started about ten minutes after then and it was ten miles to Cambridge. [laughter] So I got a parking space. I had to speed to get to...I knew to get the experiment to work I had to go faster than the speed limit to get them on the scope. This is not...biologists normally don't have to do this.

CARUSO: Right, right.

GOLDSTEIN: You don't have to break...

CARUSO: ...break laws to...

GOLDSTEIN: Someone told me that if the Cambridge police ever read the materials and methods in my paper, they'd give me a ticket, [laughter] if they could put together how long this was. This was fun, to see that you could make predictions for animals that were then regrouped in areas where we didn't expect. And parts of phylogeny we didn't expect it when predictions bore out. So, this was an experiment to study how development evolves. It told us that even the very first step, specification of the embryonic axis—the initial axis—can evolve in ways that appear, at least to me, to be pretty dramatic.

So, I wanted to do a postdoc studying this. And I was inspired by experiments from two people's labs, Sean [B.] Carroll and Nipam [H.] Patel, who still do some of the best experiments in this field, in evolution of development. Nipam had been developing antibodies to recognize proteins that are conserved, that work similarly in lots of different organisms. Normally, if you want to know where a protein is in one animal during development, which can be an important part of understanding how a protein functions, you can generate an antibody to it. But if you try using that same antibody to look at the distribution of a similar protein in another organism, it typically doesn't work. So, what he had done, that was really nice, was come up with ways to get antibodies that will work in different organisms. But they were very rare. There were only two or three proteins where you could do this very effectively. But those antibodies were like gold, in that you could continue to ask really interesting questions about how development evolves using them. And so, what I thought is, "I want some antibodies like that to study something that I'm interested in." What I wanted to study was evolution of mesoderm specification among a group of about ten phyla—about a third of the animal phyla that are known as the spiralians because they all have spiral cleavage. They're now known as the lophotrochozoans, for reasons that probably aren't worth explaining now. This was my plan. And what made me think it might be possible was an experiment by Grace Panganiban [Boekhoff-Falk], from Sean Carroll's lab, where she had tried to make an antibody to a protein called distal-less, which is a protein that has a homeodomain, a piece of protein that can bind DNA and turn on or off genes. Normally, when you're going to make an antibody, you can express some protein in something simple like bacteria, make a lot of that protein and then inject it into an animal like a rabbit and get an immune response to it. If you collect the blood, then you can get from that the antibodies that'll recognize the protein.

She wanted antibodies that would recognize distal-less, this homeodomain protein, in a bunch of different organisms. And the trick she did was to inject a piece of protein that contained a piece that was identical, the homeodomain part was identical between flies and butterflies. And she was doing injection after injection after injection and looking for an immune response and was not getting what looked like a very good response. At least, she wasn't getting good antibodies to the proteins she was injecting. And then, on about the thirteenth injection, which is unheard of—normally it only takes two-three-four injections and almost no one goes this far—she decided to just inject the homeodomain and not the rest of the sequence she had been injecting as well, and she got a really good response that recognized the homeodomain really well. Based on this, the conclusion was that maybe you can boost an existing, but low-level, immune response to a conserved piece of a protein. And basically, rather than...you can imagine one way you could go about making antibodies that would recognize the piece that exists in lots of different animals would be to just inject that piece. You don't always get a strong immune response from a little piece. The other way you could think about it is you could let the animal find that piece for you. And Grace's experiment suggested you might be able to let the animal find that piece for you.

My plan was inject a protein made...derived from gene sequence from one animal, boost with protein from another animal, but using related proteins and hope that the immune response finds the conservative piece. It wasn't clear how much sequence similarity you needed to do

this. It wasn't clear what worked. So it was a big risk. I think it's unusual to base an entire postdoc on something that risky, but I felt like my Ph.D. had gone really well, my first postdoc had gone well, that I could take a risk and do something, and if it didn't work I would try to get a job quickly before it became too obvious. This is exactly how it happened. It didn't work and I got a job before it became obvious it was a failure.

CARUSO: And this was in David [A] Weisblat's lab?

GOLDSTEIN: So, actually, I initially approached Nipam Patel about this and Nipam seemed very receptive until I visited him. I actually visited him—it was in 1995, fall of 1995—I visited him on a weekend in Chicago [Illinois] when it was so hot that a lot of people... I think a few hundred people died that weekend! And I stayed on a couch in his living room. He had air conditioning in his bedroom, but not in the rest of the house. I was perfectly happy to be in the un-air-conditioned part, because he was in the bedroom. He was very nice to me. But he did say that he had decided that he didn't want people working outside of the arthropods in his lab anymore, and this is exactly what I wanted to do. So, he proposed other projects for me to do with 90 percent of my time and he says, "Maybe in the other 10 percent, you can do the thing you want." And so, I remember sitting on his couch, sweating profusely, the last night, and he's, kind of, a quiet guy and I can be quiet at times, too. We were sort of staring at each other, and he said, "So. What are you going to do now?" I said, "Well, I think I'm going to look for other people to work with." We were both dripping sweat. That didn't go so well. Actually, I like Nipam now. He does some really cool science, but that did not work out so well. Then I scrambled and looked for other people I could work with, to do this with. I wanted to do that project. There aren't so many postdocs who do things this way anymore, where they know exactly what they want to do and they find someone to do exactly that with. There are some, but it's not that common. And David was a person who was working on these problems just in leech, which is one this large group of animals and had had some data that might have been helpful to get the first steps toward this, and so I went and tried it there.

I tried making these antibodies using *Drosophila* and leech sequence. So, at the time, the understanding of the animal tree of life suggested that *Drosophila* had this spiral cleavage in its ancestry. That was reorganized near the end... now we're about midway through this postdoc and it became almost impossible that *Drosophila* had this in its ancestry. So, I was using *Drosophila* sequences and leech sequences to do something that... it may or may not have worked. In the end, it didn't work, probably because there wasn't enough sequence conservation to get the rabbits to make a good immune response to conserve pieces. I did, at the same time—knowing that it might not work—I made specifically leech antibodies so I could see, at least, how do these proteins... how are they distributed in leech embryos, and the answer was mildly interesting.

CARUSO: So, while this project was going on and it wasn't necessarily going great, you decided to start looking for faculty positions. Were you applying anywhere for anything, or did

you have, in your mind, an idea of where you wanted to be, what you wanted to do, what sort of relationship...?

GOLDSTEIN: I applied a year before I felt I really needed to. My Ph.D. advisor always recommended people try to get at least one interview a year before they're serious. But I also thought if I applied only to my dream jobs the first year and I got one, I'd be finished. And I applied half for evolution of development positions and half for cell and developmental biology positions, so the two areas that I liked to think about and work in. I only applied for about a dozen positions at maybe six or seven places; a few at Berkeley, [University of] Colorado, Athens, [University of] Georgia, here [University of North Carolina, Chapel Hill], I think maybe Tucson [University of Arizona]. A lot of liberal academics have this hit list of towns that includes here and Austin and Athens, Georgia and Tucson and Madison, Wisconsin. These are the places a lot of us like to be. I knew UNC [University of North Carolina, Chapel Hill], there's some people who I think are fantastic here. So I applied to these places and I got interviews at UNC, at Duke—so this is unusual. They're only 10-15 miles apart from each other—and at the University of Minnesota. I met my wife during my postdoc in David Weisblat's lab. It's a funny story. I had a girlfriend for three years when I was in England, and when I left, I left on my own because I had a long-term plan not to get married until I was at least forty. I'm only forty now, so I blame my wife for ruining this plan, but I'm very happy it was ruined.

I think it was inspired in part by seeing all these people who played music in Austin and had very happy, carefree lifestyles. I suppose it's not uncommon for males not to want to get married for a long time. So, I had another friend in—a friend I met through my girlfriend in England. My girlfriend in England was named Sue [Susan L.] Dyos. She had a friend whose name was Steffi [Stefanie] Reichelt. Steffi moved to Berkeley soon after I got there and appeared in the hall one day, on the floor I was working on. I said, "Steffi, what are you doing here?" She said, "Oh, I'm starting to work in Beth Burnside's lab," right across the hall from where we were. I said, "I'm leaving, in a few days, to go to Ireland with my mother. You just arrived, would you like my house and my car for a week and a half, until I come back." And so, she said okay. The lab she came to work in, my now wife was working in there, although I didn't know her. And Steffi became good friends with her right away. And so, my wife was actually in my car and in my apartment before I met her. This was kind of weird.

When I got interviews... we had moved in together in Berkeley and I got these interviews [...]. I got these interviews, and this was our first big decision we were going to make together. We had decided we were going to move somewhere together and it was, maybe, our first small decision, too. We really hadn't been together very long. When we met, I knew very soon after we met that my plan was ruined, that something was up here. We had decided we were going to do this together. The first interview I got was at University of Minnesota. I thought, "Okay, this is our first big decision. We'll sit down and discuss this carefully together." I said, "Well, I got an interview in Minneapolis [Minnesota]." She said, "I'm not moving there. It's too fuckin' cold."

CARUSO: [laughter] I was going to ask...if you're not from the upper Midwest, its' not necessarily a place that most people...

GOLDSTEIN: So, my wife is from Scotland. She's from Aberdeen [Scotland]. She didn't want to go someplace that cold or colder again. So, little by little, I'd heard what a nice place Minneapolis is and the potential colleagues there were going to be terrific. We were talking about how nice Minneapolis was. We decided I'd go on the interview. And it couldn't hurt to interview. The place I was interviewing was a med school and it turned out, like, I didn't really want to be in a med school. I wanted to be on the main campus in the biology department, where I could run a smaller lab—an active, but smaller lab—without, it would just be a different environment and have more diverse colleagues.

CARUSO: So, did Minnesota have the Academic Health Center combined at this point? Because I know they had separate schools.

GOLDSTEIN: I don't know. It was undergoing a big rearrangement at the time. The chair who interviewed me was about...ended up leaving soon after. So, there were a lot of changes going on.

CARUSO: Okay. Because I know they did wind up unifying the system to make it into a collective identity...I was just curious if that happened.

GOLDSTEIN: I suspect that was before then. I met with people, both in St. Paul [Minnesota] and in Minneapolis.

CARUSO: Okay.

GOLDSTEIN: [I] drove across in between. There's clearly a big separation among the people I'd be interacting with, but it's not...I went back there recently and had a great time meeting with the same people. Somehow they all become very Midwestern, but in the best possible way. I went on this interview and while I was on the interview...so, a couple interesting things happened. One was my friend Dave [David] Zarkower had taken—who was one of the postdocs in Cambridge that I'd interacted with a lot—he had taken a job in Minneapolis and agreed to put me up, for a couple days, after the interview. And during that time, I went sledding with five assistant professors...it was the end of January. Actually, just before we left, our apartment in Berkeley got robbed and I lost—it was very strange—what I lost was my

winter jacket, my suitcase that I needed for the trip, a VCR that I needed to play a tape that I was going to use during my talk. We lost almost only things that we needed, I needed, for the trip.

CARUSO: Are you sure it was a break-in then? Maybe...

GOLDSTEIN: [laughter]. We made sure the police came and they dusted for prints and everything. It was clear what had happened, in the end. Maybe I'll ask Jenny, [my wife], about this. So, the other unusual thing that happened was at one point I was in Dave and his wife, Vivian's [Bardwell], house. And I talked to my wife on the phone and told her everything went really well. It was quiet for a moment on the phone and she says, "I rented *Fargo* last night." [laughter] I said, "Yes." She goes, "I don't think we're going to Minnesota." [laughter] So, we didn't end up going there.

I interviewed here and at Duke. I did consecutive interviews, and I absolutely loved it here. Here there are a lot of...there actually aren't all that many developmental biologists. Developmental biology has grown a bit since I got here, but there's a lot of fantastic cell biologists and, really, just your world-class cell biologists, a lot who study motility, the cytoskeletal motility—the nuts and bolts of the developmental systems I was studying had to do with cytoskeletal motility. I thought this would be great; to be surrounded by people who think about this much more seriously than I do, and maybe some of it will rub off. In both places, here and at Duke, there was one colleague who I absolutely wanted to be near. It was [R.] Bruce Nicklas at Duke, had done some really nice direct manipulation experiments having to do with mitosis. And Ted [Edward D.] Salmon, here, is a lot like John White in that he develops technology for imaging...develops new kinds of imaging that really make huge differences, but uses them to study biology, to study cytoskeletal dynamics. And he also—I knew from his publication record—the guy was publishing at some absolutely crazy speed. I met him. He seemed like a very nice guy, very calm. He was not rushing to get a paper off to the FAX machine as we talked or anything. Then I walked around his lab and there were five or six people doing exactly what they wanted in a very well-equipped lab. It was not a mega lab, where there was a factory going on producing these papers. I thought, "This guy would be the perfect role model," him and several other people I really thought highly of.

So, it was that and I really liked the lifestyle in Chapel Hill...that, for a while, I walked to work before we had the kids. I now drive to preschool in the mornings, But I could walk into work. The campus was pretty. There was a very civilized lifestyle. The grad students would get out and drink together. Actually, when we first moved here, my wife went back to school to retrain as a genetic counselor, and she did it in Richmond, Virginia. So, for the first two years, I guess twice each year, for three or four months at a time, she would be away on weekdays and come back here on the weekends. And Friday evenings, I'd go out with the grad students and the postdocs on Franklin Street, the main street going past campus and go out for a beer, and they would talk science and they would talk non-science. This was the atmosphere that I saw a little bit of when I interviewed and got very excited about. There are a lot of places where

faculty don't interact very well, faculty and grad students. The postdocs don't interact well. The grad students go home at the end of the day and don't talk with each other. So here, it just seemed like a nice atmosphere for doing science.

CARUSO: One thing you sort of half mentioned, I'm just curious about it. How was your family responding to all of your decisions?

GOLDSTEIN: They were proud. I have one significant thing I didn't mentioned is that the day after I left for England, my father presented divorce papers to my mother, and we found out afterwards, had been working towards a divorce for almost a year. When he left—this was unusual—he left without leaving an address or a phone number. He disappeared for a few years. Actually, he disappeared from contacting us soon after that for a few years. And then when I was going to get married, my wife and I decided we should talk to him and try to work out something. We were going to get married in Scotland, so it was a long way away and my mother grew up in Ireland and a lot of her family was there. We knew a lot of her family would be there, and we didn't want to have a fistfight at our wedding. So, we decided to invite him to go for a dinner instead, and this was, really, the first step toward reconciling and being able to talk with him a little bit again. I see him about once a year now and talk a few times a year.

But you were asking how people respond to...everyone was supportive and seems proud enough. My brothers make fun of me, in a nice brotherly way. Both of my brothers do really interesting things. My older brother started a company of his own. He installs sprinkler systems in people's lawns on Long Island, which, on Long Island, is a good business.

CARUSO: Yes, definitely.

GOLDSTEIN: Or at least has been for a while. And he has a small company doing this. Him and a few guys do this. He does seasonal work, and each winter he does something creative. It's always as the season winds down and then his off time starts. First we notice it started because he starts communicating a lot more, whereas when he's working, he works really hard and it's hard to...and he starts telling us what's on *Jerry Springer*. [laughter] And then, usually after a few weeks to a month or so, the crazy ideas start coming. The last few years he's been doing something really neat. He built a snow machine. You can find videos on the Web, but he's got a company called Neighborhood Landscaping. It's now Neighborhood Irrigation, switched from Landscaping to Irrigation. And there are videos on there where you can see him—the news has come out a few times to show him making his snow. He found some designs off the Web. He improved them somewhat and made something that, overnight, can make several feet of snow on his front lawn...a few feet of snow on his front lawn. So, he did it one year because he and his family went to Ireland, to visit family in Ireland. When they came back, they had missed the big snowstorm, and then the rest of the winter there wasn't snow but it was cold enough. And so, he started looking into this because his kids were crying that they

wanted snow. He said, "I've got time. I want to make snow." It's very funny. He said the first time he made it, and I guess every time since then in fact, when he makes the snow, when cars come down the street, every car comes to a complete stop. I guess people called the news and the news called him and came out. One morning they went and filmed it from about 5:00 in the morning until about 11:00 in the morning. They had someone there who, every 20 minutes, would come out of their truck and do another short interview with him for a minute or two. It's hilarious to see. Every year we wonder what it's...one year he did the genealogy. When he was younger, before he was married, every winter he'd get himself into trouble doing something he shouldn't. So then, after he got married, he just became very...he used his power for good instead of evil.

I like to think that the kind of science I do is somewhat creative science. It feels like a creative process to me and I kind of like that my older brother works in a completely different area. And with his hands and he has muscles and I don't, right? But also has a creative mind and really comes up with fun things.

My younger brother does computer programming and Web programming and also has a devious, creative mind. I like doing a little bit of Web programming and he's taught me all of it.

So my family was supportive. I think my mother wished I was closer. We were happy, actually, to be on the East Coast so we would be close to my family and closer to Scotland. It's that much closer a flight. But my mother would have been happier if I was on Long Island.

CARUSO: Yeah. Okay. So you came to UNC. You received the offer you wanted to come here. What was it like starting up your lab?

GOLDSTEIN: I did not have a clue how to start a lab. And I think a lot of people say this, but I think it's probably more so true for me than most. I worked independently a long time. [...] I got postdoc funding [(Gary Freeman shared a set of NSF proposals with me that he was reviewing in the last year of my PhD)]. I have graduate students now, when they write their thesis proposal, they're using the format of a postdoc application. The postdocs, I get involved with...actually, the grad students and the postdocs, I get involved with reviewing grant applications for the lab. They look at the grants I write and give me comments. And then sometimes, when I review grants, and certainly when I review papers, they get involved and we have discussions.

Boy, I was blind to almost all this stuff. David Weisblat had showed us once when he was writing a grant. We gave him some comments and we helped him with photocopying at the last second. So I knew what the mad rush looked like and I'd seen a grant application once before, but I really didn't have a clue what I was doing. And the first proposal I wrote, I'm embarrassed that I even submitted it. I did write it. Jenny and I got married just before we came here. So, we both finished in Berkeley, we got married in Scotland. We went on a honeymoon in Hawaii...almost the other side of the earth. But she had already been to some

nice places in Europe and we both wanted to go to Hawaii sometime, and we knew we had to get back to California to our stuff anyway. So, we went to Hawaii.

And then we got in our car in Berkeley, at the end of the honeymoon, and spent two months driving across the U.S. Starting out heading...actually via Reno [Nevada] up to Seattle. After a month, we were in Arizona, the state next to California, having seen most of the west...well, not most of the west, but having traveled through most of the states of the west. It was fantastic just to get in the car and go. It was an old car that all our friends asked us, "Are you really going in that car?" We said, "Well, we're going to start in this car." So, we spent two months driving out here.

We actually arrived here a little bit earlier than we needed to and we found a place much quicker than we needed to. I walked into a restaurant near where we [Goldstein and Caruso] had lunch. There were two guys talking about this neighborhood and I talked to...actually, my Ph.D. advisor's son [Ketil Freeman] was a graduate student here in urban and regional planning. And then a friend of mine who played Bluegrass music, a very good banjo player named Tim Ziegler, in Oakland [California], had an old friend who was in urban and regional planning here. We asked each of them where should we live, and they said, "Come to the center at Carrboro [North Carolina], it has a great sense of community." So we arrived in town, went to the restaurant. We heard people talking about the neighborhood. I said, "Are there places to rent in that neighborhood?" And this guy next door [Robert Harwell] said, "I have a place." [laughter] So, when people asked me, "How do you get a mill house in the middle of Carrboro?" I explain that story and they're, "Oh, great. That's no help." So, we arrived here. In that day or two we were here, looking for a place, we stayed at the Carolina Inn one or two nights, and then we stayed one night on the floor of my office because we'd been camping across the U.S. anyway and staying with friends on couches and things like this. We decided to save the money and stay one night on the floor of the office. I remember one of the cleaners opened the door and, in my confusion—it must have been 3:00 or 4:00 in the morning—I sat up and said, "We're looking for a place to live," as if this was an explanation. A couple years later, when I was writing a grant application in the middle of the night was the next time I saw this woman because she only worked overnight. And I said, "Do you remember that time you opened the door and we were in here?" She said, "I sure do!" There was no way she was forgetting that.

We arrived here and I remember the first week I got to my office, I felt like a fraud. I felt like someone was going to figure out that I was in this position and I shouldn't have been. And then, I do remember clearly a mistake I made, which I like to tell to young faculty now because I'm sure people who have worries never make mistakes like this. One morning I was going in and I had a pair of sneakers and the sole had split off it a little bit. I stopped at the drug store and picked up some crazy glue. And then, when I got to work, I thought, "I'll just glue this shut and get on with my work." And I managed to glue my foot to my shoe through my sock." This is another moment when I thought, "Maybe I'm not cut out for this." This is probably not a common experience for new faculty. I was very lucky in that I had a postdoc applicant—I used to get postdoc applicants...from when I was a graduate student I started getting postdoc applicants only because there was a confusion about someone who publishes a paper alone: the assumption was, they had their own lab. And most of them were the kind of

postdoc applications that they didn't appear to know what I was working on anyway, so I'm not sure they were really serious applications. But, while I was a postdoc in Berkeley, I got a fantastic applicant, Jean-Claude Labbé, who ended up being my first postdoc. I interviewed him. He first wrote to me and said, "I would like to be a postdoc in your lab," and I wrote back and said, "I, too, am a postdoc." [laughter] And I said, "I wouldn't be in Berkeley. I just got this job at UNC." Actually, I got the job and then waited. I delayed a year before coming because I really liked being a postdoc. I interviewed him during a visit out to here. Jenny and I visited here once together so we could decide together if we wanted to move here, and she liked it very much here as well. And then he visited, and it was funny because I flew in one day and then he flew in the next day and I picked him up at the airport as if I was welcoming him to a place I knew, but I hardly knew the place.

He was thinking about a bunch of places, and I told him what I tell all my postdoc applicants. I said, "You can do anything you want." I said, "I'll never say, 'don't do that experiment.'" We discuss experiments. We argue about whether something's the right path to take. But in the end, it's their path to take and I support when they decide to do the exact opposite of what I recommend. Because I felt like that was the kind of system in which I could flourish, and I'd like to see people be able to flourish in that kind of thing. And sadly, there aren't enough places where you can do that, where you can go and decide what you want to do and have someone who'll support you with equipment and as much as possible to do that.

Jean-Claude decided to come. He started just, I think, a couple days after I...he started very soon after I did. And then I took on a graduate student. Rebecca Cheeks was my first graduate student. Jean-Claude was probably as apt, if not more, to run a lab as I was. I felt very fortunate that I was the one put in this position and not him, even though he'd be better at it in some ways. He's gone on. He now has his own lab in Montreal. I'm going to visit him soon.

CARUSO: So what was it like transitioning also to becoming a professor? Had you done much teaching?

GOLDSTEIN: Yes. When I was in graduate school, when I was ready to drop out at any time.

CARUSO: Mm-hmm.

GOLDSTEIN: I TAed some, near the beginning. And then I went on an NIH [National Institutes of Health] training grant. NIH training grants had—I don't know if they still have these—but they had payback agreements where, if you didn't stay in science, which was fairly broadly defined, but in science for some number of years after you finished, you had to pay back all the money they gave you. Now they weren't giving us that much money, but I thought if I wasn't in something I had trained to do, I wasn't going to be making much money either. And so I decided that I was a bad bet for this and that I should come off the training grant, which I

feel terrible about now because I know people work very hard to get these training grants and they're very proud when they get them, that they can support a lot students from them. But I had fear of this payback agreement. And so I ended up TAing almost my whole way through graduate school. I was teaching almost every semester. So then, I had some experience teaching. And then, some of those I really was teaching new material, and some I was just a typical TA, not really teaching, just helping students. I've had some experience presenting new material like that, but when you start a PI position, typically, you were trained to do bench science and then you have a job where you teach, you administrate a lab, you handle the money, you do all these things that you were never trained to do. It's a really unusual training program. If you haven't been in places where they train you, specifically, to do these things, and some places actually do that more and more now, I think, you're doing a lot of things you've never done before, and it definitely felt like that.

I didn't teach my first semester. I did teach my second semester. When I started teaching, I was very nervous at the beginning. I decided, in the end, that I do very much enjoy it and I think I do okay at it. I hope I do well at it. But it took the first couple rounds of teaching the same course once or twice before I really started to enjoy it, because it was a mad dash to prepare enough for the first time. Now I go back to the lectures I already have almost every time I go to teach, the day before or the night before, and look at the material and look up what's new and search around on the Web for stuff and find interesting things. And I replace stuff that's not absolutely necessary with really interesting things and new things and more and more with the experiments so they can see how science is done rather than, "Here are all the facts you need to know."

I teach cell biology. For whatever reason, I've never been that excited about mitochondria. There are certain parts of biology that... anything that has moving parts, I get very excited about. It's interesting to think of parts and cells as little machines that are regulated in interesting ways. So, when I teach about the mitochondria, I teach primarily about the hypotheses that were tested about how mitochondria work, and I teach about how the moving parts work, that there's an interesting rotary motor, basically, in the mitochondria. And so, when I teach, I have a tendency to give more experiments in ways of thinking and clever mechanisms than a comprehensive view of how everything works. And then I just ask them all to read the textbook and tell them there'll be a few questions on exams from that, so that they also get a comprehensive view of how things work.

CARUSO: Sort of like the professor you had in college.

GOLDSTEIN: Yes. Although, I'm teaching a core cell biology course, so there is a certain amount of material they have to know. I do a compromise where I try to insert some of that stuff. I [also] teach evolution and development. I do a half a course of each, each year. And when I do that, it's much more discussing papers and original experiments.

CARUSO: How do you find balancing all the different responsibilities you now have as...the administrative duties, the teaching, the reviewing articles, and getting your own research done?

GOLDSTEIN: The one thing that I try to do, that I guess not every PI does at this stage, is that I like to do my own experiments. I do some of my own experiments. I don't do nearly as much as some do, but I do a lot more than most, I think. When I took the job here, before I came, I had a year to think about it. I'd say about a year, year and a half really [between accepting the job and arriving]. Every time I ran into a PI that I knew who did their own experiments, I asked them how they did it. And everyone had a different answer, but I think just about everyone I talked to had an answer that helped me think about this in advance. My favorite was Jim [James H.] Thomas at the University of Washington told me, "Say no to everyone, absolutely everyone at all times anytime you're asked to do anything." I don't know if he follows that or not, but it'd be tough to be a respected colleague doing that. So, you have to take on a certain amount of things. Luckily, the things I've taken on have been, mostly, things I'm inspired to do. I'm co-chair of the seminar committee in our department. I like that we're a broad biology department. So, I'm in a broad biology department. I like listening to colleagues from ecology and evolution talk about what they do. I have one colleague, Ken [Kenneth J.] Lohmann, who studies how sea turtles find their way onto the beach and around the Atlantic. In some ways it's, conceptually, very similar thinking to what we do. We consider potential spatial cues. We move the spatial cue to ask if it's really acting as one. But we're looking on a microscopic scale; he's looking on a big fraction of the earth.

But I love when ideas come from far out like this. Often, I think of new ideas thinking of stuff like this. So, with the seminar committee, it was something I was really driven to think about and do. We try to do as much as we can to get seminars that'll appeal to the whole department, so that we'll remain as one department, so that we can continue to have these interactions. The other thing we did was, at one point, we realized that every year our top two or three speakers would decide not to come and those were the people we wanted most. So, we invented, really just out of thin air, me and the co-chair, Christina [L.] Burch, invented a distinguished seminars series. And it was nothing more than, we called the first two people we wanted to invite, who were at the top of the list each year, and we told them, "You are the distinguished seminar speakers." [laughter] And that was it. Actually, for a little while, we got some funding for it because we had a distinguished seminar series that there was a group that wanted to give money to it. And then we decided to use the money for something that we still actually do, although it doesn't come from the same funding source.

Chapel Hill has a lot of...there are bands that come from here. There are bands that move to Chapel Hill, which surprised me because it's a pretty small town. But it's seen as like here and Athens, Georgia and some other places are pressure cookers for young bands, where there's a supportive environment. There's a lot of recording space and practice space and things like this. So there's a microscopic music industry that goes on here. I found some screen printers. There are a few people who hand screen print beautiful posters for bands. And I always admired them, especially when my wife was out of town, I would walk to and from work, when she was retraining in Richmond, Virginia. And if I'd see a really nice hand

screened band poster where the date had already passed, I'd take it home, and I've got a few of these. They're really beautiful ones. It seemed like people were really putting a lot of effort in and making these posters. So, we have some of these people now make our distinguished seminar speaker posters, and they're these 9 inch by 22 inch, very tall, posters that are adapted for telephone poles that we use in that same format. We always give them to the speakers, too, and they like the story. They're just beautiful posters.

So, the things that I have decided to take on, I take on things where I've got some sort of inspiration to do it, and I try to resist stuff where I don't. I used to do a lot more reviewing papers and I realized at one point when we submit a paper, if we submit it to one journal and we get three reviewers, I'm incurring three other people's work from somewhere else. If we have to submit it to a second journal and it's three more reviewers, I'm incurring six people's work. This added up so the total number of papers we're submitting each should be about what I'm doing if I'm equaling...I was way beyond that for a while. And just because I just didn't want to say no and I wanted to read everything that was coming out. So, I've sort of scaled back on some of those things.

I'm trying to think how else I balance that. The teaching...there has to be a compromise between how much effort I put in and how much I take away from the other things I'm doing. So, actually I very much enjoy teaching and I like trying to do a good job of it. But I try to do an efficient job, too.

CARUSO: I'll just skip ahead a little bit. You mentioned, at one point, there was a woman coming in for a job talk, when you were, I think it was, a graduate student. She came in eight months pregnant and in some ways that stood out. Did your family life or your desire to have children ever play a role in your professional consideration such that, "Well, this might not be the optimal times in terms of my career to have kids, so I'll hold off," or, maybe, that faculty would look down on you for having kids at a certain period? Did that ever come up?

GOLDSTEIN: No. I think there's a nice atmosphere here...first, the faculty talk to each other for the most part in much better ways than they have in other places where I've worked. We tend to have smaller labs than, say, at Berkeley where I was. In Berkeley, there are some labs that have thirty to forty people, where, if that lab got together, they filled any reasonable-sized room. Here we have...our cytoskeletal group gets together, once every two weeks there's an informal meeting where someone talks about their research and everyone gives input. There'll be five-six-seven different labs in there, maybe even more, where the PIs, postdocs, and grad students are all sitting in the room together and people talk with each other. And I think just being able to have interactions like these and having doors open everywhere and those people are very friendly—I think maybe the weather helps a little bit, too. People tend to talk to each other a lot more and I think it diffuses at least some of the concern about this kind of thing. Now, I would have a very different experience from this as female colleagues of my same age. And I know concerns, from some of them, from talking about these kinds of things. For me, I had a good friend who did not get tenure shortly before I came up, and so that scared me a little

bit, but I thought I'd be safe and so, I wasn't that worried about it. I think in my tenure talk, I did show a picture of my son. I think it probably come across as a plea, like, "Please don't kick my daddy out. I'm hungry." [laughter] So, maybe I tried to use them to my advantage instead! But, no. My wife and I decided we wanted to have kids and we tried to time the first one. The second one, we decided we'd like to have a three-year gap between the kids and two years, four months was when the second one came, so we were surprised. We wanted to have a second one. I'm trying to think how else this has affected. I have changed...the way I work has changed a little bit since I had kids. I feel like I do make an effort to work a lot more efficiently, to get home and be with them. When my first one was born, when Duncan was born, I made a conscious effort to make sure I was at home with him more often than I would have been otherwise, if I was working like I did before. I've never been the kind of person who's tried to show how hard I work to impress people.

In fact, I remember, at one point, when I was working with Steve Hird and noticed...when I was in Cambridge, for a while, one night a week I would go to a violin-making place and try to learn how to make a violin. I have about one sixth of a violin made, which unfortunately doesn't make one-sixth the sound. It makes no sound until the last step. And I would leave right after the department meeting. And Steve Hird said to me once. He goes, "What are you doing?" He goes, "Everyone's going to think you leave at five o'clock every day." I said, "Well, what do I care what everyone thinks?" He goes, "You want them to think that you work hard." I said, "No, no. I said you want to do just the opposite. So, for the amount of research you're able to publish and get out, you want them to think you're doing the least." I didn't really mean that but I was trying to show him that you could think of this in the exact opposite way, that you don't look any more clever by trying to work hard.

So, there are times when I've worked very hard, but I try to really reign...but I didn't do that all the time before we had kids, and then I tried to reign in it a little bit after having kids. At one point, when our older son was about one and half or two, he switched preschools. We took him from a very nice home daycare to a bigger preschool, where there'd be more kids exactly his age in his classroom, which turned out to suit him very well. But at the beginning, it was a difficult transition. One morning I said, "Why don't we go for breakfast." And when we went out to breakfast, we'd start talking about preschool. I think it was an easier transition than going straight from the home, whisked off to preschool, and dropped off. Breakfast became just, I'd have a cup of coffee and we'd split a muffin at the coffee shop down the street. It doesn't take any more time—maybe it takes a few more minutes than eating breakfast at home—but it's the two of us, one-on-one, and we sit down and talk face-to-face for a little while and then we go to preschool. This has become, for me...for him, I don't think he needs it anymore. For me, it's become a complete quality of life issue. I'm absolutely addicted to these coffees now. I take both my kids every morning and we all sit down for ten minutes and split a muffin. I get my coffee and it seems like a very civilized way to start the day.

I give them their baths almost every night at night, and so I make sure I'm home for dinner and the baths, then it's time with my wife. I think that has affected how I work a little bit. Most nights I'm back on the computer in the evening, but doing things I'm really driven to

do, usually not out of obligation to race to do things, except at times when grants are due and I really need to do that.

CARUSO: So, since you just mentioned grants, within a year of starting your position, you had the March of Dimes Basil O'Connor Starter Scholar [Research Award] grant, and you also had the Pew [Scholars Program in the Biomedical Sciences] Scholar grant. Had you heard of the O'Connor grant before? Had you heard of the Pew grant before? And if so, how had you heard about these?

GOLDSTEIN: I guess there's a handful of junior faculty awards that are out there. I'd asked around from faculty at UNC and at Berkeley, where I was, what people knew of, and, again, sort of collected what I thought was, essentially, the complete set by asking people. The Basil O'Connor, I remember, it was that if you worked in developmental biology and you did good work and you had no other funding, you'd be very competitive for one. The Pew, like the [Kinship Foundations] Searle [Scholars] and things like this, is more of a long shot and I felt very lucky to get it.

CARUSO: I know at some locations someone from the university will go to...or someone from your department will go to you specifically and say, "Hey, we want you to apply for this." Some places, they leave it a little more open. They make the announcement and then they see who applies. Were you told by someone in your department that you should be applying for this Pew scholarship, or was it purely...?

GOLDSTEIN: I don't know if that was the case for the Pew. For some of them I think I was...my chair at the time was a paleontologist, who worked in a different building, so we weren't in communication as much as some chairs are with junior faculty. I forget if people had recommended it or not. The first guy who contacted me from here was Mark Peifer, a developmental biologist who works on *Drosophila*, who's got tons of energy and gave me loads of advice. I'm sure he must have mentioned it at some point. But I don't think I had the experience that someone came to me and said, "You should be the one."

CARUSO: And so, I'm assuming you developed the application. Was the Pew application similar to other applications, from what you remember? Like, were they asking for similar things? Were they looking for different types of science or scientists than some of the other applications that...?

GOLDSTEIN: Oh, for the junior faculty ones?

CARUSO: Yeah.

GOLDSTEIN: Does Pew ask you to ask these questions? [laughter]

CARUSO: They give me some freedom.

GOLDSTEIN: I see...some. [laughter] Okay. No. It was certainly similar to Searle and things like this. I knew from the Pew one that you could put creative work in there and that would be respected. And certainly for an NIH R01 [National Institute of Health Research Project Grant Program] application, some of the things I proposed for the Pew I never would have put into an R01 application. So, probably, almost half the experiments we do in the lab I would never put into an R01 and I would definitely put into something like the Pew because long-shot creative approaches are not...it's very hard to get funding for. But it's not hard to actually do them when you get funding for something, as long as they're not too much of a tax on the resources.

CARUSO: So do you remember what you proposed for the Pew?

GOLDSTEIN: I don't.

CARUSO: Okay. So I may...this is my own sort of shorthand notation: "Asymmetric cell division in *C. elegans*." You were planning to combine genetics with live cell imaging; you were interested in intracellular motility and the use of beads to study flow.

GOLDSTEIN: [laughter] So, the beads never worked out. Everything else, actually, worked out well. Rebecca Cheeks did some of this stuff. Jean-Claude Labbé, the first postdoc, did some of this stuff. The beads idea was to...I was interested in the movements within the cytoplasm that we could see happening, that other people have now studied very well, as well. So, we published a paper and Ed Munro, who works in Friday Harbor now, published a paper around the same time on them,⁸ and his was very revealing for understanding how these movements work and what they can do to accomplish to move materials around cells to get specific proteins down to one side versus the other side, to set up these initial asymmetries.

⁸ E.M. Munro, J. Nance, and J. Priess, "Cortical flows powered by asymmetrical contraction transport PAR proteins to establish and maintain anterior-posterior polarity in the early *C. elegans* embryo," *Developmental Cell* 7 (2004): 413-24.

The idea with the beads was to inject beads of all different sizes and ask: Can the flows do something purely physical just by the meshing properties and the capturing? Can things get captured in shear zones? It was thinking in very naïve physical terms about what the flow itself is like, wondering could certain size classes of particles get trapped in specific places without having...you can imagine certain proteins might get stuck in one place during a flow because there's an anchor specifically for that protein in one place. But you can also imagine there'd be physical mechanism that would segregate particles of different sizes. And so, the idea was to inject those. It's very hard to deal with beads when you're trying microinject them because, what typically happens is, you load them into a needle and they pack and it's very hard to push them out of the needle. I did order the beads. I tried putting them in a needle and tried doing some injections, but it didn't go much further than that.

CARUSO: But everything else worked out pretty well?

GOLDSTEIN: Yes. A lot of it worked out well. We definitely used the funding for other stuff, right? So, we did whatever creative experiments we wanted at the time. We started working on gastrulation which, now, a little bit more than half my lab works on, and, if we have a focus, that's the focus in the lab. And that was, one of my first graduate students, Jen-Yi Lee, was doing experiments. I think it was one of these cases where she was doing experiments during the day and the scopes were free overnight and she came up with a nice experiment to do overnight where she was...so, she loved that we could do these cell manipulations and she became very good at them very quickly. But she was really interested in morphogenesis and not...so, how changes in the cell shape can drive changes in tissue shapes that can move things around to give the proper shape of the organism instead of just a pile of cells. So, she was interested in how these kinds of movements occurred. And she said, "Wouldn't it be nice if you could use these manipulations to study morphogenesis?" because most of the people who study morphogenesis, typically they either study it in a system where you can push tissues around, or a system where you can do genetics, and not a system where you can do both, or where you can easily do both, at least. So, her idea was to do this in *C. elegans*. And this was one of these cases where I said, "That's great. But it'll never work." And luckily, she defied me and decided to do the experiments anyway.

So, what she would do is...she wanted to know did gastrulation happen? So, when you first have the endoderm moving to the inside of the embryo—which is a much better place for your gut to be than on the outside—when the gut first moves to the center, she wanted to know: Does that happen when you take the envelopes off of the embryo and you just have cells in culture and just the embryo itself a naked embryo in culture medium. And so, what she did was film a couple...there were two of these 4D scopes set up. She filmed two of them each night for about a week and came back at the end and said, "This happens every time just fine." I told her it wouldn't work because we knew that something went wrong in morphogenesis, that you didn't get a worm shape out at the end of an experiment like this. But I'd never looked specifically at specific morphogenetic events. It turns out, gastrulation works just fine, but something later goes wrong. So, this started work on gastrulation that I think is some of the

most fun and exciting. It's one of the unique contributions we've made, because there aren't many people studying this and I think it's a useful place to study. So, that was funded by the Pew money as well.

You know the way labs work. It's a little hard to know what was funded by what money after a while because we don't bring in a box of yellow tips and say these are the Pew yellow tips and these are the NIH yellow tips.

CARUSO: Right, right. In terms of the award though, were you a bit more free? I mean, it sounds like you were a bit more free than you might have been with other grants.

GOLDSTEIN: I don't know if I should have felt this or not, but I felt absolutely completely free.

CARUSO: Just to use the money in whatever way, whatever direction?

GOLDSTEIN: So, any time we had a wacky idea, we felt comfortable that we could do it because of that. I mean, to some extent, we do that with any funding. When we've got an idea that we'd like to test, we go ahead and test it. Even with NIH money. If you come back and show that you published X number of papers in reasonable journals and you're learning important things, if it's not exactly what you proposed, you can get away with it just fine. With the Pew, my impression was, this was encouraged.

CARUSO: In some ways, I find it interesting that you phrase things this way, only because a lot of the other scholars have mentioned that the sum, in and of itself, isn't really significant compared to a lot of the other funding that you would get as a scientist. And the award, at least for them, was more...it wasn't so much the currency, in the sense of the dollar amount, but what having the Pew award actually meant for you, in terms of your career and things along those lines. But you would actually say that the money helped you...

GOLDSTEIN: Well, I'll tell you. Each is true in the sense that I did not absolutely have to get an R01 from day one because I had the Pew and the March of Dimes. So, between startup money and those two...normally, when someone gets a new faculty job, they get enough money to support their summer salary and some students and this sort of thing for a year or two, until they get their first grant. I knew I could go three or four years and do what we wanted and explore a few different areas, rather than have everyone focus on one problem and only one problem. Maybe I'm overly affected by the way I like to work, but my feeling was that people having some freedom to test their own ideas makes a world of difference for their own motivation. I couldn't be the kind of PI who comes in and says, "What time did you get here

this morning? What time are you leaving tonight?” When people tell me they’re going to be off for X amount of time, if I think it’s too much, I say, “Hey, it’s your career,” and they tease me about it. I feel like they have to be self-motivated and the way to get them to be self-motivated is to really let them do what they want.

I can actually steer that a fair amount by what we read and what we discuss. We talk a lot and people get excited about what their neighbors are talking about, in the same way as I do by talking to my cytoskeletal dynamics neighbors and other PIs. But I give them a lot of freedom. Having the Pew allowed me, I think, to start a lab that was very much the way I wanted to have a lab and the way I felt fortunate to be able to work. So it allowed us to do specific experiments, but then I think it also bought time until the first R01. That meant that we could really start, from the beginning, doing the kind of work we wanted rather than working toward completing the aims of a grant immediately.

CARUSO: So, I think...I know that we’re running out of time for today. One thing I think we could end on is just talking a little bit more about, not so much the Pew award, but the Pew program. Obviously, there isn’t a whole lot that’s required of you other than attending the conferences. So, I was just wondering if you could tell me a little bit about your impressions of those conferences: what you thought of them, their intellectual utility, things along those lines.

GOLDSTEIN: Uh-huh. The people who win the awards are a real mix of characters. You probably know this much better than I do, right? For the most part, they’re very talented people who are very bright. There are some very big egos. There are some people who are absolutely a delight to interact with. And there’s some people who are both, who are both big egos and a delight to interact with. I know of one specific character, in my class, who I think is absolutely both.

I think it’s been terrific to be able to meet the people I’ve met in this group, and especially, I’ve told you about some of these people, but [R.] Dyche Mullins [Class of 2000 Pew Scholar], I look forward to interacting with him every chance I get. Rebecca W. Heald [Class of 1999 Pew Scholar] was in a year before me. I really think highly of what she does and she’s a very nice person. And I’ve met, just, tons of people like this, that I really like interacting with. There’s not an awful lot of people in my class who I keep in contact with a lot, but they’re people who I assume I’ll run into again and still have a good time talking with again. It was a shock to go. You go to the first meeting and you’re treated like royalty and scientists don’t expect that—at least I didn’t. I don’t know many scientists who expect that kind of thing. I remember the first meeting I went to, Rebecca [W.] Rimel [President and CEO of the Pew Charitable Trust] stood up, so, she’s still the...She stood up at the end and she flew in and gave this speech and thanked us all for dedicating our lives to science and to giving up the other things in our lives so that we can do science. And we’re all...we sit there, we’re having a great time talking to each other because we have similar interests. We’re all doing the drinks with the little umbrellas sticking out of them and we think, “Who is she talking to? We haven’t

sacrificed anything. We're doing what we love, right?" [...] I think it [felt] very nice to be appreciated for sacrificing something, even though I didn't feel like I'd sacrificed anything.

CARUSO: What about the format of the meeting? Is it relatively traditional in terms of a lot of the scientific meetings that you attend?

GOLDSTEIN: The one thing they do, that's absolutely revolutionary, but it may not seem like a big deal on the surface, is that they have these chalk talks. So, they have short talks by everyone and then they have—or when I was in it—it was the first and last year people.

CARUSO: It still is.

GOLDSTEIN: And then they had these chalk talks, where people will give half-baked ideas, ideas that are somewhat developed, areas that they're moving into that wasn't necessarily what they'd been studying for a while. And that just leads to a lot of really interesting discussion.

CARUSO: And although you haven't been against collaboration, did you make any connections or interactions at these meetings? I know you wound up seeing seven years worth of scholars in your four year time there. Are there any people that you thought, "You're doing some great stuff. I want to come out to your lab for a little bit," or, "You should come visit me"? Any sort of collaboration on that level or beyond?

GOLDSTEIN: I don't think so. I've had some people for seminars and talked. You know, we've shared ideas, but not material collaborations. I can't think of anyone...if there's anyone I published with from one of those groups. I hope I'm not forgetting anyone.

CARUSO: Is there anything about the Pew award or the Pew meetings that you think should be different in some way?

GOLDSTEIN: You really were commissioned by them to do this, weren't you?

CARUSO: Actually, no. I don't think they want me asking that question.

GOLDSTEIN: Oh, I see. No. I think it's absolutely fantastic the way it is. I really do. It was fantastic to be able to go to these things. I was bummed when they cut from twenty scholars down to fifteen a year, and I've heard recently...

CARUSO: It's back up to twenty.

GOLDSTEIN: So, that's great because the more people that can experience this thing, the better, I guess, if they're getting great people. No. I was really happy. The year before my mother passed away, she came with us to one. So, my wife and I went and then my mother came along. Actually, a lot of Pew scholars do this. They'll go to the meeting and then, at the end, they'll go with family or their husband or wife for a little trip afterwards. So, this was in Puerto Vallarta [Mexico] and she had a fantastic time and met a lot of people. Then at one point, when they were having the banquet at the end, she looked around and she says, "I'm going to have to report this. This doesn't seem right. You people are being treated too well." I said, "It's a private fund. It's not like they do this every night. This is a once-a-year—" No. I think it's fantastic. And it really is fantastic, not just because we're treated so well, but because we interact. Getting to interact with people you really admire and who you talk well with. That's the most fun.

CARUSO: Okay. Well, I think that's good for today. Thank you very much.

[END OF AUDIO, FILE 1.2]

[END OF INTERVIEW]

INTERVIEWEE: Robert P. Goldstein

INTERVIEWER: David J. Caruso

LOCATION: University of North Carolina, Chapel Hill
Chapel Hill, North Carolina

DATE: 25 April 2008

CARUSO: Today we're going to start backtracking a little bit. Bob, you mentioned that there are some things that you remembered that you'd like to mention that we could talk about, so, I'll just turn it over to you.

GOLDSTEIN: Yeah. So, we were talking, I think a lot, about academic experiences that affect the way I think or approaches I take, and I remembered a couple of non-academic experiences that have affected a lot. One was, when I was in junior high school, I guess seventh or eighth grade, we took classes on BASIC [Beginner's All-Purpose Symbolic Instruction Code] programming on computers, and then my parents got me a computer one year for Christmas. I had a Commodore [International] PET [Personal Electronic Transactor]. This was one of the original home computers that had 16K [KB] of memory.

CARUSO: So, this was before the [Commodore] 64.

GOLDSTEIN: So, I, at one point, upgraded to the 64. The Commodore PET, it was a single unit and it came with a cassette tape drive. I think the only software it had in it was the operating system. Each program you would load in, using the cassette player. So, they got me this. I was in one of these programs for the...these gifted and talented programs for the nerds who, instead of playing with their friends after lunch, go and do something academic. So, there were a few of us who learned to do BASIC programming on a computer. And then, once I got one of these, I was addicted for a while. There were times when I would be up all night writing programs to try to get it to do something. And it was BASIC language, so it wasn't anything that complicated. Maybe it was just me being slow that it took so long. But there were a lot of times I remember, on weekends, still being up as the sun came up in the morning working on something that I had just developed a mental addiction for.

CARUSO: What sort of programs were you trying to...?

GOLDSTEIN: Well, I wrote some just to get the computer to do things that I wanted to try to do. So, there's one of the classic early videogames, called Breakout, where you use a paddle to hit a ball and knock the walls out. And I thought, "I wonder. Could I make something that just would make a ball move around and sense where there's a wall and bounce off of it?" And so, I started making that and then started building things onto it. But it was never as complicated as even the simplest videogames out there. And then, for a little while, there was a company near where I grew up—I think it was a small company run by one guy—that sold software and he commissioned a couple things on educational software. I remember clearly writing one on geometry, on triangles and similar triangles and geometry of triangles. But usually, I was doing things just to see, could I get the computer to do something that I'd dreamt that it might be able to do. I still, actually, occasionally will program, and I only know how to program in BASIC, which almost no one ever uses, but there's online communities of people who still like to use it. There's emulators, where you can get your expensive computer to behave like an old one. And then, occasionally, I'll actually test hypotheses. Sometimes we discuss hypotheses in the lab and I think, "I could actually do a quick simulation and test a hypothesis with it." There have been a couple times where I've come back with something that affected the way that we think. But it's rare that I'm able to, because I only know how to program in BASIC.

CARUSO: Right. I only know Fortran, which again, is not one of those relatively common programming languages.

GOLDSTEIN: We thought of the Fortran people as being very advanced.

CARUSO: [laughter]

GOLDSTEIN: So, that was one thing. The other thing is, when I was a graduate student, I started off living on my own and then I had one of the friends I made, through friends at the radio station—it was a guy named Jarrett Paschel, who later trained in sociology. So, we lived together, I guess, my second and third year in grad school. My fourth year he had moved to start a sociology graduate program at University of Washington. He really affected my approach to academics and serious thinking about academics, about subjects that, often, people think of as only academic subjects in that he was, for most of the time I knew him... at first he was a student, and then he went through a year before he went to grad school when he was still in Texas. We used to go see music a lot and we spent a lot of time together. He spent a while when he was unemployed. For a while, he was working for the state board of insurance, dealing with their files, and it was a time in Texas when a lot of the insurance companies were going under, and he was the person on the other end of the phone. When someone called their insurance company and the insurance company didn't exist anymore, the call was patched through to him and often he would have to tell people that they'd lost their insurance. So, he got very frustrated with this and quit his job and was unemployed for a while. He eventually reapplied for jobs and got a job, again, with the state board of insurance, and, again, handling

these files, but now, literally, handling these files with like forklifts and boxes and stuff, in the warehouse. But all through this, maintained, really, just avid interest in all sorts of things. I guess I've met several people like this, but he really strikes me as one person who had it especially strongly, this real natural intellectual curiosity about all sorts of subjects, just to understand the world around him. I think it helped me see these kinds of pursuits as not being just a part of a program. I wasn't doing research because I was in a graduate program. I was in a graduate program because I was driven to answer interesting questions. I think that's it for the stuff I've forgotten.

CARUSO: Okay, okay. So, I thought we could continue on with hearing a little bit about where your research went and what you were doing post-Pew scholarship and, maybe, talk a bit about the grants that you've received. I know you had an NSF [National Science Foundation] IBN [Integrative Biology and Neuroscience] for 2003 to...or two of them.

GOLDSTEIN: Uh-huh.

CARUSO: ...in 2003, and R01 in 2003. And then, recently, you received a Guggenheim Fellowship. So, if you could just tell me a little bit about how...or what you were doing in the post-Pew time and what these grants were about, what you were looking to do.

GOLDSTEIN: So, I've got a way of viewing grants that...some scientists see things this way and some don't. I feel like we have to have enough funding to do everything we want. With the grants, we have some flexibility as to exactly what we do. We always intend to do the experiments we apply for money to do. But then there are lots of experiments we want to do that we never write in any grant application because they're not as sure a bet. As you know, the granting agencies, for the most part, outside of Pew and things like this, tend to be very conservative. So, we write up, really, the safest things and then do what we want. So, the funding...I don't tend to apply for funding at the start of a project—and I think this is the way many people do it. Instead, I apply for funding when we need funding, right? So, the lab is pretty much at capacity right now. I think a lot of people say that and then years later they have three times as many people, so, it'll be interesting to see if that's true or not. But I think it's about at capacity right now, and we have enough funding, right now, to do the research we want to do. Most of that is funded projects, but not all of it. Some of it is projects that are unfunded. You almost have to do it this way. Because to start anything new, now, you have to be a paper or two into it before you can get the funding, and that's a lot of work. So, I guess I don't naturally organize it in my head with regard to the funding.

So, the research I started out doing here, I kept doing experiments myself, doing experimental embryology to get at a question having to do with Wnt signaling. Wnt is a protein that's made...it's a family of proteins made in a lot of animals, including humans, that's involved in...it's a signal that cells send to other cells to tell them to do something. And the

way that's received and what happens in response varies from one cell type to another. But in humans, when Wnt signaling goes wrong, it can lead to developmental defects and it can lead to cancer, and these are two really important things.

So, I'm interested in the basic questions, but I'm also interested in it because there's a potential to make some impact in important areas, in medically important areas. So, when I found this interaction I'd found in graduate school between these two cells at the four-cell stage, I put this down and started working on other things. And while I had done that, other people found what was the molecular basis for this interaction. And it turned out to depend on one of these Wnt proteins. And this signaling pathway in the receiving cell was a classic Wnt signaling pathway. It had a lot of the components that, in humans, are proto-oncogenes, genes that when mutated can cause cancer. So, I got interested in what exactly Wnt proteins do for cells. I did a search just recently and there were over seven-thousand papers on Wnt proteins, and the diagrams that show every protein that's known to be involved now have sixty to seventy proteins listed on them. So, it's gotten to be such a big and busy field that it's becoming hard, if you aren't already in that field or trained by someone who's been in it for a while, it's hard to know what the big questions are except the big questions that people say. In reviews, people tend to write questions that are open questions, but they tend to write the ones that they're working on already. So, there was a big open question, and the way I became aware of this is first, when I was a postdoc, I was right next door to Peter [A.] Lawrence, who was really interested in these sorts of questions. He's a *Drosophila* biologist. And then also, I was discussing...when I'd discuss Wnt signaling with colleagues and I'd ask them...I had one question I was especially curious about that I would ask them, and the question was: when Wnt signals to another cell—and often cells in respond what they do is they polarize. They move proteins to one side or either to the side where the signal was presented or the other side of the cell, or the division machinery aligns with where that signal is presented—does the position of the Wnt signal really matter? Or could it be that the Wnt signal's just flipping a switch that allows the cell to respond to another signal, maybe an unidentified signal. So, I came back to asking questions about this. And there's a paper I published a couple years ago on this that describes a lot of this stuff. But it was nice, I thought, that I could do the experiments in the lab.

When I started, I set up a bench for myself in the lab and, eventually, when a few people were working in the lab, I gave away the bench to a rotation student when they'd start, and then I'd get it back. That became a problem for working in the lab. Then at times when I'd had a bench that I'd safeguarded, I would come to it and I'd be missing some of the equipment. The pipette would be missing or something and I'd go collect that. But then the thing that made it hardest to work in the lab was, I would sit down to do an experiment, and by then there were several people working in the lab, and they'd all go, "Oh, what are you doing?" And so, I'd have to stop and describe what I was doing. And they were so shocked to see me doing an experiment that it became hard to actually do one. So, eventually, I moved my microscope and my bench into my office. And so, I've got the one chair and I can swing back and forth between the desk and the bench. I don't do experiments as often as I'd really like, but I do them enough to keep me happy.

It is funny. When I'm doing experiments I find...I usually wake up pretty happy and interested in what I'm doing enough to be happy to get out of bed. But, when I'm doing experiments, I just about jump out of bed, and that's probably a natural sign of something. That I should probably stick with it because it's keeping me going. So, those were experiments I knew I could do on my own in the office.

CARUSO: Now, these experiments, are they somewhat similar to what you were doing with...I remember, in the previous session, you mentioned trying to find out if the location of the sperm entry was specific or if it was just a switch. So was it...?

GOLDSTEIN: They are conceptually similar to that, in that we're trying to understand what the [spatial] cue is and shifting the position of the cue. But they're, in practice, even more similar to the experiments I first did in graduate school, where I'd found this interaction, except now the cells I was manipulating were missing specific proteins that we knew were involved in the interactions. So, it was kind of funny going back to the exact same kinds of manipulations, but it was asking slightly different kinds of questions that I thought were important questions to answer.

At the time, I was using cells that lacked specific proteins to do this. Now cells on their surface have tons of proteins, and I was doing experiments with cells that were lacking just specific proteins, but still presented tons of unknown ones on the surface. And so, at the same time I had my first—actually my second—graduate student, Jen-Yi Lee, [thought about trying to express] *C. elegans* Wnt proteins alone in a fly cell line—S2 cells—to see, could we present just the signal alone to do the same sort of thing. I think we talked about this a little yesterday. She was the one who, near the end of her rotation project, figured out a neat way to study morphogenesis using *C. elegans* instead. And so, she left that project, and I encouraged her to do so because I was really excited about what she'd found.

But now I've got a student who's come back to this. Minna Roh [now Minna Roh-Johnson] has collaborated with a lab [Roel Nusse's] at Stanford [University] that's very good at producing purified Wnt proteins and keeping them active. Wnt proteins are sort of trouble to work with because if you look at them the wrong way, they become inactive. So, there's a lab there that's very good at making them and keeping them active. And then we're presenting them to single cells and looking at responses. I've often done cell manipulations, and I do them in these little depression slides where there's just a little well on the slide and I have tools in my hands that I'm using to do the manipulations, to do them by hand. It was always hard to do the manipulations and image them really well at the same time because I have to get my hands in there and the tools in there. Minna came up with a really nice trick for doing at least one kind of manipulation, under glass in a cover slip, so that we can do really nice imaging of this. And there's a description of this in press now. So, this was one line of work.

The other things that were going on is my first post-doc, Jean-Claude Labbé, had really diverse interests and came in with an interest of purifying P granules. So P granules, they're

little RNA—protein particles that get segregated during cell divisions to just the cells that are going to form the germ line. And they're of great interest because the germ line gives rise to the eggs and sperm of the next generation, and that's a cell line that goes on forever, or else we wouldn't see worms today—or we wouldn't see humans today! So, how the germ line remains around and all the other cells stay around only for so long and then die. The difference between germ line and other cells is of great importance. And the P granules are one in to studying this. So, his goal was to purify P granules and study what they're made of. It's the Bermuda Triangle of *C. elegans* projects. We've lost a lot of good people in the field to this project—to trying to purify P granules—and there are several people still in the field who survived relatively unscathed from failures in purifying P granules. But he was a biochemist who had purified ribonucleoprotein particles from *C. elegans* before and he seemed like the perfect person to do it. And what he discovered, early on, was that he didn't have the reagents he needed to...the reagents that were available weren't good enough to do the purification. But at the same time, he became really interested in what our neighbors, Ted Salmon's lab, does and developmental roles of the cytoskeleton and microtubules and did a really nice project with that.

So, we did some work on asymmetric division at the one-cell stage, so, how once the sperm enters, how what it brings in causes that first division to be asymmetric. How do you first set up these differences between one side of the embryo and the other? And then I had a graduate student, Nate [Nathaniel] Dudley, a really interesting guy who had come...he was a technician in a *C. elegans* lab before and he knew, already, how to do a lot of the techniques in *C. elegans*. And he was interested in doing a screen using RNA interference, which was fairly new at the time, to identify genes required for early development, and specifically the kind of things we were thinking about: how you set up the initial differences between one side of the embryo and the other. And at the time, not an awful lot was known about...some of the genes had been identified through much earlier screens. But there was a lot left to be learned and not many people had yet published these kinds of screens. Soon after he did this work, or while he was doing the work, several papers came out doing these screens en masse. So, I'm glad we're not doing that anymore because it's a heavily populated area. So, he started doing this and he found something that was a complete surprise. He ended up finding genes required for RNA interference instead. So, it was a neat story, and it's one...I think we talked about it briefly, but maybe during lunch yesterday when we weren't recording. It was a story where we wrote it up, almost exactly, historically how it happened.

CARUSO: I think that was...

GOLDSTEIN: We had a fortuitous result that we followed up on and it led to an area we hadn't expected.

CARUSO: And so, are the three grants based on those areas?

GOLDSTEIN: No. Mapping the grants to the projects, that's [laughter]... This is an interesting thing. So, having the Pew and the March of Dimes and my startup money allowed me to go longer than usual until I needed my first funding. My first R01 I wrote was awful. I'm embarrassed that I even submitted it. My second one had risen to being just bad. I think I went through a few rounds before I even came close. And then I had a not-bad score... I forget the details of it now, of the history of these. But there came a point—if it got those in 2003, it must have been sometime in 2002—when I started to panic that, if I didn't get something soon, there was going to be a problem on the horizon. And so, I wrote up a few of the things we were doing. I wrote one grant on all the asymmetric division work at the one-cell stage. I wrote one on the RNAi [RNA interference] work and I wrote one on tardigrades, something I don't think we've talked about yet at all. And all three of them got funded on the same round. So, I went from concerned that we had no funding, to no concern at all.

CARUSO: So, what happened in between for you to... I mean, it sounds like you really didn't know how to write a grant.

GOLDSTEIN: Yeah. [laughter]

CARUSO: And, I mean, we talked about this yesterday. In some respect, it was because your advisors weren't necessarily showing you. So, how is it that you went from not necessarily knowing how to write a grant to then having three successful grants? Was there...?

GOLDSTEIN: Well, it did take me a while to learn how much preliminary data you really needed to have, at least at that time, to convince people that the project was worth funding. So the two NSF grants I wrote were loaded with preliminary data. With the RNAi one, we had a paper out in *PNAS* [*Proceedings of the National Academy of the Sciences*]⁹ already, by the time I applied for it. And we had a method that, the exciting thing about the paper is... well, some of the genes that I've identified is that we had a method to do something... to do the next step. And so, I felt it was easy to write a grant that, at least to me, sounded convincing that we could do these next steps. This was exactly how the project was geared.

The tardigrade project was an interesting story, in that I had done some evolution of development work before with *C. elegans* and Nipam Patel, this guy who I almost did a postdoc with, invited me to speak at a Cold Spring Harbor [Laboratory] meeting on evolution and development. And I was excited to go and I had planned, at first, to talk just about the nematode evolution of development work and then later decided to talk, a little bit, about these

⁹ N.R. Dudley, J.-C. Labbé, and B. Goldstein, "Using RNA Interference to Identify Genes Required for RNA Interference," *Proceedings of the National Academy of Sciences of the United States of America* 99 (2002): 4191.

tardigrades, which was...they started as a project that, it was really more a hobby than...I never actually planned to have funding on it. I probably dreamed that, at some stage, it might lead to that, but it was one of these cases again where we had microscopes that weren't being used overnight and I could see an area in biology where it was very quiet and there wasn't much work and where there were some very interesting questions that might be addressed, at least initially, without that much extra work. So, I ended up talking about both *C. elegans* and the tardigrades. Now, the tardigrades, their common name is water bear. You probably haven't heard of them. Most biologists have never heard of them.

CARUSO: No.

GOLDSTEIN: But they're one of about thirty phyla of animals. So, they're a significant proportion of the diversity of animals we've defined in nature. There are about 1,000 species. They live all over the world, but they're microscopic and so, you've stepped on plenty of them, but you've never seen one probably, right? There's something charismatic about a water bear, and I can't put my finger on exactly what it is. They have a very clumsy walking, and people who see them often just fall in love with them when they see how clumsy they look. And I can't figure out what else it is. I often, now, get together with *C. elegans* colleagues and you'd think we'd sit and talk about common interests using *C. elegans*, and we very often spend the whole time talking about water bears. So, when I spoke, I spoke half about *C. elegans* and half about water bears at this meeting. People were very excited about the water bears and I had tons of questions. But like I said, it was something that was very new. Maybe it made sense that they had a lot of questions.

So, then one of the organizers of the meeting did something very kind, and I'm not sure he even realizes what he did or that it was so kind. There was a session where Judy [Judith E.] Plesset, a terrific program director from NSF who recently retired, was talking about funding and funding sources and what the NSF will fund and that sort of thing. And Richard Behringer, one of the organizers, raised his hand and made a comment about how conservative funding tends to be and asked would the NSF fund a new project, something that's unusual and sort of a pilot project, and he used the tardigrades as an example. Judy Plesset, maybe partially defensively said, "Yes. We would definitely fund something like that." That was the exact moment when a light bulb went off in my head that my little hobby could be a fundable project that we could keep, not as the major focus of the lab—at least it hasn't been. It's been 10 percent to 15 percent to 20 percent of the lab's effort, all that time. But something that we could keep funded and work on avidly, without taking too much of the stuff that...the funds that were designated for *C. elegans* research. So, then I applied and got it on my first try, which I feel really lucky to have gotten.

CARUSO: Now, had that not happened, in terms of seeing someone who actually was from the NSF...most of the scholars I've spoken to do not have NSF funding. It's almost entirely NIH. What is, or what do you see as, the difference between NIH and NSF in terms of going to them

for funding? Is it something that's really tangible, or is it just sort of, "Well, okay. Let me try this institution instead of this other one"?

GOLDSTEIN: There is. NIH will fund health-related research and basic research with some relevance to health. And if you look at an NIH application these days, for basic research, the relevance to health is often not the focus of the application. It's something that's mentioned as an aside to motivate all the research but then all of the basic research. And actually NIGMS [National Institute of General Medical Science], the institute that funds me right now, has a very articulate pamphlet they've put together about basic research. I think it's called something like, *Curiosity Drives Cures* or something like this.¹⁰

NSF funds basic research without necessarily having any health relevance at all. NSF also cares about—what'd they call it—their broader impacts. Impacts are: Are you training graduate students adequately? Are you involving undergraduate students in the research? Do you involve minorities and underrepresented populations in the research? It varies how much weight is put on these broader impacts. But, at least in name, they appear to care about these sorts of things. So, the tardigrade project, at least when it started, there was no way we could get NIH funding for that, whereas it was the perfect thing for an NSF grant. There was an NSF panel that met to review grants specifically in developmental biology and in evolution of development. And about half of their applications were in evolution of development, and this was clearly a pilot project in that area, so, it fit exactly that.

There was no NIH panel that met on anything like that. There was evolution of genetics and some areas vaguely like that, but no real sort of evo devo, evolution of development. The RNAi grant really could have gone to either, but we were doing it on a scale where an NIH grant, it would have to have been a very, very small one. And, along with reviewers being conservative in what they'll fund, they're conservative in what they expect to see. So, if you apply for something that doesn't look like an NIH grant, they agree that it doesn't look like an NIH grant, and they tend not to fund it. One sign of this is that, if you ask anyone how many major aims, specific aims should you put in a proposal to the NIH, everyone will tell you number three. Right? And I actually was sitting in a study section once where someone had seven aims and someone said, without knowing anything about the research yet, just hearing that there were seven aims said, "That's too many aims. No one can complete seven aims," without even hearing the size of each one. It seems to me like you could break—anyone I think—that you could break up an amount of science you plan to do in a number of possible ways, one of which would be in three big parts and others would work just as well. It's hard to apply to NIH, I think, for a project that...it doesn't already smell like an NIH project.

The RNAi, there was one graduate student working on this who ended up...an undergraduate, who was very good, ended up staying on as a technician, Ty [Thurston]

¹⁰ National Institute of General Medical Science, *Curiosity Creates Cures: The Value and Impact of Basic Research* (NIH Publication No. 05 5493, Revised November 2010, <http://publications.nigms.nih.gov/curiosity>).

Lindberg stayed on as a technician and worked with the graduate student, Nate Dudley, who was working on this. And then some other people made some contributions to it as well. But it was the perfect size for an NSF grant. It's hard, also, at NIH to convince people...we were not at the time, and we never have been the best lab working on RNAi. We haven't been close to that because we're not doing biochemistry of the components and that sort of thing. And that's really, I think at least now and for the last few years, that's one of the really important things that's made differences in understanding how it works. So, we knew we weren't going to be competitive with these sorts of people. But on the other hand, we knew we had a niche where we could make very important contributions on a smaller scale. So, that's the other reason I considered NSF.

CARUSO: And can you tell me a little bit about the Guggenheim Fellowship?

GOLDSTEIN: The Guggenheim...so, this was specifically for a sabbatical project. So, I was on sabbatical for the past year—I just got back in March—in Cambridge, England. And it was to interact with colleagues in Cambridge and to try some experiments with *Drosophila*. So, when I was leaving, all of my lab's funding was coming up for renewal, so, the grant on asymmetric division was ending from the NIH, and I planned to apply for a new grant on gastrulation work instead, which I now have, but I didn't have when I left. Actually, I don't necessarily have it now. I have a score that suggests I'm almost certain to have it. And our tardigrade work was...the funding was coming up for renewal. So, I knew there was a chance that, instead of doing experiments, I might end up having to spend a lot of time writing grants. So, I went there. I got back a score for the gastrulation grants, which didn't get a score that would be funded. And I panicked and started writing grants like mad. So, I wrote five grant proposals. I did a little bit of work in the lab, but ended up not doing nearly as much as I wanted, and interacted with colleagues there and went to seminars and gave seminars and traveled some as well and gave seminars. So, it was a terrific year and I think it worked out well in that the major thing it accomplished was recovering funding for the lab so that we could continue when I come back. But experimentally, a lot of experiments that I wanted to do I ended up delaying until I came back. I've changed my mind about the kind of experiments I wanted to do. I'm back now I'm doing *C. elegans* experiments and tardigrade experiments whereas I'd planned to do *Drosophila* experiments.

CARUSO: So, since we're, just generally, on the topic of funding and it's clear that, based on what you said, there are some issues with the way the funding works: you need data in order to get a grant and generate data, that your funding can dry up as a scientist, which means everything ends. Do you have any feelings towards the way that funding is done in the U.S.? I mean, comparing it to your postdoc experience in John White's lab where you needed something, you asked for it, you got it. Now, I know that's partly because the lab had developed a lot of equipment. But it also seems like things are a bit easier for scientists there. That could be a gross generalization that's incorrect, but I was wondering if you could say a little bit about this.

GOLDSTEIN: I got to see, again, where I used to work. Although I was in Cambridge again, I wasn't at the same place. But I saw how people there...they have historically put a cap on lab size there and that cap has risen so that there are people who have labs around the size of mine now, and mine's not especially big, but there are people with similar size labs. I was very jealous to see them operating without worrying about grants and all. And they would discuss science and think about science. On the other hand, they have pressures, too, that are slightly different. So, the pressures I could see they have is they need to convince people, continually, that they're doing valuable work in other ways and in ways that there's...our system isn't perfect, but it's, for the most part, transparent, or at least as transparent as I can imagine it is possible. Whereas there, the system is a lot less transparent, I have the impression. People just thought you were good or didn't think you were good and it was very hard to know who was making the decisions and why you were promoted or not.

So, I have a love/hate relationship with the funding system here. It's terrible that very talented people...I see talented colleagues who lose funding, who were doing terrific research, but there's only so much money out there, and especially now. The last few years the money's been very tight for U.S. science research. It's terrible to see them lose funding, and especially with junior faculty at the time. We went through a doubling of the NIH budget, over a quicker time than inflation would have doubled it, and then it flattened out dramatically for a while. During that time, universities—at least ones that I could see—were expanding very quickly. Here we were expanding very quickly, taking on a lot of new faculty. Although there's more money than there used to be, there's tons more people applying for it. And so, it's gotten really difficult. Your question was about the...?

CARUSO: Just about the general process and your impressions on funding.

GOLDSTEIN: The way it works by anonymous peer review, in general, I think is a terrific system, and yet you're throwing the dice an awful lot because the two or three people who are the main reviewers of any grant have a lot of say and they don't necessarily see things the way you do or the way your closest colleagues do. The people who think about the problems from day to day, you don't necessarily get the best pick of them, but I don't know how else you would control that.

There are differences between how NSF and NIH does this that are interesting. So I've sat on panels for each of them and NSF, they will have a panel meeting where there'll be, usually, two reviewers assigned to a grant. But then, as well as that, they use mail-in reviewers. So, they get a lot of outside opinion. Of course, a mail-in reviewer who only sees one grant or two or three grants in a cycle when they score them on a scale that goes good, very good, excellent to outstanding, these sort of things, it's very hard to know what their judgment means because they're not comparing with as many as you are when you're looking at a dozen or so. But I think the program directors that I've dealt with...Judy Plesset was fantastic at navigating

through this, or at least it appeared very good to me sitting on the other side of it. At NIH, they don't use the mail-in reviewers. So, whoever's sitting on the panel are the people that really matter to you. On the other hand, they're more transparent than that. They tell you who's on the panel so you know...you can picture who your audience is going to be. Usually, up to about half the panel can be people that you didn't necessarily expect because they weren't recruited until later. And then, people who are on the panel sometimes will sit out in one of the panel meetings. And so, it can happen that you don't actually get who you expect at all. I mean, you look at the panel numbers and you're not absolutely sure who you get. But for the most part, *C. elegans* grants will go to at least one *C. elegans* reviewer, if not two, and so, you can make a guess who you'll get.

CARUSO: What about this whole notion that you need data in order to generate data? I mean, to me it seems a little contradictory. "Can I have some money to continue with the stuff that I'm already showing you kind of works?" instead of asking for money to get something going. "This is something that hasn't been looked at. I think we should look at it. Can you give me some money to do experiments on it?" Even if, let's say the NIH wanted to say, "All right, for those types of grants we're going to give you much less in terms of funding. It's not going to be a full project. We'll give you a little bit to see if it works"

GOLDSTEIN: Well, they have programs like this. But I've had colleagues who've applied for these things tell me...a colleague in this department who applied for one of these smaller ones at NIH that was told by the program director this was the best one [R21 proposal] they'd reviewed in years, and no, it wasn't going to be funded.[laughter] Because it wasn't good enough. So, I think what happens is, inevitably, as reviewers review these grants...and I know when I've reviewed grants, I've had the same feeling. Inevitably you look at that and you realize this is up against grants from people who've already done the experiments to tell you that this is going to work and how could you not view that as a better thing. So, inevitably, in a system where there's not enough money, that's what has to happen.

At NSF, I have seen Judy Plesset, at the end of a discussion on a panel, ask, "Is there anything that you knocked down a rank, because of lack of preliminary data, that you thought was really very exciting and you wish could be funded otherwise?" And at NIH, the program director is an administrator. At NSF, the program director makes the decision of what will be funded or not, making use of the panel's recommendations. And so, I don't actually know which ones she funded and which ones she didn't. But she at least asked the questions to circumvent this natural tendency to be conservative.

CARUSO: Interesting, interesting. Now, I guess one of the things...I guess this is for my own education/clarification. I go around interviewing a lot of biomedical scientists and they come from a lot of different fields, right? Some people are working on specific viruses, Kaposi's sarcoma. Some of them are looking at the way molecules move in cells, the way that proteins are regulated, lots of different things, yet everyone is called a biomedical scientist. And what

I'm not really sure of is what biomedicine actually is. Do you have anything that you could say...are there any parameters that you have in your own mind that says, "Well, this is biomedicine, this is not"?

GOLDSTEIN: My graduate advisor, Gary Freeman, had, maybe, a bad attitude about doing research because it has medical relevance. I think there are certain people who think you should only do research in biology that has medical relevance. There other people who see that you should do research because you're curious about how things work and that in many cases, but not all, that will end up having medical relevance. And I think it's becoming more and more clear that doing research just for curiosity can have dramatic effects, specifically in medicine. Rarely am I defined on paper somewhere as a biomedical scientist. I think the Pew is one of the cases where I was. But I don't see it as inappropriate; it's just not the label I would normally use myself. It's appropriate in that we're asking really, I think, fundamental questions about how proteins involved in cancer and in human development function. But we're asking them, for the most part, because we really want to know how they work. To me, it's like...I had a good friend in Berkeley, who I knew from college, again, from working at the college radio station. She worked in a company in town. It had nothing to do with academics. They were making programs for companies. She used to tease me about it. She'd say, "Is this some kind of welfare program for you guys? They're just giving you some money to keep you out of trouble or something?" And I'd try to explain to her. The only time I think I ever really got it through to her, where she really completely understood the point, was I said, "Astronomers look up into the sky because there's a lot going out there and we don't have a clue what going on and we want to understand what's around us. And there's probably a lot of really interesting things going on." I said, "This happens on the other scale of size, too, that the tiny things that are all around us and that make us up, we can be ignorant of. And there's a lot of fascinating things happening and it gets to the heart of how we work, why humans are here, and how they function. But also everything we see, all the organisms anyway, we see around us and in nature as well. And how could you not look when given a chance to look? You'd be crazy not to look."

So, I'm glad that it has medical relevance and it can be funded for this reason and hopefully it will help people at some stage. I do occasionally think, especially with my family history of multiple sclerosis, I do occasionally search through the literature on multiple sclerosis and other autoimmune diseases and look for genes and occasionally see the *C. elegans* have a very similar gene. I actually found one recently that I'm tempted to...I might start an experiment soon on. But for the most part, I'm not doing experiments for that reason. For the most part, I'm doing them because I'm very curious, and that's true for most of the people in the lab and most of the people I interact with in science.

CARUSO: I guess the last question...I'll say it's the second to last...I won't say question. I'll say topic that I was curious about, and this is based very much on what you've described to me in terms of, during graduate school and whatnot, your activism, to a certain degree. A lot of people...maybe I won't phrase it that way. People do criticize specific political/social/cultural

groups for waging a war on science. Jack Keene, who I was speaking to earlier, feels that the current Bush administration really has not helped science in many ways. He referenced Hillary [Rodham] Clinton's use of the term "war on science."¹¹ She wants to stop the war on science. Do you feel, as a scientist, that you should be... Well, one thing is, do you see there being a war on science? And as a follow-on, do you feel that, as a responsible scientist, you should be in the trenches in that war fighting battles to make sure that funding does not go away or things along those lines?

GOLDSTEIN: Yes. I mean, I think there are some well-documented cases where the Bush administration has twisted scientific facts or selectively presented scientists' facts to make a lot of points that seem awful, that they clearly shouldn't be doing. My activism in the past was, in part, driven just by an adolescent anger, maybe as much as my real concern about issues. But I am active now. North Carolina has a lot of poverty. I'm really proud to be working at a state university that serves the public. When I interviewed at UNC and Duke, one of the faculty of UNC teased me by saying, he said, "Oh, you're from Long Island? You'll love it at Duke. Everyone's from Long Island." [laughter] The flip side of that was, at UNC, they require a minimum of—why it's 82 percent, I don't know—but a minimum of 82 percent of each incoming class must come from the state of North Carolina. In each basketball game that's shown on TV... So, basketball is the way everyone in North Carolina learns that there is a university. At each basketball game they used to have this quote from Charles Kuralt, who came from the University of North Carolina, where he makes... it's really almost a socialist rant, where he would say, "What is it that ties us to this place." They'd show pictures of ivy-covered walls and this sort of thing. Then he goes through, "Is it this? Is it that?" At the end, he just said, "It is because, it is as it was meant to be, a university for the people." It feels great to be at a place where, when I go teach cell biology and there's one-hundred and fifty students in the class, I look out and it's the proportion that are African American or Hispanic or Asian are the proportions that you see, roughly, in the state. That feels much better than teaching to one-hundred Long Islanders. I've got nothing against people from Long Island, but it feels good to be able to know that you have, at least, a potential to make an impact on people more generally, and people who are traditionally underserved in education.

Now, in North Carolina... North Carolina is well into the bottom half of states as far as how much they fund per pupil for education before they get to the university. And so, the students we get in, they do a nice job at the university, I think, of making sure they get students that represent the state by having an unwritten rule that they'll take the top few percent of every high school in the state, and that means high schools funded as well as Chapel Hill/Carrboro schools are, but high schools funded as poorly as some of the others are. And so, then the incoming class looks like the state.

They have a program now—they call it the Carolina Covenant Program—where students who come in, if their family makes less than—it used to be less than one and a half times

¹¹ Hilary Clinton, "60th Birthday Speech," (New York: Beacon Theater, 25 October 2007).

poverty rate and then I think someone noticed how low the poverty rate is and they now make it less than double poverty rate—they're guaranteed to be fully paid. The difference between what they can pay and their need is fully covered, and fully covered without any loans, which is the important thing because a lot of kids at that age are just afraid that the loans will bury them. And they make a very clear, simple promise. "If your family fits this, you'll be fully covered, and that's it." Now they actually don't pay the whole thing themselves. They help the students apply for grants and then they cover the excess. They also make this advertisement that, I think, honorary chair, or some title given for the program, is the basketball coach [Roy Williams] who makes the announcement during the games. So, on TV, people around the state see, when their kid's watching basketball on TV, "Any student who's bright enough, and even if they don't have enough money, can come to this university." It feels great to be teaching in a place like this. So when the students come in is the part I said I was active in. Last year I volunteered for this Carolina Covenant Program as a mentor for some of the incoming biology students. And we took a bunch of the students to a basketball game. We went for a dinner with them and then I met with some of them here, in my office, and then I'm available to meet with them at various times. Because I think, often, when kids come in and they don't...for most of these kids, they've never had anyone complete a four-year university before in their family. In fact, I was the first in my family to do so. They come in and they're confused about what's going on. They don't know their professors. If I'm teaching cell biology and there's one-hundred and fifty students, they don't necessarily know their professor. So, this is a chance to have some personal contact with someone in the university who they can talk with. I don't actually see very many of them very often, but I think they appreciate having some contact like that. So, I'm much more interested in this sort of thing where...I think there is a problem with science funding and there is an attack on science. And I do my part to try to help when we've got a funding crisis, to write letters to congressmen and that sort of thing. I try to articulate what we're doing to people anytime someone's interested, because I feel like it's a part of the responsibility of having public funding. But I'm much more interested in the day-to-day problems of kids coming in from poverty and coming to university and being able to...there's a lot of really bright minds who would go wasted if they weren't looked after.

CARUSO: So, the only other thing that I have. I actually like to end the interview with asking you if there was something that you expected me to cover that we haven't, or something that you would like to talk about that I have haven't asked you about. If not, that's fine, but I just like to...

GOLDSTEIN: There is one thing that really stands out, which is almost anyone in science I talk to who knows what we're working on says, "Why on earth are you working with water bears and how did that come about?" So, I'd be happy to talk about that.

CARUSO: Sure, sure.

GOLDSTEIN: So, I'd done some experiments in evolution of development during my first postdoc. And then during my second postdoc, I was studying a question that was intended to be a project that addressed how development evolved. When you're studying about the broad question of how morphology evolves through changes in developmental programs, you want to identify the genes that are going to be important for this. And when you identify the genes that are going to be important for this, you make use of, usually, a model system. So, there are a lot of people, like Sean Carroll and Nipam Patel, who've done well by studying, instead of *Drosophila*, they study other arthropods and they make use of the huge body of knowledge from *Drosophila* to guess which genes might be controlling changes in morphology.

When you do this, you always know you're making a good bet when the gene you're studying is involved in controlling development in *Drosophila* and in another model organism. But the other model organism is often a mouse or something that's so distantly related that your success rate is not going to be as great as you'd like. So, in my mind, I thought you could make unique contributions if you could find a new system that was related to a couple of model systems; not just one, but two models systems. And while I was in my second postdoc, it was...this animal tree of life was dramatically reorganized by a paper by Aguinaldo et al¹² that found that *Drosophila* and *C. elegans* were much more closely related to each other than previously suspected. I didn't really believe the paper at first, but after a while and seeing more data pile onto this, I started to believe that this was really true, that [...] *C. elegans* and *Drosophila* are much more closely...nematodes and arthropods are more closely related to each other than we thought. Now, this reorganization put with those two phyla, with nematodes and arthropods, they've put a lot of organisms, a lot of other phyla, for which there's very, very little data on how they develop. So, the other groups are...so, there are only about 30 animal phyla and most of these phyla you will have heard of, like mollusks and there a lot of these words that are at least familiar to...If you look in this group, there are words that most biologists have never heard before. So they're the onychophorans, the tardigrades, the kinorhynchs, the priapulids. Most biologists haven't heard of them. Most biologists can't even pronounce them, right? People in my lab affectionately call them, they say in this phylum is arthropods, nematodes and a bunch of losers. [laughter]

I was familiar with a lot of the really old literature, the old embryology literature, through my graduate advisor imploring that we read this and reading and discussing some of this stuff. And I knew there were these old developmental biology textbooks by Libbie [H.] Hyman, who...they're actually invertebrate zoology textbooks that had developmental biology sections in them. There's an old French set of books that are similar, *Traité de Zoologie* that also cover very old embryology.¹³ And these groups were almost absent from these books. So, I knew not much was known in these things. Onychophorans, there had been a little bit of interesting work on. The others there wasn't so much. So I decided...is the tape okay?

¹² A.M. Aguinaldo, J.M. Turbeville, L.S. Linford, M.C. Rivera, J.R. Garey, R.A. Raff, and J.A. Lake, "Evidence for a clade of nematodes, arthropods and other moulting animals," *Nature* 387 (1997): 489-93.

¹³ Pierre-Paul Grassé, ed., *Traité de zoologie, anatomie, systématique, biologie*, 52 vols. (1950-1979).

CARUSO: Yeah. I'm just making sure the battery is ok.

GOLDSTEIN: Okay. I decided to see if we could adopt one of these in the lab and try making films and see if any of them had small and clear embryos, so that we could do this 4D imaging. So, the 4D imaging depends on being able to do optical sectioning through an embryo and it would have to be clear enough to do that. Big embryos tend to be filled with yolk and you can't see through them very well. And so I thought, if I find small ones and then I put them on the scope and they look clear, maybe I could start to reconstruct how they developed by just watching cells divide the way people did in *C. elegans*, as opposed to the way people track cell lineages in other organisms, which is by injecting lineage tracers into cells. It was actually David Weisblat, my second postdoc advisor, who developed this method. So, I thought if I could do this optically, I could literally set up a film on that scope at night, come back the next day, and reconstruct the lineage in a day, at least the beginning of the lineage in a day. And so, I started collecting tardigrades. So, I got some from the wild. I say the wild, but I found some moss outside and shook it out in some water and some fell out.[laughter] Those were wild tardigrades. They can dry out. When they're dry, they're rumored to blow around, all around the earth. So, a lot of species live all around the earth. When they dry out, they enter this resistant state in which they're famous for being resistant to almost anything. They can survive a vacuum, close to a space vacuum. They can survive low temperatures down to below one degree kelvin, where all molecular motion stops at close to there. So they survive crazy things. In fact, someone recently put some on a Russian rocket and opened the case and left it open for six or seven days and then brought them back to earth and we're waiting for the report on whether they survived it or not.

CARUSO: Wow.

GOLDSTEIN: I think these sorts of stories and how cute they are make them famous. People who have seen them, love them. People who have not seen them, have never heard of them, right? It's a strange dichotomy. So, I got some from the wild and then I got some from biological supply companies, from Ward's [Natural Science] and Carolina Biological Supply [Company]. And the people at these companies, I was surprised to learn, will gladly share their protocols for raising these things. So, there was a problem in that people couldn't raise them through many generations in the lab. There was someone who had raised them through about six years in the lab, although it wasn't completely clear from that paper whether it was the same collection they were looking at all that time. But the record wasn't as long as we'd like, and in most cases, they weren't lasting through many generations. But at the biological supply companies, they were keeping them at least through some generations. So, they told me how they did it and I start filming embryos and looking at these. People in the lab laughed. My postdoc, Jean-Claude Labbé, thought it was hilarious that I was doing this and was not discouraging, but did not understand at all why. I would explain my interest in it, but it was so far removed from his interest trained as a biochemist that I think he really didn't understand.

[laughter] So, I filmed some of these and I saw that, in fact, there were some of the small and clear embryos. And then I went to a *C. elegans* conference and saw an old friend and colleague Mark [L.] Blaxter, who's at the University of Edinburgh. I feel like I spread myself thinly, a little bit, working on too many different things. Mark really goes crazy with this. He does all different things. And so, we were talking to each other—this was at UCLA [University of California, Los Angeles]. I remember standing on the steps of Royce Hall and he said, “What crazy things are you working on?” and I said, “Tardigrades,” and he looked at me like I was nuts because he, too, was working on tardigrades.

CARUSO: Oh, interesting.

GOLDSTEIN: So, he thought I was nuts, but he understood. So, he was sequencing genes from a species of tardigrade and he'd collected a bunch of EST [Expressed Sequence Tag] sequences. And we agreed that it would be best if I was doing my developmental studies on the same species that he was doing the sequencing from. And so, I got some of his. Actually, his lab sent me tardigrades a couple times and they kept arriving dead, which wasn't good. And then eventually when...either they would arrive dead or they would die soon after arriving. At one point, I asked someone in his lab to send the protocol for how they kept them and I noticed on the protocol it said where they got them from. And so I called up. It was a biological supply company in England called Sciento, run by a guy named Bob [Robert] McNuff, and he sent me some and there were loads of them and it turned out to be very easy to keep them.

At one point, when I was working on them, after I'd worked on them for a while, and the scientific work is all described in papers, but there's an interesting story that wasn't, which is, at one point, I had called him and asked him how long...how often he re-collects to continue his culture. He said, “Re-collect? I got these in 1987. I've been using them ever since.” So, I said, “Bob, no one in this field can grow these things through generations.” It was quiet for a moment and he said, “Are there many people in this field?”[laughter] And admittedly there weren't, right? At that time, the last paper on their development that, at least in our mind, was very informative, was published in 1929 in German. There was one interesting paper in between, but not so relevant to what we were doing, by Jette Eibye-Jacobsen, I think in Denmark.¹⁴ And then while we were working on them, a paper came out from another lab on them, not on the species we were working on, but another. So, you could read the entire literature in an afternoon. If you don't read German, you missed most of the literature, but you could read all you can in an afternoon.

Okay. So, I asked this guy, Bob McNuff, when he got them, “You've had them all this time.” I said, “How do you keep them? What kind of medium do you keep them in?” He said, “I raise them in Volvic.” I said, “Volvic. I've never heard of that.” He said, “Volvic...bottled

¹⁴ Jette Eibye-Jacobsen, “New observations on the embryology of the Tardigrada,” *Zoologischer Anzeiger* 235 (1997): 201-16.

water.” So, I thought this can’t possibly be, that this guy’s been raising them in bottled water and no one else can raise them. It turns out, he’s also feeding them a unicellular algae and it may be that there’s something essential in the algal culture that people weren’t giving them before. I did try growing them—we grow them in Crystal Geysir [Alpine Spring Water], the local bottled water. I did try them in Dasani once, which is Coke’s bottled water that has...it’s distilled water and they add the minerals back in, and I couldn’t do it, but I don’t know if it was my own inability or just Dasani does not support tardigrade development as well as Crystal Geysir does. So, we keep them quite easily in the lab. I don’t have any right here, but people do have them in the lab, in little Petri plates. Being able to keep an animal in a Petri plate is what allowed the microbiologists of the 1950s and 1960s to switch to studying animals. Later on they thought, “If we can grow them and treat them like viruses and bacteria, we can do experiments.” And so, I’m sort of pleased that we can keep them in something as simple as a Petri plate with very little care.

Bob McNuff, his company Sciento...I did a search for it on the Web when we were first interacting and I could not find anything about it except for a couple of school sites that said, “This is where we get our tardigrades from,” or other...He sold a few other organisms. And when I phoned him, he or his wife would answer the phone and they’d say, “Hello?” [laughter] They would not say, “This is Sciento.” So, I had a feeling this was a small operation. I did notice, although when I searched Sciento I wasn’t finding much, when I searched his address, I would find a lot. What I would find is a pub that would appear repeatedly when I’d search for this. And there were loads of instances on the Web where the pub had this address. And so, at one point, when I was talking to Bob about something I said, “I hate to be prying, but are you selling these out of a pub?” And he said, “Oh, no. That’s a few houses down from where I am. There’s a pub and I often get their mail. They’ve got a mistake in the address.” But because this pub had this address all over the Web and his company didn’t, I was still suspicious. [laughter] So one time, when my wife and I were visiting friends, and we were actually quite close to this address and I had taken the address with me just in case we had gotten that close. I wasn’t sure how close...this was outside of Manchester [England]. We had friends who live near Manchester. I wasn’t sure if we’d be near or not. So, when I realized that we were that close and we wanted to stop somewhere for lunch, I said, “Let’s go find this pub.” And so, we went to the pub and I phoned Bob, but he wasn’t in, so I haven’t gotten to meet him in person yet.” And sure enough, the pub was not his address. It was a few houses down. Behind his house, there is a small shed and I think that’s where he runs the company out of and he sells just a few things out of there. He was very kind to give us his culture methods because this is the way he makes his money. But he sells them pretty cheaply and I guess it’s probably to his benefit, in the long run, that other people are adopting this organism and other people are looking at it, that there’s more people know that that’s a place you can get it from. So, hopefully he’s selling more, although he’s not selling them for enough money to make too much on it.

He’s an author on our paper in return for putting his culture methods in the paper. You don’t often get to write something like this in a scientific publication but in the abstract, we could say, “These can be raised for decades.” It had just been two decades, so we could justify saying decades with an S at the end, and normally you can’t say you’ve done anything for

decades because you can't normally work on that until the first publication. It was nice to be able to recognize his contribution that way. And I guess all the rationale for working on the tardigrades and what we're finding with them are just described in the papers.

CARUSO: Okay. Is there anything else you'd like to mention or talk about?

GOLDSTEIN: Boy, not that I can remember right now. I'm sure once you leave I'll remember a whole bunch of things.

CARUSO: Okay. Well, you can always add them later.

GOLDSTEIN: Right.

CARUSO: All right. Well, thank you very much.

GOLDSTEIN: Okay.

[END OF AUDIO, FILE 2.1]

[END OF INTERVIEW]

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