INTERVIEWER: Today is March 2nd, 2010. I am Karen Arenson. I'm speaking today with H. Robert Horvitz, the David H. Koch Professor of cancer biology at MIT, who shared the Nobel Prize in Physiology or Medicine in 2002 for discovering and characterizing the genes controlling cell death in microscopic worms known as the C. elegans. Bob, who's a 1968 graduate of MIT, is also an investigator for the Howard Hughes Medical Institute and for the McGovern Institute for Brain Research at MIT, and a member of the MIT Center for Cancer Research. Bob, thank you for talking to us.

In your Nobel speech, you noted that your parents raised you to ask two questions, how and why. How important are those questions in science and what makes them important?

HORVITZ: Well, I think I would back up from that a moment and say what my parents taught me most was to respect and appreciate other people -- something that is important in science and life well beyond that. Asking questions about what goes on around you is something that I believe all people should do.

But, of course, asking and then attempting to find ways to answer questions is at the core of scientific inquiry. So growing up hearing what is this, how does it happen, what's the basis of it, why, how? Those are really at the core of science and I think although we certainly didn't know it at the time were key in setting the stage for the subsequent scientific careers, not only of myself, but also of my little sister.

INTERVIEWER: Who went into biology also.

HORVITZ: Who went into biology also, although with a completely different history, a completely different set of early interest, and a completely different approach and interest in the field of biology. But yes, we both ended up as scientists, we both ended up as biologists, and people are often amused when they discover we're related.

INTERVIEWER: You also said that your parents' belief in you gave you the confidence to go into science. Can you talk about the role that self-confidence plays in science research?

HORVITZ: Well, again, I would say confidence is key in all walks of life, and it's just very important for any individual, and in science in particular where you're exploring the unknown. You have to have the faith that one, you can do something, and two, that it might be of some earthly interest, at least to you, if not beyond that. And what my parents did, and, you know, I think it's something all good parents should do, is basically reinforce over and over the statement "do your best -- if you do your best, that's all we ask." And whatever happened, sometimes good, sometimes not so good, they would say "if you're doing your best, we support you."

INTERVIEWER: That's actually a heavy burden I think to feel like you've got this whole open-ended quest to do well again and again.

HORVITZ: But the best doesn't necessarily mean be manic and unilateral -- best means approach life in some way that's reasonable. So I think I learned from them not only to strive, but also to balance. And, you know, they again, taught me about people -- you know, do things that are going to be helpful to people. My father always had a smile for everybody around, he learned bits and pieces of more languages than I can even name and could often talk to people a little bit in each of their own languages. And he carried in his pocket candy, and if he saw a kid he'd give the kid candy, if he went to a teller at the bank and the teller was scowling, before he'd say anything he'd take out a piece of candy and the person would smile, and, you know, that is doing your best, it's doing your best in all walks.

INTERVIEWER: Tell me some more about your parents -- who were they, what did they do?

HORVITZ: Both of my parents were first generation born in the US from parents who had come to the US from Eastern Europe, basically. My father wanted fundamentally to be a professional baseball player, but he couldn't see -- his eyes were at least as bad as mine, and he also was too poor to afford a pair of glasses. So he didn't get to play a lot of baseball, and at one point in school one of his teachers actually bought him a pair of glasses, which helped him with the school work, but I guess not enough to do baseball. He was always, again, asking questions like why. He was very interested in science. He wanted to become a chemist, but he had to earn a living, and so he didn't do that. He went to night school in basically accounting and he became involved in finance, eventually moving to be vice president of a company in the US based upon his knowledge of accounting and finance. And again, with all of that he really dedicated himself to the field he was working in.

One of the things that has amused me is that in this context he ended up at a variety of meetings where finance and accounting were intersecting with the emerging world of computing machines, first accounting machines, and then a little bit later computers. And one of the final sentences in an article he wrote in the '50s, which has always echoed with me, is he says "The possibility that computers might have business applications is something that should be considered seriously." So that was prescient, and what was striking about him that I think really I absorbed was the fact that he loved numbers. He played with numbers, numbers were his friends, he always enjoyed anything that involved numbers, and I think he instilled that interest in numbers in me and no doubt was very much related to what much later eventually sent me to MIT.

My mother grew up at a time when opportunities for women I think were rather limited. She became a school teacher, a very dedicated, and from what her students have told me, the ones that I've encountered, a very good school teacher. Her area of expertise was really English literature, but as elementary school teachers progressed, they often moved to areas that they had less training in, and she ended up as a teacher basically of science, and went and got a Masters Degree in astronomy at one point so that she could better teach science. And so she was always at home, you know, thinking first about English and then later about science, and I grew up in an environment where I had the math from my father -- I also had the English from my father. He could work a double crostic or a crossword puzzle, even one of the diagramless crossword puzzles by just sitting down and filling it in -- never flinched, never erased anything, he just did the whole thing. His knowledge was amazing, and he was vastly smarter than I ever hope to be. And so he had the combination of the English and interest in science, and my mother had the interest in English and science, and all of that instilled in me I think a great respect for both areas of inquiry.

INTERVIEWER: Did you have any friends or relatives who were scientists?

HORVITZ: Yes and no. Not really any friends or relatives, except a cousin who was a few years older than me and actually very instrumental. And he, like I, had grown up in Chicago. He, unlike I, was very involved in sports. He became a serious football player who was recruited to play college football, broke his nose three times, decided this was not the way to live, went back to school and became a biologist. And he was the one who interested me in biology, he supplied me with fruit flies drosophila to do a science fair project when I was in high school. And much later when I was thinking about what to do for postdoctoral research, I talked extensively with him and he encouraged me to basically enter the area that has really been the basis of my career ever since. So, he was very influential in science, and also he moved to Europe for his own scientific inquiries and encouraged me with the idea that broadening one's experience in that way would be a good thing.

INTERVIEWER: With all these little relationships to science, it wasn't really till your senior year of college that you decided to head in that direction yourself. Are you surprised in looking back that it took that long for it to flourish within you for that kind of passion to begin to develop?

HORVITZ: I'm not sure that I've ever, to this day, decided on a direction. I've tried to follow my interests, and my interests have always been very broad. So, as an undergraduate, I majored at MIT both in math and in economics, and I took many courses in both computer science and psychology. So there were a variety of interests. I became very involved in student government, and that led me into thinking about other possible professional pursuits, maybe law, maybe business. There was some temptation of medicine. So there were many, many different fields that I was considering. And indeed, it wasn't until my senior year that I ever took a course in biology. I had in my junior year been exposed to an unusual course that was co-taught from the humanities electrical engineering and psychology departments by Jerry Lettvin, of course, called "The Biological Basis of Perception and Knowledge." And that intrigued me with the possibility of maybe using some of my math to understand biological problems of the brain, but it wasn't really a course in biology.

I did take a course in biology my first semester of my senior year because an ex-roommate and good friend, Al Singer, said to me biology had become interesting. My exposure to biology previously in high school was basically dried plants and stuffed animals and a lot of formaldehyde and it didn't seem very lively. But I took a course from Cy Levinthal when I was a senior, and I loved the relationships between chemistry and biology that emerged very early on in that course.

And, in fact, it was Cy who was pivotal in encouraging me to pursue a possible interest in biology. I went to him six months, I'm sorry, six weeks into the course and I said Doctor Levinthal, I'm taking 701, your introductory biology course. I'm majoring in math and economics, I know nothing about biology other than what you've lectured on, and I'm thinking maybe I want to go to graduate school in biology, am I crazy? And what Cy said was my undergraduate degree was in physics, my PhD is in physics, and I'm teaching your biology course -- you would be starting early. And importantly, in response to my question, he said, and I'll write you a letter of recommendation. So, that moved me into biology.

But even then, it was an experiment. I had no idea if I would like it, I had no idea if I would be able to do it, and I felt that if it didn't work after a year of graduate school I could go back and do something else, maybe go work for IBM -- something I had done for four summers before, or pursue some other interest. So it wasn't a decision, it was an experiment, and frankly, that's the way I regard all of life -- there shouldn't be decisions, there should be experiments, and if the experiment doesn't work, you do something else.

INTERVIEWER: You seem to have always been an incredibly hard worker. You talk in your Nobel biography statement about when you studied, I think, in high school, how you tried to think of every possible question a teacher might ask on a test and then wrote down both the questions and the answers, how did you develop that approach and why -- I mean it seemed some very focused and disciplined.

HORVITZ: Excessive might be a description. But I tended to do things very thoroughly. And in studying I found that writing things out put them in my brain much better than simply reading them. And so I tried to write out what I could. I would write notes from course material, and the easiest way to study I found was to think about what kind of questions might the teacher ask. So I would write them down, and then having written them down, I would write down the answers. And then I would study these until I could do all answers from all of the questions and all questions from all of the answers. And it probably was a bit of overkill, but frankly in the grand scheme of things, I don't even think I spent all that much time on it.

INTERVIEWER: Interesting. Did your friends work that hard? I mean did you have a circle of people, or did they say gee, whiz, why do you do this, or did they not even notice?

HORVITZ: I don't know if it ever was a topic of conversation. Certainly, my friends were highly varied in the degree to which they took academics seriously -- some were very, very serious. One of my high school friends was Marty Chalfie who received the Nobel Prize recently in chemistry, and he was a very serious student, he was also a very serious swimmer. Others of my friends were not serious at all. So I think we each did our own thing. It wasn't that we did this together, but rather that we each pursued what we thought was appropriate.

INTERVIEWER: What do you think made you work so hard? Does it get back to your parents telling you to do your best, and when you thought about best, it was really saying I need to think about what it takes and do it?

HORVITZ: You know, so this is basically a nature/nurture question. So, to what extent was this intrinsic in me, and to what extent was it imposed by my environment, and as an experimental scientist, I can say there's no experiment, there's no control, so there is no me separate from either my environment or my parents. So I can't really say what it was. There's no question that my parents instilled in me a sense of responsibility and a desire to "do my best," but at the same time, you know, there was something in me that really did drive me to do this, and in thinking about it, you know, my sister also has always been an incredibly hard worker and very, very dedicated and probably works harder than I do to this day.

INTERVIEWER: Do you employ this kind of exhaustive approach in your science and is part of what's contributed to your success, do you think?

HORVITZ: I think I've always tried to be thorough in my science, but it's not possible to be exhaustive, because the universe of science is far too broad. So what I try to do is to learn things broadly, think about problems in terms of what seems appropriate to try to approach, and again, do my best. But exhaustive is not possible in this context.

INTERVIEWER: Although, I mean in thinking about your initial research with the worms in England, it sounded like one of the attractions of studying that, both for other people who focused on it and for you, was that there were a limited number of cells in this animal, and that you could in some way begin to take them systematically and look at all of them, which I think you did do, which in the end turned out to be an enormous amount of work, but a surmountable one.

HORVITZ: Right. So, the animal I worked on, the roundworm, the nematode C. elegans, Coenorhabditis elegans, indeed is the simplest animal that has been studied in any detail at all, and that was what really drew me to this animal. I mean just as an example, if you look at a nervous system and you say how many nerve cells do we have -- we have about 10 to the twelfth, 10 to the eleventh to 10 to the twelfth, a billion billion nerve cells. How many does C. elegans have? 302. And we know them all -- each one has a name and it's been possible to define the entire wiring diagram of the animal. So, this cellular simplicity really offered in the beginning the promise, and today it's much a reality of an analysis at a level of resolution that simply isn't possible with more complicated animals. And, in fact, I have one scientific publication in Chinese, which I can not read and I wrote in English and was translated by a student, and the title of it is Toward the Complete Understanding of an Animal. And the promise of the article was that because C. elegans is so simple, we could imagine understanding its biology at a level of resolution that couldn't be matched by any of the other organisms that tend to be studied.

INTERVIEWER: I think one of the things that was interesting to me as I looked at your career, was that you do pay attention to detail, and yet you seem to keep the big picture in mind, too -- it's the forest and the trees. And you've said that in graduate school you learned to focus on important questions, ones you thought tractable, but also worth pursuing. How did you learn that? I mean that seems like an important lesson.

HORVITZ: Well, I have been extremely fortunate in my mentors throughout my career. I mean as an undergraduate here at MIT I did a thesis in mathematical economics with Bob Solow. The experience could not have been more stimulating or more humbling. I then went to Harvard and worked with Jim Watson, James Watson of Watson and Crick, double helix, and Wally Gilbert, one of the pioneers in methodologies for DNA sequencing. And after that, I went and worked as a postdoc with Sydney Brenner, who is a brilliant and highly creative scientist. So, all of these people, plus mentors I've had since then, have been extremely influential. And I think the basic principles of how to approach science were really principles I learned from Jim Watson. And what Jim said in essence, was first you ought to do something that's tractable -- the most important problem in the world you won't get any place if you can't do something. And second, it's just as easy to work on an important problem than an unimportant problem, and so do something tractable that's important. Now, identifying tractable and identifying important is another issue, but as principles, I think those two are fundamental and really what I've tried to adhere to throughout my career, and I think they came from Jim.

INTERVIEWER: Do you recall how he conveyed it? Was it over a year or two of working, or did you sit over a beer one day and he said let me tell you about science and how to approach it? How did it come through?

HORVITZ: I'm sure it was neither. It was implicit and everything that went on, and Jim has never been one subtle with words, and I'm sure he made those statements explicitly many times, not casually over a beer, but just in the context of the science that went on in the laboratory.

INTERVIEWER: And those are probably lessons that are appropriate for graduate level researchers to think about more so than undergraduates? I mean in thinking about education and what to give students when, and as you're training researchers, even undergraduates at MIT, are those things you can begin to introduce or is it too early?

HORVITZ: I think the ideas can be introduced very early, but the opportunity to really explore, and in particular, to make mistakes and to de-bug problems and to then move forward require more time than most undergraduates have, at least in biomedicine. So, they can get exposed to the principles, but it's very hard to learn by doing in a project that's independent and where you are responsible, you take ownership for solving the problems, and that's what you really have to learn to do to become a good scientist.

INTERVIEWER: Are there ever times when you don't see a big important question that also seems doable or tractable and where you might be tempted to say well, I'll work on these smaller things for the moment and it'll come along, or do you sit back then and say hm, it just doesn't pay to do it that way, let me just sort of bide my time, or what's the pacing like?

HORVITZ: Small and big are not two distinct categories in this context in science, and they interplay. So, in order to make any kind of big discovery, you have to be doing something that's very nitty-gritty. At the same time, and something I believe very firmly, if you pursue at an appropriate high level of resolution and analysis, something in detail that interfaces with a problem that's general, you're going to find out something new and that something new is going to be important.

So, I think to really be an experimental biologist, you have to love the mundane, you have to love doing the boring, you have to love doing the same thing over and over again just because it's fun and you get a little bit of a puzzle here and there. That people who go into this research because they want to make a breakthrough that's going to land them on the New York Times front page, I think hardly ever make progress. You have to go into it because there's something in you that says you like the puzzle solving of doing science, and if you do that well and choose a problem, you're going to find something that will be interesting. But it should be all balanced in an appropriate way.

INTERVIEWER: As you began your research on the worms in England, how conscious of all of these questions and answers were you? I mean part of it was you had though about where did you want to live and where was there a lab you could work in, so there were lots of factors coming into play, but were you also thinking about these lessons from Dr. Watson?

HORVITZ: Going to England was a personal experiment, just like entering biology was. I had actually never been in Cambridge, England, I had never met Sydney Brenner, I did something I would never advise any of my own graduate students to do, which is just go dive in and see what happens. And what appealed to me was the level of unknown and the apparent potential of working with this organism. But the animal was essentially unexplored experimentally. The techniques for its study were almost nonexistent. People told me that it would likely be a career dead-end to go to England and work with Sydney Brenner on a worm. But when I looked at it, it seemed to me that there was potential. So, it was potential to do something different and it appealed to me, but I had no idea if it was going to work, and again, I figured if it wasn't working, I would find something else to do.

I can say that the group of us working on the worm in these early days never dreamed that we would make contributions that have gotten the kinds of recognition that the contributions I've achieved, and we talked about that -- I remember talking about it with John Sulston in Stockholm. You know, who would have ever guessed, and the answer is not us. We were doing something because we found it interesting, we found it challenging, and it was coming from within us to pursue it. And I think one has to remember, these were very early days, and when you do something very early, it's not popular. By the time it's popular it's late.

So, people were very skeptical. It was exceedingly uncertain. We had no idea where it was going to go. We had no idea if we would find anything interesting, we have no idea if we would find anything general -- we were working on a worm. And yet what emerged were findings that are of essentially universal nature in animal biology and fundamental to human disease and have opened whole areas of inquiry, and also novel approaches to human therapeutics. Could we have known that in the beginning? Absolutely not. Could we have hoped we would find something of interest? Sure, but we did it because our hearts drove us to do it.

INTERVIEWER: Do you think you felt less pressure in terms of time and maybe money than graduate students or postdocs do today, that there was something -- that there's something now that just pushes -- puts more pressure on people to feel that there are going to be payoffs when they make decisions to take next steps that you didn't, or did people feel it then too, and you were more of a free spirit in some ways?

HORVITZ: I think there's a lot more pressure that people feel today. Now, people is a broad word, but there are kids who are worried about getting into kindergarten. What school can they go to in elementary school or middle school or high school, and getting into college today. I mean the difference between what I did in college applications and what high school students are doing today in college applications is not describable, it's just incredible. And I think this pressure continues throughout. I think in general graduate students feel a lot more pressure, postdocs feel a lot more pressure, junior faculty -- a phrase that I hate because I don't think there are junior and senior, I think there are younger and older and less experienced and more experienced -- but the younger faculty feel enormous pressure. And everything has metrics that are externally defined, and I think it is completely counterproductive to both science and humanity, and it's something that I care very, very much about, because I think this pressure doesn't do people any good, and actually doesn't do the scientific progress any good.

INTERVIEWER: Do you find ways to diffuse it so that it doesn't impede work, say, in your lab?

HORVITZ: Well, I try to talk to the people in my lab and other younger people that I can chat with about these issues and about taking chances and about following what's in their hearts rather than following what they should do. I mean a student recently came to me and said, I'm not sure I want to go on and do a postdoc in an area related to what I'm doing, and I said, that's fine -- there's no reason you have to do that, you should think about what you want to do and go on and do what's inside you. So I do have those conversations. I also have had the privilege to be able to think about some of these things on a larger scale.

So, recently I was a member of a committee that was established by the American Academy of Arts and Sciences, located here in Cambridge, and the committee was to basically look into issues of science and technology in the United States, not just biomedicine, but the whole issue of science and technology and what are the problems beyond there's not enough funding, because everybody knows there's not enough funding, that's categorically true, but the mandate of this group was to say what beyond simple dollars is a problem in the country. And the group was very diligent and looked into many of the science and technology agencies and groups in the country, including NIH, NSF, NASA, DOE, DOD, we could go on, and what we found was striking, because there was a commonality of issues. And what we ended up very simplistically was with two recommendations and then a variety of ways to think about implementing them, and the first recommendation relates directly to what we've just been talking about, which is the issue of young people and the ability to really explore. And we focused in particular on beginning investigators, people in a first "academic" or equivalent job, and said that the way everything is structured in this country today stifles creativity, makes people encouraged to do the mundane, to do the safe, instead of doing the riskier things that could lead to bigger discoveries.

And then related to that, but also separable in some ways, is the fact that all of the funding that goes on basically discourages high risk, high reward research, okay, young and old. And what we argued is that nationally we should find mechanisms to support younger people better in their most creative years, and more generally support high risk, high return research. so, we'll see -- that's a relatively recent report. While it certainly has had visibility, we'll see if it has impact.

INTERVIEWER: Interesting. Let's go back to your time at MIT -- how did you get here, what prompted you to come to MIT as a student?

HORVITZ: Another experiment. I grew up in Chicago, actually in the City of Chicago until my last year of elementary school, 8th grade there, and then in a nearby Chicago suburb. And the expectation was from peers and relatives, college is good, and the college of choice is the University of Illinois. If somebody were to do something really out-of-the-box, you would go to another Midwest school, the best being discussed at that point was the University of Michigan. So, my expectation was I would go to the University of Illinois, and if I wanted to explore I would think about the University of Michigan.

Two things happened. First, I went to the University of Michigan to visit on the weekend of a Michigan-MIchigan State football game, and what I experienced said I don't want to be here, and Michigan was out. I was then scheduled to go to visit the University of Illinois on the weekend just after JFK was assassinated. Everything stopped, I never got there, and so I never saw it and it became a question mark. In the meantime, I had applied to MIT. I had applied to MIT not because it had ever occurred to me to apply to MIT, but because I had a guidance counselor who said, I think you should apply to one school in the East. I said, okay, I don't know anything about East, you pick it, I'll apply. So she picked it, she picked MIT and I applied. So I had applications into Illinois, and I never actually sent one into Michigan, MIT, and also Cornell, because I knew it was a good school, it was almost East. And then I met a couple of people from MIT and I liked them, I liked the students, and they told me about it and I was interested and I said, okay, I'll do that. So I came to MIT having never seen the campus, having never been in Boston -- another experiment.

INTERVIEWER: What were your first reactions when you got here and you said, hm, and now here I am for four years?

HORVITZ: Well, I think one of the memorable first experiences was sitting in Kresge Auditorium when the then dean of students, Fred Fassett got up front and expressed what was then the MIT philosophy. And what he said was look to your left, look to your right, one of you is not going to be here when it's time to graduate. It was a memorable statement. And it was a statement that, you know, sort of echoed the you have to do it philosophy, but I think misstated the kind of supporting environment that MIT could really be for people who fit appropriately, and I think most people certainly did fit appropriately. But that was a very early image of MIT.

After that as a student I got very involved in many aspects of MIT, and the more I did the more I loved it. Now when I say loved it, what I would say I loved is the experience. I'm very hesitant to say that I loved the institution, and the reason from that comes from another one of my mentors. After I came back to MIT as a faculty member, one of the people I had the real privilege of having lunches with almost every day was Salvador Luria. And Salvador -- I've had very few heroes in my life, and Salva was one of my heroes. He was incredibly wise and deeply knowledgeable.

And I remember one of the first things he said to me, he said, never be loyal to an institution, be loyal to people. People may be key in an institution and that will drive your involvement, but it's not the institution that matters, it's the people. Now Salva was one of the leaders at MIT, he founded the MIT Cancer Center, he was a Nobel Laureate for pioneering the modern field of molecular biology, but he was very smart. And I always try to keep that in mind, people.

INTERVIEWER: What were your classmates like at that time? Did you arrive here and say gee, they're a bunch of people like me, or had you had that experience in high school and so it wasn't such a change?

HORVITZ: I think MIT at that point, and probably now but I'm not so sure it's as much true, was quite varied and with unusual people. Most of the people if you really thought about it had something that was a little bit unusual about them, and that was very stimulating because you got to know, I got to know different kinds of people, people with different interests, different backgrounds, and very often people who had some passion about something. And it was that passion that I think really was fundamental to the MIT student community. Some students were passionate about their studies, some students were passionate about other things, but it was just an interesting group of people. And some of the people that I knew then, I do still have some contact with. Of course, I could say the same thing about my high school, that I still maintain contact with some of my friends from high school as well.

INTERVIEWER: What made you choose to live in a fraternity when you came, and that was a decision you had to make pretty early.

HORVITZ: I think what I learned about the fraternity, and of course, it was very hard to learn much in the few days that one had to examine these things, appealed to me because of the independence of the living group. So basically the fraternity was run by the students. The students had responsibility for management of the finances, for hiring and firing the cook, for keeping things clean and neat for the upkeep of the building, and basically, you went in and suddenly you were an adult. And it appealed to me and I think I learned an enormous amount from it. I can't do the compare and contrast -- if I had lived in some other living group I'm sure the experience would have been different but also very stimulating and it would have learned a lot from it, but the experience that I had for me was I think very formative.

INTERVIEWER: Given your reaction to the Michigan campus at football time, you didn't say is this culture going to be a little bit of that partying rah-rah, whatever, that apparently turned you off there.

HORVITZ: Well, fraternities have had for many years labels associated with them, and I have to say that the fraternity experience I had was a little different from those classic labels. So when the fraternity I was in talked about competition, there was some talk about sports, but a lot of it was we want to be academically better than, and then they pick some other fraternity in competition. So academics were very much a part of the fraternity mentality, and, in fact, achievement and involvement in student activities. You know, the number of people from the fraternities who got involved in a diversity of student activities was huge and very, very much encouraged. So it was responsible involvement rather than irresponsible involvement that I saw as very much the theme.

INTERVIEWER: You were involved in quite a few extracurricular activities and pretty intensively. Can you talk about some of those?

HORVITZ: Sure. I mean I began with an involvement in the student newspaper, The Tech. I had been very involved in my high school student newspaper, and in fact, my high school student newspaper was run by the senior English teacher who informed me with great dismay that if I went to MIT it would be a personal disaster because all of my interest in English and literature would disappear forever. But despite that, I came, I think that didn't happen, but I did continue with my interest in journalism in the school newspaper. So, I began with The Tech, and on the feature staff, my first article had to do with high-speed ground transportation in the northeast corridor, a problem that remains to this day. My peak article was when we came out with The Tech and beat the Boston Globe and the Boston Herald to the stands with an article about the New England blackout in November of 1965 -- that was a great coup, and luckily the elevator I was in when it began, although it shook, didn't close until I got out. And I had lots of experiences there with the paper. I became Features editor and then later managing editor. As managing editor, I got to spend overnight twice a week at the Cambridge Chronicle on Mass Ave where I learned what Irish whiskey was really about and somehow managed to put the paper to bed at the same time. I was also involved on the finance board and the activities board and--.

INTERVIEWER: Of the student government.

HORVITZ: Of the student government, and very involved in student activities in general. And then had the honor of being elected undergraduate association president where I was the representative of the student body to the students, to the administration, and to the outside public, and that gave me a phenomenal opportunity to meet and get to know a variety of people including, you know, many really key people at MIT. So my student government activities were major and probably took more time than my studying.

INTERVIEWER: But you seem to have done well in your studying also. How did you balance the two -- did you sleep at all?

HORVITZ: Yeah, balance was not the operative word. My grades were fine but my studying, no doubt, suffered because I spent fewer hours on it than I should have. I often left studying to the very last minute, I did lots of things I would never suggest to my daughter or my students, but at the end of the day, you know, I got a pretty broad exposure to a variety of areas of academic interest, and I think I learned a lot both from the courses and also from my other experiences.

INTERVIEWER: What made you decide to run for student government president? Had you ever held elective offices before? Where did this come from?

HORVITZ: One of the responsibilities of the student government president, the UAP, was responsibility over the many student activities, and I had spent an enormous amount of time with a great diversity of student activities and I felt I understood what was going on in terms of student activities. At the same time there were issues concerning students at MIT that I felt I would like to be able to express and maybe help make some changes. So I had causes that I believed in. Now, of course, in the grand scheme of things and looking at the world many years later, some of these causes might have been a bit parochial, particularly when you think about what was going on in the world in the late 60s. But nonetheless, they were important to us and I felt I could help with them and I really dedicated myself to trying to do that.

INTERVIEWER: Do you recall any of them in particular?

HORVITZ: Well, there were a number of them. One that I felt very strongly about was that the way freshman were introduced to living groups was, in fact, I would say very one-sided -- they came for a period of time before classes started called rush week, and they were introduced to fraternities but not really introduced to any of the alternative living accommodations, like dormitories. And one of the things that I helped change was to change rush week to a residence week where residences were more generally shown to incoming students.

Another thing that got changed that was one of our causes and it got changed I think soon afterwards, but maybe at the same time, I don't remember the details, had to do with the living accommodations of women on campus. Women had to live in a dormitory -- off campus for women was off limits. Men could live off campus but not women, and that didn't seem right and that got changed also. So, accommodations, how people live, what kinds of responsibility students were allowed to take for their own lives with something that was very important. And then there were lots of other things that got altered, something like field day, which is an opportunity for one class to murder another class got modified in a way that became a little less destructive to human bones.

INTERVIEWER: Have you been politically active since that election? I mean did it wet your appetite for being a political figure?

HORVITZ: Well, political is a funny word because, you know, in a sense being UAP was political because there was an election and a vote, but the job obviously involved things that were political only insofar as they meant dealing with people. When I think of political today, I think do I interface with the governor or the president, and so on and so forth. And the answer there is yes, I have. I've met four presidents, including our current president, President Obama and chatted with him in different contexts. I've been involved in a variety of campaigns in the last two elections. I actually helped write some of the science position paper statements for the Obama campaign in this last election. And I've also been very involved in issues that interface between science and politics.

So for many years I've worked with a group that has as a focus inside the beltway activities of educating congress about science, and particularly biomedicine, and advocating for appropriate support for scientific endeavors. I was very involved and a member of a committee that was established by the U.S. Institute of Medicine, National Academies of Science on human embryonic stem cell research, and our committee basically came up with guidelines for how stem cells could be used in ways that would be, I think, ethically important, and these guidelines have now provided the basis for institutional policies for organizations around the country and actually around the world, and were, in fact, the basis for the executive order that was issued by President Obama just a month after he came into office changing the way the government deals with stem cell policy. And in part because of that involvement, I had the honor of being on stage with President Obama for the signing of that executive order. I watched over his shoulder as he used five consecutive pens to do two letters here and two letters there as he signed his name so that five different people would get pens from the signing -- I didn't get a pen.

INTERVIEWER: You have to do another bill. So, you see the political process as one that can be used and shaped and influenced and you've been willing to take that on in ways that you thought were important to science and biology.

HORVITZ: Well, obviously, politics are very important and very complicated. And my feeling is that the best way I can have impact is take an area I know something about, which is science, and particularly biomedical science, and try to influence policy. I mean what I think is crucially important is that political decisions, and let me word it another way, decisions made by politicians, because political decisions might have a different meaning, decisions made by politicians should be based on a knowledge of science where science can have an impact on them. Science shouldn't be ignored, science should be a driver. We should understand the scientific implications of our current state of knowledge, we should understand what we know and what we don't know, and policy should be based on that. Science shouldn't be ignored, and science shouldn't be modified to fit a political agenda. And so I feel very, very strongly about that and have expressed that view in a variety of ways many, many times.

INTERVIEWER: Have you ever taught a course here at MIT or anywhere else in science policy or do you talk to your -- the people in your lab -- postdocs, grad students, undergrads about science policy and how it gets formed and how you can get involved in the formation?

HORVITZ: I haven't taught a course per se, but recently there has been a group of graduate students who are interested, and from a variety of departments at MIT who are interested in science policy. And I recently met with that group and shared with them some of my experiences and thoughts and encouraged them, if it were their interest, to become actively involved, either as students or later in other contexts because there are many opportunities for people knowledgeable about science to try to use that knowledge to influence policy. And the more scientifically knowledgeable people are involved in policy decisions, I think the better it is for everybody.

INTERVIEWER: When you delivered the Killian lecture a few years ago, you decried the reduced funding for science research, which is a kind of policy outcome as well. Can you talk about what's been happening on that front and why is going down rather than up and whether you think there's a way to reverse it?

HORVITZ: Well, it's going down because money is tight. Money is always tight and one has to define priorities, and the priorities can be complicated. Is it better to pay for heating for poor people or the next scientific experiment? And that's not a question that's easy to answer. What one has to do is really evaluate in some meaningful way what the value is of scientific progress. And in many ways that's easy -- we can just look around the world and see, in terms of our lives, how science has influenced our lives and our health. But people don't always do that in an appropriate way. So when one looks at the funding for science in this country, it has really suffered from what it was, let us say, right after World War II where Vannevar Bush from MIT, in fact, had a real impact on advancing the investment of government in science.

In recent years, particularly in biomedicine which I know best, science funding in real dollars has simply gone down from year-to-year. And this is disastrous because what it means -- I mean it reminds me of the Cultural Revolution in China where there was a period of ten years from 1966 to 1976 where science stopped. Well, science stopping doesn't just leave a gap, because what it does is well beyond that, because for years, decades after that, the people who were driven out of science are gone forever. So when a drop in funding occurs, young people are discouraged, older people are discouraged, projects are stopped, they can't be restarted when people have been fired, and the whole enterprise starts to fall, which is particularly disastrous in the context of the kinds of opportunities that are available today to really make an impact on knowledge and application.

So I feel very, very strongly about it, and there are complicated issues, because it's how much money, and it's also what the money is used for. And something, again, that should be obvious but isn't always paid attention to, is that the real driver of scientific knowledge in biomedicine and other areas of science is basic science. This is where the discoveries come from that allow us to build and do things that are new. And if we simply take today's knowledge and try to apply it, we can do that and that will be good but there'll be no tomorrow. It's as if with the building of an airplane by the Wright Brothers, people would say well, we solved the problem, now we can fly. And the number of feet that that airplane would go is as far as any airplane would go today -- it's not the way it should be. We need the basic science to be the driver of new knowledge, which is then the driver of application in all walks of life. And that has suffered greatly in recent years.

INTERVIEWER: How far off course are we, and how much would you say needs to be put back in to put us where you think we should be? Is it possible to just grab it?

HORVITZ: I think that's a very complicated question and I can put numbers on it but the numbers won't be in context unless we had a very long discussion. So what I would say is they are way off, and they're actually way off by historical standards if you do the proper analysis. You can see that they're way below what they should have been based upon historical trends. And that's true in biomedicine, it's true in other areas of chemistry, physics, computer science, we can go on and on. All of those areas that we at MIT know and love really have been underfunded.

INTERVIEWER: Going back to your academic experience at MIT as an undergrad, how did you choose your majors actually, and -- how did you choose your majors?

HORVITZ: I came to MIT with an interest in science and math, and the two areas that I was most interested in when I began were chemistry and mathematics. And in thinking about that, I decided that meant that my major should be chemical engineering. So I went to one lecture in a course on chemical engineering and decided my major should not be chemical engineering. I like chemistry in math, which is different. I then registered for organic chemistry my first term of my freshman year because I had placed out of a year of introductory chemistry, and that course met at 9 o'clock in the morning. I didn't meet at 9 o'clock in the morning -- that was the end of chemistry. Although, I continued with the organic chemistry laboratory course with Daniel Kemp, and that was a great course, but I didn't really know what was going on since I wasn't taking the lecture course.

So that left me with math, so I became a math major, and I took the series of math courses and really enjoyed them, they were challenging. Some of them really typified MIT. I can remember one exam where the exam was open book, open note, open end, began after dinner. You were allowed to leave and come back -- some people went out and went to the movies at LSC and came back. And the exam was ten questions, true-false. And the true, if it was true you had to prove it, and if it was false you had to come up with a counter example. And it was one of the most challenging evenings of my life and it was incredibly stimulating and really indicated, you know, the way the way MIT taught its courses. So I loved the math and I took all the courses. And because I came in with a lot of credits and tended to overload my courses, I discovered I was in trouble. I was about to graduate in three years. Graduating in three years would be a disaster. First of all, I didn't want to leave, and secondly, I was interested in student government and I couldn't run for president if I wasn't going to be here. So I had to find a way to stay a fourth year, and the easiest way to do that was to do a second major, and I thought about the courses I had taken and my interest, and I decided economics would be a good choice for a second major, and then added the courses, took the appropriate hours, stayed the fourth year and did a proper undergraduate degree.

INTERVIEWER: Did you think of continuing on in either of those areas?

HORVITZ: I thought about both math and economics. The math, it was always clear to me I wasn't a mathematician. I did fine in my math courses, I did fine on math tests, but there were students here who were mathematicians. These were students who could go to bed at night with a math book under their pillows and wake up in the morning with visions of manifolds going through their heads and understand all of this stuff. I had to study, and I knew that my intuition wasn't at the level of the people who really were mathematicians. So I never thought I would be a professional mathematician.

Economics I found very interesting. As I mentioned earlier, I loved working with Bob Solow on my senior thesis, and found that very, very tempting. But I think what happened was in part a consequence of it being the late 60s, and there was so much going on in the world that I felt my opportunity to do something first in math, the impact of doing theoretical math would be at most, at best 100 years in the future, and in economics there was a lot of potential in economics, strictly the economics that might be relevant to the developing countries, but I was a little dissatisfied with some of what I was doing with economics or at least some of what I'd been exposed to because when you did mathematical economics, as with any math, the arithmetic was dependent on the assumptions. But the assumptions for math and the assumptions for economics were very different in their nature and it was really hard to know which assumptions in economics were going to prove to be valid. And so I wanted something that was a little bit harder science, as I began thinking about a potential scientific career, and that helped lead me into the biology.

INTERVIEWER: And you thought for a while maybe about law, too, as a field? Did you probe that at all?

HORVITZ: I thought very seriously about law. I mean I had lived my senior year as undergraduate association president in a three-piece suit and talking to people and I took a course in torts.

INTERVIEWER: At MIT?

HORVITZ: At MIT, yup, from the Sloan School.

INTERVIEWER: Dan Earnhardt?

HORVITZ: I don't remember who taught it. And I decided torts weren't for me. But there were many aspects of law, and also the possible interface of law in politics that I found appealing, but when all was said and done, the notion of doing something in science just appealed to me more. It was a compare/contrast rather than a yes/no. It just had more appeal maybe because it was less known and didn't involve three-piece suits.

INTERVIEWER: How much of an education was your year as president of student government?

HORVITZ: That was a real education because it offered me the opportunity to interact with marvelous people and marvelous minds. And I got to know a bit people like James Killian and Jerry Wiesner, and Jay Forrester. I remember Jay Forrester telling me one time life is short, don't do the same thing throughout, anybody smart changes careers every seven years -- something I haven't quite done. But I have thought about that and actually changed some of the focus of the way in which I spend my time. And there were just many people whose doors were open to me because of that position and whom I got to know and got to learn from. So, I think it was an incredibly valuable life experience to me.

INTERVIEWER: How different do you think undergraduate life in the 60s was from the way it is today. Do you have enough of a handle on MIT today to make any kind of comparison?

HORVITZ: I'm not sure I can say -- answer that question in a meaningful way because I think every generation has concluded that the later generations are less mature than they were. So, I think when I was an undergraduate, undergraduates really did have a lot of responsibility in many ways, and maybe were a little bit more grown up. I compare myself at 19 or 20 to the 19 and 20 year olds today, and clearly they were much younger, but I suspect that if the same question were asked to people who were equally older than me at that time, they would have made the same statement. So I think it's hard to say. I do think that the MIT undergraduates tend to be more nervous about their futures, maybe a bit more constrained in some of the thinking about what they might do, and I think that could be opened up. I don't know the extent to which it's overall the culture in the country, in the world, to what extent it's a change in the way young people grow up, and to what extent it's a change in the admissions policy of MIT, because I think MIT is choosing students in a way that is at least different from the way students were chosen when I came.

INTERVIEWER: Were there any research opportunities open to students? As an undergraduate, do you remember thinking, oh, here's something I could do or should do or were they just not on the table in the same way as they are now?

HORVITZ: I don't think they were as explicitly present as they are now. Certainly the notion of allowing an undergraduate to have a meaningful research experience has grown with time, and I don't think it ever occurred to me to really do research -- not that it wasn't done, I knew people who did do some research in different areas. But I think it was less frequent and also my extracurricular activities were focused in a different way. So I never really explored that at all.

INTERVIEWER: When you decided to go into biology in your senior year, how did you decide where to go? You did your doctorate at Harvard, what brought you there?

HORVITZ: I looked into a relatively small number of biology programs in part because I was looking into programs in all sorts of other areas as well. And harvard appealed to me, one, because I knew the biology going on there was very good, although I actually knew very little about biology, but was soon to discover. And also because I had a preference for staying in the Boston area and I knew it wouldn't be a good idea to stay at MIT. Even though I hadn't been a biology major, I just thought I should have some other experience. And so Harvard appealed in that way to me.

INTERVIEWER: How different was the culture when you got there and understanding that there are certainly major differences between being an undergraduate and a graduate student?

HORVITZ: Yeah. There also were for me very big differences in field. So suddenly I was in biology. Many of the people around me had been in biology and knew the language in the field vastly better than I did. So, I was very much over my head academically. I mean I had to go back and take undergraduate courses. I had no idea how to do anything or even how to think about things. So I don't think I have -- you know, I think the experience was so much out-of-the-box for what I did at MIT as to not be comparable. And, of course, at MIT much of my emphasis was extracurricular. So, the class work at Harvard, there were similarities -- you went the lectures and there were courses, actually Harvard I went to lectures, at MIT I didn't quite get around to that. But, you know, you had books, you read books, you learned material, you took tests -- that was all pretty similar. The class sizes and the interactions with faculty, you know, were not all that different. Harvard, of course, had a Harvard mentality, which one could feel. Harvard and MIT have always had sort of a different kind of base and approach and you could sense that.

INTERVIEWER: How would you describe that?

HORVITZ: MIT has always been, I think, from the beginning much more blue collar and work and engineering application focused, whereas Harvard has been, I would say, more elite-oriented, more with an attitude of its obvious international leadership than MIT has classically had, although today if you go to Asia and you ask what's the most famous university in the world, people will say MIT. You go to Europe, people will say Harvard. So, there are differences there, and also, you know, Harvard's football team had a status that nothing at MIT could match.

INTERVIEWER: And what are the implications of that kind of different culture, say, for both doing biology and teaching and learning biology?

HORVITZ: As a graduate student, I think it's not so much the institutional culture as the local culture. What lab are you in, with whom are you working, and that was very much the case. The place where institution interfaced with my graduate education was basically in 1970 when much of the unrest about the Vietnam War came to a fore. Classes were canceled, people went to Washington, and it was just a completely different world, but that world wasn't Harvard-specific, it just happened that I was at Harvard at that point in our country's history.

INTERVIEWER: And so even your biology lab work got suspended, or did you just keep -- did the labs keep going?

HORVITZ: Everything stopped. I mean at that point I wasn't yet in a laboratory, because I had to do a lot of course work before -- I mean, I was in a laboratory, but I wasn't really spending much time in the laboratory. Because I had a lot of course work to do. And it was courses that really stopped.

INTERVIEWER: You started in one lab at Harvard when you did move into a lab and then you moved into a different one. Was that an easy process, and --

HORVITZ: It was very easy.

INTERVIEWER: You went to the first one and the second one.

HORVITZ: So, the first lab I went to was the lab of Matt Meselson, who's a very famous pioneer in molecular biology, and actually I bumped into him here at MIT last week. And Matt was one of the people who really proved that the double helix of DNA is as Watson and Crick had proposed it, and he is a brilliant scientist, and when I went to Harvard I began in his laboratory. At that point, Matt had taken on some bigger issues, and he, in fact, was spending a lot of time in Washington advising the government about issues related to chemical and biological warfare, and was spending less time with his laboratory. Because I was totally ignorant, more than totally ignorant, I needed an environment that basically had a little more daily current feeding, and it was at that point I talked, for example, to Jim Watson and decided that that laboratory would be better suited for my ignorant state.

INTERVIEWER: His was an interesting lab in the sense that he had already won his Nobel Prize by the time you got to his lab. Was it hard to approach him and did you think twice about it or did you simply say he's doing work I want to do and knocked on his door?

HORVITZ: He was always very accessible to students, and I just went and chatted with him. The way that laboratory worked was very interesting and I don't know of any match to it, because there were really three faculty members who worked together running one lab. Jim Watson, Wally Gilbert and Klaus Weber, and the three of them are all spectacular scientists and very complementary. Jim had a phenomenal intuition for important biological problems, and actually for people. Wally was very critical and could see the problems with any experimental design or any experimental interpretation faster than you could even describe a result, and Klaus had magic fingers and was able to develop techniques that were brand new and incredibly powerful. And the three of them worked together and together advised a series of students and postdoctoral workers, and the environment was just stimulating beyond any imagination. It was very exciting and you just couldn't help but learn, really, what science was all about.

INTERVIEWER: And did you know what you wanted to do there or did they give you a here's what we need to do next?

HORVITZ: I knew nothing, and so when I went to chat with Jim Watson about the possibility of joining his lab, basically what he said to me is -- Cold Spring Harbor, and Jim went on to be the director of Cold Spring Harbor and actually had just started, but was still in both places at that point -- Cold Spring Harbor has its annual symposium coming up very soon on transcription -- how RNA is made from DNA, why don't you come and listen to the symposium and then we'll talk.

So, I came, discovered that there was no room and slept on the floor of a dormitory because there was no place to stay, listened to the symposium. The symposium ended, and I didn't know what I was supposed to do. So I went to Jim in his office and I said, okay, I listened, what now? And Jim said, okay, well, when you get back to Boston, talk to Klaus Weber and he'll set you up. So, I guessed I was accepted into the lab. Went back, talked to Klaus Weber, we discussed a project and I got started.

But the project, I think, was very much driven by things that were ongoing in Jim's lab and also in his head. And, in fact, it was interesting because head comes first. Jim wrote a classic, the classic book in molecular biology called *The Molecular Biology of the Gene,* a book that I had actually read through before I had started graduate school because I didn't know anything. And in that book he basically explained how certain aspects of biology work. The only problem was there were no data supporting what he explained in his textbook, and my first project was to obtain data to show -- I think to test the idea -- but to show that what he wrote in his book is gospel, actually had some relationship to biological reality, and it turned out Jim was right.

INTERVIEWER: And it worked out.

HORVITZ: And it worked out.

INTERVIEWER: So you got to the end, you got your doctorate. And then?

HORVITZ: And then I was looking for something interesting to do. I had a desire on a personal level to live in Europe, and I explored a number of European laboratories, and I was told about a laboratory in Cambridge, England run by Sydney Brenner where Sydney was studying a "new" organism, this worm, C. elegans, and that he was trying to understand how a nervous system developed and worked. And one of the drivers in my entering biology had been an interest in the nervous system and the brain and how does it form and how does it work, and the idea of taking a very simple animal and analyzing that problem appealed to me enormously. So I wrote a letter to Sydney and I said I'm interested in your work -- do these worms have memory, can they learn? And he wrote back Horvitz -- he never said dear -- Horvitz, he said, I have no idea if they have memory or can learn. How would you think about working on TRNAs in the worm? And I wrote back and said I didn't really want to do TRNAs, but I was interested in the biology. He wrote back and said, okay, come. And that was it. So, I appeared there and then chatted with people and got started on--.

INTERVIEWER: How different was that lab culture? In other words, as you moved to a different country?

HORVITZ: That was very different. The difference -- the intensity at Harvard, for example, could be typified by a Saturday morning about 8 o'clock in the morning in the lab when Jim came in and balled-out one of the graduate students for not having been there late the night before, and the student said my wife and I hadn't been out for three months, we went to a movie, and Jim said you'll never be a scientist. okay. So it was a pretty intense environment. Going to Cambridge, England, we had coffee at 10 o'clock, an extensive lunch at noon, tea at 4 o'clock, and lots of conversation that was much more intellectual and less time for experimental. But the intellectual wasn't bad. And it wasn't that people weren't serious. I mean I would find myself sometimes in the lab at 2 or 3 o'clock in the morning and I'd go into the tea room to get a cup of tea and rattled my spoon and Sydney Brenner would be working across the hall hearing me there and he'd come in to want to chat at three in the morning when what I wanted to do was finish and go home. So there was an intensity, but the intensity was integrated with much more conversation and much more blue sky thinking about problems. Whereas in this country my sense was it was do, do, do and things will emerge. There it was think, do, think, do and figure out how to do the thing that's going to make them emerge best.

INTERVIEWER: How much of the Nobel award was for work that you did in England, or was it really just you got your toe in England, and came back and did it here? I mean is it possible to define it that way or measure it that way?

HORVITZ: Yes and no. My Nobel Prize was shared with two others -- Sydney Brenner, who was my mentor in Cambridge, England, and John Sulston then who was my colleague in Cambridge, England, and we worked together in Cambridge, but I would divide our contributions into three components. Sydney was the one who identified the worm C. elegans as a promising experimental organism and basically established the methods for its study and figured out what could be done. John Sulston worked out what's called the cell lineage. So when any animal develops, you start with a fertilized egg and it divides to make two and those divide to make two each, and so on and so forth. And that set of cell divisions ultimately leads to any organism, like ourselves, and a lot of cells that do different things. C. elegans, because it's so simple -- there are only 959 cells -- it turned out it was possible to describe all the cells, and John worked out a way to figure out the entire pattern of cell divisions from that fertilized egg to adulthood, okay. And I helped on that while I was there, but it was fundamentally a contribution of John's. In the course of those studies, John discovered that some of the cells that are generated during the development of this worm die. They commit what's called program cell death, and that coupled with Sydney Brenner's foundations of the field basically left me poised when I came to MIT to begin to analyze mechanistically how program cell death occurs.

And so I would say Sydney founded the field and established the techniques, John established the biology of program cell death and of cell lineage, and I in my lab here basically did the experiments that worked out the molecular genetic mechanisms responsible both for program cell death and the other part of the Nobel citation, which is called organ development, and that work was done here, but it was very much founded on what was done there, and some of the beginnings of it started in Cambridge. But all of the molecular genetics of program cell death were done in my lab at MIT and for many years only by graduate students, and there are then more recently have been contributions made by postdoctoral researchers. But it's MIT work that was honored for me, but it was work that was based on what I had learned there.

INTERVIEWER: What was it like in the Cambridge lab and figuring out what to do and how to do it and proceeding how much -- well, describe.

HORVITZ: Yeah, that was very independent, because I came in and I chatted with Sydney Brenner, and he had an idea for a project and I said no, and I talked to other people around, and then I had things that looked interesting and I started doing them and I worked very closely on many things with John Sulston who was a great colleague, a great friend and phenomenal scientist, and we just got started doing some things together and then some of them I took in one direction, some of them he took in another, and all of it was very synergistic, but it was extremely independent. And I would say the work I did as a graduate student also was very independent. As a graduate student, I published four papers and I'm the only author on all four of them -- there's--.

INTERVIEWER: Although, I think you said that somebody else had kind of defined the problem that you were trying to pursue or pursuing.

HORVITZ: In the beginning, yes, but the culture at that point, and it's a culture that has certainly changed, was that your adviser, at least Jim Watson, Walt Gilbert, your adviser didn't put his or her name on a paper -- and it was mostly his at that point -- didn't put his or her name on a paper unless they felt they had had real contributions of substance, rather than just why don't you try this. Today most places that wouldn't happen.

INTERVIEWER: You had funding that you brought with you to the Cambridge lab, I guess from the United States.

HORVITZ: Right.

INTERVIEWER: How important was that to giving you the independence to saying no, I don't want to deal with your question, here's what I want to pursue?

HORVITZ: It was much more than independence. If I hadn't had that funding I couldn't have gone, because there simply wasn't funding available there to pay for a visitor from the United States. It was the Muscular Dystrophy Association that funded my initial studies there, and that was key. I could not have done, I would not have done what I've done if it hadn't been for the MDA.

INTERVIEWER: What did it take to line that up? I mean as a grad student about to finish -- get your PhD, did you look around at a bunch of places, or was this an obvious one? Had you had conversations--?

HORVITZ: I was interested in nervous system and neuromuscular interactions, and I put together a proposal -- I mean in today's context it was laughable because I only had one citation, because nothing was published about C. elegans, and the reference actually wasn't a citation at all, it was personal communication. So it was all very, very conjectural. I suspect that an application like that would not get funded by anybody today. But the MDA was very progressive and they said okay, go ahead and explore. And there was nothing tying me to do anything that I proposed. The project I proposed and the project I did were not the same. They gave me money and I was free to do something.

INTERVIEWER: Did you have to stay in close touch and report back, or what kind of strings, if any?

HORVITZ: No, there were no strings. Eventually, I told them what I had done -- nobody complained, they didn't ask for the money back. But they were very good about supporting it. It's one of the things I feel very strongly about is mechanisms of support for young scientists, nationally and internationally both. There are opportunities, but often times they do come with strings, often times they're limited and there's not enough. We have many more talented young people than we can support in appropriate ways.

INTERVIEWER: When you were about to leave England, how did you end up coming to MIT?

HORVITZ: Another accident. So, I was advised by Sydney Brenner that there was a job opening at Brandeis and he said it would be a good idea for you to put in an application. So I put in an application, but having done that, I decided that I might as well apply a number of other places as well. So I did, and one of those other places was MIT. So, I came from Cambridge, England to the US for a set of actually 11 different interviews, and I started at Brandeis and they said well, there was some misunderstanding, they didn't actually have a job but they were happy to meet with me. So there was no job, and suddenly here I was applying for jobs -- I didn't really want to leave England yet anyway -- and I came to MIT, and I met the people here, I told them what I was interested in doing and they offered me a job.

INTERVIEWER: Was there an open slot or did they just create one because they wanted you?

HORVITZ: That's also a little bit complicated. There had been a job opening and they had offered the job to someone else who had accepted it and was coming -- somebody who was and still is at UCSF. And what happened was one of the people at UCSF who happened to be his mentor died unexpectedly. And then UCSF asked if he would be interested in basically taking over the lab and the responsibility, and he felt he both wanted to do that and couldn't not do that. And so he contacted MIT, MIT then had a job opening and they offered it to me.

INTERVIEWER: What was it like to set up your first lab? Where'd the money come from for that? Did it come from MIT or from outside? And how did you think about how to define it and how big and so forth?

HORVITZ: So, at that point, start-up packages in the field were nothing like they are today. Today they're quite substantial. What I got was a file cabinet and an IBM Selectric typewriter -- that was my start-up package, okay. I had written a number of grant applications and I received two grants from the National Institutes of Health, and those were the funds that I had available. The funds were not huge and I actually went on weekends to flea markets to buy things like lights where I could buy a light for $1.00 instead of having to spend my precious grant money, and it was very much hand to mouth for a number of years. There were people who were very generous at a variety of stages. In fact, my first day at the lab, Salva Luria, a pioneer in the field came to me and said, here, I'm going to give you a centrifuge, and he gave me this old, rusty desktop centrifuge that looked as if it had been around for 100 years, maybe 50, but it worked and I used it and I still have it -- it was a special gift from Salva.

A few years later -- well, actually two things happened. One was -- that are very related -- one was that after I had accepted the job, I was contacted by Gene Brown, who was then the chair of the department, later became dean of science at MIT, and Gene said, well, here's your laboratory, and I looked at the drawings and all of that and there was only enough room for four people, and I thought well, maybe that's a little small. I was really nervous. He was coming to MIT for another visit and I came and I started by talking with him and I said, Dr. Brown, is there any chance that you might find a little bit more space? And by the end of the day he had another room for me that was twice as big and it was done. And that actually presaged something that came later.

So after I outgrew that bigger room, Gene was still department chair -- actually, I think in the beginning it had been Boris Magasanik who was chair. Gene was department chair and I went to him and I said, Gene, I need more space. I've got literally people sitting in file cabinets, that was true. File cabinet open and legs in between, I need more space. And he said let me think about it. And his solution was to empty the lab across the hall from me, which was his. He moved his own entire laboratory to a different floor to give me more space, as department chair. That was incredible at the time and with hindsight, and just indicated the kind of support that colleagues and the administration department, department of administration had.

As time went on there was some support that came from MIT -- I was given a microscope, I was given a few other things, but most of the support was NIH, and certainly my fundamental research program was established by NIH. And this is something, also, I think very important, because there's no disease agency that would have funded me to study dying cells in a worm -- it just would not have happened. It was basic research -- how does this come about. And NIH had the vision and the wherewithal to say look, we know basic research is going to be important, National Institutes of Health is going to be important to health. We may not know today how, but we have to support this, it's absolutely fundamental and that's where the breakthroughs are going to be.

INTERVIEWER: Do you have any sense of how much was truly vision on their part that they understood in some way that this was a good, basic science building block, and how much was the pedigree you were coming in with by then? You had worked in a lab of a Nobel Prize winner, you'd put in time in England -- any sense of what counted?

HORVITZ: It's very hard for me to evaluate what went on behind closed doors in those early days, but I think there was a very, very strong mentality of good, basic research will lead to breakthroughs. And it was a time when people were beginning to move away from bacteria and bacterial viruses to animals with their complexity and wide open world, and I know that people who were involved in reviewing my first grant were people who believed that such exploratory science would lead to fundamentally new findings. So I can't say that the pedigree was irrelevant, and I would like to think that people did look at what I had done. But when I came to MIT, I had no publications from my postdoctoral work, they hadn't been published yet.

INTERVIEWER: Had you put them in? Were you giving them drafts?

HORVITZ: I had one draft of one paper. I can't imagine somebody being hired in that circumstance today given the kind of "scrutiny" that goes on. When I got my first grants, two of them, I had no publications. It wouldn't happen. So, it was just the idea that was sufficient to entice people here to give me a chance, and to entice people at NIH to give me a chance.

INTERVIEWER: But you were also able to describe a very defined body of work that you and John had done in Cambridge -- that sounds -- now it sounds pretty--.

HORVITZ: For the cell lineage, yes, but I would say that John was the driver in that work. I had begun the genetic studies, and there were genetic studies that had been done -- they hadn't been published. They indicated that there was a new world, but we have no idea what that world was going to be, and we had no idea how tractable it was going to be.

INTERVIEWER: Where in this process did you get tenure? When the department chair was emptying his lab for you, were you tenured yet? Do you recall off-hand or was it still pre?

HORVITZ: I think that was pre-tenure when he did that.

INTERVIEWER: Probably three or four years in maybe.

HORVITZ: I'd have to check those dates. But what happened was I had people come into my lab, there was a small area in which I had two freezers, and I took the two freezers and moved them to another room, and put in three small desks and had people sitting there. And then on the long lab benches, there was a place where there was literally a cabinet, and I took the door off the cabinet and had somebody sitting with his knees in the cabinet.

INTERVIEWER: What was bringing people to your lab at this point? You didn't have these publications -- was it simply your teaching?

HORVITZ: I think students, I mean these were graduate students, and I think graduate students are excited about things that are new and different, and this was new and different. I mean the graduate students who came to my lab in those early days are just a phenomenal group of people. I was incredibly lucky with the combination, and they really just did very, very well. And those students, and students in post-docs who have been in the lab since then, you know, they basically built the C. elegans field in this country, in the world, and I can look at those early students -- I look at one who's a professor at Columbia, another University of Chicago, another Caltech, and I can go on and on, I'm just thinking the first three. You know, they've done very well because they were very exceptional people.

INTERVIEWER: And you'd been in a couple of different labs with different styles. Did you have a notion of how you wanted to run your lab, was it modeled after the coffee/tea conversation model in England, or after Harvard because it got things done and this was America, or did you somehow fashion your or did it just sort of happen?

HORVITZ: It was a combination and a bit of a variation. So, I firmly believe, I believe then, believe today, that the way to help train a student to be a good scientist is to give the student sufficient independence to do something on his or her own, okay. And then that student will learn to do good science and will be able to do good science in the laboratory and beyond, okay, and that's very different from saying I have my pet projects and I want someone to do them so I can check this box and send it back to the granting agency, and students may do very good science in that context, but they're not going to learn the same way. And more than that, I believe that the approach that I've tried to foster in my lab not only trains the students better, but because they become independent, they actually do better science in the lab. So the science in my lab, I think is better because I've allowed students to develop independent abilities to define and pursue their science.

Now, the kinetics are different, okay. so if I told somebody exactly what to do they might get started and go like this very soon. whereas if they have to figure it all out they start very slowly, but then they do much better, and ultimately, I think create much more science than I would be able to define on my own. And that is really the philosophy that I've had to have, to have students be very independent, and that also means that there's been a breath of scientific topics in the lab so that everybody is elbow-room. If everybody is working on something that's very closely related, student a discovers something and it now interferes with what student b is doing, that's not so good. I mean there's a lot of things we don't know anything about, let people explore it and then pursue what they think is interesting.

INTERVIEWER: Do you get more applicants than you have room for, and if so, how do you select among them and are you able to judge which ones will thrive with the independence and which ones might be less likely to?

HORVITZ: So, historically I had a lot of applicants for the lab and I always try to choose and I always recognize that I'm choosing based on somewhat arbitrary criteria. For postdocs you can ask what have they done already and that gives you some hint, but not always failsafe. For graduate students there's no precedent because it doesn't really matter what they've done, nothing is close enough to what they're going to be doing, so it's very, very hard to predict. But nonetheless, I interview people, I think about it, I make choices and do the best.

Interestingly in recent days, I would say I've had fewer applicants than before. Two reasons, I'm older and students often like to work with younger people, but I actually think the Nobel cut down on the number of applicants in part, I've heard, because people are intimidated. They're afraid that if they write to a Nobel Laureate they'll never get in so they don't bother, and I've had a number of people tell me that. So I've actually had, I would say, fewer applicants of really incredibly high promise than I had before the Nobel.

INTERVIEWER: Are there other ways in which winning the Nobel has changed your life or your science or your career?

HORVITZ: Well, it's a label that is going to always be there. So if people know, they point and say ah, Nobel Laureate. And, in fact, one of the realizations I had right after the announcement was now everybody I knew knew a Nobel Laureate -- something that seemed astounding. The label can be helpful, so that, for example, in my work in Washington, I think being called a Nobel Laureate has helped open some doors on occasions and facilitated some conversations, but it also has some bizarre repercussions. And one of the things that I try to always remind people is I don't actually know more post-label than I knew pre-label, and that's particularly true in fields about which I don't know so much.

So, for example, at one point I was invited to an international conference on world peace, and I wrote back, I said I think world peace is good and I don't think I have anything to contribute to this conference. Now, having said that at a later stage, I actually did do something that was focused on world peace, but it was integrated with global health in a way that I did feel that I could make some comments that would be reasonable. But it is a forever label, and for those people who know, they tend to look at you in a different way. Now, one thing I'll say is that in the U.S. I can walk down the street and, at least outside of Cambridge, most people don't know -- in Sweden, when I've walked down the street, people will walk up to me and say oh, I know who you are. So, different awareness in Sweden.

INTERVIEWER: You've done some research outside of MIT, too -- you've worn a number of different hats and gotten -- can you talk about some of that and why one does research in different places and whether it's different?

HORVITZ: Well, I've had a number of hats often worn simultaneously. So my major research effort has been for, you know, the 32 years here at MIT. And mostly it's focused on C. elegans or things that relate very much to what we've done with C. elegans. For the last 20 years, I've had a second academic research interest, which for most of that time was at MGH, Massachusetts General Hospital in the Department of Neurology with a good friend and collaborator with a neurologist, Bob Brown, and there we worked on human neural degenerative disease, particularly Lou Gehrig's disease, ALS, amyotrophic lateral sclerosis. And in that effort, we basically have focused mostly on the genetics of ALS using genes to help us find molecules that are involved in the disease process. That collaboration, as I say, has been going on for 20 years. Bob recently moved from MGH to the University of Massachusetts at Worcester, and we've continued that collaboration.

Now in that collaboration, the work has been done in Bob's lab. I have had employees and occasionally undergraduates who have worked there. I have never put a graduate student or postdoctoral researcher on that project because much of the project. I think, doesn't make for as good training as the kind of training that we can do here, plus the training I like to do when I'm closer than I am to either of those institutions. But that's been a very active effort and I've been very involved in ALS and other neurodegenerative disease research now for many years.

Then I have a third "research" hat, but it's a little bit different because I advise but don't instruct, and that's with a commercial eye. And the idea is, you know, worms we discover basic biology, human disease we figure out what goes wrong in people, and then in the commercial setting try to do something about it. And so I've been involved in the biotechnology industry for more than 20 years, and I've also worked with a venture capital company and with a major international pharmaceutical company as an adviser, again, trying to take the science and bits of biomedicine that I know and figure out how to apply it to make a difference. And these kind of three legs of a triangle are not just an arrow in one direction, because I find that each interfaces with, and is actually synergistic with what I'm doing in the other areas. So some of the things that we do in my MIT lab come from ideas that I've had in working on human disease or in working in pharmaceutical discovery and development. And so it's all in my head very much mixed together, and frankly, very stimulating. It keeps me from being bored. INTERVIEWER: Was the ALS research challenging in different ways, did it call on different kinds of science thinking or puzzle solving than your worm research did all those years?

HORVITZ: Well, in many ways you could say it's different, but I think that the science basically is critical evaluation of technologies that are available or might be available coupled with the problem and the definition of the problem and interpretation of data. So the grand scheme of things is not so different, most people might not agree with that. But it also helped me to really learn about human genetics, and also aspects of what became human genomics. Now, a lot of human genomics actually is derived from the worm, because the first animal genome to be analyzed and the first animal genome to have DNA sequence in its entirety was that of C. elegans, driven by my friend and colleague John Sulston. And when John did that -- something that many people said would be impossible -- he moved on to the human genome project and really was pivotal in founding and driving that project, and I was involved as an adviser to the Institute that he founded in England, the Sanger Center, then the Sanger Institute that was the British arm of the human genome project.

At the same time, I became an adviser to the American arm, the US arm of that project to the Genome Institute of the NIH, which was then headed by Francis Collins, and I was on Francis's council, during relatively early stages of the Human Genome Project. And Francis now, of course, has moved on and he's now the director of the NIH in Toto. So my ALS research gave me very direct experience with thinking about human genes, which is more complicated than thinking about worm genes. When you study worm genes you can take two worms and do a cross. When you study human genes you can't take two people and do your cross -- you've got to take the crosses that have already happened.

INTERVIEWER: You talked about when you initially came to MIT as a professor, an assistant processor, a couple of other professors sort of, I don't know if they swooped in, but they came in and were supportive in different ways including providing you with some equipment. You said the start-up packages are better, but does the department support newcomers in that same way or was it always a matter of a few individuals who did this kind of thing? Is there a way to systematize it, and does MIT as an institution help in any way?

HORVITZ: I think the department actually has evolved, so I think when I came, the departmental administration took responsibility for supporting people and a few people did it individually. But since then there's a mentor program that's evolved, it's systematized, it's much more defined -- I don't know if it works better or worse, but it's at least much more explicit and I think it would be harder for somebody to fall between the cracks. But when I started, I mean I can't complain. I had really outstanding colleagues who were very supportive of many different things that I was thinking about and trying to do.

INTERVIEWER: When you were coming back from England, you said you applied to a number of different places and you looked around the field. Do you think you could have done the same work almost anywhere or at least at a handful of other institutions, and what were the important elements in ensuring that you could do the work that you've done over the years?

HORVITZ: No controlled experiment, so I can't say. When I was offered the job at MIT, I took it -- period, full stop, didn't consider anything else.

INTERVIEWER: And you had at least one other and maybe some others.

HORVITZ: I had one other offer and a number of discussions ongoing, but MIT first was unequivocally a, and maybe the leader in the field of molecular biology, the field that I felt was at the core of my intellectual base at that point. MIT gets great students. The graduate students in the MIT program were and are absolutely exceptional, and as a young faculty member, much of what you do is going to be driven by the graduate students, it takes some years before you get postdoctoral fellows, although again, I it was incredibly lucky with my early postdoc fellows. And the colleagues -- I liked the people, I'd liked the diversity of areas within enough of a focus that I thought there was an intellectual hole. So, I didn't flinch for a minute. I remember getting the phone call, I was in Cambridge, England eating a spaghetti dinner, and Boris Magasanik was on the phone and he said you're offered and I said yes. I think it was as fast as that. I didn't even say what, I just said okay, you got it.

INTERVIEWER: You bargained later.

HORVITZ: The interesting thing was I was advised get it all in writing, make sure you get -- I didn't get anything in writing and what I got was more than they offered.

INTERVIEWER: You talked earlier about having been given the advice, I think by Sal Luria that what was important was people not institutions. And yet don't they come together in a way? In other words, is there something about MIT, and particularly MIT being focused on science and engineering that attracts a certain type of people and creates a comfort level? Again, I guess you haven't worked--.

HORVITZ: I think that's absolutely true, and I think Salva was just saying, you know, step back from his humanistic perspective and just make sure you always know your priorities, and actually it was resonant with the message I got growing up from my parents. It was always people matter first, and Salva basically said the same thing in a different context many years later.

INTERVIEWER: And as a biologist at MIT, to what extent have you interacted with people in other departments at MIT? Is there much interaction, and also with administrative people?

HORVITZ: That's varied over the years. So as an undergraduate, of course, I interacted with a lot of people because of the position of student body president. On the faculty, I would say for my first years, not so much. Then I became much more involved with what was then the psychology department, it evolved into brain cognitive science because of my interest in neurobiology, and I was on search committees and I was on committees, and now I'm joint in the McGovern Institute for Brain Research, which is fundamentally with me, housed in the neuroscience building. So I've certainly had interactions at that level. People in other departments, there are a number of people in other science departments I've interacted with. There's a physicist who's now moved into the biology building with whom I'm collaborating. There's some of the engineers I've gotten to know. Some of them I get to know in an MIT context, some of them I get to know outside, so Bob Langer is somebody I've gotten to know quite well, but I'm not sure it was because of MIT, but our MIT connections certainly have made us closer. So, I do feel like I know a fair number of people, but there are an enormous number of people at MIT I've never crossed paths with and I read about and I say hey, I'd like to know some of these folks some more. Also, there are committees.

INTERVIEWER: We are out of time. Thank you very much for your pictures of MIT -- past, present, future.

HORVITZ: Karen, thank you very much.

INTERVIEWER: My pleasure.