



Nobel Voices Video History Project, 2000-2001

Interviewee: Johann Deisenhofer and Kirsten Fischer-Lindahl
Interviewer: Neil Hollander
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HOLLANDER:

If you could please tell us who you are.

DEISENHOFER:

My name is Hans Deisenhofer. I'm currently professor at the Southwestern Medical Center of the University of Texas. My main interest is structural biology; in other words, the structures of protein molecules, and we determine such structures by a technique called x-ray crystallography.

HOLLANDER:

Can you tell us exactly why you won the [Nobel] Prize?

DEISENHOFER:

The official citation was for the determination of the three-dimensional structure of a photosynthetic reaction center. Now, what is all that? Photosynthetic reaction centers are large protein molecules, which sit in a biological membrane, that is, a little sheet of fat molecules that surround all the cells in living organisms, and these proteins have very specific properties so that they can feel all right in such a fat environment, and these very properties made them difficult to treat with the normal technology that we have in treating proteins, bringing them into solution and purifying them, sorting out all the different types of proteins and also making them into crystals. So that type of thing had never been done before to a so-called membrane protein. That was one part. And the other part is that reaction centers are at the heart of photosynthesis, which is the process that generates practically all biological energy on the earth. It is also responsible for maintaining the oxygen content of the atmosphere, and it's the basis of life as we know it.

HOLLANDER:

Is there some way we can draw a line from what you are doing [unclear]?

DEISENHOFER:

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Yes, going to a more general aspect of the methods we use, we determine, as I said, structures of proteins. Some of these proteins are very important for understanding live processes. I mean, all of them are very important for understanding life processes, but especially understanding what goes wrong with life processes in disease. They are targets for drugs that are produced and taken by people who need them, and I would like to mention an example from our latest work that concerns a molecule that makes—how do I say? That makes a precursor molecule for cholesterol. So most, or two-thirds, of the cholesterol in our body is produced by the body itself, and the rest is taken by food.

If we usually, as usual, take in too much cholesterol by food, so we have high concentration in the blood, that over time leads to diseases of the arteries, the clogging of the arteries, and eventually the major cause of death in civilized countries, the heart failure or stroke. There have been since a number of years drugs that were known to lower cholesterol, and the way they do this is to bind to that enzyme that we study, inhibit the function of that enzyme, and in that way lower or inhibit the production of the body's own cholesterol. That leads to an increased uptake from the blood and a lowering of the blood cholesterol level.

So our work comes in to understand exactly how these inhibitors interact with the enzymes, and what we do is we isolate the enzyme, actually only the so-called catalytic part of it, and study its structure, study its structure when an inhibitor is found, and in that way, first of all, understand how the inhibitors work; second, look for possibilities whether we can make better inhibitors. I think that, in part, answers your question.

HOLLANDER:

Are you inventing a new process?

DEISENHOFER:

No. This process is called rational drug design for reasons that are not entirely logical, because most of the drug design is in many ways rational. But this way is drug design or drug discovery on the basis of structural information, and that has been done in several cases or has been tried in many cases, has been successful in some cases, like, in part, the drugs that are used now against HIV infection, the so-called protease inhibitors, HIV protease inhibitors. They were the result of such studies where you determine the structure of the target, this protease, protein, and think about what kind of molecule would bind to this structure so that it cannot perform a function anymore.

HOLLANDER:

How has the Nobel Prize altered your life? Or has it?

DEISENHOFER:

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Yes, it has. One can say so. Following the discussion this morning, the first thing that happened was a name on my parking lot [laughs], which could be bad news according to Professor Schwartz, but it is quite convenient, I have to say. And it allowed, or it led to changes in the funding of my research and in my personal status at the Medical Center that made it easier to pursue more crazy projects, if you know what that means, things that other people prefer not to do because the likelihood of success is somewhat lower than in other projects.

The only problem with this is that the people who work with me and do not have this status, they are working under a more high-risk atmosphere than they probably would like. So I have to constantly try give them the confidence that I will stand for them, even if the crazy projects don't work. But overall, of course, I mean I would not be sitting here without the Prize. That is one of the changes that happen.

HOLLANDER:

Does your wife treat you differently?

DEISENHOFER:

Not really. She wasn't my wife when I got the Prize. We were together, but we were dating, let's say. I think there was a short period when she was treating me somewhat differently, but it was over pretty soon, yes, which is good, because it is hard for me to be something special. I don't really enjoy that.

HOLLANDER: [unclear] crazy project?

DEISENHOFER:

In retrospect, of course not, but especially my colleague, Hartmut Michel, with whom I got the Prize, he heard a lot of comments that said, "Why are you trying something that is impossible?" So in other words, there was a firm belief in the community that what he tried was not feasible, and it took quite some stomach to fight this off and continue, and it certainly helped him, like me, to be a native of this area who are known as being very stubborn.

HOLLANDER:

When did you or how did you first become interested in biology? What [unclear]? Was there a turning point? Was there a particular incident where you said, "Okay, now [unclear]"?

DEISENHOFER:

Yes, I started out as a physicist, so I originally wanted to become an astronomer, and then

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thought perhaps it's more realistic to study general physics, and I was doing something related to what [Douglas D.] Osheroff and [Robert C.] Richardson did, low temperature physics, as an undergraduate.

Then my professor at that time, who lives at the shores of this lake further to the west now, and he's retired, he volunteered for some reason to give a course in biophysics. So when you came into his office, he had big piles of biology books on his desk, and his mind was totally into biology, so it was hard to talk to him about physics. He was always straying off into biology. And that perhaps was the decisive influence that made me decide or made me want to go into biophysics.

Then there was the opportunity of the opening of a new group at the Max Planck Institute for—at that time it was called [German], very interesting name. Its new boss was a very young man named Robert Hoover, who is a participant in the meeting. He was looking for students, and he accepted me, and that's how I came.

HOLLANDER:

What was the actual name of the [unclear]?

DEISENHOFER:

The physics professor's name is Klaus Drumsfeld [phonetic]. Before he retired, he was professor at the University of Constance, but at that time he was at the Technical University, Munich. Very interesting man. He had gone through Bell Labs that were mentioned today, and was perhaps part of the explosion of physics at this place in the 1950s, sixties.

HOLLANDER:

When you look back on your career, is there anything you regret?

DEISENHOFER:

Well, as far as the projects I tried to do, no. As far as differences with people I had, yes. So, biological science and probably all science is always very competitive, and sometimes this competition becomes so intense that it is personal. And in retrospect, I mean, always every time or every incident of this sort is totally unnecessary. It's motivated by our ambitions, by the seeming needs of the moment, and I have to regret a few times that I conducted myself perhaps with less grace and with less understanding of others than I would have liked.

HOLLANDER:

[unclear]?

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DEISENHOFER:

In personal relations with nonscientists, you mean, or—

HOLLANDER:

Either.

DEISENHOFER:

No, it has helped. I mean, I have a lot of friends among my colleagues, at least I believe so, and I know a lot of people that I would have never known without being in that field. Probably would have been the same in other fields, but in that sense, yes. My acquaintances are all over the world, so it's another of the privileges of being a scientist, that you really meet people from all parts of the globe.

HOLLANDER:

[unclear] photosynthesis. Essentially in many ways you studied life.

DEISENHOFER:

Yes.

HOLLANDER:

I'm compelled to ask you, what is the meaning of life? Why are we here? This is a question everybody asks of oneself somewhere along the way. You are researching the very elements of life. What is it and why?

DEISENHOFER:

Well, I don't think we are researching what your question aims at. What we are researching is, how does life work. We may even research, or some of us do research, how might it have come about. But what it means, that is a very different question. Everybody may answer that in a different way, and this is a totally nonscientific issue. So I can only go back in history and say if you want to have a useful life, you have to do something that is remembered by the people who come after you or something of that sort. Life, I mean, in its most elementary way has the mission to reproduce itself, and in that sense I have failed.

HOLLANDER:

The question of why. The person things I can ask you. What governs your approach?

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Where are you coming from and why? What is life on this planet [unclear], discovery of possible water on Mars. What is your—

DEISENHOFER:

Well, I would be extremely surprised if Earth were the only place where life developed. I think the properties of the chemistry of matter is the same, no matter where we look. All we need is a constellation of favorable conditions, and life has to develop. Some sort of life has to develop. There is almost no doubt in my mind that this is inevitable. That doesn't mean we understand how it came about, but all we know about life nowadays and fossil records and so on points to a very early occurrence of life on the planet, which means automatically that the occurrence of life is a likely event.

HOLLANDER:

But on the more metaphysical level, what is your thinking?

DEISENHOFER:

Well, I can only tell you how I feel, myself. As I said before, I think we can all be satisfied if we have done something that makes a difference for other people. If you haven't violated the rights and the interests of others more than—well, if you haven't done too much of that violation, and if we leave a world that is not much worse than it was when we came into it. Right now we probably cannot say that the world becomes better over time, but we can work on trying to make it better.

HOLLANDER:

Where do you think the world is going?

DEISENHOFER:

Well, I have to say I am somewhat pessimistic about our ability to continue the lifestyle we are used to, and I believe that the Earth will go or the humanity will go through a series of crises that are probably as bad as the twentieth century's crisis and maybe even worse. This is a consequence of our numbers increasing and our resources decreasing and our inability to, as a collective species, to put our individual interests after the interest of the species. So everyone tries to behave as if he or she is alone, and that will bring us into much more trouble, I believe.

In other words, wars, fights about the resources, and maybe the outcome will be a largely diminished population with a different attitude, with a different attitude to life. I mean, there are all kinds of prophets. Some say, okay, we are going probably through cycles where we almost extinguish ourselves and then recover, and then remember that for a while and then explode again and then extinguish ourselves again. I hope that this will not be the case, but for the near future, I have some concerns.

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HOLLANDER:

What's the most amusing thing that happened to you [unclear]?

DEISENHOFER:

There were many amusing things. What is the most amusing thing?

HOLLANDER:

First one to come to mind.

DEISENHOFER:

Well, right now I cannot think of anything. [Laughs] Right now I cannot think.

HOLLANDER:

Have you ever been embarrassed?

DEISENHOFER:

Oh, yeah, many times, many times, yes. For example, when I had to give my first talk in a scientific meeting, I was extremely—how do you call it? I had a lot of stage fright. Practically, I didn't know what to say when I was given the microphone. I had totally forgotten what I've ever done, and I was totally paralyzed. The chair of the session was one of the participants here, Bill Lipscomb, and he was so kind and nice and understanding, and he somehow made me talk. That was a big embarrassment. Of course, I was eager to present what I had done, but it was just impossible.

The most amusing things, well, one thing was certainly to watch my colleague named Alvin Jones, who is a professor now at Upsala University, fall in love with almost every beautiful girl that was around. It was a predictable event that when he came somewhere and there was a charming female, he would automatically end up being totally lost, and that was an interesting process over the years. But he's about my age, and you can imagine that also he's going slower in that respect.

HOLLANDER:

Do you have a favorite science joke?

DEISENHOFER:

Science joke? I cannot tell jokes. That was never a gift I had, and of course, when I'm

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asked I cannot think of one. When I'm back in there, I will—

HOLLANDER:

[unclear].

DEISENHOFER:

Yes, yes, okay. [Laughs]

HOLLANDER:

If I have a chance to see you again, [unclear].

DEISENHOFER:

Okay.

HOLLANDER:

Are there any questions I should ask that I didn't?

DEISENHOFER:

That's completely up to you, what you're asking.

HOLLANDER:

Suppose I were to come to you, [unclear] and I said, "Doctor, what do you think I should do? Where do you think I should go? What should I study? And please don't tell me, whatever I need to." [Deisenhofer laughs.] [unclear]?

DEISENHOFER:

Well, I would say the field in which the most discoveries are still going to be made is the life sciences, and I may say that simply because I'm working in that field. And Richardson may be right, I mean, the speaker in the panel discussion, that we are in a similar situation as physicists were at the turn of the nineteenth or the twentieth century, that people believed it's only a matter of filling in some gaps and everything will be known. Of course, they were proven extremely wrong, and maybe I'm proven extremely wrong about physics, simply because I don't know enough about the subject.

But I'm absolutely sure that life sciences will have an enormous stream of new discoveries, and there are countless unsolved problems that have to be worked on and have to be solved, and if we ever want to understand a living cell, we have to generate a

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computer model. I cannot think of any other way of proving that we understand the cell in which all the whole chemistry is simulated. And even though nowadays computers are getting better every year doubling, or every two years doubling their capacity, we are so far away from having computers that can do that and having algorithms that can simulate so complicated systems, that there is really a very rich field of activity and discovery. I would say if the person who asks the question has any affinity to biology, that is the way to go, and it is almost irrelevant in which part of biology.

HOLLANDER:

What single book should I read?

DEISENHOFER:

What single book? Hmm. Well, I can only say what I enjoy. It was a very interesting experience to read *The Double Helix* by [James] Watson, because it showed the paths of the discovery, and it also showed the human nature of the participants. That was an eye-opener, in a way. Especially if you're sort of idealizing scientists as kind of holy people who have nothing in mind but their science, it's very useful to read that book, and you learn a different story. So this one I would recommend. There are many others, of course.

I enjoyed very much, if you want to learn about—now I'm straying off. I'm not keeping in line with my arguments. But a very good book is *The God Particle* by Leon Liderman, where he describes the course of events of the particle physics, and it's written extremely well. For someone who wants to get some history, it's beautiful. There are many books that are not really suitable for beginners, but which are very, very interesting, too.

HOLLANDER:

Do you read outside of your field?

DEISENHOFER:

Oh, yes, yes, I do. For example, right now I am reading a book by a famous German historian—

[Taping interruption]

HOLLANDER:

Doctor, start again.

DEISENHOFER:

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So about my reading outside the field, I was always very interested in history, and right now I'm reading a monumental book, or series of books, on Roman history by the German historian Theodor Mommsen, for which he actually got the Nobel Prize in Literature in 1902. It was written 1850s, 1860s. It's a really thorough treatment of Roman history from the start of the city to about the middle of the age of the Caesars. It's fitting well together with Gibbon. Gibbon starts at, I mean, second century A.D., and Mommsen goes in about second, third century A.D.

But I'm fascinated by the similarity of the political problems of that time to what we have now. It seems as if human politics have not changed at all in three thousand years, or two and a half thousand years. This is a really fascinating—it could read as if it were yesterday. So that fascinates me. It brings me to some very different ideas, and I like that.

HOLLANDER:

[unclear]?

DEISENHOFER:

Yes.

HOLLANDER:

[unclear] in the fall, do you think?

DEISENHOFER:

Yes, the fall came relatively suddenly for the people who lived at that time, or they had the impression that this empire was so large it cannot be thrown down, and it was. There are many, many similarities, like the wealth, that wealth that made it unnecessary for people to invest themselves in the common interests, and the people who overthrew the empire, of course, they're not wealthy, and they had a lot more to gain from risking something. And so it may be that we're approaching a similar situation, that there is a large part of the world in which people are infinitely less wealthy than we are, and we may get tired and saturated and no longer able to produce new things.

If you think of the United States of America, in many ways the progress of that country is guaranteed or is enacted by people who migrate to the country, not so much by the natives or at least the migrants, the immigrants, make a lot of contributions. As long as that lasts, the country will do well. But if you look at the long-term Americans, they are less likely, let's say, to study natural sciences. It's too difficult, or you cannot make money as rapidly with that, and so on. They have high expectations into everything and are less likely to make sacrifices in their life. That may threaten the existence, the very

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existence of that country and of the western world as a whole over time.

HOLLANDER:

So you're pessimistic about it.

DEISENHOFER:

Yes, yes, yes. Yes.

HOLLANDER:

But you're not pessimistic about science?

DEISENHOFER:

About science, no. I don't think that the whole human race will lose its curiosity. Science will go on, no matter where on the planet. But it will go on. We are, as I said, very far from having a complete understanding of the world, and so I'm sure there will be science hundreds of years from now. If there are people, there will always be science.

HOLLANDER:

Thank you very much.

DEISENHOFER:

Okay.

[Taping interruption]

HOLLANDER:

Could give your name and introduce yourself?

FISCHER-LINDAHL:

My name is Kirsten Fisher-Lindahl. I am the wife of Johann Deisenhofer, and I am a colleague of his, too. We both work in the University of Texas Southwestern Medical Center, where we met thirteen years ago—no. Yes, thirteen years ago, when he was interviewing for a job.

HOLLANDER:

What is it exactly you do?

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FISCHER-LINDAHL:

I study the immune system, and in particular, histocompatibility antigens, and right now we are working on the sequence of the mouse genome and the mouse matrix compatibility complex.

HOLLANDER:

What is that [unclear]?

FISCHER-LINDAHL:

Well, it's a group of genes that together have the major influence on compatibility of tissues and the ability to exchange tissue grafts. We have also learned that, in fact, the cornerstone of the immune system and what we can make immune responses to when it's the central piece of an immune reaction. We are trying to figure out what all the pieces are and how they came to be together and what they do.

HOLLANDER:

This has a direct link, then, to our health.

FISCHER-LINDAHL:

It does, indeed, yes. Susceptibility to a number of different diseases, lupus, diabetes, arthritis, and how we can respond to infections like malaria, are all controlled by the system.

HOLLANDER:

Turning to the Nobel for a second.

FISCHER-LINDAHL:

Right.

HOLLANDER:

How has this changed your life in a personal sense?

FISCHER-LINDAHL:

Well, we met the year that he got the Prize, and it was a very exciting year. In a personal sense, obviously, it's almost hard to separate the two, because we met and fell in love at

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the same time all these external things were happening.

The Prize, what difference has that made, if you didn't have it? I think it's given more security and lots of opportunities for interesting trips and meeting interesting people and attending events.

HOLLANDER:

It hasn't interfered with your personal life?

FISCHER-LINDAHL:

No, I can't see any, no.

HOLLANDER:

Unfortunately, he's almost within earshot.

FISCHER-LINDAHL:

Yes. [Laughs]

HOLLANDER:

We can't talk about him now. Could I get you to give me a description? And, please, not "warm, generous, loving," but really a real description of Dr. Deisenhofer, a profile.

FISCHER-LINDAHL:

Yes. He is a very quiet person, as you could think, quite introverted, and at the same time has a tremendous security, a self-confidence. He just trusts himself and his instincts and that life will be all right. It makes him a very easy person to be with.

HOLLANDER:

Do people get along with him quite easily?

FISCHER-LINDAHL:

Very easily, yes. I don't know that he has any fights. He doesn't make a big fuss. In fact, he has, rather, difficulty expressing his opinion and doesn't normally get into an argument, so just avoids it.

HOLLANDER:

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Does that create a problem for you? Do you get into arguments with him easily?

FISCHER-LINDAHL:

No, I would see the problem would rather be if there was something that we should argue about, he wouldn't express it, but rather just be discontent, and you have to be sensitive to that. You have to realize that—

HOLLANDER:

What are his dislikes?

FISCHER-LINDAHL:

Chicken. [Laughs] And stupid people, I think, people who talk a lot and don't say anything.

HOLLANDER:

And his likes? If you were going out to buy him a gift and you wanted to please him some way or another, what would it be that you would get?

FISCHER-LINDAHL:

Well, for example, I was the one who organized the Roman history. You know, you have to think about it. Books that would interest him would be a good choice. Music he likes very much, classical music, and that's you would think of. He doesn't have any expensive habits that I can think of, but one thing we both share is a love for the outdoors.

HOLLANDER:

Do you hike?

FISCHER-LINDAHL:

We hike. We have a condo in Jackson Hole, Wyoming, and we ski in the winter, downhill skiing, and hiking in the summer. That's what we do. I guess the other thing he like is things with buttons, you know, any kinds of electronic gadgets.

HOLLANDER:

What was the last gift you gave him?

FISCHER-LINDAHL:

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Before that, that was actually *Caesar's Gaelic Wars*, and Gibbons, exactly. And before that—

HOLLANDER:

What kind of [unclear]?

FISCHER-LINDAHL:

Well, we exchanged. We normally end up getting the same things for each other, so we exchanged cross-country skis this Christmas, and the Christmas before that it was snowshoes.

HOLLANDER:

Deliberate or accidental?

FISCHER-LINDAHL:

No, it's deliberate. We both have a hard time thinking of gifts.

HOLLANDER: Do you have any pets?

FISCHER-LINDAHL:

No, we don't, because we travel so much that we don't have time to—we wouldn't be home enough to care for a pet properly. He likes cats very much, and we would like to have one if we weren't away so much.

HOLLANDER:

Can you think of a humorous story about him?

FISCHER-LINDAHL:

I heard you ask him about jokes. The problem, I'm very bad at remembering jokes and coming up on the spur of the moment.

HOLLANDER:

What's the most humorous thing that's happened to both of you professionally?

FISCHER-LINDAHL:

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I just—no, I wracked my brain already. I couldn't. It just doesn't come. That must be a specialty thing.

HOLLANDER:

Are you optimistic about the future?

FISCHER-LINDAHL:

Yeah. [Pauses] It's—I am, yes.

HOLLANDER:

Do you share his views?

FISCHER-LINDAHL:

Yes. Right. I would not disagree, you know. I may be not think something will happen, you know.

HOLLANDER:

Are there any causes or organizations that you especially identify with or support?

FISCHER-LINDAHL:

Yes, things that have to do with conservation, and particularly we like the Nature Conservancy, that sort of uses the capitalist system to preserve. They actually buy pieces of land that they want to protect, rather than just hoping that people will protect them. And wildlife organizations is what we particularly—

[End of interview]