Nobel Voices Video History Project, 2000-2001

Interviewee: Edmond Fischer
Interviewer: Neil Hollander
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HOLLANDER:

Professor, if you would, introduce yourself.

FISCHER:

My name is Edmond Fischer. My friends call me Eddie Fischer. I'm a Professor Emeritus of biochemistry at the University of Washington in Seattle.

HOLLANDER:

What is it exactly that you do or you did at university?

FISCHER:

Well, I have been for the last forty years interested in the regulation of cellular processes, the mechanisms by which cell transduce their signals, how enzymes are activated and inactivated, so, in general, cellular regulation.

HOLLANDER:

And you won the Nobel Prize for—

FISCHER:

Well, we won the Nobel Prize, with my friend Edwin [G.] Krebs, for having discovered the first reaction in which an enzyme was activated and inactivated by a mechanism which we call phosphorylation, by a phosphorelation/dephosphorelation reaction. Of course, when we found that, we thought it was a nice system. We had no idea that this particular mechanism would become or would be found to be the most prevalent mechanism by which cellular processes are regulated. So this is the draw, this is the luck of working on basic systems.

HOLLANDER:

You had no idea you would win the Nobel Prize.

FISCHER:

No, no. No, you don't. I mean, this is something—the Nobel Prize came as a big, big surprise. It did.

HOLLANDER:

You felt you didn't deserve it or—

FISCHER:

Well, it's not that. I mean, the fact is that so much beautiful work is being carried out that you can't prevent yourself of thinking—and I'm sure many others do—I mean, why were we selected over other people? It's a funny thing about the Nobel Prize, you know. On the one hand, it's an exhilarating experience, and on the other hand, it's—I wouldn't say disturbing, but, nevertheless, you have a funny feeling, not of guilt, but nevertheless—let me try to explain that.

I was wondering why, in fact, if you win a Gold Medal in an Olympic game, you know darn well why you got it, okay? You trained like crazy for a number of years with that idea in mind, and then you went over there, you competed with the other guys, you came first, and there's no question that you have earned your Gold Medal.

Not with the Nobel Prize. With the Nobel Prize, first of all, you never work in isolation. You always work with many collaborators, superb young men without which you could not have done what you did. Secondly, as the field develops, hundreds of people throughout the world contribute to those advances, so a Nobel Prize should see a sort of a celebration of the field of everybody's contribution, even though you, in our case, we were singled out for getting the ball rolling, you see, to get started. But I have very strongly the feeling that we could never have done what we have done without the help of some superb collaborators.

HOLLANDER:

Do you have the feeling that the Nobel Prize, as it's given out yearly, that this is the case?

FISCHER:

Yes. I mean, choices have to be made. You see, when Alfred Nobel established his will, if you want, he felt that the Nobel Prize could only be shared by three people—one person getting one half, two others getting a quarter each. But if you think of the number of investigators at that time compared to today, today is huge. Some difficulties in certain field, there are too many people who made basic contributions, and even if you give three Nobel Prize, you might always leave one or two out. It can be very unfair for

those people. So it's rare that, you know, you have a hole-in-one, like in golf. Usually many people have contributed to the advancement of the field.

HOLLANDER:

After you received the Prize, did you feel guilty when you went back to your lab?

FISCHER:

No, absolutely not. No, absolutely not, because we were awarded the Prize for work that had been done thirty-five years before, in the mid-fifties, for getting the ball rolling. You know, at that time, with my colleague Ed Krebs, we were just working, the two of us, in a lab. We had maybe one technician and perhaps one student each, nothing more than that. Of course, as the field developed and our groups grew, we added post-doctoral fellows, collaborators, people coming, spending sabbatical leave for a little time. But no, absolutely not, none of this.

[Taping interruption.]

HOLLANDER:

Let's continue a bit. As you were just saying, you're from Geneva.

FISCHER:

Yes.

HOLLANDER:

Could you tell us why, how, what happened to bring you into biochemistry and where?

FISCHER:

Well, it's quite simple in my case. At age fifteen, I wanted to become a microbiologist, and I had read the books on Louis Pasteur and others, and I thought, "That's what I want to do." For my—I don't remember—my fifteenth or sixteenth birthday, I asked for a microscope and, in fact, my brother was older than me. He was at the polytechnical school in Zurich, and he got a secondhand, a very nice Leitz microscope with an immersion objective. It was a real serious professional microscope.

Then when I reached university, I went to the professor of microbiology and I said, "I would like to go into microbiology."

He said, "That's a good idea, but you know you don't make any money there. You have to have some kind of a diploma. If I were you, I would take a diploma of chemistry, for

instance. One uses more test tubes than microscopes nowadays." You know, he was very farsighted, and so this is why I went into chemistry, organic chemistry.

Then I did my thesis. My mentor was a person by the name of Kurt [H.] Meyer. He was working on macromolecules, on the structure of starch, the structure of lycogen, huge, huge molecule. At that time, that was before the war, just before the war, people had no idea that starch were molecules in the million of lycogen. They didn't believe it. Many of the chemists said it's thermodynamically impossible that you would have a molecule with maybe 100,000 or a million glucose residues.

So to dissect these molecules, he needed enzymes to cut them, specific enzymes. So I started working on the enzymes that degraded starch and lycogen and the lasers. And this is how I got, in fact, in the field of enzymology.

I must tell you that biochemistry hardly existed in Switzerland at that time. People who synthesized a lycogen, like Paul Carer [phonetic] or Muchiska [phonetic] working on steroids, were considered biochemists. Biochemistry was very advanced. There wasn't even good books on biochemistry in Switzerland.

I remember just after the war I succeeded in getting from America some volumes, advances in biochemistry and I read these, you know, avidly. So, very soon I decided I wanted to go to America to really work in the field of biology or biochemistry. I went to Caltech. I wanted to work with Max Stelbrook [phonetic] on bacteriophages. But certain things I wanted to do and he had none of those instruments, chemical or biochemical instruments. So I worked with somebody else, Henry Borsuk [phonetic], a marvelous person, on the synthesis of hemoglobin. But I realize that I did not really know the field of biochemistry.

That was '53, and then something else happened which sounded almost miraculous or crazy. I had friends in America. I arrived in New York, and friends from Geneva who were in Pittsburgh invited me to give a talk. I said, "I can't go to Pittsburgh. I have my plane ticket for Los Angeles. I have to go to Pasadena."

She said, "Don't worry about that. Just come to Pittsburgh. They will pay you a plane ticket. Come and give us a talk."

So I went to Pittsburgh, gave a seminar, and they offered me a job. Then they said, "You have to call Henry Lardee [phonetic]," a good person I knew in Madison.

Henry said, "Come to Madison and give us a talk." So I went over there, and I gave a seminar, and they offered me a job.

Then I arrived at Caltech, and there was a letter waiting for me from Hans Neurath, who was the chairman. Though I had read his article, I knew what he was doing, I knew him well from the literature. He was at the University of Washington. I will never forget this

letter. I opened it, and it said, "Dear Dr. Fischer. I heard from Professor Max Delbrook [phonetic] that you would be spending some time at Caltech, and I would like to speak to you of something that might be of mutual interest."

So, you know, I asked the guy across the desk, "What does he mean by that?"

He said, "It means he wants to offer you a job."

And I said, "Those are crazy." It was a time where they were building medical schools all over, and jobs were very plentiful, whereas in Switzerland, jobs were one in a million. This is why I came.

So I was in Los Angeles. He invited me to come to Seattle. For me, Seattle was halfway to Alaska. I had no idea I would be staying in this country. I went over there and gave, I think, one or two seminars. They offered me a job, and I took it. I took it because you know the State of Washington looks very much like Switzerland with a lake, the mountains, the trees. So I have been very happy over there.

HOLLANDER:

Going all the way back to the beginning, when you just got interested in chemistry as a child, was there any significant event or anecdote or book or something that took you from one direction and pointed you in another?

FISCHER:

Not really. You know, if you are asking me now, and I try to find like when you go to confession, you know, perhaps because my father had tuberculosis. In fact, he died of tuberculosis. He was in China. I was born in Shanghai. Maybe that induced me to go into that area. You know, as a kid, you want to cure all the ills of the Earth.

But I was torn between two possibilities. I was at the Conservatory of Geneva in piano, so I was very, very involved in music. I would have never become a concert pianist. For that, you have to be a virtuoso at age thirteen or fourteen, like tennis players. And I never would have had the fingers to become a virtuoso, but I would have probably gone into conducting.

So there was the music on one side and then science in the other. And I don't know. I had music on a pedestal. It sounded sort of gross to make money out of music, whereas it wasn't the case for science. So I always kept music for the pleasure and went into science.

HOLLANDER:

Did you ever have any regrets that you didn't become a conductor?

FISCHER:

No, no, not at all. I would probably have been a lousy conductor. [Laughs] I don't know. No, not at all. I enjoy music enormously. I like chamber music. I like to play with friends of mine, accompany friends of mine, in Lieder, Schubert, Brahms, Beethoven, I don't know, Mozart. I like piano violin or piano cello, chamber music. No. In fact, I'm very satisfied. I have been very happy in my life. There is nothing that I would do differently, looking back.

HOLLANDER:

That's a very rare thing to be able to say.

FISCHER:

Well, I don't think so. I think I have been lucky. I have been very lucky in my professional life, in my personal life. I'm still alive, which is an achievement at my age. And really, there's nothing. People ask me, "Would you do things differently?" No, never.

HOLLANDER:

Doctor, where do you think we're going from here in terms of science? Where do you think the future is going to lead us?

FISCHER:

I think that it's a difficult question to answer. First of all, I'm very optimistic in terms of science. Some people say, "Have we discovered everything in science?" If you ask me that question how much we know of science, I would say, "Zero-point-zero-zero-zero-something-one." I think still everything is to be discovered. I really do feel that.

We can't imagine where science will go, because you can't imagine what you can't imagine. You can't extrapolate the present to guess where we will be in fifty years and a hundred years or whatever.

On the other hand, sure, at the local level, I mean, just right now, we know that you need funding for science. We know that more and more, and there was a whole discussion about that, I think, yesterday morning, that governments, administrations are pushing for or favoring targeted research. Also the industry. There's nothing basically wrong in targeted research. As a matter of fact, many fundamental discoveries were made in applied research, for instance, in the work of Louis Pasteur a century ago. Nothing wrong except if all the money is being funneled in that direction, and that would be an enormous mistake, because in targeted research, you develop one particular area without

realizing that science is a huge edifice and you can't build one area without building all the others. Science builds on science. You cannot solve a problem by throwing millions of dollars at it. That's not the way science proceeds. That's not the way scientific creativity develops.

And so many of the discoveries, the great discoveries, come really from serendipity. I don't want to mention everybody knows them, but for instance, the work of Mendel, who discovered the laws of classical genetic by looking, asking the question, "Why do peas when they grow can have white or pink flowers?" He developed the methodology to solve that problem.

Or Roentgen, who was interested in what happens to electrons when they bounce against a cathode, and who happened to discover that you know those mysterious rays which he called *x* could go through solid objects, thereby, you know, paving the way to probably the greatest discovery ever in the field of medicine. I'm saying that because if Mendel or if Roentgen had applied to an institution like the NIH [National Institutes of Health], supposing it existed at that time, there's not a chance in a million that the application would have been approved. So you have to be very, very careful. There's a real need for basic research, research done for the pleasure of solving a problem, whatever it is, without commercial or other motivation.

HOLLANDER:

This problem-solving attitude, or disposition, which seems to be at the root of many scientists, in your case, where you do think it came from? How do you think you became a problem solver?

FISCHER:

I don't know. I don't know. It seems to me absolutely natural that when there is something there that you don't understand, that you want to understand what's going on. I know several of my students over the years come to me to do an experiment, and it flops. I mean, it doesn't go at all the way they expected it to go, and they are depressed. I said, "Terrific. Great. Maybe it's a dumb mistake, but maybe it's something new." I think that this is the fun of it. This is the fun of being a scientist, particularly a basic scientist, the fun of knowing where you take off from, but never knowing where you will end up, and this is marvelous.

HOLLANDER:

Is this what you look for when students come to you?

FISCHER:

No, not really, because you cannot predict that you will find something unexpected.

HOLLANDER:

No, I mean in terms of a disposition or an attitude or a questioning mentality. How do you decide which students you will take and which you won't?

FISCHER:

Oh, well, that is not difficult. You want somebody with imagination and enthusiasm. You know, a scientist, when he selects a problem, really serves the function or behaves like a creator, like a painter, has a blank canvas and creates a work of art. He uses his imagination to invent a field, invent a problem. He has to rely on his imagination to select the proper approaches. I mentioned that in one of the discussions. I don't remember if it was yesterday or the day before. So his success will depend on his imagination.

But then very soon there is a dichotomy between science and the arts, because in the sciences, every result attained has to be proven and reproven. You know that at any time what you have found might be shown to be wrong. And I mentioned that Einstein once said that "No amount of experiments can ever prove that I'm right. But a single experiment done anytime anywhere can show that I am wrong."

So at that point, science really builds on science. In other words, every data you obtain, every result you obtain, will automatically suggest the next logical hypothesis or the next logical experiments. The results you obtain there will suggest the next one, so that inevitably what is not done by one scientist one day will have to be done by another tomorrow. In other words, for me it's a sobering thought that nobody is really indispensable in science. What you don't do today, somebody else will do tomorrow, because it follows a logical path.

I asked the question to the panel, I said, "You know, what would have happened if Newton would have never existed, or Bohr, or Einstein?" You know, they made tremendous contributions to science. Obviously, it would have affected the course of science, the pathway, the development of science, no question. But you know, somebody else, maybe twenty years later, fifty years later, would have found everything they have found, and it would probably not have altered the end product, where we are today.

In other words, what that means is that in science nobody is really indispensable, whereas if Mozart had never existed, nobody would have ever written his G-minor Symphony or *Cosi fan tutte*, or *Don Giovanni;* Schubert's *Die schoene Muellerin*, or *Die Winterreise.* Not in a million years. So this, I think, really marks the difference between science and the arts.

Secondly, it's another big difference as Nadine Gordimer, the Nobel Laureate

poetess/author from South Africa, once wrote—I think she wrote that in her Nobel address. She wrote, if my memory is correct, "Authors are not orchestrated. Poets sing unaccompanied." Scientists do not sing unaccompanied. The complexities of science are such that you cannot work in isolation by yourself. It doesn't exist anymore. I don't know if it could exist at certain times, possibly. It's no longer possible today. Collaborations are really indispensable between colleagues, between institutes, between continents, and whatnot. So again, this is a big difference between the arts and the sciences.

HOLLANDER:

Doctor, one or two quick last questions on a very personal basis. What are some of the things you dislike?

FISCHER: The most?

HOLLANDER: The most.

FISCHER:

Bigotry and fanaticism. You see, I think this is the importance of science. As I told you, in science you're never certain that what you do is right. As Einstein said, you know, "Anytime somebody can prove that I am wrong," which means I might be wrong. I think this is, for me, the principal lesson of science. It teaches you that no matter what, you might be wrong. If everybody had the same attitude that they might be wrong, it would be the end of all political, moral, racial, and particular religious bigotry and fanaticism.

HOLLANDER:

Do you do any work in any of these fields outside of—

FISCHER:

No, I don't. No, not really, no.

HOLLANDER:

In a person, what do you dislike the most?

FISCHER:

If those people are opinionated, which for me is a form of arrogance. [Laughs] Until somebody croaked and finally the guy died, so immediately he started his visit. The first guy he visits, said, "*Oh, Monsieur Dumas. Vous avez du devenir par le premier corbillard.*" "You must have come by the first hearse." [Laughs]

HOLLANDER:

But you don't [unclear].

FISCHER:

They are. They are abandoning them now.

HOLLANDER:

My wife teaches at P_____, and she had to make the visits.

FISCHER:

Really.

HOLLANDER:

Oh yes. This was—oh yes. She never would have been elected.

FISCHER:

Oh, for Christ's sake. [Laughs]

HOLLANDER:

I mean, not so much—I mean, this is not [unclear]. Still, she was obliged to do it. She needed the votes.

[Taping interruption]

HOLLANDER:

Why are there so few women [unclear]?

FISCHER:

I don't know. In my field, which is biology, there have been quite a few, not very many, but there are many problems attached to that. Nowadays, in biochemistry, for instance, in my department, I think there are as many women graduate students as male graduate students. Same for the medical school. There's a very large number of women. Some are exceedingly bright, but they are faced with problems that often men don't have, particularly if they get married, if they have children, those are sometimes difficult situations for them to overcome. It is difficult to equate a career in a science where you

want to devote all your energies, all your thoughts, and a family.

I have had some difficult examples of post-doctoral fellows of mine who were married and the wife wanted to go into post-doctoral fellowship elsewhere. The husband couldn't, because he had a position that he couldn't abandon. And a couple of times, it ended up in a divorce. So those are very difficult situations, but no question that women are just as bright as men.

HOLLANDER:

Madame Curie.

FISCHER:

Ah, yes. That reminds me of a story. Madame Curie wanted to be elected to the French—I'm not sure that story is true. She wanted to be elected to the French Academy, and at that time in the early 1900s the age of the members of the French Academy was—you had about average age around 125, I think. And, secondly, you had to wait until somebody died so that the position was open. And then you had to visit the members of the Academy and pay your respects to them. From what I understand, the first fellow she visited asked her, "Madame Curie, I mean, what makes you believe that you deserve to be admitted in our institution? I mean, whatever put in your mind that you as a woman deserve to be admitted in our Academy?"

And she was so pissed, that she didn't say a word. She grabbed a piece of paper and she wrote, "Prix Nobel," and she stuck it in front of his face. And he said, "Prix Nobel? Nobel? Nobel? Is he one of ours?" [Laughs]

[End of interview]