



Nobel Voices Video History Project, 2000-2001

Interviewee: Paul Greengard
Interviewer: Neil Hollander
Date: No date
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HOLLANDER:

Would you introduce yourself and tell us who you are and what you do.

GREENGARD:

My name is Paul Greengard. I'm a professor at the Rockefeller University in New York City, and I study the brain.

HOLLANDER:

What exactly about the brain is it that you study?

GREENGARD:

I'm interested in the molecular and cellular mechanisms by which nerve cells communicate with each other in the nervous system.

HOLLANDER:

How does that work?

GREENGARD:

How does what work?

HOLLANDER:

How does this happen, the communication within the brain? I'm fifteen.

GREENGARD:

You mean you want me to tell what we found?

HOLLANDER:

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Well, I'd like—well, I'll ask you another one.

GREENGARD:

See, I'm trying to get a feeling what is it you want, yes.

HOLLANDER:

Let me ask. Doctor, you just won the Nobel Prize. What did you win the Nobel for?

GREENGARD:

Okay. Damned if I know. [Laughs] Let me think about this just for a minute.

HOLLANDER:

Let me start in another direction.

GREENGARD:

Right. I'll be all right. I just have to kind of get into the right wavelength you're on.

HOLLANDER:

Doctor—you are a doctor?

GREENGARD:

Well, I'm Ph.D. No, I don't have an M.D., right.

HOLLANDER:

You're a scientist.

GREENGARD:

Right.

HOLLANDER:

How did you get into science? Why are you a scientist and not a plumber?

GREENGARD:

Because I would be a terrible plumber. [Laughs] I'm trying to think more about how to

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go about this now that that I understand a bit more about what you want.

HOLLANDER:

When was the first time that you recognized science as science, or you decided, “I want to be a scientist”?

GREENGARD:

Okay. My name is Paul Greengard. I—no?

HOLLANDER:

You don’t have to [unclear].

GREENGARD:

It’s easy for me to do it that way.

HOLLANDER:

However you like.

GREENGARD:

Okay. My name is Paul Greengard. I’m a scientist. I study the brain, and I work at Rockefeller University, which is located in the east side of Manhattan in New York. I studied for the last half century. My interest has been in the biochemical basis by which nerve cells function and more specifically by which nerve cells communicate with each other in the brain.

There are about 100 billion nerve cells in the brain, and they communicate with each other to a very complex arbrization [?]. Each nerve cell on average receives signals from a thousand other nerve cells and, in turn, sends signals to a thousand nerve cells.

I’ve been interested in the biochemical basis by which nerve cells do what they have to do and by which they talk to each other. What nerve cells have to do is to take the messages from the incoming cells and coordinate all that information and then send it out in a signal, which then is distributed to lots of other nerve cells.

The way this happens is that an electrical signal, which begins in the sensory part of the nerve cell, there’s a cell body and then there’s a tree of sort of antennae called dendrites, that are connected to cell body. Then that has a long process called an ax____, which goes out to distant nerve cells and sends signals to them. There’s an electrical signal that comes along from the receiving part of the antennae to the nerve cell body, and then

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another electric signal that goes down the axon to its nerve terminal, where a chemical is released.

That chemical is called a neurotransmitter, and it diffuses across a region called the synapse, and the distance between the sending cell and the receiving cell are about a few hundred angstroms. Then when that neurotransmitter reaches the receiving cell, it's detected by a family of molecules called receptors. These are proteins. And when those receptors are activated by the neurotransmitter, they generate a signal.

There are two kinds of communication between nerve cells, referred to as fast and slow synaptic transmission. Fast transmission, the time it takes to leap from one cell to the other, the signal, is about a thousandth of a second or a millisecond. This fast transmission has been studied electrically. What happens is that when the nerve transmitter gets released from the presynaptic terminal, the sending terminal, it diffuses across the synapse to the receptor on the post-synaptic side. It causes an opening of a protein, which allows ion channels to go through. Those ion channels then, by carrying different amounts of current, different amount of ions through them, generate electrical signal, and that could either be inhibitory or excitatory and generates this fast transmission.

The work that we did, which was recognized by the Nobel Prize, had to do with elucidating the mechanism by which slow signals work. There are basically two fast signals, one of which is excitatory and the other which is inhibitory. They can almost be considered the hardware of the brain.

There are about ten compounds that are generically put together called biogenic amines, and over a hundred other molecules which are proteins or peptides, all of which, all of these ten and one hundred biogenic amines and peptides are neurotransmitters, but they work the very slow processes which can have durations of either anywhere from a few seconds to many hours.

My colleagues and I worked out the mechanism, the general principles, and a few specific examples of how these slow-acting neurotransmitters, as they're called, produce their slow-acting effects in their target cells.

HOLLANDER:

If we could go back in time, Doctor, all the way back to when you were a child, when was it that you first decided to become a scientist? What made you head in this direction?

GREENGARD:

I think my natural abilities lay more in quantitative types of thinking. I would, for example, have been a terrible plumber. I'm mechanically a moron, as everyone who's ever been associated with me tells me. I sort of have a natural inclination towards

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mathematics and precise sciences. So since I seem to do better in those than in other things, my interests naturally went in that direction.

I'd thought at one point of becoming an engineer. During the Second World War, I was in the navy, involved in the development of microwave radar, which was going to be used—which was used, in fact—by the United States armed forces, particularly the navy, to try to detect low-flying Japanese aircraft. In other words, the suicide planes or kamikazes, they were called, would fly very near the surface of the water. Since the Earth is curved, you couldn't pick them up with radar systems at the top of a mast of a ship. So the concept that evolved was to have these planes flying in the air at 20,000 feet, and then you could detect these suicide planes much further out. I got very much involved in that and got involved, as a result of that, in more of electrical kind of field, electricity and magnetism.

When I went to school after the war, I majored in mathematics and physics. Then when I graduated from college, which was in 1948, I wanted to go on to graduate school. I discovered that the main way of getting support was through the Atomic Energy Commission. That was a very short time after the dropping of the atomic bombs in Japan, and I didn't want to let any talents I might have that might lead to the discovery of anything be misused.

I had a roommate in college whose parents were both M.D.'s, and they talked to me a lot about—I was very close to my roommate and his parents. They talked to me about this emerging field of medical field or biophysics; in other words, the application of principles of physics to biology and medicine. So at that time there were only two departments in the country that did biophysics. One was at Berkeley, University of California, Berkeley, where they were studying radioisotopes, and the other was a group at Penn [University of Pennsylvania], which was studying electrophysiology of the brain, the electrical properties of nerve cells.

So I started working in that area. I chose to go to Penn and joined that department, started studying the brain by doing electrophysiological studies. During my first year of my thesis, two men in England, named [Allen] Hodgkin and [Andrew] Huxley, discovered the ionic basis for the nerve impulse; in other words, the electrical signal that goes down from the cell body to the terminal. I felt that biophysics was going to be—it would be a long time before biophysics—.

I may be dry. I think I need some water.

[Taping interruption]

HOLLANDER:

Doctor, you said “misused,” science had been misused. What did you mean, “misused”?

GREENGARD:

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To kill people. That's what I mean. Very simple. I didn't want my work to contribute to more powerful weapons of mass destruction.

HOLLANDER:

You've always felt this way?

GREENGARD:

I don't think one has that kind of conscience until you're three or four or five. I don't recall what—I don't think I had an attitude about those things before that. I don't know at what age I would have felt that way had I been, you know, younger when the atomic bombs were dropped. But certainly after that, I felt that way, and I was eighteen or nineteen at the time.

HOLLANDER:

What did you think of the scientists who did contribute their work to [unclear]?

GREENGARD:

It was a very difficult situation. It was the Second World War, there was Hitler, and, you know, it was one of the few wars where there were good guys and bad guys. I think most wars, it's all gray. Those are bad guys, and, you know, I'm not judging those people. I might have done the same thing myself. One never knows how one would react in another situation. But I do feel that—I did feel that at the end of the Second World War, with the demise of Hitler, that, you know, I didn't want to be involved in that kind of research which would lead to more powerful weapons of destruction.

HOLLANDER:

I can't help but ask the question. For example, Norman [F.] Ramsey, who won the Nobel a number of years ago, at Harvard, designed the casing for the bomb. What do you think about him? [unclear]?

GREENGARD:

Yes, I've never thought about him. In fact, I didn't even know about him. I don't know. I'd have to know more about it to tell you my own personal opinion. Because I'm not saying that those people did anything immoral. I might have done the same thing. I don't know what I would have done had I been in that situation. I just know that in 1948, I did not want to do work which would lead to more powerful bombs.

HOLLANDER:

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If you look back at various physicists, which physicists would you say, going back, influenced you the most? Or medical people. Or people in science.

GREENGARD:

Well, I mean in physics, Albert Einstein stands alone. There is nobody in his class. There are a few other great geniuses below him, and, you know, those are fantastic minds.

The ones who influenced me in my own work, I don't know that I can answer that. I'm trying to think. See, for example, in that nuclear physics that we were talking about, there these great men very much influenced. There was a kind of a sequence of things where, you know, Dr. A did some work, but then it stimulated Dr. B. to do that, which stimulated Dr. C., and so on. In our area, I can't say that there was a direct—there was not a direct—there was not a single individual who greatly influenced in work.

In fact, what I did was considered very heretical at the time. That is to say, it didn't come out of any other tradition, and it was a long hard fight. I was starting to tell you before, when I complained about my mouth getting dry, that having heard this work of Hodgkin and Huxley, where they felt that they couldn't, you know, they didn't—as a result of their work, there was nothing much more that could be done in physics in the near future, and that turned out to be correct. It was another couple of decades before some new techniques were developed measuring single ion channels by two scientists named [Michael] Mayer and [Bert] Sakmann, that next big events were made.

So I wanted to study the biochemical basis of nerve cell function, and to do that, to show you how there's no tradition, I actually had to take—had a professor in my department, which was basically physiology department. Biophysics, physiology, and electrophysiology were all kind of different names for what was the same study at that time. I had to have one professor from there and one professor from the biochemistry department to supervise my work.

When I went to through postdoctoral studies, I had to go into a department which is neither biochemistry nor physiology, because the mindset at that time was that the people doing physiology believed in measuring electrical properties of nerve cells, and it was heretical to ask biochemical questions. I mean, people just didn't do that.

Biochemists, on the other hand, would take a brain, like they'd take a liver, and throw it into a Waring blender and homogenize it, and then measure, you know, chemical reactions there with no relevance to what was going on in the cell. I felt it might be possible to understand the biochemical basis of how nerve cells function, how electrical signals go along ax____, but more importantly what are the biochemical methods by which an electrical signal is converted into a chemical signal at the nerve terminal, the sending cell, and what are the mechanisms by which the chemical signal is converted

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back into an electrical signal. And that's what I spent much of my career doing.

At the time I started doing this, there was very little support for it, intellectual support. I was fortunate in getting grant support. I mean, I'm an intelligent person, and people said, "This guy's nuts, but let's give him money and let him play with his thing." So I always had the good fortune to be well supported, but most people, even after we had published a lot of evidence in support of some of these ideas, it was very slow for them to accept this new way of thinking.

I found the same thing with myself in other areas where, you know, somebody comes up with something that's very different. I think I say, "He can't be right." I think we all do that, scientists and nonscientists. You set certain formulas for encompassing the bewildering world we live in. And in science, it's particularly clear you have certain either explicit or implicit ideas that help to focus your work and tell you what to do next. Some new idea comes along that threatens to fragment your idea structure and therefore threatens to interfere with the way you perceive the universe and how you create things. It's unpleasant to have to incorporate that into your thinking. So I think a lot of other people felt that about what I was doing, and I felt that about many other things.

HOLLANDER:

Doctor, personally, did you find this very difficult to take kind of a heretical point of view, putting yourself way out on a limb, and having people say, "He's nuts"?

GREENGARD:

No, I sort of liked it, not because I wanted to be a heretic, but because there are more excellent scientists today than there are excellent problems, and I was dealing with a problem that I thought was very exciting, and I was happy that not too many people believed in what I was doing. It had its downside. I mean, you know, you get up and lecture, and sometimes people were hostile in their questioning. Most of the time, they were not, you know. But what I was saying was in disagreement with how they thought, and so we'd have a nice intellectual battle. So most of the time it didn't bother me. Just occasionally there would be somebody in the audience who was very hostile in their questioning that would make me kind of irritated.

But, you know, overall, I mean, I was getting funding for my work, I was being invited to meetings. If I had been treated like a pariah, you know, people didn't invite me to meetings so I couldn't interact, that would have been bad. But I went to meetings, and people didn't all walk out of the room when I got up to talk. In fact, even at the times when my work was very controversial, people participated in the discussions. There were large audiences, even when—it's very interesting. I hadn't thought about this, really. But even when the work was not at all accepted and there was like very kind of adversarial questioning, there were large audiences in the seventies, for example.

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So I guess you could say I had mixed feelings. I would have liked people to say, “Wow, that’s great,” but they’re not going to go into that area, you know. It was kind of the advantage was that people didn’t move into the area. The disadvantage was, I wasn’t getting the kind of immediate reward, namely, the admiration of my colleagues, for what I was doing. But it was not like, you know, they were all saying this was nonsense. They were saying, “Maybe it’s right, but you haven’t proved it.”

HOLLANDER:

Did anyone ever say to you directly, “Doctor, you’re nuts”?

GREENGARD:

They wouldn’t have used those words, no. It would be more like, “Poor Paul has gone astray. He’s a bright chap, and undoubtedly he’ll get back on the correct path.” It would be more like that. It was not all like put out into the wilderness. I was in the mainstream of scientific collegiality. Just, you know, what I was doing was not considered to be likely to be right. I’m oversimplifying, because certain parts of it, an increasing percentage of it, began to be accepted as the years went by.

I have to say that at the time I first started making these conjectures about how nerve cells released neurotransmitters and how other nerve cells respond to them, I didn’t think it would be possible in my lifetime to prove or disprove my ideas, but the technology advanced so rapidly that it was possible to evaluate these things.

HOLLANDER:

One detail. Could you just quickly explain the difference between fast-acting and slow-acting transmitters?

GREENGARD:

Yes. Fast-acting neurotransmitters, there are two. One is called glutamate, and that is excitatory, and it binds to a protein, the receptor, and the target cell, and it causes a conformational change, a change in the structure of that receptor, so that it allows sodium ions to flow in. That causes a depolarization of the membrane and causes a firing of a nerve impulse. So that cell responds in a positive way. Glutamate is by far the major excitatory fast-acting neurotransmitter.

There’s another called gamma aminobutyric acid, or GABA, G-A-B-A, which is the main inhibitory one. It does an analogous thing, but it changes a different protein, a different receptor, and allows chlorides to flow in, and that causes a hyperpolarization of the membrane, and that’s inhibitory. And these things that I mention take about a millisecond. All it means is for the neurotransmitter to just touch this one receptor, and

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ions flow.

In the case of slow-acting neurotransmitters, it's a very complicated series of steps involving the binding of a neurotransmitter to its receptor, the formation of what's called a second messenger. That second messenger then activates an enzyme called a protein kinase, which then adds a phosphate group to a whole bunch of key molecules, which also do different things in those nerve cells.

All these steps that I just told you about are, in turn, modified, modulated by many other steps, so it's an extraordinarily complex signaling process. I mean, I could show you a scheme, but, for example, one cell type we've studied which involves a neurotransmitter, dopamine, with this cell, we analyze how the dopamine produces its effects on the target cell through this complex series of biochemical steps, and we've shown that other neurotransmitters which act on the same cells also work with complex series of biochemical steps, but they overlap. In fact, they converge on a particular cascade of biochemical reactions, and then they all diverge again.

So the effect is that these neurotransmitters reach a common path where they regulate the state of activity of a very key molecule, which controls how much phosphate is on different downstream physiological effectors that control the permeability of the cells, the metabolism, the way ions are pumped in or let in and pumped out and so on. So it's an extraordinary complex series of reactions, but the more we learn—what's interesting is, the more complicated it gets, the more simple the concepts which emerge.

HOLLANDER:

Doctor, would it be possible to draw a line from your research to something very practical, something that we're going to use either now or in the next year?

GREENGARD:

Yes. A scientist named Arvid Carlsson, who—well, three of us received the Prize together in medicine this year, a man named Arvid Carlsson and a man named Eric [R.] Kandel. There's a very logical connection between the work of the three groups. Arvid Carlsson in the fifties discovered this neurotransmitter dopamine, which I mentioned earlier, and he obtained evidence that—his work led to the discovery that this neurotransmitter dopamine is deficient in Parkinson's disease. He also showed that by giving a precursor to dopamine called levodopa, which is now widely used, that you could get animals to restore behavior, Parkinsonlike models of animals to have normal behavior. That work, it turns out what we now know today about this neuro, it turns out to be an incredibly important neurotransmitter. It's one of about ten or some biogenic amines I mentioned.

But abnormalities in dopamine signaling are involved in several major neurological and psychiatric disorders. The four major ones are Parkinson's disease, schizophrenia, drug abuse, and Attention Deficit Hyperactivity Disorder. And there are several minor

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diseases also in which abnormality in dopamine signaling are also involved.

Okay. Where did his work and mine converge? I was interested in studying how slow-acting neurotransmitters produce their effects, and the one I studied most thoroughly is, in fact, dopamine. The reason I studied it most thoroughly was because of its clinical relevance. The principles that we found by which dopamine produces its effects on its target cells are very similar to the ones used by other neurotransmitters, other selecting neurotransmitters. So that's the connection between Arvid's work and my own.

Eric Kandel was interested in finding—he had the courage to believe that it might be possible to understand the molecular basis of learning and memory. At the time, almost the entire neuroscience community was very skeptical about his work, just as he was about mine. Eric and I knew each other quite well; we were colleagues. And we discussed the possibility that some of these long-term changes, which he was studying in simple organisms, particularly aplesia, sea slug, that the biochemical pathways that we were studying might be the underpinnings of these long-term changes that turn out to reflect learning and memory.

So we did some experiments together and found that that was the case. In fact, when I mentioned a few minutes ago that the technologies advanced to the point where we could test some of my ideas, one of the experiments that was done, we prepared one of these enzymes. It's a very large molecule, which if you put it on the outside of a cell, it won't get across the membrane. But we made this molecule, and it was injected by Eric Kandel into these nerve cells, and it produced the response predicted by the model. So then that was very good, because it supported the biological importance of the chemical reactions we had found, that we postulated mediated slow synaptic transmission, and it provided a very nice starting point for his studies of learning and memory.

HOLLANDER:

How does this relate to something very practical that we're going to use or not use [unclear]?

GREENGARD:

I'll repeat the question. I'm finding I'm a slow learner. Okay. The way in which this works relates to things of practical use is as follows. It's best explained by a couple of examples. In the treatment of Parkinson's disease, one administers this, and patients take this drug, levodopa, it gets converted into dopamine, and then dopamine relieves the symptoms of Parkinson's disease. These patients, however, after a short time, unfortunately, get refractoriness to the beneficial effects of the levodopa. A plausible and possibly the correct explanation for this refractoriness developing is that the receptors for the dopamine become desensitized, and so the dopamine can no longer work on those cells.

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By our understanding what happens downstream with the receptor, it provides a whole bunch of new targets so that you can develop substances which will either mimic or antagonize certain intracellular biochemical reactions, in this way mimicking the effect of dopamine and hopefully having the therapeutic effects without the side effects or the refractoriness of the levadopa treatment.

Another example is schizophrenia. All drugs in current use for the treatment of schizophrenia work by a mechanism involving blockade of a specific type of dopamine receptor. In addition, these drugs are used in a very large number of Alzheimer patients to control agitation. So basically all schizophrenics and probably half of the Alzheimer population which are on these drugs. They have terrible side effects. We have found out that dopamine actually branches out and does a whole bunch of different biochemical things. By our being able to go into the cell and target one or another biochemical reaction, our hope is that it will be possible to develop improved anti-psychotic drugs which will have the therapeutic effects without the unwanted side effects.

HOLLANDER:

If we could jump to the Nobel, could you just briefly tell us where you were and how you learned about it?

GREENGARD:

I was in bed, sound asleep, and the phone rang. I made a comment to my wife about the intelligence of the caller, which was 5:15 a.m. I asked who this idiot could be calling at this time, since we have a portable phone we couldn't find. [Laughs] So then she says, "It's probably the same idiot who called at midnight," and when she answered the phone, the person hung up.

So I picked up the phone. Our daughter is staying with us. She's in transition, moving from Atlanta to New York. I heard her on the phone saying, "But it's the middle of the night. He's sound asleep. Do you want me to wake him up?"

Then I heard this voice saying, "Well, my name is Hans Jörnvall. I'm the Secretary of the Nobel Assembly, and it's important that I talk to him."

I just heard that part, so I said, "Hello, hello." I felt like saying, "Don't hang up. It's all right. Wake me up." That's how I heard about it.

One thing I didn't know is that all these institutions all over the country, they have their public relations people wake up—they set their alarm clock and they wake up on whatever date. They know which days the Nobel Prize in the different fields are going to be announced, and they have a whole network. So there's one person responsible for picking up the news as soon as it's announced. That person then tells like three or four people, who tell three or four other people, so that by an hour later, the whole university

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is mobilized, and all the press are there, all the television and radio station people with cameras and microphones. It's amazing how quickly this whole thing happens. I didn't even know there's this whole infrastructure in universities, and the probability of any given university of winning a Nobel Prize in any given year is quite small, but these poor blokes have to get up every year, you know, like, I guess—I didn't know that before—it's the first Monday in November. The first Monday or the second Monday in November—excuse me, October. I guess it's the second Monday in October it's announced. So all these schools know this, or at least all the biology and medical schools know this, and so they have this thing all organized. It's the same for physics and chemistry.

HOLLANDER:

Did you roll over and go back to sleep?

GREENGARD:

No. One of my grandsons was sleeping on a mattress on the floor in our bedroom, and so he and my wife were immediately told, and my daughter and her husband. Then I called my other children and my sisters, woke up a couple of close friends, woke up Angus [C.] Nairn, a colleague of mine who was working with me for twenty-one years.

HOLLANDER:

How was the Nobel affected your work?

GREENGARD:

Well, the Nobel has affected my work in the following way. I haven't been able to get any work done for three weeks. [Laughs] But it's been a very pleasant time.

HOLLANDER:

I heard that you gave the money from the Nobel away.

GREENGARD:

Yes.

HOLLANDER:

Could you tell us what—

GREENGARD:

I gave the money, my portion of the Nobel Prize, to an organization that we set up, my

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wife and I set up, two years ago. I won a prize that was given out by the Metropolitan Life Insurance Foundation for—we had done work on Alzheimer's disease, and I won a prize. It was \$50,000. My wife and I took that money, plus another \$50,000 from our own savings, and used it to establish an award. The university, through various donors, came up with matching funds, so there was \$200,000 in the award.

The award is for the purpose of honoring once a year an outstanding woman working in the field of biomedical research. I have taken the Nobel Prize money and added it to that so it's now over a half a million dollars. The university is going to try to get the money up to a level. The goal is to get \$2.3 million, because then they can have an annual prize—this is what I wanted—of \$100,000 each year. These foundations work at 5 percent, so you need \$2 million to give \$100,000 prize, and \$300,000 to pay for the dinners and the transportation of the speakers, and so on.

HOLLANDER:

Why particularly did you focus on this issue?

GREENGARD:

Well, I've observed a great deal of discrimination in academia. I've worked in both. I was in a pharmaceutical company and in academia, and, unfortunately, one would think that with the supposedly enlightened attitude we in academia have, that there would not be this sort of discrimination. And it certainly is gradually disappearing, but not fast enough. There's still a great deal of discrimination against women, both conscious and unconscious. You know, I think the younger people have less of a bias.

When I grew up, we all believed that women were not as intelligent as men. I mean, anybody who says that is not true is lying. Everybody believed that. Women who went into mathematics classes were told that they were, you know, lesbians. It was just an incredible attitude, in retrospect. It's taken a lot of education to get people to treat women as equal, and we're not there yet.

I had one request in connection with this money, which was that the award be named in honor of my mother, who died giving birth to me, and I did that because, you know, it was clear that had she lived, she would have been subject to the same discrimination that all other women of her age were. So it seemed an appropriate way to do something about discrimination and to honor the memory of my mother.

HOLLANDER:

Can you think of any particular outstanding women of science that, for example, have influenced you or that you would reward?

GREENGARD:

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I would like to see this prize have a great deal of distinction, prestige, you know, be a tremendously important recognition for women scientists, and that the women who would get it would be, you know, of the quality of candidates for a Nobel Prize. Right now certainly I could name ten outstanding women. I'm not going to do that, and the reason I'm not going to do it is because I don't want to interfere in the process. These are my requests, that the prize is given by a committee of five professors at Rockefeller University. They have the voting power, and they can get advice from, you know, colleagues all over the world, and I would hope that they would. But the charge is entirely their responsibility, and I felt it would be inappropriate for me to be on that committee.

So I'm not going to name who my candidates would be. I have, I told the president, who I think would be some of the more excellent choices within the university to be on the first committee, and the idea they'd be on for five-year terms, staggered. So it would be every year one would go off and a new person would come on.

There's not a large number. Certainly I can think of ten superb women scientists today. My hope is that this prize will, you know, increase that number a great deal over the many years. The reason there is so few is because usually people by the time they've done work of that quality it takes them many years, and there's so much discrimination that—in the younger faculty there's a lot of women now. A lot of graduate students and postdocs are many women. I guess we're somewhere fifty-fifty now, so it's just a matter of time until this is overcome. Certainly the percentage of women at senior levels is very, very small in most of the top universities, so that there's a smaller population to draw from to give the prize.

HOLLANDER:

As you look back historically, who do you think are most important women scientists [unclear]?

GREENGARD:

Well, the most famous by far is Madame Curie. I think she won two Nobel Prizes.

HOLLANDER:

Any others that stick in your mind?

GREENGARD:

There was a woman crystallographer named Dorothy Crowfoot Hodgkin, who was a tremendous scientist. There have been—I think I forget the number. I think in the last thirty years, there have been—I'm sorry, I misspoke. I think in the last twenty years,

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there have been thirty Nobel Prizes in medicine. I didn't say that right. In the last twenty years, thirty individuals have been recipients of the Nobel Prize, and I believe of that number something like five have been women. These were obviously all very talented women. I remember a couple of their names. I don't remember all of them.

HOLLANDER:

Do you have a favorite science joke?

GREENGARD:

No.

HOLLANDER:

o? You're without humor?

GREENGARD:

Oh, I have a lot of humor, but I just—I mean, the jokes about science have to do with absentmindedness, you know, and I can't—I don't think I can remember any of those. Let me think for a minute.

HOLLANDER:

Can you think of something humorous or embarrassing that happened to you in the lab?

GREENGARD:

I can think of something humorous that's happened since I won the Nobel Prize. The night that I heard at 5:15 in the morning that I'd been the recipient of the Nobel Prize—by the way, they just recently started doing that. My understanding is that years ago there was a press conference at 11:30 in the morning in the Stockholm and there were all the international press corps there to get the names of the recipients. So the Nobel Prize winners would hear from newspapers and televisions, you know, that they'd won. So what they started doing is calling people fifteen or twenty minutes ahead of time to let them know that they were about to be deluged by the media.

Anyway, I heard this at five o'clock in the morning, and then there was a dinner party that evening. At the restaurant, I told Angus Nairn, my colleague that I mentioned earlier, of twenty-one years, I said, "Angus, this is good news, because we have a grant due at the National Institute on Aging next Monday, and we're behind. Now we have an excuse to get a week's extension."

So Angus called the National Institute on Aging and talked to the appropriate officer

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there and said, “Well, Dr. Greengard won a Nobel Prize, so now we’d like to get a week’s extension. That will be all right, won’t it?”

They said, “No, we can’t make any exceptions.” I think the concept was that, you know, what if anybody who won the Nobel Prize asked us for a week’s extension, what a terrible mess we’d be in. [Laughs]

HOLLANDER:

Changing gears again, will you talk a little bit about your perception of the relationship between creativity in art and creativity in your field or science? You mentioned an article about your wife, an artist who works in wood and other media. Is there something that you could say about that, what is the relationships there?

GREENGARD:

Yes, my wife is an artist, a sculptor, and we’ve often talked about the similarities and differences in the creative process between these two fields which seem totally unrelated, but there’s a lot of similarity, I think. Creativity, nobody really understands it. I’ve heard people usually interview Nobel Prize winners and ask them how they got their idea, and people have done Ph.D. theses on creativity, and there are lots of study of it, papers have been written on it. But there’s a simple generalization, I think, that one can make with a fair degree of accuracy, and that is that creativity, nobody understands where it comes from. I remember there was one fellow, a man named [Melvin] Calvin, who won a Nobel Prize for—he was in Berkeley, and I don’t remember exactly what. Something on photosynthesis, I think. They asked him where he got his great idea from, and he said, “I don’t know. I was sitting in a parking lot while my wife was in a supermarket, and it just came to me.”

I have my own view on this. I think that what we call intuition is a kind of an unconscious logic. Our brains are working through problems all the time. Otto Loewi, who was a very famous physiologist, had a dream about an experiment. He wanted to test whether cells communicated with each other through electrical or chemical means. He thought of an experiment as to how to do this, and the way he thought of it, he woke up in the middle of the night. He dreamed about it, and woke up and said, “Oh, that’s great. I’ll do that experiment in the morning.” He went back to sleep, and he couldn’t remember it the next day. [Laughs] So the following night, he had the same dream, and then he quickly got up and wrote it down and went back to sleep, and then he did that experiment.

I think a lot of what of we call intuition is really an intuitive step forward, is attributable to our unconscious doing analytical kinds of things that we’re aware of when we’re doing them consciously, and it all gets worked on and a solution comes and suddenly it pops through the level of consciousness. I mean, it’s the only way that makes any sense to me.

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HOLLANDER:

Would you consider yourself an inventor or artist?

GREENGARD:

Yes, yes. That won't help, will it? [Laughs] I don't understand why they don't have—I think it would be much more interesting to have questions than answers.

HOLLANDER:

Well, because nobody's really interested in what I have to think.

GREENGARD:

Well, then you should get better at your job. No, I mean, nothing is more interesting than hearing somebody interviewing somebody and hear what the reaction is.

HOLLANDER:

We may have a question and answer format for young people. There would be a question on the screen, do you consider yourself an artist or inventor, where do your ideas come from, and then we would have a choice [unclear].

GREENGARD:

I see. What was your question? I've forgotten now.

HOLLANDER:

Do you consider yourself an inventor?

GREENGARD:

Whether I consider myself an inventor or not depends on how you define an inventor. I mean, inventors do creative things. I try to do creative things. Sometimes I succeed. So in that sense, I'm an inventor. There are very different kinds of minds that have been very successful in science. Some people are extremely intuitive. Others are very analytical. Some are both.

Just like there are many different kinds of intelligence. I mean, intelligence used to be based—people's opinions of people's intelligence was based on either an I.Q. test or on performance as related to I.Q. tests. But it's becoming increasingly clear that there's all kinds of intelligence, and they often are correlated with each other within any given person, but they often are not.

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It's been my own impression that great scientists also can have very different kinds of minds. Most highly successful scientists have very critical minds. Some of them are very imaginative, some of them are not, but I think one thing that almost all of them have in common is that analytical, critical kind of mind. But that's not always the case. I'm not going to mention who I think are great scientists who don't have such minds, but I know such people.

HOLLANDER:

Where do you think you got this critical capacity? I mean, can you look back in the years, back in high school or before, and say, "That's where I get [unclear]"?

GREENGARD:

It may be politically incorrect, but I think it's mainly genetic. [Pauses] You want me to say something else?

HOLLANDER:

You mentioned your mother died in childbirth. Did your father spur you or encourage you to think in this way, or any childhood influences? It wasn't your mother.

GREENGARD:

No, I was actually very much discouraged by my family from going into any intellectual pursuits. It's a kind of complicated situation. I don't want that on the record, but it had to do with a stepmother and my father and a rather traumatic childhood, and I'd rather not go into that.

HOLLANDER:

Was there somebody outside of your family who did influence you, then, [unclear], a teacher or a positive influence?

GREENGARD:

I understand you want it for these kids, but—

HOLLANDER: [unclear].

GREENGARD:

No, I mean, I can only say—again, this is all off the record. I can only say that I decided that—since it's off the record, it shouldn't matter how I'm standing or [unclear]

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HOLLANDER:

It's not off the record.

GREENGARD:

No, then I won't discuss it.

HOLLANDER:

Evidently it's not a positive [unclear]

GREENGARD:

There was no positive influence. There was no positive influence in my childhood, right.

HOLLANDER: We can't look back to a teacher or something [unclear]?

GREENGARD:

But I will say something about that. I do think that a lot of the most talented people in science and other fields were very driven to do something with their lives, and the reason that they were driven to do something with their lives had to do with childhood experiences that raised serious doubts in their minds as to their own inherent value. So you hear many of the most creative people I know, whether it's in the world of science, the world of art, lawyers, doctors, you know, when you get to know them well and they trust you that they can confide in you, will tell you pretty horrendous experiences they had. So, you know, if your audience is composed of people who are fifteen to twenty who want to be very creative people, I wouldn't advice them to go and retrace their steps and have a traumatic childhood. And that's not always the case, obviously, but I'm always amazed at the remarkably high percentage of highly creative people who had very sad childhoods.

HOLLANDER:

I'll quickly ask this one. Were you a good student in high school?

GREENGARD:

I did not get good grades, no. I did not get good grades in high school. I was pretty much in a state of turmoil at that time, and it took me, you know, a while to get myself together.

HOLLANDER:

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At that point in your life, what were you interested in [unclear]?

GREENGARD:

I think I was very shy. I spent a lot of time studying chess, and I didn't have a very active social life in that period you're talking about, you know, when I was in high school.

HOLLANDER:

Science, then, came really later to you, at university?

GREENGARD:

Well, in high school, I wasn't particularly interested. I think there was a maturing process when I was in the navy during the Second World War, and when I came out, I decided I wanted to study physics and mathematics. But I would not say I was interested in science before that, when I was in high school. I didn't have a focused view of the world, and I don't think there's much that anybody, any younger people could learn from hearing the details of my own high school experience.

[Begin Tape 1, Side B]

GREENGARD:

—some inner thing that gets into overdrive. I think it's trying to prove you're not a piece of shit, basically.

HOLLANDER:

I think what you're saying is quite right. You're either compelled to do something, or you're not compelled. And I think that's [unclear].

GREENGARD:

I wasn't compelled at that age to do anything. It was a matter of survival. It was just emotional survival. It's just as simple as that.

HOLLANDER:

Growing up without a mother.

GREENGARD:

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It wasn't just without a mother. It was a very abusive home atmosphere. But I swear, I know two dozen—I'm actually, whereas I was very shy, now I'm very interactive, and I have, I'd say, two dozen people who I know that I consider very good friends, who all went through the same—I mean, stories much worse than mine. I thought and think that my childhood was horrible. Of those two dozen, I'd say one dozen had worse childhoods, and it's incredible when you get into these things. I mean, it's partly because it's an area I'm in, too, neurology and psychiatry and so on. So I think about it a lot.

HOLLANDER:

Something that drives you into yourself.

GREENGARD:

Yes. But you have to have talent, obviously. What do people do who are very talented and had happy childhoods?

HOLLANDER:

[unclear].

GREENGARD:

I don't know. I guess they get nine-to-five jobs.

HOLLANDER:

And then become insurance salesmen.

GREENGARD:

Or even—you know. Yeah, exactly.

[End of interview]