CHEMICAL HERITAGE FOUNDATION

FRANZ HILLENKAMP

Transcript of Interviews
Conducted by

Michael A. Grayson

at

University of Münster
Münster, Germany

on

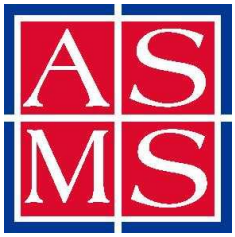
20 August 2012

(With Subsequent Corrections and Additions)

ACKNOWLEDGMENT

This oral history is one in a series initiated by the Chemical Heritage Foundation on behalf of the American Society for Mass Spectrometry. The series documents the personal perspectives of individuals related to the advancement of mass spectrometric instrumentation, and records the human dimensions of the growth of mass spectrometry in academic, industrial, and governmental laboratories during the twentieth century.

This project is made possible through the generous support of the
American Society for Mass Spectrometry.



CHEMICAL HERITAGE FOUNDATION
Center for Oral History
FINAL RELEASE FORM

This document contains my understanding and agreement with the Chemical Heritage Foundation and the American Society for Mass Spectrometry with respect to my participation in the audio- and/or video-recorded interview conducted by Michael Grayson on 20 August 2012. I have read the transcript supplied by the Chemical Heritage Foundation.

1. The recordings, transcripts, photographs, research materials, and memorabilia (collectively called the "Work") will be maintained by the Chemical Heritage Foundation and the American Society for Mass Spectrometry and made available in accordance with general policies for research and other scholarly purposes.

2. I hereby grant, assign, and transfer to the Chemical Heritage Foundation and the American Society for Mass Spectrometry all right, title, and interest in the Work, including the literary rights and the copyright, except that I shall retain the right to copy, use, and publish the Work in part or in full until my death.

3. The manuscript may be read and the recording(s) heard/viewed by scholars approved by the Chemical Heritage Foundation or the American Society for Mass Spectrometry unless restrictions are placed on the transcript as listed below.

This constitutes my entire and complete understanding.

(Signature) 

FRANZ HILLENKAMP

(Date) November 14, 2013

OPTIONAL: I wish to place the following restrictions on the use of this interview:

_____

_____

Regardless of any restrictions that may be placed on the transcript of the interview, the Chemical Heritage Foundation retains the rights to all materials generated about my oral history interview, including the title page, abstract, table of contents, chronology, index, et cetera (collectively called the "Front Matter and Index"), all of which will be made available on the Chemical Heritage Foundation's and the American Society for Mass Spectrometry's respective websites. Should the Chemical Heritage Foundation or the American Society for Mass Spectrometry wish to post to the Internet the content of the oral history interview, that is, direct quotations, audio clips, video clips, or other material from the oral history recordings or the transcription of the recordings, the Chemical Heritage Foundation and the American Society for Mass Spectrometry will be bound by the restrictions for use placed on the Work as detailed above. Should the Chemical Heritage Foundation or the American Society for Mass Spectrometry wish to post to the Internet the entire oral history interview during my lifetime, I will have the opportunity to permit or deny this posting.

I understand that the Chemical Heritage Foundation and the American Society for Mass Spectrometry will enforce my wishes until the time of my death, when any restrictions will be removed.

This oral history is designated **Free Access**.

***Please note*:** Users citing this interview for purposes of publication are obliged under the terms of the Chemical Heritage Foundation (CHF) Center for Oral History to credit CHF using the format below:

> Franz Hillenkamp, interview by Michael A. Grayson at the University of Münster, Münster, Germany, 20 August 2012 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0704).

Chemical Heritage Foundation
Center for Oral History
315 Chestnut Street
Philadelphia, Pennsylvania 19106

FRANZ HILLENKAMP

1936 Born in Essen, Germany, on 18 March

Education

1961 MS, Electrical Engineering, Purdue University
1962 Diploma, Electrical Engineering, Technische Universität München
1966 PhD, Electrical Engineering, Technische Universität München

Professional Experience

Universität München, Germany
1962-1963 Research Assistant, Institut für Strahlenbiologie (Institute for Radiation Biology)

Gesellschaft für Strahlen und Umweltforschung (National Laboratory for Radiation and Environmental Research), München, Germany
1963-1968 Research Scientist

University of Maryland, Munich Campus, München, Germany
1963-1976 Part-time Lecturer of Physics

Gesellschaft für Strahlen und Umweltforschung, München, Germany
1968-1976 Deputy Head, Department of Coherent Optics
1976-1986 Research Consultant

J.W. Goethe Universität, Frankfurt, Germany
1982-1986 Professor, Medical Faculty

Harvard Medical School, Boston, Massachusetts
1985-2006 Visiting Professor

Massachusetts General Hospital, Boston, Massachusetts
1985-2014 Research Physicist

Università degli Studi di Napoli, Napoli, Italy
1986 Visiting Professor, Seconda Facoltà di Medicina

Texas A&M University, College Station, Texas
1999 Visiting Professor

Universität Innsbruck, Innsbruck, Austria

2000 Visiting Professor

Sequenom Inc., San Diego, California

2001-2014 Chief Consultant, Mass Spectrometry

University of Illinois, Champaign-Urbana, Champaign-Urbana, Illinois

2003 G. Frederick Memorial Lecture

Honors

1997	Award for Distinguished Contributions in Mass Spectrometry of the American Society for Mass Spectrometry
2000	Award for “Molecular Bioanalytics” of the Deutsche Gesellschaft für Biochemie und Molekularbiologie
2001	Wolfgang Paul Lecture, German Society for Mass Spectrometry
2001	Member, Academy of Sciences of the State of North Rhein-Westphalia Germany
2003	Award for "Outstanding Contributions to Biomolecular Technologies and Applications" of the Association of Bioanalytical Research Facilities (ABRF)
2003	Thompson Medal of the International Mass Spectrometry Society.
2003	Fresenius Award of the German Chemical Society (GDCh)
2003	Beckurts Preis of the German Helmholtz Association
2006	Torbern Bergman Medal of the Swedish Chemical Society
2011	Caroline and William Mark Memorial Award of the American Society for Laser Medicine and Surgery
2012	Honorary Member, German Society for Mass Spectrometry

ABSTRACT

Franz Hillenkamp was born in Essen, Germany, one of four children. The family, except for the father, who had to remain in Essen because he was a judge, soon moved to Düns, Austria, because of World War II. Hillenkamp's early life in the mountains inspired a lasting love of mountains and mountain sports. After the War the family moved back to Germany to live with Franz's maternal grandmother. Hillenkamp credits his grandmother with much of his love of learning.

Having chosen the science and math track in the *Gymnasium* Hillenkamp went on to major in electrical engineering at Technische Universität München (TUM). He interrupted his diploma thesis on vacuum systems to accept a Fulbright Scholarship to Purdue University, where he obtained a master's degree. Returning to TUM he finished his thesis and married.

Hillenkamp's first job was with the Federal Department of Science and Technology, where he taught himself lasers and worked with them for fourteen years. During this time he also got his PhD, writing his thesis on energy meters for Q-switch lasers. Hillenkamp met Raimund Kaufmann and the two began a long-lasting collaboration; eventually this collaboration led Hillenkamp and Michael Karas to the invention of, first, laser-induced microprobe mass analysis, or LAMMA; and then matrix-assisted laser desorption ionization, or MALDI, which has been profoundly important in biology. Researching the safety of lasers led Hillenkamp to found a laser-tissue interaction laboratory; this lab became the prototype for the Wellman Center for Photomedicine at Massachusetts General Hospital.

Hillenkamp held a position at J. W. Goethe Universität in Frankfurt before moving to the University of Münster, where he became chair and Director of the Department of Medical Physics and Biophysics. At that time Münster was considered the center of mass spectrometry in Germany. Hillenkamp has also held visiting positions at Harvard Medical School, Massachusetts General Hospital, Università degli Studi di Napoli, University of Maryland in Munich, and other places.

He talks about the many important changes to mass spectrometry, including FAB, SIMS, and electrospray, and their influence on biology and medicine. He laughingly describes the contortions needed to install his first LAMMA in the Deutsches Museum; he laments having overlooked the surgical benefits of lasers in his early studies of lasers' dangers. Hillenkamp explains some of the intricacies and drawbacks of patents, emphasizing the importance of the exchange of information in science. He maintains that his professional relationships were collaborations or friendly competitions, good for all. He never used a commercial spectrometer, except for the first LAMMA he invented.

Hillenkamp retired but continued his work and his play. He says he can no longer work well in the lab, so he mentors and helps others. He helped develop a submission for the Excellence Initiative before he retired. Unfortunately, a recent accident has put a crimp in his first love, skiing, but he spent his seventy-fifth birthday skydiving. He has included in the interview letters pertaining to the award of the Nobel Prize to Koichi Tanaka; Hillenkamp is still disappointed about what many spectrometrists consider a serious error by the Nobel Committee, but he is not bitter. Hillenkamp has won many other awards and has published many oft-cited articles and a textbook that is now in its second edition. He believes that his lab's work focused most importantly on the contibutions of MALDI to biology and medicine.

INTERVIEWER

Michael A. Grayson is a member of the Mass Spectrometry Research Resource at Washington University in St. Louis. He received his BS degree in physics from St. Louis University in 1963 and his MS in physics from the University of Missouri at Rolla in 1965. He is the author of over 45 papers in the scientific literature. Before joining the Research Resource, he was a staff scientist at McDonnell Douglas Research Laboratory. While completing his undergraduate and graduate education, he worked at Monsanto Company in St. Louis, where he learned the art and science of mass spectrometry. Grayson is a member of the American Society for Mass Spectrometry (ASMS), and has served many different positions within that organization. He has served on the Board of Trustees of CHF and is currently a member of CHF's Heritage Council. He currently pursues his interest in the history of mass spectrometry by recording oral histories, assisting in the collection of papers, and researching the early history of the field.

TABLE OF CONTENTS

ILLUSTRATIONS

INTERVIEWEE: **Franz Hillenkamp**

INTERVIEWER: **Michael A. Grayson**

LOCATION: **University of Münster**
Münster, Germany

DATE: **20 August 2012**

GRAYSON: Now we're recording. So usually I start these things by saying that this is the twentieth of August 2012. My name is Mike Grayson. I am in Münster, Germany, interviewing Professor Franz Hillenkamp. I believe that's all of the important stuff that has to be in front. So whoever picks this up, knows what it's about.

HILLENKAMP: Right.

GRAYSON: And doesn't have to figure out what's going on. Who are these two people and why are they talking about these things?

So typically what we like to do is find out how you got to where you are in your career. A lot of that depends on your parents, and their education, and their parents' education, and a little bit of background, so could you describe something about your parents and then your forbears before that?

HILLENKAMP: Okay. So I was born on March 18, 1936, in Essen [Germany], which is relatively close by here. It's actually the center of the industry, of the coal and steel industry in Germany, which is important for what comes now. My father [Ferdinand Hillenkamp] was a judge, and his father was a judge, and his grandfather was a judge. All male members of his family were in law, somehow.

GRAYSON: Interesting.

HILLENKAMP: So that might have been one option for me, but I chose not to go into law.

My mother [Charlotte Hillenkamp née Russell called "Lotte"] had an education in what we might call home economics, but she was never professionally active. As was typical for a

bourgeois family, the wife would not work, but she would take care of the children. Both parents are from this area of Germany, called Westphalia, actually. However, the family of origin of my mother originally came from England. Her maiden name was Russell. [. . .] So I have three sisters, one older, [Beate, called Ati] and two younger sisters, [Annette and Bertheide, called Heide]. They were all born also in Essen. However, when I was four years of age, in 1940, World War II started, and there was the expectation that pretty soon Essen would get bombed by the Allies. A colleague of my father had this small vacation house in a very small village in the Austrian mountains. He offered my father that he could use that for his wife and the children. Everyone expected the whole war would be over within half a year or so, which, of course, didn't happen.

So the most important years of my growing up were actually in this remote, small village. I went to school there, elementary school, four years. This was a one-classroom school, one teacher, which in a way gave me the opportunity to learn whatever was taught within the first two years, or three years.

But I must say, this teacher was the best I've ever had. He was extremely good. For example, he taught us the law of conservation of energy. Now, we didn't call it that way, but he taught it in a way that was of interest to the farmers there. That is, he had this set of pulleys, and his statement was "what you gain in force, you lose in distance." Then he was pulling the string and showed that the more pulleys there were, the longer stretch you had to pull for the same lifting up of a weight or something.

GRAYSON: This is in grade school.

HILLENKAMP: [Yes]. This was in grade school. [Yes], really good.

GRAYSON: What was his name?

HILLENKAMP: Oh, what was his name? Hagg [. . .] but no one would use last names in that village. He was called, you know, the teacher is "ein Lehrer" in German. He was called in the dialect, the "Lähr", but Hagg was his last name.

GRAYSON: He was just "Teacher."

HILLENKAMP: He was just "Teacher," right.

GRAYSON: Everybody knew that, and that was it. They didn't need to know any more.

HILLENKAMP: [Yes].

GRAYSON: So he's teaching conservation of energy <**T: 05 min**> in grade school.

HILLENKAMP: [Yes].

GRAYSON: So how many people were in this small one-room school?

HILLENKAMP: Well, in my grade . . . do you say grade for . . .

GRAYSON: [Yes].

HILLENKAMP: . . . for year, [Yes]?

GRAYSON: [Yes].

HILLENKAMP: In my grade, there were three. In some other grades there were a few more, but as far, as I remember there was a total of [about] twenty-five . . .

GRAYSON: Altogether.

HILLENKAMP: Altogether, right.

GRAYSON: Let's see. There was a point I wanted to ask about, but it escaped my mind, so let's go on and . . . so you said, you spent four years at this one-room . . .

HILLENKAMP: Oh, yes.

GRAYSON: Would it be not more normal for a woman to teach in these schools? Or, like in America, generally . . .

HILLENKAMP: Yes. In grammar school, it would be women.

GRAYSON: [Yes].

HILLENKAMP: It is still so in Germany. I think it was that way in Austria as well, but I didn't know. You know, I mean, this was the only teacher I knew about. You know, in this village, there wasn't a single car. There wasn't a single tractor.

GRAYSON: What was the name of the village?

HILLENKAMP: Oh, the village is Düns [. . .]. And it's in the state of Vorarlberg. [. . .] This is actually very close to Lake Constance, and the Swiss border. So we could look into Switzerland, though during the War, of course, we couldn't go there.

GRAYSON: Well, did the War affect this area? I guess that's why you went there. Is it didn't really affect . . . you weren't as affected . . .

HILLENKAMP: [Yes]. The way I grew up, we children didn't have [a clue about] the War. The only thing that was different from what might otherwise have been, was that my father just came for Christmas and during summer vacation. Because a judge, he had to stay back in Essen, of course, where his office was, and his court.

It was a real small village. As I said, no car, no tractor. One horse for the whole village, [Yes]. A few oxen to pull cars when there was need.

GRAYSON: There is an expression in America for a small town. It's a one-horse town.

HILLENKAMP: Okay. This absolutely was a one-horse town. [Yes], right. The area there is very Catholic. Both my parents were Catholic, so I served as an altar boy. Generally, you know, life was simple but very good for children. Everything that happened, children could understand. It was quite a bit dominated by Christian holidays. We went on these long pilgrimages. You know, like, eight hours or so, over the mountains to some other place, and then back at night.

But anyway for small children, I think, this is the ideal way to grow up. The fact that we were fully immersed in that life, we . . . how do I say that? We understood things, which gives you self-confidence. It's not like in the bigger town, or where there are many things going on that children don't understand yet. So I was very fortunate, I must say, to be given that chance.

But it lasted until 1947. The area was occupied by the French Army. They insisted that we go back to Germany, because we were Germans and not Austrians, and, of course, Austria separated from Germany at that time.

GRAYSON: [Yes]. Was there a language problem in Austria versus Germany? Because they have slightly different . . .

HILLENKAMP: Yes, and no. Of course, German is the language in all of Austria, but in this village <**T: 10 min**> they spoke a dialect which is almost a different language. Actually, you may know that in Switzerland, you have four languages. You have German, French, Italian, and the fourth one which most people don't know about, which is called Romanic. This dialect in this village was sort of a mixture of German and Romania; [yes], *rumantsch ladine* is the right word for that. We would . . . the children would speak, of course, the dialect to all the other children, and to all of the adults in the village. But with my mother, we spoke High German. My mother learned to understand the dialect, but she never spoke it.

GRAYSON: Yes. So High German has its own grammar, primarily, right.

HILLENKAMP: [Yes]. But here it's more vocabulary. The vocabulary was very different. Actually the teacher, the Lähr, would teach in dialect. When he wanted to teach us some High German, he would defer to my sister and me, how that is. [Yes]. Sometimes we had to laugh, because he would literally translate it. It sounded very strange for us. [Yes].

In order to have enough food to survive we ran sort of a small farm enterprise . . .

GRAYSON: Oh.

HILLENKAMP: We had some fields and planted vegetables, potatoes, and what have you, and got also some from the village people.

GRAYSON: So would you work in the fields then?

HILLENKAMP: Oh, [yes]. Oh, yes. Oh, yes.

GRAYSON: You were . . .

HILLENKAMP: Yes. I learned how to do that. [Yes]. It was good that my mother had some background in it, so she helped. Actually, early after we arrived there, two other cousins came, of my sister and myself, so we were all there together, six children and my mother. So that was my early childhood, so to speak.

If you ask me where I really feel at home, it's still there. It's in the mountains, and it had a strong influence on my later life. You know, I did rock climbing, and mountaineering, and skiing. Actually in winter, we couldn't go to school without skis. Now there was much more snow for that.

GRAYSON: So it was at altitude . . .

HILLENKAMP: Not very high, around eight hundred meters, I think. But enough snow, [yes], at least for some time.

Again, back in 1947 we had to go back to Germany. Now Essen was almost completely destroyed. There was no room, no houses, no apartments to be had. But my grandparents [Karl Russell and Beate Russell née Schweling], my mother's parents, had a summer house just north of this industrial area, south of Münster not very far from here, actually. My grandfather had died by then, but my grandmother lived there, and we moved in with her.

GRAYSON: So the war had . . . by 1947, the war was kaput, finished.

HILLENKAMP: Oh, the war finished in 1945. And it certainly finished by then, but even in 1955, when I went to Munich [Germany], Munich was half destroyed. I mean . . .

GRAYSON: Oh, [yes].

HILLENKAMP: Half of the buildings or so were in rubbles. So the [Freiherr vom Stein *Gymnasium* in Lünen, Germany, about four miles from where we lived] that I went to had been bombed. So it was still . . . you could certainly still see the signs of war, and for a couple of years, until about 1950, food was very scarce. So we were hungry quite a number of times.

GRAYSON: So the French were essentially . . . this would have been after the war, their partition of Austria and Germany . . .

HILLENKAMP: They . . . well, Austria was separate. It soon became independent again where Germany stayed occupied to various degrees until about 1955 or so. This area here was occupied by the British Army. The French had the southwestern part, and it was bordering France.

GRAYSON: Okay. I think Vienna [Austria] was also partitioned.

HILLENKAMP: Oh, Vienna and Berlin [Germany] were both partitioned among the four Allies, you know, but . . .

GRAYSON: Because that's where the *Third Man* . . . movie about the *Third* <**T: 15 min**> *Man*[1]. . .

HILLENKAMP: [Yes], [yes], in Vienna, [yes], certainly. With the very famous Harry Lime melody . . .

GRAYSON: Yes.

HILLENKAMP: [Yes], of course.

GRAYSON: We were there and apparently there's a picture show house—movie house—that shows this movie every Friday night at the end of the day. So, you know, it's really kind of fun to go there.

HILLENKAMP: It's almost as famous as *Casablanca*.[2]

GRAYSON: You're right, it is.

---

[1] Graham Greene, *The Third Man*, directed by Carol Reed, London Films, released 2 September 1949.
[2] Juliua J. Epstein, Philip G. Epstein, Howard Koch and Casey Robinson, *Casablanca*, directed by Michael Curtiz, Warner Brothers, released November 26, 1942.

HILLENKAMP: You know, all of these war . . .

GRAYSON: It is, and the fact that you had been traveling in Vienna, then you can see the movie, and the same places you traveled, but ravaged by war is really striking.

HILLENKAMP: [Yes]. So . . .

GRAYSON: So you're back in this part of the country, then, in 1947.

HILLENKAMP: Then in 1947, we came here, and then . . .

GRAYSON: So your education is still . . . you're in grade school still?

HILLENKAMP: Well, I went to grade school for a few months or so, but didn't do very well. One of the reasons was that I wasn't used to speak High German in school, you know, and during breaks I would stand together with my sister, and we would speak the Austrian dialect. Then the other pupils didn't like that, so we had a pretty hard time. Then in 1948 or so, the high school, which was called *Gymnasium* in German, in the nearby town of Lünen . . .

GRAYSON: Let me get *Gymnasium* in here.

HILLENKAMP: *Gymnasium*, [yes]. [. . .]

HILLENKAMP: Okay. So that's high school. I well remember when I got there, I jumped the first grade in the *Gymnasium*, because I had been taught some Latin by a retired priest back in Austria, and my parents thought that I should keep going with my education.

But the first day we went there we were shown the classroom. The classroom, there was no glass in the windows. There were no desks, no chairs. We had to sit on the floor. We had no books. We had almost no paper to write on. It was a very strange situation. I think it didn't have much effect on the long run, but for a while the school life was somewhat different from what you would otherwise expect.

GRAYSON: Now your father stayed in . . .

HILLENKAMP: In Essen.

GRAYSON: Essen. So did he have any . . . I guess he experienced some difficulties with the War, because he was in Essen during the whole war period, right?

HILLENKAMP: Right.

GRAYSON: So was he ever . . . did he ever talk about feeling threatened by . . .

HILLENKAMP: Yes, actually, very much so. My father was brought up very Catholic, actually. My mother's family was not Nazi, but right wing. There was some other more conservative parties originally. My father was the only one in the larger family who was not on this political ticket, let's say. After the War, actually until he retired, he suffered from the fact that he thought he should have done more against the Nazi regime. But, you know, with a family of four small children, what can you do?

GRAYSON: Well, it was difficult, because people who expressed themselves too strongly were stepped on.

HILLENKAMP: [Yes], true.

GRAYSON: So . . .

HILLENKAMP: And also the judges in Germany are public servants. They are not elected. They are what we call the third power in the state, and they are not supposed to be very active politically. We tried to convince him that he did what he could have done, but that didn't help all that much.

There was also the other problem: judges cannot be moved around from one town to another. The town they start out, they will stay with. So he stayed in Essen, it's for life-long, and he only came for the weekends. So essentially I grew up without a father. I cannot recall that I suffered from that, or that I thought something was <**T: 20 min**> missing. My mother was a very strong personality. She made up for it, let's say.

GRAYSON: Well, it's interesting that she had English roots, right?

HILLENKAMP: [Yes].

GRAYSON: But she had more sympathy apparently with the right wing in Germany than your dad did, it sounds like.

HILLENKAMP: That's right.[3] But you see, the connection to England was long ago, and the last person or first predecessor that we know of in her family was a British officer who came to Germany, to an area north of Münster here, when the House of Hanover took over the throne in England [1714].

GRAYSON: Oh, okay.

HILLENKAMP: Okay. So that was quite some time ago.

GRAYSON: [Yes]. [Yes], okay.

HILLENKAMP: And . . .

GRAYSON: So she was basically . . . she had English roots, but basically . . .

HILLENKAMP: [Yes]. But no, by that time, it was a German family, no doubt about it.

GRAYSON: So you're still finishing off grade school, basically. Now you're in *Gymnasium*.

HILLENKAMP: [So now I am in] the *Gymnasium.* . . . well, the whole schooling was thirteen years. Okay. So nine years of *Gymnasium*. There was sort of an intermediate exam after the sixth year in *Gymnasium*, and just a special name which is not important here, but at that point I

[3] Hillenkamp qualifies: To do justice to my mother: she was apolitical as most women in bourgeois families at that time.

was given the choice whether I wanted to specialize on math and sciences or the liberal arts. I choose the [mathematical and science branch], and we were the first year that this was allowed; normally, the *Gymnasium* was strictly liberal arts with Latin and Greek as foreign languages, and so on. I never had to take Greek, actually. I took English and Latin.

I chose the mathematical, scientific branch. To be honest, I don't know exactly why. When I think about it, [yes], I had relatively good grades in physics and mathematics. We had a very good teacher in those two topics, which is important, and our teachers in German and English were not very good. There was another reason in my grandmother, who we were living with in her house.

GRAYSON: This is your mother's side.

HILLENKAMP: My mother's side grandmother, right. She was always well-to-do. My grandfather was the director of a coal mine. She never had to work, so she spent all her time educating herself. So, for example, she would know almost the whole *Faust*, by Goethe, by heart.[4]

GRAYSON: Oh, wow.

HILLENKAMP: You know, I have considered that I got much more education whenever I was with my grandmother than in school, but nothing about math and sciences. So anyway, I had a good teacher. That's, I think, something that's very important.

GRAYSON: Now, this division . . . does that go on in today's *Gymnasium*, or they still do that?

HILLENKAMP: The German *Gymnasium* has gone through dozens of reforms. Just last week, my oldest granddaughter started *Gymnasium* in Kiel, in the town of Germany. She decided, or her parents decided, to send her to a classical *Gymnasium*. So she will start with Latin and her school is actually called the [*Gelehrtenschule*], School of the [Scholarly Ones].

GRAYSON: School of . . .

[4] Johann Wolfgang von Goethe, *Faust: Eine Tragodie.* Tübingen : in der J.G. Cotta'schen Buchhandlung, 1808.

HILLENKAMP: The [Scholars]. *Gelehrtenschule*. It exists since 1200-something. So very, very long tradition, but there are other schools which start with English or with French. So since then a lot of things have happened.

GRAYSON: The *Gymnasium* is administered or formed by the federal government, by the . . .

HILLENKAMP: No. No. All what we call "cultural activities" are state activities. The states are <**T: 25 min**> very jealous of the federal government, that the federal government might interfere with their decision-making, which has as a consequence that teachers, for example, have a hard time to move from one state to another. Let's say when I was moving to Münster and if my wife would have been a teacher, it would have been difficult for her to get a job here. Also for children, when parents moved, it's not so easy. So this is strictly a state affair.

GRAYSON: So Westphalia would be the state that controls . . .

HILLENKAMP: North Rhine-Westphalia. So the most southern point is about Cologne, [Germany], and the most northern part is Osnabrück which is north of us, not very far.

GRAYSON: Okay.

HILLENKAMP: So . . .

GRAYSON: So then that entity is able to control its own educational system.

HILLENKAMP: Right.

GRAYSON: Okay.

HILLENKAMP: Right. So except for very few private schools, schools are run by the public servants. Teachers are public servants, almost all of them.

GRAYSON: Do you have any sense of whether they're well paid? I mean, most teachers in America, I think . . .

HILLENKAMP: First of all, in the first number of years in *Gymnasium*, the question was not how much you get paid, but how to get food. That was a much more difficult task.

No, I think teachers are reasonably—were, and are—reasonably well paid, I would say. If you ask a teacher, you may [be told differently].

GRAYSON: [Yes], right.

HILLENKAMP: No. I think it is a respected profession. Let's put it this way, that's certainly true. So . . .

GRAYSON: So let me . . . when you moved here . . . you just mentioned food again. So how did . . . what were the exact kind of problems you had getting food when you came back to this part of the country? Was it just that there was nothing? Or, I mean . . .

HILLENKAMP: Oh, it was . . . for example, there was a huge garden with the house of my grandmother. Most of it used to be flower gardens. So that was all converted into vegetable and potato garden. We had chicken and we had rabbits.

GRAYSON: *Hasenpfeffer*, huh?

HILLENKAMP: [Yes], right. For example, when the farmers would harvest their potatoes, after they had cleared a field, we would go and look for what was left and collected potatoes. Same is true for corn. So to get enough food was a concern, originally. Later on, let's say from 1950 on or so, things normalized and you could buy whatever food was needed.

GRAYSON: What about meat? I guess chicken . . . like you said chicken and rabbit was the meat you served for protein. You wouldn't have cow or pork?

HILLENKAMP: [Yes]. [Yes]. Actually, because of the special "*Küche"* [cooking] we would say in Austria, we had meat only once in a week, only on Sundays, even then sometimes not. We would have different dishes which were very tasty, and are good enough to grow up on. You know, so the meat wasn't that much of a problem, I must say. It was more simple food; potatoes, in particular, not that much pasta then. Okay.

So I grew up in a family where education was considered very important, both by my parents, and by my grandmother. Actually my grandmother was sort of the role model for us. Still from that time I like poems. I learned many of them by heart at that time.

GRAYSON: [Yes]. It's interesting.

HILLENKAMP: [Yes], right. So in school <**T: 30 min**> I was never a straight-A student or so. Maybe I could have, but I didn't care. I had too many other interests, let's say. In between once, in the third year of the *Gymnasium*, my parents got a letter at Christmastime that there was no chance for me to make it to the next grade because my grades were all C's and F's.

My mother was, of course, really concerned. She went to see my math teacher. He told her, "You know what? I have been observing Franz, and I think he's going to make it. There is some switch that hasn't been powered yet, but he will make it." Actually, by Easter—that's when the school year ended—by Easter, I had not a single grade less than a B. I mean, it was strange. But other than that . . .

GRAYSON: But, I mean, you'd get negative feedback, or positive feedback from your parents about your grade situation that motivated you? Or . . .

HILLENKAMP: No. I think it wasn't a question of feedback. It was one special, actually, way in mathematics of . . . and I don't really know how to say that in English. In German it's called *Dreisatz* [rule of proportion]. It's, like, "If ten people need four pounds of meat, how much meat will seventy people need?"

GRAYSON: Word problems.

HILLENKAMP: Word, [yes], and more difficult than that . . .

GRAYSON: [Yes], [yes].

HILLENKAMP: So all of a sudden, I understood what this was all about. I couldn't remember why I had so much difficulty. This gave me self-confidence in the other topics as well. I think that's what it was. So I remained a B to A student throughout my school time. But I must admit that . . . well no, let me first say, I liked to go to school. I liked to learn. But I liked to learn only what I liked to learn, and not what the teachers wanted me to learn at times, which made it difficult.

The best example of that was that every time we got our certificates—you know, once a year—my teacher in physics and maths would look at my certificate and say, "You know this is ridiculous. You have an A in physics. You have an A in mathematics, and you have a C- or an F in chemistry." So I didn't like chemistry when I was in high school. I don't know why. But it has been, I think, a theme throughout my life that I mostly did what I liked to do, and didn't want too many people to interfere with my plans. So I graduated from high school in 1955.

GRAYSON: Okay.

HILLENKAMP: Then the question was what profession to go into? Now my father, I know, would have liked to see me go to law. But I told him that I wasn't interested, and he didn't insist, really. You know, he let me do what I wanted. And I decided to take up a curriculum in electrical engineering, for no good reason. I don't know.

One sign of that is that about a half year before graduation we had to write a paper about our future plans. [Yes]. And in that paper, of course, I wrote I wanted to be an engineer. When our German teacher returned that to us, he wrote that . . . he said, "You know, if you want to go into engineering, you should at least know how to spell 'engineering.'" It would be as if I would have in English spelled engineer with only one E at the end. [laughter] So that was . . . it was just my choice <**T: 35 min**>.

I also decided to register at the Technical University in Munich. The reason there was obvious. I wanted to get back close to the mountains, because that was where I felt at home.

GRAYSON: So this process of selecting schooling after high school, was it . . . you know, in America now it's very intense. You sent out applications to all over the world and all this business. But, I mean, did you just select the TUM and then go there, or did they . . . do they . . . do you have to be admitted?

HILLENKAMP: [Yes]. It was not the TUM, yet, at that time; it was *Technische Hochschule*.

GRAYSON: Ah, okay.

HILLENKAMP: All right. It later became a university. Now it has a medical school and all that. At that time it was strictly engineering school, but at the level of a university. And no, they had limited admission, so I had to take an entrance exam. I thought after I came out of that exam I'd flunked it, but apparently others were even worse than I was, so I got admitted.

GRAYSON: Was it . . . well, many, many people applying, more than there were positions do you know? Or . . .

HILLENKAMP: I don't know. I would . . . if I try to recall the lecture hall where we took the exam, maybe twice as many applications as there were positions in available, something like that. And . . .

GRAYSON: But you selected the school primarily because . . .

HILLENKAMP: I selected the school, but, you know, if I would have failed that exam, I might have selected Aachen [Germany] for example, would have applied there, and gone there. But I wanted to go to Munich and I passed the exam. So that decided that I would go there.

Now during the first four semesters, the first two years of engineering curriculum, we mostly had lectures in mathematics, in physics, in chemistry, in [technical] drawing . . . basic fields, let's say. I wasn't sure how well I was doing, and I worked pretty hard during those first two years.

Then after those two years, there was what we call the pre-diploma, an exam, all written actually. You could go on with your studies only if you passed that exam. They posted a list of all students and how well they did in that exam. It turned out to my great surprise that I was among the top 10 percent. That was the good side. The bad side was that the very moment the more specialized lectures and laboratories on electrical engineering started, I found out I wasn't interested at all.

I thought that I would be better off if I would switch to physics. I tried to do that, but the system was very rigid. They said I would have to start from scratch again, which would have cost me two years, and I didn't want to do that. So in reality I finished my curriculum in electrical engineering, but never intended to work in that field, and in fact, I never did. For my diploma thesis, I picked a topic which was more in physics than in engineering, already.

GRAYSON: What happened to those students who at the end of their two years in pre-diploma did not pass? What happened to them? Did they have any options, or they start out their career at a lower level?

HILLENKAMP: Well both, I think. There was no organized way for them to . . . what to do at that point. But we also now have these sort of engineering schools which are somewhat below the level of a university, and how do they call themselves? [They are called Universities of the Applied Sciences.]

GRAYSON: There's what they call "trade schools" in the United States . . .

HILLENKAMP: [Yes], and that's what it would be. And they were not in existence then. So I think those students either took up another career field, or just dropped out <**T: 40 min**>, and took up a job, most probably.

GRAYSON: So did your engineering ever come in handy at all? I mean, I know that you didn't pursue it as a, you know . . . I mean, in the process of your career . . .

HILLENKAMP: [Yes], [yes].

GRAYSON: Having knowledge of the electrical engineering, I would assume helped you along the way.

HILLENKAMP: Before I was allowed to enter the university, I had to do hands-on work in a machine company for half a year . . . and during my curriculum, again in electronic company also, and I learned a lot there. For example, I had learned how to operate a lathe, or milling machine, or to draw pieces. That has helped me a lot later on, when I was designing and constructing my own mass spectrometers. So that . . .

GRAYSON: That would be mechanical . . . what we call mechanical drawing . . .

HILLENKAMP: [Yes], right. Right. It was more, the mechanical part of it than the electrical, actually.

GRAYSON: So this is a two-[times] six-month requirement for all students.

HILLENKAMP: For all engineering students, right.

GRAYSON: Okay.

HILLENKAMP: Again that has changed meanwhile. Now it's only quarter of a year, and . . .

GRAYSON: But they still have to kind of . . .

HILLENKAMP: [Yes], some hands-on work to get a feel for what is good for . . .

GRAYSON: And they do that after their degree . . . or some of it during their studies?

HILLENKAMP: Some of them before, and some of them during their studies. Okay. Because we have long summer vacation in universities, so they do . . .

GRAYSON: So what is the school year?

HILLENKAMP: Well, a typical school year would start in May and end in July/August and then start again in October and end in February.

GRAYSON: So you had two breaks.

HILLENKAMP: [Yes]. Now again, the school year has been extended somewhat, but during my time that was a typical school year. So as I said, I finished the engineering curriculum and then I had to take the main exams for the diploma. There were no master's degrees then. Afterwards, I had to write a diploma thesis, which would typically have taken a year, one and a half years.

There is a real break in my development at that point, because I had just started my diploma thesis when I got awarded the Fulbright Scholarship. I had applied for the Fulbright Scholarship. Actually, I had learned about the Fulbright program from my aunt. My mother had a much younger sister, sixteen years her junior. She was in diplomatic service. She spent all her time as a cultural attaché at first the German general consulate in New York, and then at the embassy in Washington. So she was very familiar with the US, and the options. So she told me, "Why don't you apply for Fulbright Scholarship?" I did, and I got it for whatever reason. My English certainly wasn't very good then, but . . .

GRAYSON: Now were you taught English in school?

HILLENKAMP: Yes. I was taught English in high school.

GRAYSON: High school.

HILLENKAMP: But you know, we learned more Elizabethan English. I still remember, "Is this a dagger which I see before me, the handle toward my hand? Come let me clutch thee!" That's [Macbeth].[5]

GRAYSON: [Yes]. That's real good English.

HILLENKAMP: [Yes]. So, I learned my colloquial English when I was in the US.

I was told that I would get the scholarship maybe in July, or so. The American school year started in October. So there was not much time, certainly not enough time to finish my thesis. You know, I absolutely wanted to go the United States. At that time, this was . . . looking from Europe it was sort of a paradise.

GRAYSON: Uh-huh, this was 1950 . . .

HILLENKAMP: That was in 1957 <**T: 45 min**>. No, no, sorry. This was in 1960.

GRAYSON: 1960.

HILLENKAMP: 1960. So I went to see the chairman of the examination committee, [Hans H.] Meinke, who was a high-frequency engineer, and was the star of the faculty at that time. I asked him whether he would grant me a year of leave so I could spend that year in the United States. He said, "No." He said, "You should finish your thesis, and after you've finished your thesis, I can always help you to get a job somewhere with a company in the US. A year at an American university is a waste of time. I'm not granting you the year of leave."

So first of all, I was . . .

GRAYSON: So why did . . . you said he . . . the American university would be a waste of time. I mean, was that because he had bias against American education? Or . . .

[5] William Shakespeare, *Macbeth: A Tragedy*, London: Printed for P. Chetwin, 1674.

HILLENKAMP: I have no idea. I have no idea. I think it was more bureaucratic. That he wanted people to stay on track.

GRAYSON: Okay.

HILLENKAMP: Okay. That was more . . . you know, he thought that I was about within a year to finish my diploma, and then I would have an exam which was similar to a master's degree in the US. So why spend another year? And I think he thought that I would goof off the year, anyway.

GRAYSON: No. [laughter]

HILLENKAMP: Well, he said, "no" so I was devastated. I was really devastated. So I think you . . . at some point, you ask about mentors and so on. I went to see what we call my diploma father. He was my mentor for the diploma thesis. Actually, [Max] Knoll was his name. [. . .] He did some very important early work in electron microscopy, actually. So I went to see him and said, you know, "What can I do? I really want to go to the United States, and the other professor doesn't grant me a year leave." He said, "Well, that's really bad. He's very powerful man. So what can we do?" Then he looked at me, and he said, "You know, I really don't have to look after you every day."

GRAYSON: [laughter] "Go away, kid!"

HILLENKAMP: That was exactly what he said. He said, "Make sure that for the second semester in that year you fill out the registration forms already, and have your friends turn them in for you." He said, "You know, if—Meinke was the other professor's name—if he finds out that you have gone, then I can't help you, because the rules are against you."

GRAYSON: [Yes], [yes], [yes].

HILLENKAMP: But . . .

GRAYSON: "If he doesn't know you're not here, then you're okay."

HILLENKAMP: [Yes], right. "But I won't tell him . . . "

GRAYSON: Okay.

HILLENKAMP: "And I won't be looking for you every day." [. . .] Meinke was in high-frequency engineering.

GRAYSON: [Yes]. So it was kind of like don't ask, don't tell kind of situation.

HILLENKAMP: [Yes]. No, he made it absolutely clear that it was my risk, not because he didn't want to help me. But if it would . . . if the other guy would find out, I was so obviously violating the rules that I would have flunked. No doubt.

I decide to take the risk, and in fall of 1960, I wound up at Purdue University.

GRAYSON: Oh, wow.

HILLENKAMP: [Yes].

GRAYSON: Now did you choose Purdue?

HILLENKAMP: No. The Fulbright Foundation choose . . . they pair people and universities.

GRAYSON: Oh, I see.

HILLENKAMP: The universities would offer positions in certain departments. Then Fulbright Commission would do that.

GRAYSON: I see. So once you accepted the scholarship, you were going to go . . .

HILLENKAMP: You were told which university to go to. I crossed the Atlantic on a boat, on what we call the intermediate deck, you know, way down by the engine, of course; the cheapest

ticket you could get. On the way over, I was so incredibly seasick. I was . . . it was a hard time for me.

GRAYSON: Oh. How many days <**T: 50 min**> passage was that?

HILLENKAMP: Oh, six days. Six days from Land's End to Nantucket Island. These things I remember because I had a hard time. Then, because I was somewhat late, Fulbright let me take a plane from New York to Indianapolis [Indiana]. My first time on a plane, it was very exciting.

GRAYSON: [Yes]. So that was . . . got you there in time.

HILLENKAMP: [Yes].

GRAYSON: That must have been fantastic to be seasick all of that time.

HILLENKAMP: [Yes]. But I was looking forward to paradise.

GRAYSON: [Yes].

HILLENKAMP: [Yes]. It was unpleasant, but it was worth it, I thought all along. Okay. So I arrived at Purdue and . . .

GRAYSON: That was in October . . .

HILLENKAMP: That was in October, [Yes], October 1960.

GRAYSON: 1960.

HILLENKAMP: Right. I was told that because I had already passed my written exams back in Munich, that only half of the money I would get would be the real scholarship. The other half I would have to earn as a teaching assistant, so I taught a laboratory course there; you know, I was supervision for the laboratory course. There was one younger professor, who sort of took care of me. In the second term, he said, "You know, you could actually teach a recitation." I

said, "[Yes], but my English is not that good." He said, "Oh, your English is good enough." It turned out that he had been standing outside of the classroom one or two times, listened to how I was doing, without coming in, because he thought he would disturb me, and I'd get nervous.

GRAYSON: So who was this guy . . . name?

HILLENKAMP: I don't remember. There, I must say, no . . .

GRAYSON: Perhaps it'll come, you know.

HILLENKAMP: No, I don't . . . I don't remember.

GRAYSON: But he helped you out, and then . . .

HILLENKAMP: Oh, [yes]. You know, he was a real mentor. For example, there was a professor in magnetism [Fritz Friedlaender] who was a Jew of German descent. He had to leave Germany before the War. He was lucky enough to leave Germany, I would have to say, as a young man. He had a very strange attitude towards Germany. On the one hand, he was very proud. He was having this small radio set by Telefunken, a German radio set. He was driving a Mercedes, at that time in the US a very unusual car. At the same time, of course he had resentments . . .

GRAYSON: Oh, sure.

HILLENKAMP: Which are totally understandable. And not so long after I had arrived, I was forced to take the prelim exams. I had never in my life taken a closed book exam. So I failed totally. I mean, you know, it couldn't have been worse. So then, he called me into his office, and got very, very angry at me, because he had originally said, "Well, wait. I was the first German student at the department after the war." He said, "Wait for the German students to come. You will see what a good student is." Here I failed him totally, and . . .

GRAYSON: So he was tad unhappy.

HILLENKAMP: He was very unhappy. I was very unhappy. But somehow this other young professor who was my mentor, heard about it. So he called me into his office and said, "You

must understand. Fritz,"—that's the magnetics professor; he said—"Fritz has a very hard time with Germany. So that's why it happens." I said, "But I've never taken a closed book exam."

He said, "Well, do you know how to prepare for these exams?" I said, "No." "Well, he said, "you know, if you go to the library, in the back end or so, there are binders of all prelims of the last ten years. What you do is, you just take them and go through them. <**T: 55 min**> That's the best preparation you can have. You just take it over again in spring," which I did. Then it was not a problem.

GRAYSON: So what department did you go to?

HILLENKAMP: Oh, it was electrical engineering.

GRAYSON: So you were in electrical engineering at Purdue as well.

HILLENKAMP: [Yes]. It was electrical engineering, but I specialized on statistical communications.

GRAYSON: Statistical communications.

HILLENKAMP: Yes, right. There was a Professor [George] Cooper. That was just a very new field at that time. That was shortly after the Shannon book, [*The Mathematical Theory of Communication*], was published.[6]

So I must say, during that one year, I worked very, very hard, because I had this threat that I might flunk my German exam. So I decided to try to get a master's degree within the one-year, the two semesters and the summer school. So I took a very high [load of] work, and actually was a teaching assistant, too, after the spring. It was a half-time teaching assistant, originally it was a quarter-[time].

So I worked very hard. But on the one hand, there was not much to be done in Indiana, in West Lafayette, Indiana, except work. Also, I realized that I had a good background from home, but I needed more practical knowledge in applications and so on. It fit together very well. So I eventually did get a master's degree, so I hold a master's degree in electrical engineering . . .

[6] C. E. Shannon and W. Weaver , *The Mathematical Theory of Communication*. Urbana, IL: University of Illinois Press, 1949.

GRAYSON: From Purdue?

HILLENKAMP: From Purdue University, [yes].

GRAYSON: Oh, okay.

HILLENKAMP: And I think that the year at Purdue has had a very strong influence on the rest of my career and my life. You know, it's not only that I learned different attitudes towards engineering, or towards learning, but it was a different language. It was different culture. It was a different environment. It was, you know, it was something that I otherwise would have never been able to experience.

GRAYSON: It's an education in its own right, just the time in a different country.

HILLENKAMP: [Yes], absolutely. Nowadays to go to the United States is almost like going from here to Munich or so. But in those days, it was really very different. During spring break, four of us, all Germans—one of them had a car—we went all the way down to New Orleans [Louisiana] and then back up on the East Coast. In fall, after I finished the summer school, I bought a car and I went all the way with two other students, all the way to California, and back. So I really got to learn the United States, and the . . .

GRAYSON: [Yes]. That was 1961, 1960, 1961.

HILLENKAMP: That was 1961, right. I came back in the fall of 1961. On the way over, back over here, the sea wasn't so rough. So we had a great time on the boat. But it was, again, on the boat.

GRAYSON: So what other experiences did you have in America at that time that you think are worth recalling at this point? You socialized mostly with other German students, or . . .

HILLENKAMP: No. In fact, intentionally I did not socialize with [Germans]. There were two other Germans at that time. In fact, I shared the office with one of them. There were actually six desks in that office. He was sitting opposite to me. We decided from the first day on that we

would not speak any German unless it was absolutely necessary to making a point or something like that.

No, no, I socialized mostly with Americans. This was a little bit difficult actually, because the majority of my fellow master's degree students were married already, and some of them had children already.

GRAYSON: Oh, [yes].

HILLENKAMP: [Yes]. For Germans at that age, and this was nothing, I thought . . .

GRAYSON: You were what . . . thirty, twenty-four, twenty-six, twenty-three?

HILLENKAMP: In 1961, I was twenty-five.

GRAYSON: Twenty-five.

HILLENKAMP: Twenty-five. You know, I had left my girlfriend back in Germany <**T: 60 min**>, but we hadn't thought about getting married then. Most of [the Americans] were already married and had children. So they invited me to their houses, but I couldn't return the invitation. Also, it was difficult to get a date on the weekend, because there were only the few home economics female students at Purdue. So it was mostly work, I must say. It was mostly work, but as I said, it had a strong influence on the rest of my life. I'm very, very grateful to the Fulbright Foundation for that program, and the opportunity I got that way.

GRAYSON: [Yes]. It's a great opportunity. I guess they continue to offer those scholarships today, to students around the world, which is really good.

HILLENKAMP: So when I came back, I was, I felt, in a little more safer position because I had the master's degree and if I would still flunk the diploma, it wouldn't be so bad. But because I had worked so hard for the master's degree, I had no time to work on my diploma thesis while I was in the US. So I had nothing when I came back. So I went to see my mentor for the diploma thesis. I think he was impressed that I had got the master's degree, but . . .

GRAYSON: Made good use of your time . . .

HILLENKAMP: [Yes], right. So he realized I hadn't goofed off. So he looked at me and said, "Well, what do we do now? Because the latest time point where you have to submit is about six weeks from now." Well, in the end he decided to write a letter to the examination committee that I had submitted a thesis that was so poor that he immediately returned it to me. He didn't even grade it. He said, "You know, chances are that the guy will not remember your name, and will not realize," which indeed happened. The rules were that [one] could flunk his thesis once. Then you would get another half year to improve your thesis and then turn it in.

GRAYSON: So there are ways around the system.

HILLENKAMP: Right, right. You know, he was really very, very helpful . . .

GRAYSON: Oh, [yes]. Well, obviously, he recognized . . . [phone ringing]

HILLENKAMP: Sorry, just a second. Could you switch it off?

GRAYSON: Oh, [yes]. [pause in the recording]

Okay, I think we're back underway here.

HILLENKAMP: So . . .

GRAYSON: So then the fact that you had actually been very industrious impressed him enough to say, "Well, we could bend the rules . . . "

HILLENKAMP: [Yes]. [Yes]. I think so. It was both. He was a nice person, but I think he also acknowledged that I had made good use of that year in the United States. [Yes], and . . .

GRAYSON: So you . . . that gave you another six months to work.

HILLENKAMP: Exactly. Right. So I . . .

GRAYSON: But you were all doing this still in electrical engineering . . .

HILLENKAMP: It was actually on vacuum systems.

GRAYSON: Oh, okay.

HILLENKAMP: So it wasn't . . . as I said, you know, it was in those days, there were still vacuum tubes, very important . . .

GRAYSON: Oh, okay.

HILLENKAMP: So it was on vacuum tubes, and the seals, the vacuum seals in tubes.

Yes. Maybe something that I forgot to say before, while I was still taking the courses in Munich, before I went to the United States, I spent a lot of time in the mountains. I was a mountain guide in the sports department of the Munich University. Most weekends, I was out in the mountains climbing. During the week, I spent a lot of time at the Music Academy, rather than in the Technical University. I tried to follow my interests, so to speak.

GRAYSON: But is your music in keyboard . . . or do you play a keyboard?

HILLENKAMP: No. I played a violin <**T: 65 min**>. [Yes]. One of the biggest mistakes I ever made in my life was that during those six months, I had to work very hard. I stopped playing the violin. Also, we had a quartet, four students of us. All the other three were gone by that time. There were different faces in the orchestra. So I gave up the violin playing, which I shouldn't. But, I mean, but you can't do everything right. This was one of my big mistakes.

Something that I did very right was that my girlfriend [Annemarie Nobbe] had waited for me. She got a job in Munich as well, so she moved to Munich. Actually, you know in the wedding ring, we usually have the date of the wedding and the date of the engagement. So in my ring the engagement date is the day I left the boat, when I was coming back from the US. Hers is . . . well, six weeks later. She still had to find out whether that was the right thing to do. We got married in 1963. Then it was appropriate, because I had [finished my basic] education. So her parents and my parents would think it was appropriate to get married, and she has been my wife ever since. She is still my wife.

GRAYSON: Wonderful.

HILLENKAMP: [Yes]. So we have [the] fiftieth [wedding] anniversary next year.

GRAYSON: Excellent.

HILLENKAMP: Wedding anniversary.

GRAYSON: Excellent. So you did spend a lot of time hiking in the Bavarian Alps, and . . .

HILLENKAMP: [Yes], right. I mean, in my free time. But after I turned in my diploma thesis, and got my diploma, I started to look for PhD work as a grad student. Because I had been in statistical communication at Purdue, and I had become somewhat interested in the biological side of the world, I thought I might try to find a PhD thesis in cybernetics, which also was a just coming up field at that time. I . . .

GRAYSON: And so this was in . . . what did you call it again . . .

HILLENKAMP: Cybernetics

GRAYSON: Oh, cybernetics.

HILLENKAMP: Cybernetics. So I went to . . . you know, I tried to find out at which universities cybernetic work was being done. I found out there were only two in Germany, one was in Tübingen [Germany] and the other was in Bonn [Germany]. Both had no openings, I went there and had an interview. So I was a little bit stuck there.

Then I asked for interviews in other maybe, what I thought related fields. One of the interviews was with the head of the department of radiation biology [Otto Hug] in Munich, at the University of Munich. You know, he said, "What do you want?" I said, "Well, I was actually looking for a place where I could do graduate work in cybernetics. But I wasn't successful so far." He said, "Well, we don't do any cybernetics, but I just got a call yesterday from a man at the Federal Department of Science and Technology about something new. Do you know what a laser is?"

I said, "No. I know what a maser is. I have seen a maser at Purdue, and a laser is apparently something similar. But I cannot claim that I know really anything about lasers." "Well," he said, "there has been a report in the *New York Times* of a medical doctor who claims

that he could heal malignant melanoma with laser radiation. And the guy at the Federal Department asked me whether we would be interested in looking into that, and find out what this was all about. Would you be interested to work in lasers?" I said, "Well <**T: 70 min**>, I don't know. I have to educate myself first."

GRAYSON: Have to find out what they are.

HILLENKAMP: Right. So I went to the library and read some papers by people like [Nicolaas] Bloembergen, and [Theodore] Maiman, and [James P.] Gordon and [Gary D.] Boyd, and all the Bell Laboratories people. After two weeks or so, I thought it sounded like a very interesting field, and I went back to this professor and said [yes], I was going to take it. It was a job that was fully paid. I got a full salary, so that was good and it was actually not a job at the university department, but at a national research laboratory [*Gesellschaft für Strahlen und Umweltforschung* (National Laboratory for Radiation and Environmental Research)] somewhere outside of Munich, where he had a [double position besides his University chair]. So for the next fourteen years, I was employed in a German National Laboratory on radiation and environmental research.

GRAYSON: Now you said that somehow along the way, previous to starting work on your PhD, that you had become interested in biology.

HILLENKAMP: Right.

GRAYSON: So when did that come about? Where did that interest begin?

HILLENKAMP: I think I just . . . from listening to seminars or reading papers. There was nothing special. It was very rudimentary at that point.

GRAYSON: Oh, [yes].

HILLENKAMP: But when I joined that National Laboratory, I made it a point that I would go to any seminar I could go to, to get more knowledge in these things . . .

GRAYSON: Because you really had no formal education in . . .

HILLENKAMP: No. I had no formal education in biology. I never got any formal education in physics, actually, the basics of laser physics. But then, there was no laser physics at German universities, because the first laser was operated in 1958. This was 1962. So it was, I would say on the one hand a difficulty, but on the other, it was a fantastic chance.

GRAYSON: Oh, [yes].

HILLENKAMP: You know, a whole new field opened, and the ones who were in that field early on had a lot of options. I said that the Fulbright year at Purdue influenced my further career very much. By the same token, I could say that lasers have been the common themes throughout my . . . all of my professional career. So at any rate, I tried to understand as much about lasers as I could, and . . .

GRAYSON: You're educating yourself in lasers and biology.

HILLENKAMP: [Yes], right. But most, you know on lasers at that point.

GRAYSON: And then you're working on a doctorate, a PhD program at that time?

HILLENKAMP: Well, there were no formal lectures, so you just have to write a thesis, and I was just starting to wet my feet. I read as much as I could, as I said. Then after a couple of months, the professor called me in again and said, "What have you learned? What do you think about applications with the malignant melanoma?" I said, "To be honest, it doesn't sound convincing. But I must say, it's non-ionizing radiation, and I don't know how . . . what the mechanism might be, how it would work. But I'm not in a position, really, to tell you yes or no."

"Well," he said, "I think you should talk to our dermatologist." So he made an appointment with the head of dermatology [Otto Braun-Falco] in Munich. I went there, and presented my case. He just burst into laughter and said, "You know, this is incredible. These Americans, they always make claims that they can't live up to. This is . . . a malignant melanoma is one of the most dangerous cancers there are and meta . . .

GRAYSON: Metastasize . . .

HILLENKAMP: [Yes]. "Metastasizing malignant melanoma, there is no <**T: 75 min**> way that you can heal that. So forget about it." By the way, the guy, I had just remembered the name

of the man who published that in the *New York Times*. His name was [Paul E.] McGuff, Dr. McGuff.[7]

GRAYSON: [. . .] But, I mean, at least you understood that it probably wasn't going to work. I mean, just from the reading that you had done and you . . .

HILLENKAMP: From the reading I had done, I was skeptical, because I couldn't see mechanisms.

GRAYSON: [Yes], okay.

HILLENKAMP: Okay. Then the very experienced dermatologist told me, you know, that people have tried almost anything on malignant melanoma. It was clear that he knew what he was talking about and that this wouldn't work.

GRAYSON: Your skepticism was proper and correct.

HILLENKAMP: Right. Right. So I went back to my mentor and said, "[Yes], Braun-Falco said, 'No way.'" He said, "[Yes], that's what I thought already. So what do we do now?" Then he said, "Do you think that lasers will ever be of any use in medicine?" I said, "You know, I don't really know. How can I know? But it's certainly a very interesting principle, and it may well be of use and value. But it would take much more work to find out." He said, "Well, then let's go on."

GRAYSON: Let's get to work.

HILLENKAMP: [Yes]. Let's get to work. So because he had the money, he got the money from the Federal Department of Science and Technology, and . . .

GRAYSON: Let's spend it.

[7] Robert K. Plumb. "Laser Tests Raise Cancer Care Hope." *New York Times* (1923-Current file), May 6, 1964. http://www.nytimes.com/1964/05/06/laser-tests-raise-cancercarehope.html (accessed June 23, 2015).

HILLENKAMP: [Yes]. Why not spend it on something interesting? So I started to work on lasers . . .

GRAYSON: And this gentleman that . . . have we gotten his name yet, the one that who said, "Let's go on"?

HILLENKAMP: Oh, [Otto] Hug. [. . .] Professor Hug. [Yes]. He was a medical doctor, but in radiation biology. So he was an MD in radiation biology. That's an important piece. So he was very research-oriented. He was not a surgeon, let's say, or for that matter, a dermatologist.

GRAYSON: Okay.

HILLENKAMP: Okay. So the next question was how to get a laser. You couldn't buy lasers at that time. So I had a fellow student who I met again, after I came back from Purdue. He had taken up a job at Siemens [AG]. I met him one night, and he said, "Well, I've heard that a PhD physicist in the Siemens research laboratory is going to start a group on lasers. Maybe you should talk to him."

He gave me the name [Dieter Röss]. I found the telephone number, and called this guy up and said, "Here I am. I would like to look at some potential medical applications of the laser, and I heard you're setting up a laser laboratory. Could we talk to each other?" He said, "Oh, [yes]. Why don't you come over?"

So I went there. It turned out at that time he was just by himself, there was no one else. It was difficult to get one or two positions from the company for at least a year or so. He said, "Well, you could work for me. The only problem is that Siemens normally doesn't let people into their research laboratory who are not employees of Siemens. But maybe you can try." So he said, "Why don't you just call the"—what do we call it—"the chief scientific officer of Siemens Company? And ask, and I will write a letter, and give you support." It was difficult, but finally I got the permission. Lasers were at that time, a magic word. Even the CSO of Siemens had heard about lasers <**T: 80 min**>. So for almost a year, I was paid by the federal government and was officially at the National Laboratory, but I worked at Siemens, and built my own lasers.

So I spent days polishing ruby rods. You know they have to be very plane parallel, the faces. Fiddling around with flash lamps and reflectors, and it was very interesting, a very good time.

GRAYSON: And who was that fellow at Siemens . . .

HILLENKAMP: Oh, the fellow at Siemens was Dr. Dieter Röss.

GRAYSON: Okay.

HILLENKAMP: We got along with each other very well. He had some very good ideas, and I had some ideas. For example, towards the end of that year, there was [an early] publication on Q-switching with rotating prisms.[8] It was not so easy to get a turbine that would be good enough for that. It took us a while and we got nervous, because we wanted to see these Q-switches.

So I thought about it, and then, I did something very simple. I took carbon paper. At that time, there was still carbon paper for making copies.

GRAYSON: Oh, on a typewriter . . .

HILLENKAMP: [Yes], the typewriter. Cut it into a piece, and then put it into the optical resonator of the ruby laser. Then I pulled slowly back until part of the ruby rod was free to oscillate. At that time, there was this buildup of inversion and of laser intensity. It would burn the carbon paper. It was a perfect Q-switch. It was a one-shot Q-switch. But at least we could see what this was all about.

GRAYSON: A manual one-shot.

HILLENKAMP: A manual one-shot Q-switch.

GRAYSON: So the Q-switching was important in the laser business because of . . .

HILLENKAMP: Well, we just wanted to be able to do as much of the experiments that people at Bell Labs, in particular, were doing . . .

GRAYSON: You were just making sure that you could keep up with what was going on.

[8] Robert Hellwarth developed the Q-switched laser while at Hughes Research Laboratories in the early 1960s and published a number of papers on it between 1961 and 1963.

HILLENKAMP: [Yes], keep up with all of these developments. So at the end—it was nine months or ten months, I don't remember exactly—Röss—of course for me, he was Dr. Röss; we would never use first names . . .

GRAYSON: Oh, yes. Yes.

HILLENKAMP: And said, "You know what? Why don't you stay? I can get the money. So Siemens can pay you." He said, "I have a clear goal. I want to be in the board of directors. I want to wind up on the board of directors of Siemens. If you stay with me, you can be in"—how do you say that—"my shadow, so to speak."

GRAYSON: [Yes].

HILLENKAMP: "You can pull up behind me, so to speak, and . . . "

GRAYSON: Riding my coattails . . .

HILLENKAMP: My coattails, right. "You can be on my coattails. You will have a chance of a very good career with Siemens."

GRAYSON: Oh [Yes]. Big money.

HILLENKAMP: Big money. So I thought about it for a while, and that was the first time that I think I made a very conscious decision that I wanted to go into science. I didn't want to work for a company. I wasn't that interested in the big money. I wanted to do research and to do self-determined research, research that I really wanted to do. So I went back to this National Laboratory, and . . .

GRAYSON: By then you knew enough, how to build your own laser.

HILLENKAMP: Oh [yes], sure. By then actually, my first laser had a reflector, which was an ellipsoid, was still made in the workshop, the machine shop of Siemens, and they allowed me to take it out.

GRAYSON: So did this guy, Röss, ever get to the top of the peak like he said he was . . . would do?

HILLENKAMP: Almost. He went in the end . . . his career took a different turn. Siemens has X number of daughter companies. He became CEO of Heraeus daughter company <**T: 85 min**>, which is you know in UV optics and lamps, and so on. So essentially, he . . .

GRAYSON: He got what he wanted.

HILLENKAMP: [Yes], right. Much later, maybe ten years ago, he was also elected [honorary member] of the German Physical Society [and president of the Wilhelm und Else Heraeus-Stiftung]. So no, he was very . . . I was lucky to meet people who were personalities and were good at what they were doing. These were good precedents for me.

GRAYSON: Oh, [yes], and highly motivated.

HILLENKAMP: Right. Right.

GRAYSON: So you're back now at the National Lab doing . . .

HILLENKAMP: So I was back in the National Lab. I was given [lab space, an office, and a budget for my work]. National labs were very well funded in these years, so funding was not a problem. Whatever I wanted to buy . . .

GRAYSON: So this was mid-1960s.

HILLENKAMP: That was mid- to end 1960s. [Yes], start in mid-1960s until late 1960s . . .

GRAYSON: Okay. So the money was coming from the national government . . .

HILLENKAMP: Right, from the federal government. Actually, 10 percent from the Bavarian state government and 90 percent from the federal government.

GRAYSON: Okay.

HILLENKAMP: At any rate, I still had to build my own ruby lasers. But soon thereafter, you could buy helium-neon lasers for alignment. Then the first argon lasers came, and a little later neodymium-YAG [yttrium aluminum garnet]. So slowly, lasers became commercially available.

GRAYSON: [Yes], neodymium . . . I've got to write these down for the . . . YAG lasers, [yes]. Okay.

HILLENKAMP: YAG, argon. YAG was really a bit later. I developed the idea that most probably lasers would be particularly useful together with microscopes, because you had a very collimated beam which you could easily focus down onto small areas. So I set up a laser set with a microscope. Then something, again, very unusual happened. I was going to a Mardi Gras party in Munich.

GRAYSON: Mardi Gras.

HILLENKAMP: Mardi Gras, yes, called Fasching, Fasching party in Munich. [. . .]

GRAYSON: Fasching.

HILLENKAMP: Fasching party. I don't know why my wife wasn't with me. Oh, I guess our first son had been born in 1966. She stayed home with the baby. Well, I went to that party. It turned out to be relatively boring, and I saw a guy sitting in one corner drinking beer. He looked bored, as well. I decided to just walk up to him and ask him who he was, and what he was doing there. So his name was Raimund Kaufmann. He's on the list of people that you have piled up, collected who is who, Raimund Kaufmann. [. . .] So it turned out, he was a physiologist with some physics background. He was an assistant as we would call it, you know—how would you say that in English, someone, you know, who gets a full salary and works at a department—anyway, in German *Assistent*, okay, at the physiology department in Freiburg [Germany]. At that time, the concept of calcium antagonists . . .

GRAYSON: Calcium . . .

HILLENKAMP: Calcium antagonists as a remedy for infarction and circulation disease were very popular. Actually, his boss in Freiburg [Albrecht Fleckenstein] was the inventor of these

calcium antagonists.[9] So [Kaufmann] was doing research on cell cultures of heart cells, heart muscle <**T: 90 min**> cells. He was looking for a method to determine the distribution of calcium ions in heart muscle cells. Okay. I said . . . and he had heard about lasers, you know. I said, "I have a laser. And you want to work with it? I've set it up with a microscope."

So we decided . . . as we spent at least two or three hours just chatting there, then we decided that the next week, while he was still in Munich, he would come to my new office, my lab. We would discuss whether we could do some joint work. Then this was, so to speak, the start of what in the end, wound up to be MALDI [matrix-assisted laser desorption/ionization].

At the same time, I got an inquiry from the Federal Department, again, whether I could do some work in laser safety, because that was all of a sudden becoming a hot topic, because there had been some accidents.

So, I mean, literally nothing was known about the interaction. So I got together with several people at the Munich Eye Clinic, because it was obvious that the eye was one of the main organs in danger. We started a series of experiments, animal experiments on retinal coagulation. Now, about maybe five, six years before that time, an ophthalmologist in Spain [J. Morón-Salas] and a German ophthalmologist [Gerhard R.E. Meyer-Schwickerath] then in Hamburg [Germany], had both experimented with mirrors and sunlight for photocoagulation of the retina.[10]

Of course, that was somewhat close to having a laser beam, and focused on the retina. Their idea had been taken up by Zeiss Company and Zeiss was marketing a huge xenon lamp photo coagulator. It was a real monster. At that time, every major eye clinic in the world wanted to have this. This was a big business for Zeiss at that time.

GRAYSON: So the photocoagulation did what for the patient? I mean . . .

HILLENKAMP: Yes. That was . . .

GRAYSON: What would it do to the eye, the photocoagulation?

---

[9] A. Fleckenstein, H. Kammermeier, H. J. Döring, and H. J. Freund. "On the Method of Action of New Types of Coronary Dilatators with Simultaneous Oxygen-saving Myocardial Effects, Prenylamine and Iproveratril. 2." *Zeitschrift für Kreislaufforschung* 56, no. 8 (1967): 839.

[10] J. Morón-Salas, "[Obliteration of retinal detachments by burning with light.]."*Archivos de la Sociedad Oftalmologica Hispano-Americana* 10, no. 6 (1950): 566-578; G. Meyer-Schwickerath, "Erfahrungen mit der Lichtkoagulation der Netzhaut und der Iris." *Documenta Ophthalmologica* 10, no. 1 (1956): 91-131.

HILLENKAMP: Well, the xenon lamp with its power supply was about maybe 5 feet by 3 feet by 3 feet. There was sort of a beam coming out. The patient would lie on a table underneath. Then the ophthalmologist would bypass with his vision, look into the eye and manipulate the beam on the retina, and would heat up the retina for photocoagulation. Does that make sense?

GRAYSON: [Yes]. But, I mean, what was the benefit to the patient?

HILLENKAMP: Oh. This was mostly used for so-called retinal ablation. There are certain diseases where the neural retina separates from the underlying retinal epithelium and the choroidea. It was actually called welding, [yes]. It has nothing to do with welding, of course.

GRAYSON: [Yes].

HILLENKAMP: What you do is, you damage the tissue, and the tissue will go through a wound reaction.

GRAYSON: Ah, okay.

HILLENKAMP: So in this wound reaction, unspecific tissue is formed that connects the two layers together. So the retina is gone where you coagulate. But the surrounding is still functional. So you would [look]. If there's a hole in the retina you would make many coagulations around it.

GRAYSON: So they were using this huge . . .

HILLENKAMP: This huge thing.

GRAYSON: To get the xenon . . .

HILLENKAMP: Okay. So we of course, wanted to use lasers, and <**T: 95 min**> we decided that the first thing we needed to do was to understand how much energy we would put in, and how much energy would get absorbed. In the retinal epithelium, there is one cellular layer, which is highly pigmented, the absorbing layer. To get some feel for what was happening there

[we tried to measure this]. There was one experienced ophthalmologist in that group. He's on your list as well. It's Peter Gabel.

GRAYSON: VP, this guy here . . .

HILLENKAMP: [Yes]. VP. Veit-Peter.

GRAYSON: Okay.

HILLENKAMP: So he's the ophthalmologist [in the group]. Later he was the chief ophthalmologist at University of Regensburg, and he's now retired.

GRAYSON: Okay.

HILLENKAMP: Okay. Then, let me see. I hired Reginald Birngruber. [. . .] So he's a physicist. He was my first grad student, so to speak. So I was his mentor from the very beginning. He came straight from university. At that time, I had several years of lab experience already.

GRAYSON: And so somewhere along here, did you take a PhD degree? Or . . .

HILLENKAMP: Oh. Of course, I did.

GRAYSON: Okay. So . . .

HILLENKAMP: I forgot about it. Totally forgot about it. Okay. We'll come back to this later.

GRAYSON: [Yes].

HILLENKAMP: No, no. After we had managed to Q-switch our ruby lasers at Siemens, we did get a spinning prism, eventually. Actually, when it turned out to be too difficult, the one we wanted, we went into a shop and bought a dentist's turbine, and put [the prism] on top of the dentist's turbine. It turned out that you couldn't measure the energy in the Q-switch pulse,

because it would destroy any meter. At the same time, a guy came who had been working at Bell Labs [Wolfgang Kaiser] for two years or so, got a chair of physics at Technical University in Munich. He was also working with Q-switch lasers. Somehow we got together and I told him that I had some idea of how to measure energy without damage to the meter. So as my PhD thesis, I developed an energy meter for measuring the energy of Q-switched ruby or other Q-switched lasers.

GRAYSON: Okay.

HILLENKAMP: It consisted of an aluminum cone, which was darkened. This is a very sturdy coating. It's not . . . you don't coat it with a paintbrush, but anodized . . .

GRAYSON: Anodized aluminum . . .

HILLENKAMP: Aluminum. The main . . . actually, the main development was to add to these cones of different sizes, actually, some resistance wire for calibration, and the calibration procedure was complicated, but that . . . right. I got my PhD in 1966.

GRAYSON: Okay.

HILLENKAMP: So [yes], I forgot . . .

GRAYSON: This was while you were working at the National Lab . . .

HILLENKAMP: Oh, I was working at the National Lab. But one of [the chiefs,] the head of the radiation department, the ionizing radiation department, also had a chair at the Technical University, so he didn't [really understand anything about lasers, but] he was kind enough to accept my thesis and asked another colleague to serve on the committee, and that <**T: 100 min**> way I got my PhD.

I think somewhere in your list there, you ask also about my mentors. In the classical sense of the mentor, I never had one. I was a self-made man. I mean, I had, like, this guy in electronics, you know, vacuum electronics, who was very friendly and helped me a lot, and Hug helped me a lot, but they couldn't give me any advice as far as my research went.

GRAYSON: How to direct your program for . . . [Yes].

HILLENKAMP: So you know, this is [the situation], if you pick up something like I did with lasers, on the one hand the field is wide open, and you had a lot of options what you can do. On the other hand, you're on your own.

GRAYSON: [Yes]. You have no guidance, no help.

HILLENKAMP: [Yes], right. Right. I don't know, are we getting too much into detail, or . . .

GRAYSON: No, no, no. This is good. Good, this is very good because, I mean, that's what we want is to find these little things. I mean, anybody can pick up the literature and read all of these papers and find out about the science. But, you know, this is about how the science got to be.

HILLENKAMP: Okay, [Yes].

GRAYSON: That's what we're about here; that kind of thing.

HILLENKAMP: But, you know, otherwise you let me know and . . .

GRAYSON: Oh, okay. Well, good.

HILLENKAMP: [Maybe] we'll change the speed a little bit . . .

GRAYSON: Good. We're good.

HILLENKAMP: Okay. So it was actually with this group from the Munich Eye Clinic that the laser-tissue interaction became my major topic at that time in my research. For example, we prepared [enucleated eyes.] We took first rabbit eyes—they were cheap—then monkey eyes—which were not so cheap—then later even human eyes which had to be taken out because of tumor.

As I told you, behind the retina is a one cellular layer, very sensitive, highly pigmented with melanin to absorb light. We prepared that single layer under the microscope and measured the absorption, and it turned out the absorption isn't in any way uniform throughout the eye

background, the fundus. It varies a lot, and partly because of different pigmentation, partly because of different geometry. You know, the fovea, which is the area of where you really see and focus, is somewhat indented in the retina. It looks much darker than it really is.

GRAYSON: So these are eyes that had been removed from the animals . . .

HILLENKAMP: Well, we started out with rabbits. [Yes]. For these experiments, we would take the eyes from the animal. We also took eyes, had a special holder which made sure that the curvature of the cornea stayed exactly what it was in the live animal. Then in the back of the eye, we drilled a little hole and then we scanned the laser beam there, because the eye is in no way a perfect optical system. Nobody knew what the size of the focus really was on the retina. So we measured that. These were more basic experiments.

At the same time, we irradiated live animals and then made follow-up studies of how the retina would develop. In the end, we would sacrifice the animal, take the eyes out and do histology and electron microscopy

GRAYSON: So this was all to develop information that you would use to determine the laser energy to do the photocoagulation thing, as a medical . . .

HILLENKAMP: Right. You know, it started out by trying to answer the question, how dangerous were lasers under what conditions, in what wavelength range, what pulse range, and what organ? But it really developed into experiments and research into the basic interaction mechanisms. For example, in dermatology there is also, of course, pigments; there's melanin there. But in dermatology, the arteries and veins are very important and [one of the questions was] can you close, for example, arteries in bleeding <**T: 105 min**> wounds with lasers?

You know, all this has to do with biology. You have to understand the tissue that you're irradiating, and its function. But it's a lot of physics, also. You have to do good radiometry. You have to become an expert in histology and electron microscopy.

So this was a very fruitful collaboration. Let me look at that list, where there was someone else on your names list who, no, I think on this list . . . it's on. Those two [Gabel and Birngruber] are indeed the most important collaborators.

GRAYSON: Very good.

HILLENKAMP: Since that was going quite well, I was asked by the Federal Department of Science and Technology [whether there was interest in other medical laser applications]. Well,

actually the guy who started the whole thing out [Dr. Straimer] came one day to my laboratory and said, "How can we . . . what can we do to get more information about laser medical applications and to foster that field?" I said, "Well, it definitely needs a collaboration between physicists and medical doctors. So far, we are doing most of our experiments in the eye clinic. But every second time when that we decide in the afternoon, we do some experiment, the ophthalmologist will get calls to a patient. We can't do the experiment. So my suggestion would be to set up a medical laser laboratory at the National Laboratory, equip it with all common lasers that we knew were useful for medical applications at that time already, and hire one or two or three physicists like Reginald Birngruber to make sure that the laser is operating properly. Then ask medical doctors to come out there, which is far enough away from their clinics that they can't be called for emergency cases, so that one can do real decent experiments."

In the end, there were five or six different medical doctors in different specialties involved. There was urology, neurology, gastroenterology, ophthalmology, okay. One of them actually took a year of leave from his clinic and he served as the chief MD at that laboratory.

GRAYSON: Oh, okay. So you had him full time.

HILLENKAMP: Right. That was, I think, the precedent for what still is the biggest and most successful laboratory on medical laser applications and other optical techniques in medicine, actually, which is the Wellman Center of Photomedicine in Boston [Massachusetts]. I'll come back to that. Let's leave that for the moment.

You know, I don't want to do any shoulder slapping, but we had managed at that time to be, most probably, the leading group on laser-tissue interaction worldwide. In 1970 I attended my first Gordon Research Conference on Lasers in Medicine and Biology, and until four years ago, I've attended every single such conference. I chaired one of them, myself, and had very, very fruitful interaction with groups from all over the world.

GRAYSON: Now is this conference in the fall, or in the spring. They usually have . . .

HILLENKAMP: That is in fall, or late summer, let's say.

GRAYSON: East Coast.

HILLENKAMP: The East Coast. Until very recently, it was always at Kimball Union Academy which is in New Hampshire, upstate New Hampshire near . . . what's the Ivy League university up in Vermont? Dartmouth College.

GRAYSON: Dartmouth?

HILLENKAMP: Dartmouth, it's very close to this. Of course, the Gordon Conferences are all held at prep schools. This was close to Dartmouth College, but on the New Hampshire side.

GRAYSON: [Yes]. There was . . . so you've been going to these for the last thirty <**T: 110 min**>, forty years.

HILLENKAMP: [Yes]. It has been going on since . . . I think the first was 1969 or so. It's not every year. It was . . . when I started, it was every year. Then I actually was the one who suggested it should be every second year, because there was not enough new material to warrant it every year. At this conference also, I met John [A.] Parrish. Is he on your list? I guess he's not. This is all the Germans. No. So maybe you want to add certainly his name and one more name.

GRAYSON: John . . .

HILLENKAMP: John Parrish. [. . .] Okay. John Parrish is a very extraordinary man. He was educated as a dermatologist and spent one year in Vietnam doing triaging, very, very . . . you know what triaging is.

GRAYSON: Triage?

HILLENKAMP: Oh, triage, [Yes]. [. . .] Triage, okay. Good. So, and which is important if you knew him well, he suffered from that much later. But he had also started to be interested in medical laser applications in dermatology, actually. We met at one of the Gordon Conferences, and I gave a paper on laser-tissue interaction. He came to me afterwards and said, "We are trying these applications and we don't really understand much about this field. Would you be willing to help us with that?" I said, "[Yes], why not?" You know . . .

GRAYSON: Sure.

HILLENKAMP: [Yes]. The next thing that happened was that the spring thereafter, [his research group at the Massachusetts General Hospital in Boston which is part of the Harvard

Medical School] had . . . ah, how do you call that? They went out for a weekend to Cape Cod [Massachusetts] to discuss their research program.

GRAYSON: A retreat?

HILLENKAMP: A retreat, right. So they had a retreat, and he invited me and paid for my trip across the Atlantic. So this was so fruitful.

Actually, the most fruitful was the car ride. He picked me up at the airport and drove me right out to Cape Cod. This car ride was essential for a lot of work that we did together later on. because we decided that what was happening was there was a big gap between the physics and the metrology of lasers here, and the tissue on the other side. In order to bridge that gap you have to have very good physics, and do very good measurement, and on the other hand, have very good, particularly, electron microscopy. So and then try to establish a relationship between the physical action and the biological reaction. So for many years the photopathology at Wellman was the central pillar of the whole thing, besides the physics, of course. So John was the MD, but he never really worked in the laboratory. The physicist is R. Rox Anderson who is now director of the Wellman [Center for Photomedicine]. Want to put down his name, Rox [. . .] Anderson, just as you . . . okay. The . . .

GRAYSON: This is all on the drive out to Cape Cod.

HILLENKAMP: Right. I mean . . .

GRAYSON: The ideas . . .

HILLENKAMP: Then we had this weekend with many more discussions. As a result, I was appointed first consultant to the . . . no <**T: 115 min**> let me start differently.

John had been able to set up a group and a laboratory. But it was small and just a few people. At that time, he was still seeing patients. He had—I don't know where and why actually—had the idea that one could use light to treat psoriasis. You know psoriasis, right?

GRAYSON: [Yes].

HILLENKAMP: He came up with a treatment called PUVA: psoralen UVA radiation. He got permission from the authorities, which is NIH [National Institutes of Health] . . . is it NIH? Or Food and Drug Administration . . .

GRAYSON: [Yes], probably the FDA, I would think, for . . .

HILLENKAMP: Anyway, he got permission for experimental treatment of twenty or so patients with this UV light, and psoralens are organic aromatic compounds. The actual story goes back to the old Egyptians. It's already in their texts that they describe that certain workers in the field never have skin diseases. It turns out that they were working with plants that generate these psoralens.

GRAYSON: What do they call these?

HILLENKAMP: Psoralens, let me . . . let me type it. [Yes]. They actually are crosslinking the molecules between the two DNA strands [when irradiated with UVA light.]

GRAYSON: Ah, okay. So if you worked in the field with plants with these compounds . . .

HILLENKAMP: Right. They were . . . they had a natural protection. Okay. So he got this permission to do a number of patients. After he had collected the twenty of them, a lady came and said could she still get—he had advertised that—could she still be part of it? He said, "Well, you know I have already twenty, and I'm not allowed to do any more." But she begged him very, very strongly and said, "I have psoriasis all over the body." So he said, "Well, the only thing I can do is put you on a wait list."

Then within a week or so, someone dropped out, so this lady was admitted to the controlled study and it turns out that she was an extremely good reactor. She reacted very positively. She lost all of her psoriasis and lost it for the rest of her life. Weeks later or so, a guy called John Parrish and said he wanted to see him. He said, "Yes, why?" He said, "You treated my wife, and we are so happy about this treatment. Could I stop by your laboratory?"

So he came; he was Mr. Wellman. He said, you know, "We want to support you. Do you need something for your work that I can help you with?" John said, "Well, I would like to have a monochromator, but that's about twenty thousand dollars, and that may be too much." "No, no, no!" he said; "Just order it. Send me the bill, I'll pay for it." You know, the check will be written . . .

A day later, the Director General of Massachusetts General Hospital called John and said, "I understand you have talked to Mr. Wellman." John said, "Yes." "I understand you have asked for a monochromator from Mr. Wellman." John said, "Yes, that's true. Was that too much? I wasn't sure what to do." Then the other guy burst into laughter. It turns out Mr. Wellman was one of the oil tycoons, very, very rich. He actually lost all his money later, because he was a gambler on oil. With the first oil crisis he lost most of his money.

But it turned out that later on he financed one of the huge research buildings at MGH, Massachusetts [General] Hospital. And one level was given to John, and he got quite a bit of money from Wellman. So that was the start of the Wellman Center <**T: 120 min**> of Photomedicine.

GRAYSON: Wow.

HILLENKAMP: [Yes]. [Mr.] Wellman came once or twice a year and walked through the laboratory for a day or two and enjoyed that he was, you know . . . somehow involved in this research and that he could finance it.

Also relatively early on John got a call from Department of Defense, DOD. The guy said, "Well, we have spent already a lot of money on the development of a free electron laser." There is actually . . . well, whether he said it the first time, I don't know. But it turns out this free electron laser was part of Star Wars . . . [Ronald W.] Reagan's Star Wars [Strategic Defense Initiative]. There was a note in the decision of Congress that 10 percent of the money must be spent to look into other than military applications, particularly medicine and what was the other . . . and materials research? [Yes].

So by then, you know, the guy had heard about this group at Harvard [University]. Would he be willing to take part in that program? I was there at that time, just by circumstance. John was coming in my office and told me the story, and said, "What do you think?" I said, "Well, I first have to educate myself about the free electron laser, and its parameters. Then, I think there would be big problems, because as far as I know the faculty here, they won't be very happy getting involved in Star Wars and so on."

So I looked into this. It was a very special type of free electron laser developed by John [M.J.] Madey at Stanford [University]. It turned out it was, on paper at least, wavelengths tunable in the UV with a picosecond structure, which was at that time, a very strange and not at all explored parameter range.

So it was scientifically interesting, but there was still the problem of Star Wars. Then John and I both talked to the rest of the group, and we said, "At least this money is being used for something peaceful rather than for destroying something. The fact that it's part of Star Wars shouldn't really bother us so much, if we tie some strings to it."

So finally the end of it was that we submitted a proposal. It clearly stated that first of all, we could not predict and promise any useful medical applications of the laser, but we would try. Secondly, that every single thing we did was going to be published, so they could not keep anything secret. That convinced the others. In the end, I think the free electron laser program went on until two or three years ago. The Wellman Center got at least fifty million dollars from that program alone.

A lot of interesting and good work, and I was always in those applications as a consultant. However, after the first two or three years, I was also appointed visiting professor at Harvard. I kept that position for at least twenty years, even though there is nothing like a continued visiting professor at Harvard. Somehow John managed that. I don't know. It was important for me, because I could use this as an argument towards my University here to spend two or three months a year in Boston.

So this is that side of my activities which is really related to laser-tissue <**T: 125 min**> interaction in medical laser applications. I still maintain some of those activities in Boston because in 1976 I moved from Munich to Frankfurt [Germany], and . . .

GRAYSON: Okay, so all of this time all this development was occurring that early timeframe, early 1970s when you were . . .

HILLENKAMP: Right, most of it was done in the time between 1963 and 1976. Okay.

GRAYSON: Oh, okay. While you were still at Munich.

HILLENKAMP: While I was still in Munich, right. But already at that time, I spent some time in Boston. So, you know, I was commuting back and forth. But my main occupation was in Munich. What happened was that I was moved from one department in the National Laboratory to another department which was newly founded. The chief of that department [Wilhelm Waidelich] I didn't get along with, so I started looking around for other positions, and took up an associate professorship at the University of Frankfurt.

GRAYSON: Okay.

HILLENKAMP: For medical physics and biophysics. My teaching obligation there was teaching physics to the medical students, and biophysics to the physics students, so I had a very heavy teaching load there.

GRAYSON: Did you teach any at Munich, when you were at Munich?

HILLENKAMP: In Munich, at the National Laboratory there was no teaching. But I had a part-time teaching job at the University of Maryland. I think I told you the other night.

GRAYSON: Okay.

HILLENKAMP: The University of Maryland was operating a campus in Munich for children, [for] what they called "government dependents." It was either military or diplomatic personnel, or other government dependents [from Europe, Near East and North Africa].

GRAYSON: The University of Maryland in Munich.

HILLENKAMP: And that . . . right. It was in Munich. It was a junior college, so it was only the first two years.

GRAYSON: So you taught there.

HILLENKAMP: I taught physics there, one semester of physics for non-science students, and then physics for science students. It was four hours of teaching per week, and four hours of laboratory work.

GRAYSON: But this was on the side. It wasn't a requirement.

HILLENKAMP: It was on the side. I needed permission to do it. It was very well-paid, I must say. It gave me a chance to keep up with my English. You know, it was very good, but it had . . .

GRAYSON: So you sought this job out yourself, though.

HILLENKAMP: Yes. Yes. I don't remember how I learned about that university. After I heard about it, I just went there and talked to the dean. After maybe fifteen minutes of talk he said, "You know, but with your background, why do you think you would be qualified to teach German here to our students?" I said, "No, no. I don't want to teach German. I thought I would teach physics." "Oh," he said, "That's very different." So then for, I think, two years, there was

another American there, a PhD, who . . . and I was his assistant, so to speak; I did the laboratory courses. And then he left for the US. I took over the lecture and the laboratory.

GRAYSON: So this was a fairly small group of students.

HILLENKAMP: [Yes]. [Yes]. The [total number of] students on the Munich campus was something like five hundred, I would think.

GRAYSON: Oh, that's a pretty good size.

HILLENKAMP: Around that. [Yes]. But, in the physics course there was never more than 20, mostly twelve or so. So it always was a question, could they afford me to teach the physics course, because . . .

GRAYSON: [Yes]. [Yes].

HILLENKAMP: So small number of students.

GRAYSON: [Yes]. That's always a problem.

HILLENKAMP: [Yes]. I learned to teach, by the way, there. And also to deal with another problem. In one year, they had a huge problem with drugs, because the whole thing was on military base in the city of Munich. There was drug dealing going on, on the base. The students became aware of it. In one semester, more than half of the students failed, could you believe it?

I taught and it was obvious that some of my students were involved in that <**T: 130 min**> as well, particularly one girl who was a very good student. All of a sudden, she almost dropped out. So I, one day, asked her to stay, and talked to her. She said, [yes], I was right, but I shouldn't worry. Next semester, it will be over, and everything will be normal again. I didn't believe it, but it happened. It was very strange.

GRAYSON: [Yes]. It is strange.

HILLENKAMP: It was methadone that they were taking, mostly.

GRAYSON: So that was just for that one period.

HILLENKAMP: It was just, sort of . . . you know, it was fashionable. But those students were strong enough already in their personality that they could pull out. Most probably, a few of them got lost. I don't know.

GRAYSON: [Yes].

HILLENKAMP: Anyway, so I did teach there. Then in Frankfurt, I taught.

GRAYSON: But that was a more responsible load in a way, because now you're in a university setting, which was . . .

HILLENKAMP: Now I was in a normal German university. This was a normal step in a career. In fact, many people remained associate professors for the rest of their life. They don't have to necessarily become a full professor in the university.

GRAYSON: [Yes]. So, I mean, you got kind of the worst of both worlds, didn't you? I mean, you were teaching medical students about physics, and physics students about biology. So, I mean, that's kind of like . . . was it . . .

HILLENKAMP: [Yes]. But it's also [interesting.] I got something out of it, because the medical students just hate physics. For their sort of prelims that they have to take, physics is the worst of all fields. To try to get across to them where physics is important in medicine [is what is needed.] I mean, you know, ionizing radiation is obvious; it is simple. But, for example, that you have a layer of surfactants in your lung, and if the lung . . . first of all, when a baby is born, it has to inflate the lung. If it wouldn't be for the surfactants . . .

GRAYSON: Surfactant.

HILLENKAMP: . . . the lung would rupture before it would ever inflate. You know, and I made it my point to—for every single part of physics—to show them where that was important.

GRAYSON: Where it fit in medicine.

HILLENKAMP: [Yes], in medicine. [Yes]. It was a high teaching load, but it was also quite good. For the physics students, they were only taught about ionizing radiation. So I added a part on non-ionizing radiation and optics and all of that. That was worthwhile as well. So . . .

GRAYSON: So how many hours did you end up teaching? Was that . . .

HILLENKAMP: Well, there was also the laboratory for the medical students, which was running four hours every afternoon throughout the semester. I had to mentor two or three groups there every afternoon. So in total it was about fourteen hours.

GRAYSON: Ooh, okay.

HILLENKAMP: That was quite a bit. By the way, we had also a very good lab course for the medical students. For example, I talked Zeiss into letting us have a number of not most modern stereomicroscopes. They are now used in almost every operating field, ophthalmology, in surgery, in gynecology, and so on. To make sure that you have stereovision on the stereomicroscope is not so easy.

So from my work back in ophthalmology back in Munich, I knew that when you make a corneal transplant, you sew it on with very fine needle and actually, originally with hairs that they used. Later on, it was very, very thin nylon threads. So I got hold of a couple of needles and they are bent actually, and of the threads, and I asked the students to feed the threads through the hole, the door of the needle . . .

GRAYSON: Eye . . .

HILLENKAMP: Eye, the eye of the needle. Unless you have good stereovision, you just can't <**T: 135 min**> do it. But it was something . . . you know it was written in the description of the experiment that whoever would go into ophthalmology might need that and things like that. Or we had a trough with liquid and electrolytes to mimic EKG. Then we also had a simple medical EKG apparatus there so the students were taking EKGs of each other, and things like that.

GRAYSON: [Yes].

HILLENKAMP: So [yes], it's worthwhile trying to convince even medical students that physics is good for something.

GRAYSON: Well, yes. But, I mean, that's the right way to teach it, to understand the reason why you want to know these things, because they could be helpful.

HILLENKAMP: But, you see, if it wouldn't have been for the MDs that I associate with in Munich, and Raimund Kaufmann, who was a physiologist, and who knew everything involved in the human body, I couldn't have done that. So that was a prerequisite for setting up the lecture that way.

But in Frankfurt, I never found a single MD. who was interested in laser applications. So I got stuck there. That's why I shifted all my activities on medical laser applications to Boston.

GRAYSON: Ah, okay.

HILLENKAMP: Okay. So that was . . . since then, it's in Boston and a little bit here, but not much happening. Parallel to this medical laser application in Munich, as I told you, I met this guy, Kaufmann. After quite a number of discussions, we decided that the only, or the most probable, approach [for measuring the Ca-distribution in heart muscle cells (see above)] would be to not only combine the laser with the microscope, and focus it to a size that is smaller than a cell, but add a mass spectrometer to see what ions you have there.

GRAYSON: You said the magic word, mass spectrometer.

HILLENKAMP: Right. This was the first time mass spectrometry entered my life.

GRAYSON: Right then. I mean, this was an idea that you had, or that came out as a result of the discussions.

HILLENKAMP: No, it came out of discussions. No. We were . . . you know, it was the laser and focusing in microscope part. Raimund would have known about it, but I had the practical, hands-on experience. So I said, "That can be done." And then we were looking for a way to measure what we were generating there in terms of ions. There were several publications at that time, where people were using emissions spectroscopy, optical emissions spectroscopy. But we did some calculations, and it was clear that would not be sensitive enough. It was too limited to only a few ions that might be there. So . . .

GRAYSON: But, I mean, did you have an understanding that the interaction of the laser with the biological material would actually produce ions?

HILLENKAMP: Ah, that's a good question.

GRAYSON: [Yes].

HILLENKAMP: It was a guess. [Yes], not quite. Let me explain to you how that all evolved.

GRAYSON: Okay.

HILLENKAMP: What I knew, of course, was by that time that you could use high intensity lasers—in a focus it's always high intensity—that you could generate the plasma. Of course, there are other ions in the plasma. We were interested in atomic ions, you know, sodium, potassium, calcium, iron, all the trace elements. Okay. So our notion was that we would focus the laser on the tissue section, or a cell from cell culture on electron-microscopic grating, would generate a plasma and look at the ions in the plasma by mass spectrometry.

GRAYSON: But there you were interested in <**T: 140 min**> ions of basic . . .

HILLENKAMP: Of elements, [Yes]. Elements of . . . atomic ions . . .

GRAYSON: Right.

HILLENKAMP: We didn't think of molecular ions then. That was . . .

GRAYSON: Okay. So you were . . .

HILLENKAMP: . . . atomic ions, and because, you know, he was originally interested in calcium.

GRAYSON: Right, goes back to the calcium in the cell.

HILLENKAMP: [Yes]. The calcium in the cell for the calcium antagonists.

GRAYSON: Then you want to know where the distribution of calcium ions was . . .

HILLENKAMP: [Yes], right. So at that time I had already been moved to the new department, and my then boss thought that was all totally crazy, and he was not willing to put any money into that.

GRAYSON: This is . . . now you're in Frankfurt.

HILLENKAMP: No, no. That was still in Munich. [. . .] Oh, [yes]. The work started around 1970, I guess.

GRAYSON: Okay.

HILLENKAMP: May have written it down there. Okay. So we decided to write the proposal to VW Foundation.

GRAYSON: VW . . . Volkswagen?

HILLENKAMP: Volkswagen. They have a foundation and they fund research. So we went through relatively great lengths to not only explain why we wanted to do what we wanted to do, but also how it would work, and why it would work. Now, I have to look for something here. Okay.

We were quite confident that we would get the money. Indeed, after a couple of months, we got a letter and we got the money. Much later, twenty years later, we met the officer who was responsible for deciding which proposals would get granted and which not. We asked him, "You know, this was a pretty risky project. Why? What made you decide to give us money?"

He said, "You know, I had been sitting there on a Friday. It was a whole day, and I had looked through something like ten proposals. They were all well written. They were all okay, but they weren't really fascinating. There was nothing really new about them. It was continuing something that people had been doing, where feasibility had been done, and they knew how to

do it, and I said, 'Goddamn it, I once want to fund something that is really high risk, high yield.'" So he realized that if [our system] would work, then that might be very useful.

And this despite, of course, he had written [external] evaluations. I can tell you now what it said. It said, "This project touches the absolute limit of sensitivity which has not been achieved before and will, in all likelihood, not be achieved by this project either." So he was courageous . . .

GRAYSON: Yes.

HILLENKAMP: In a way. At the same time, he wanted to cover his back, as well. So in the allowance letter, it also says, "After proving basic feasibility within" . . . or wait, no. "In accepting this support, you have to accept the responsibility for the high risk to successfully complete this project." So he let us know, we better be successful.

So we set up the whole thing in a room, actually outside of the department that I belong to, because my boss didn't want to see that there. Added actually, to the laser and the microscope, we added a quadrupole mass spectrometer, which Balzers loaned us. We didn't need to pay for it. Then we took cover glasses, microcopy cover glasses, and evaporated aluminum onto it, and put it in our machine, and banged it with the laser. We found out that we needed something like a thousand shots to just trace out the aluminum peak <**T: 145 min**> in the mass spec and it took forever, a full day or so, just for this little bit.

So we quickly decided the quadrupole wasn't the right thing to do. The other thing we realized was that our notion of generating the plasma was totally wrong. So we sort of did the right thing—and this might come up again later—we did the right thing for the wrong reason. If we cranked up the laser to the point that we generated plasma, we saw big humps of whatever, something, which we couldn't make any sense of. So this was when the laser desorption was born.

We found out you have to be just at the border, where you perforate, let's say a tissue section or a cell, but not much more. Then you could see the ions we wanted to see.

GRAYSON: So it was just a matter of getting it just right.

HILLENKAMP: It's the right fluence or the rate of exposure, irradiance. They are different terms. Intensity, if you want, though that's very unspecific.

GRAYSON: [Yes].

HILLENKAMP: Also since it was clear that we should not use too high a laser power or energy, we looked at different tissues. Originally, we just made blood smears, you know. We saw that with the ruby lasers that I had for erythrocytes—the red blood cells—that worked very nicely. But for white blood cells it didn't. And the reason was that in order to perforate the white blood cells, or anything else that was non-absorbing at the ruby laser wavelengths, we needed much too much laser energy. So I added a frequency doubler to the ruby laser. So we went from 694 nanometers in the far red to 347 nanometers [in the UV].

I don't know . . . you know, I have prepared a number of pictures. Do you want to look at them now?

GRAYSON: That would probably be fine.

HILLENKAMP: Because you know, some of that . . . then we can transfer to . . . maybe you switch that off for the moment.

GRAYSON: Well, I'm not sure . . .

HILLENKAMP: Oh, okay if it doesn't bother you. Well, first of all, since we were talking about the Gordon Conferences, this is John Parrish. [Fig. 1] This is at an afternoon . . . you know, at Gordon Conference the afternoon is always free, so we went on a hike for one of these mountains there. We did many hikes together, actually; White Mountains, and so on.

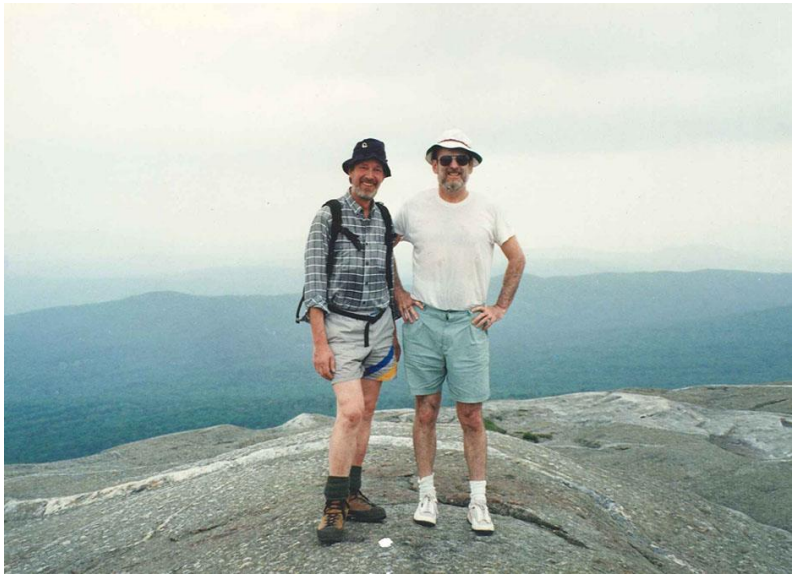


Figure 1. John A. Parrish and Franz Hillenkamp on top of a New Hampshire mountain

This is Richard Haglund from Vanderbilt [University] on a different mountain and this is a different Gordon Conference. [Fig. 2] It was a Gordon Conference on lasers, [not] on medical laser applications. So there was a certain pattern to my going to the US, and we will come back to that later. On your list is Peter Roepstorff.

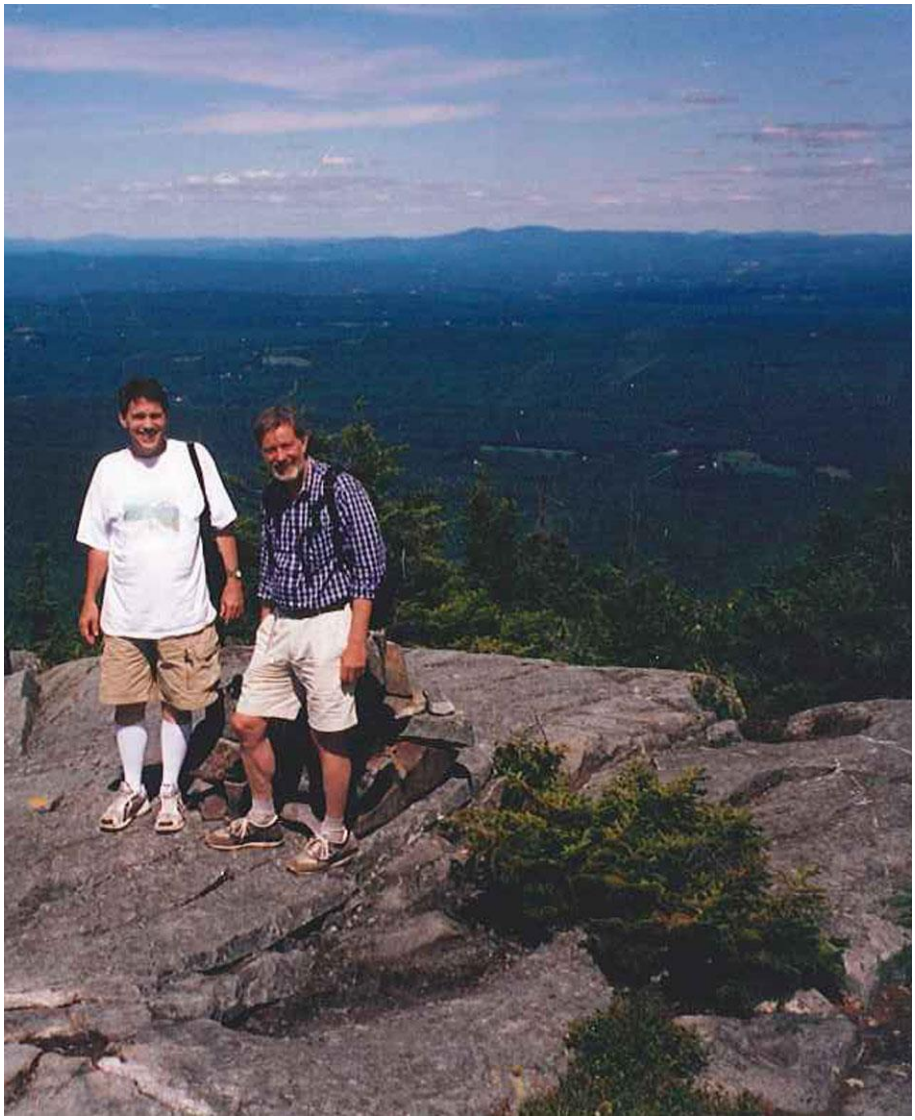


Figure 2. Richard F. Haglund and Franz Hillenkamp atop a New Hampshire mountain

GRAYSON: Ah, okay.

HILLENKAMP: This was when we got the ABRF [Association of Biomolecular Resource Facilities] Award in Denver, and he was there. We were just sitting in front of the hotel. [Fig. 3]

I think my wife did shoot this. Just to show you how much I am part of the group in Boston, the Wellman faculty, it's like a professional second home. [. . .]

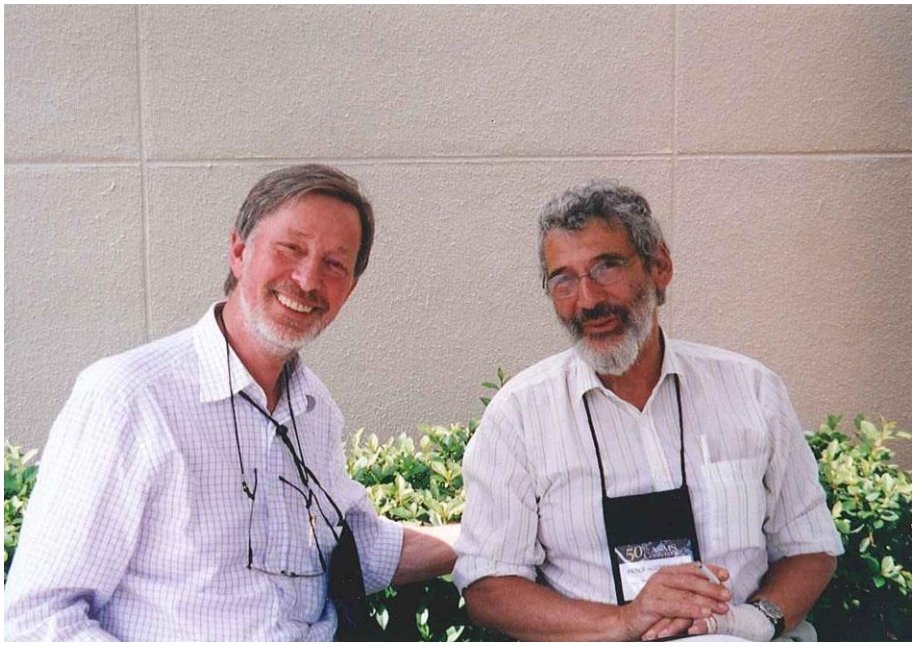


Figure 3. Peter Roeppstorff and Franz Hillenkamp 2003 in front of a Denver Hotel

GRAYSON: Very nice.

HILLENKAMP: [Yes]. So this is the [Wellman faculty] and it was taken when I was there maybe last year or so. [Fig. 4] I don't remember exactly. So this is . . . where's Rox . . . no, there's Rox Anderson <**T: 150 min**>. And John Parrish is not on that anymore, because he retired from that. I have brought them from home, these are the other photographs I want to show to you. Okay.

Figure 4. The faculty of the Wellman Center for Photomedicine, 2012. Hillenkamp third from right.

These are just PowerPoint slides but they can be transformed. This is the [feedback from the VW Foundation], what I just read to you. "This project sets the limit of the . . . ." Of course, it was written in German. Okay. Okay.

Okay, these are red blood cells. [Fig. 5 and 6] These are perforations with a laser. [Left] was a free run ruby, and [right] was Q-switched ruby. And you see that to some extent the action of the Q-switch is more vigorous because you get bigger holes. Still for other reasons, we had to stick with the ten-nanosecond Q-switch laser, because otherwise we couldn't frequency-double. This is . . . of course, these are pigmented. They have hemoglobin, right.

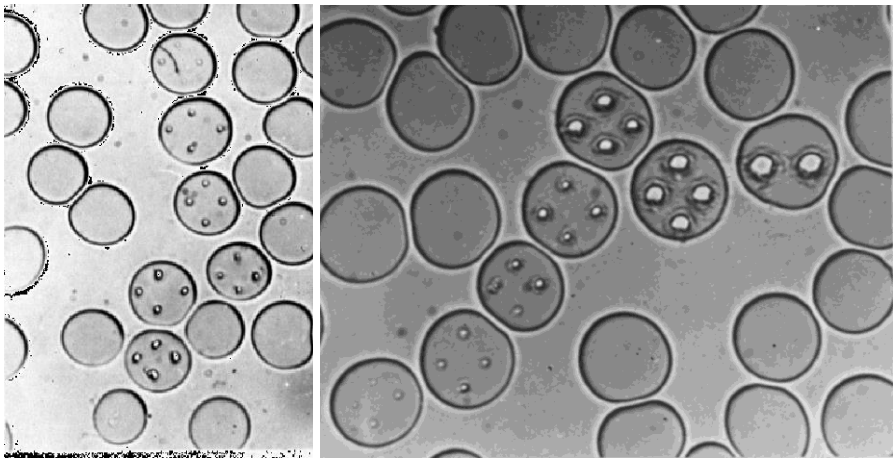


Figure 5 and 6. Laser perforations of erythrocytes with a ruby laser at 694 nm wavelength left: τ = 1 ms; right: τ = 20 ns obtained with the first laser microscope

GRAYSON: Right.

HILLENKAMP: This is non-pigmented cells, and you see these three holes here, which were done at three forty-seven [nanometers]. See these holes? [Fig. 7]

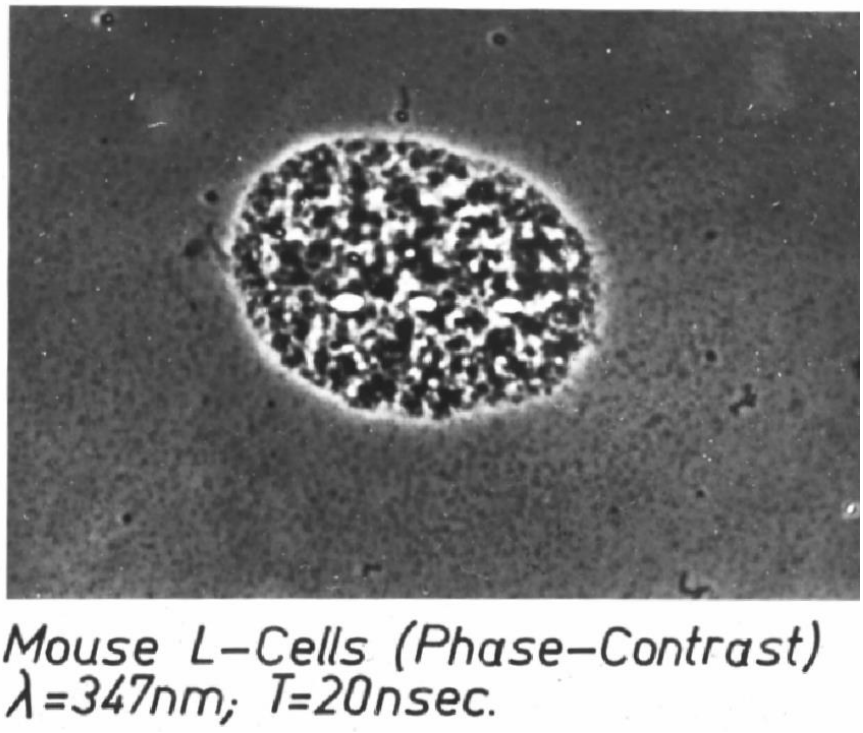


Figure 7. Laser perforation of a non-pigmented cell

GRAYSON: [Yes].

HILLENKAMP: It's a granular cell, so it's a little bit difficult to see, but that's where it is. [. . .] You see, this was done on twenty [nanoseconds] and Q-switched laser, and frequency doubled.

This now was the first instrument which, this is still in Munich, from which we got presentable results, let's say . . . we decided to [not] use the quadrupole and go for time-of-flight. [Fig.8] See there is a vertical time-of-flight tube. The laser is back here, and well, the electronics are there.

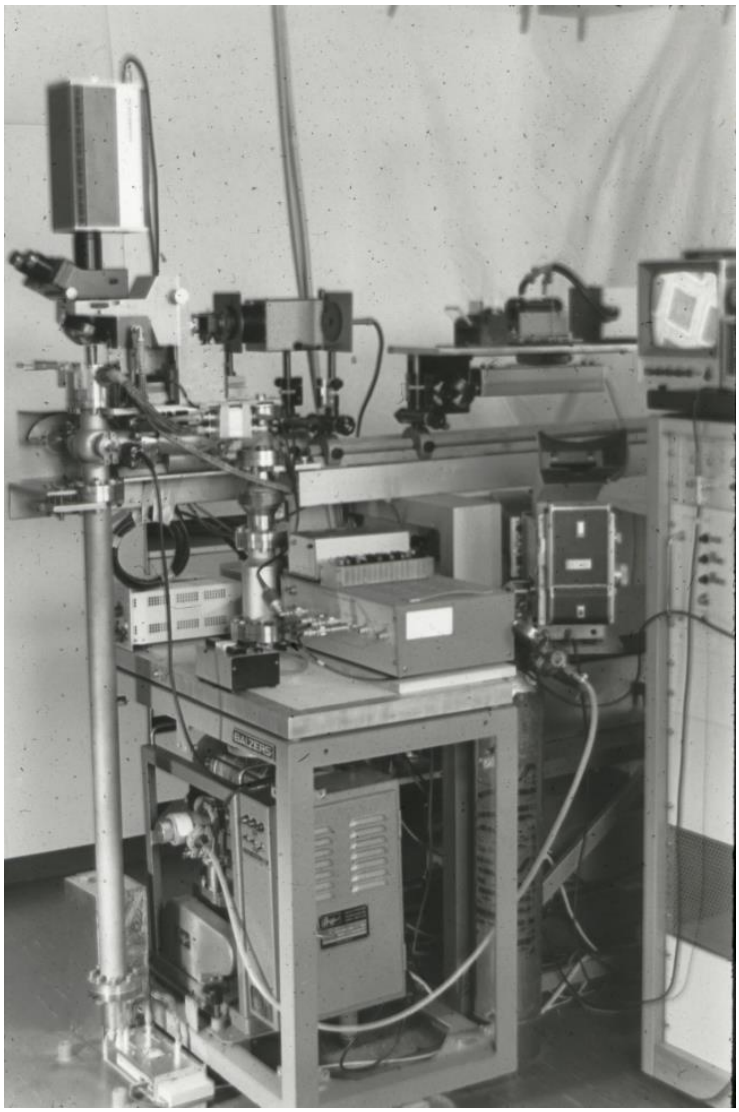


Figure 8. The first lab version of the LAMMA 500 development. ca. 1973

But at that time we had to record all the spectra on a strip chart recorder. There were no transient recorders available at that time. That came quite a bit later. So here's the microscope. So we essentially took the microscope apart into pieces and assembled it on top of the time of flight tube.

As I said, the objects were thin tissue slices as you produced them on the microtome. Of course, there must have been a vacuum seal there. The feed through, the vacuum feed through were just spark plugs from a car. We didn't want to wait too long for high voltage feedthroughs. In fact, they were difficult to get at that time. So we just used spark plugs.

GRAYSON: That worked, I guess.

HILLENKAMP: Yes. Of course, it worked.

GRAYSON: Worked well.

HILLENKAMP: There's nothing wrong with them.

GRAYSON: I like that.

HILLENKAMP: Except that they're more difficult to seal, because they have a somewhat conical thread . . .

GRAYSON: [Yes]. [Yes]. It's not . . . well, it's designed for a vacuum system. But . . .

HILLENKAMP: So and this system we call LAMMA for Laser Microprobe Mass Analyzer. So this is the first LAMMA instrument ever set up. Again, this was for elemental or atomic ions . . .

GRAYSON: Right.

HILLENKAMP: Okay. So let's . . .

GRAYSON: Were you even thinking about molecular ions, at all?

HILLENKAMP: No. At that time, we didn't think about molecular ions at all. I'll tell you in a moment how that came about. At any rate, after VW <**T: 155 min**> Foundation had financed the feasibility experiment, and we had proven that even though the mechanism was different, it was doable. VW said, "We are not going to continue to finance projects. We just want to give seed money."

So we had to look for other funding, and went back to the Federal Department of Science and Technology. They said, [yes], they would be willing to finance it, if we would team up with a company. So we went around a variety of companies. Of course obvious choices were the optical companies Leitz and Zeiss [. . .]. Then Balzers for the . . .

GRAYSON: Mass spec . . .

HILLENKAMP: Vacuum technology. None of them was willing to enter into an enterprise like that. But we finally came to Leybold-Heraeus in Cologne, which was originally a company that made equipment for physics teaching in schools. But they also had done some vacuum equipment and so on. They were willing to join in with us. They built commercial instruments.

The one for the thin slices . . . that was our interest for tissue slices, was called the LAMMA 500. Then they were also interested in using it for semiconductor chips, to look at failures in their chips. That was then not a transmission arrangement, but an arrangement where the laser beam was coming under an angle, and the ions were extracted under a different angle. This was called the LAMMA 1000. [Fig. 9] This is the final version of the LAMMA 1000 as they sold it.

Figure 9. Laser Microprobe Mass Analyzer LAMMA 1000, Leybold Heraeus, Cologne

In total, I think we sold something like between fifty and seventy. I don't know the number, tally of these instruments. At that time, already half a million Deutschmarks each. So it wasn't a big business, but it was a fairly successful business. Then the company decided to stop their whole program on vacuum technology and analytical instrumentation and the LAMMA went down the drain with that. [. . .]

Okay. This is at a very early time. This is Raimund Kaufmann, the only picture I could find of him. [Fig. 10] He was just two years my senior. This is somewhere in the laboratory. I'm soldering some circuitry. He's just watching, very skeptical. He was very bright, but he was very critical. You had to have strong ego to survive with him. If you had a strong enough ego, then it was a very, very fruitful collaboration. But he was too impatient to deal with people who said, "Yes, yes," when he said something. You had to fight him. Okay, that's . . .

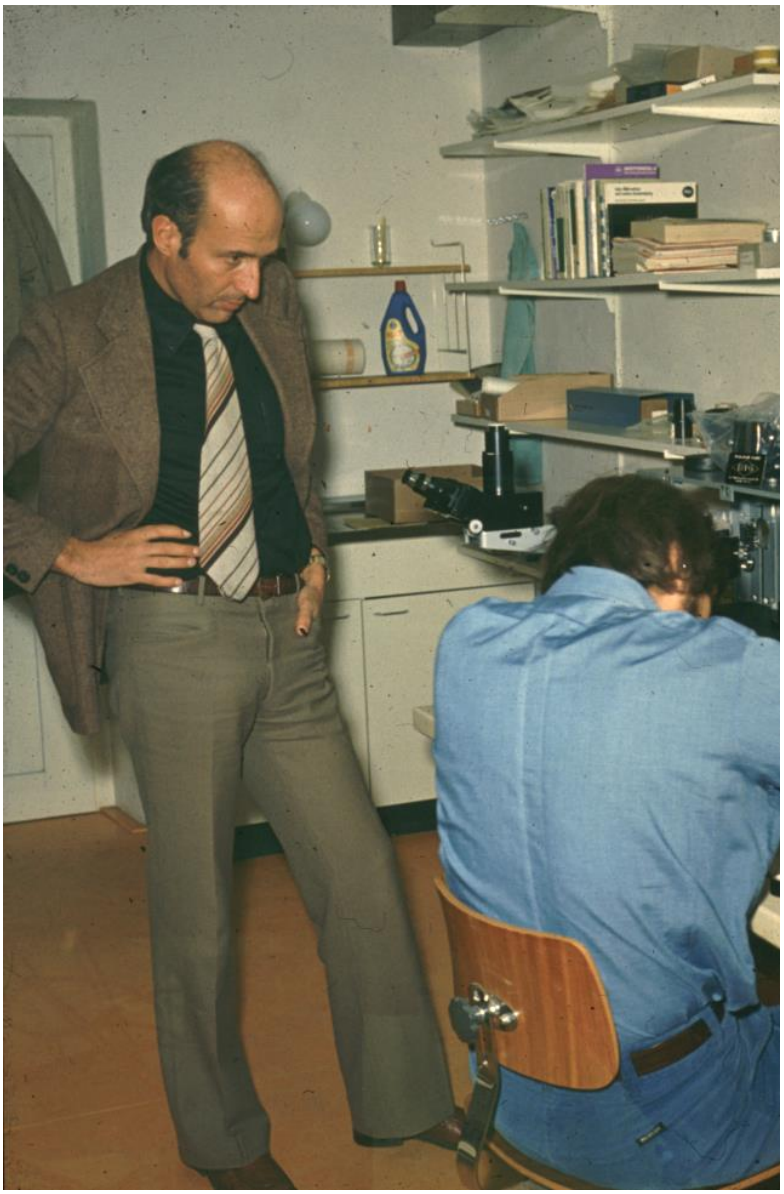


Figure 10. Professor Raimund Kaufmann during the early stages of the LAMMA development

GRAYSON: I'll be able to get an electronic copy of this, right.

HILLENKAMP: [Yes], [yes]. These are . . . as I said, these are PPT files. We transfer them afterwards, okay?

GRAYSON: Sure.

HILLENKAMP: That's okay. Now, over the last few years, imaging MALDI has become one of the major fields of application of MALDI. We couldn't do really imaging MALDI [then], but the idea we had already and did it then. This is a kidney tissue section. [Fig. 11]

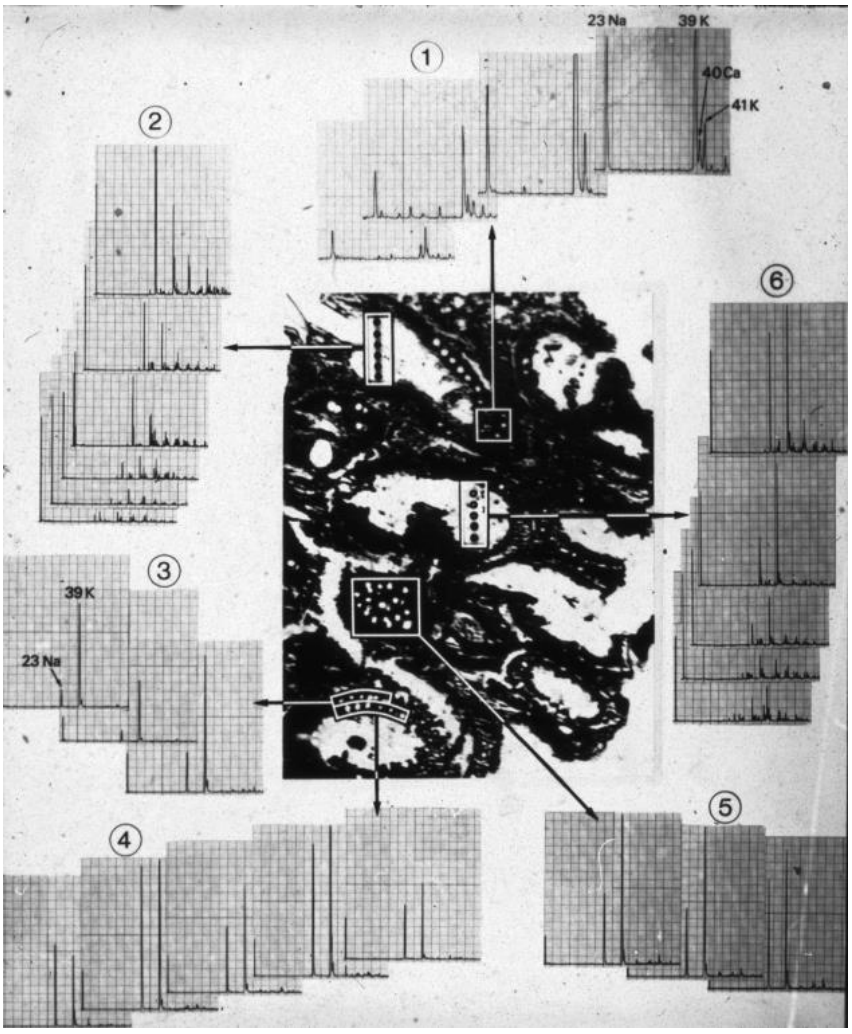


Figure 11. LAMMA 500: Analysis of a kidney tissue section

There are these little tubes in there where the exchange of electrolytes takes place. We wanted to look there where the potassium and the sodium which is, of course, driven by direct potential. There you see we looked at different areas here. But for every single shot, we had to

take a spectrum on the strip chart recorder and then, take a ruler afterwards to measure what ion it was. So it was very tedious and certainly not practically useful at that time.

GRAYSON: [Yes]. Well, and it's like the early mass spectra that were taken where you adjust the magnetics through current <**T: 160 min**> then you get . . .

HILLENKAMP: [Yes], [yes], [yes]. Or photo plates, you know, and looked at that. So the ideas were there already.

GRAYSON: [Yes].

HILLENKAMP: But the time at that time it wasn't right.

GRAYSON: And the technology was . . . [yes].

HILLENKAMP: [Yes]. Actually what happened [next] was we had this very fast . . .

GRAYSON: Oscillographic . . .

HILLENKAMP: Oscilloscope, Tektronix . . .

GRAYSON: [Yes].

HILLENKAMP: It had only four-by-six-centimeter screen. Not every shot was a success, of course, you can imagine. So I would be sitting there getting my eyes dark adapted for ten minutes or so. Then fire the laser and then, *vpppp*. And something passed by. And you had to be very fast to see whether it was worthwhile to capture that or not capture it. We had these very sensitive Polaroid films which lasted only in the refrigerator and then, only for four weeks or so. So we kept ordering them.

So it was not a high throughput method back then. But you know, it worked on tissue sections as we . . .

GRAYSON: And what year would that work have been there . . .

HILLENKAMP: This was still in Munich, so that would be something like 1973, 1974, I would imagine.

This is . . . I added this. It has nothing to do with LAMMA. This is work on the rabbit eyes. [Fig. 12] You see the rabbit here. The laser is here, and then there is fiber optics and we guided it into the rabbit eye. In fact, in this particular case, we wanted to know how dangerous Q-switch lasers were, not only in the retina, but also on the eye lens. So we focused into the eye lens and generate these huge bubbles here.

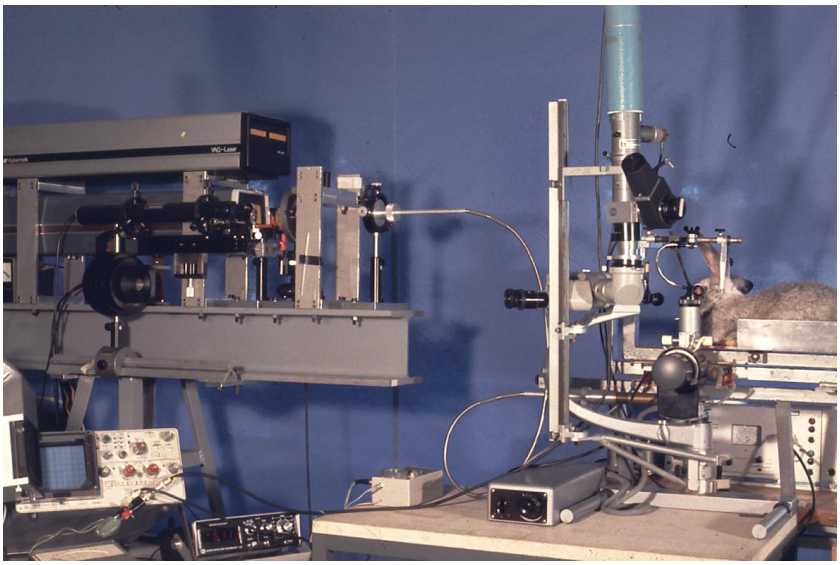


Figure 12. Irradiation of an anesthetized live rabbit with a Q-switched ruby laser λ = 347 nm, τ = 20 ns

Of course, this again, this is histology after we took the eye out. [Fig.13]

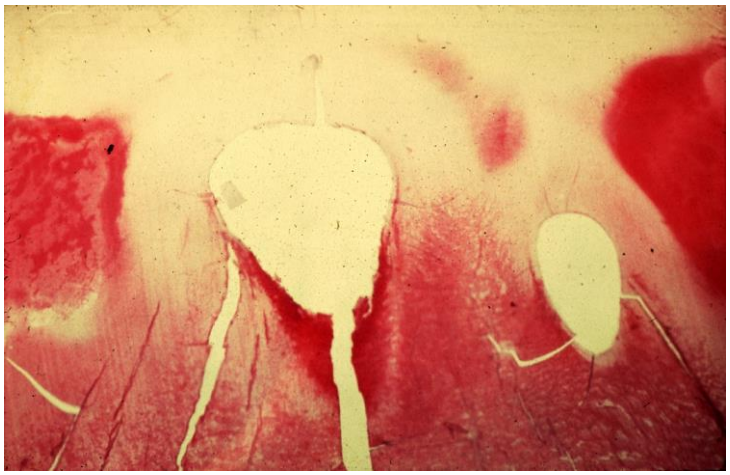


Figure 13. Lesions in a rabbit eye lens irradiated with a Q-switched ruby laser (λ = 347 nm, τ = 20 ns)

It also tells a story. We presented that at an ophthalmology conference and said, "This shows that one should be even more careful with Q-switch lasers, because it can produce much more damage than the free run. So, you know, stay away from Q-switched lasers, so to speak. Only two years later or so, independently an ophthalmologist, [Aaron-Rosa] a woman in Paris, [France], and an ophthalmologist who we had collaborated with in Switzerland [Franz Fankhauser], in Bern found out that you could use these Q-switched lasers to cut membranes in the vitreous. This is now a standard method in ophthalmology. So we missed out on that. We only looked at the danger, and didn't think enough about the potential use of that. That's why I put it in here.

Okay, so that much at the moment for LAMMA. When I moved on to Frankfurt, I took the LAMMA 500 instrument along, because that belonged to me and not to the National Laboratory, because I brought in the money. After two or three years, Leybold had finished their first prototype of the LAMMA 1000. That was set up in my laboratory in Frankfurt as well. So in Frankfurt, we used the [two instruments] . . . no, let me say it differently.

I had an agreement with Raimund Kaufmann that he would pursue more the biological applications, and I would pursue more the applications of such microprobe in materials science or physics. So among others, what we did was look at . . . we took carbon foils or metal foils and looked at the cluster distribution. That was also a very popular field of research in those days by SIMS [secondary ion mass spectrometry], by plasma desorption, by many different methods. You know, if you have carbon for example, pure carbon foil, just graphite and you bang it with the laser, then you get a distribution <**T: 165 min**> of carbon 1, carbon 2, carbon 3, carbon 4, and so on. So if you want . . . so they are molecular ions, but that's not what they are called.

GRAYSON: [Yes]. They're clusters . . .

HILLENKAMP: Clusters, right.

GRAYSON: Clusters.

HILLENKAMP: [Yes]. We published quite a number of papers on clusters . . .

GRAYSON: Go ahead. That's fine.

HILLENKAMP: [Yes]. There is also . . . and we saw differences between, let's say, SIMS and laser. We got bigger clusters than SIMS could ever get, for example, because it was softer. You

know, the generation of the clusters. We also . . . very well or very courageously left out a chance that we might have had. One day one of my students came to my office and said, "I can't get the machine to run. Can you help?" I went over, and at that time, we had the first transient recorder, Biomation, and it was set in the wrong timescale. I started to fiddle with the transient recorder and all of a sudden there were these huge signals. But they were in totally the wrong mass range. But guess what they were.

GRAYSON: Like buckyballs . . .

HILLENKAMP: They were buckyballs. We had no clue that could even happen. I mean, sometimes you come across something and only much later you realize that could have been something interesting. But you know, to be understood that I don't claim anything to having been the first one to see [buckyballs.] I had no knowledge about how carbon bonds were formed at that time. Yes, there were magic numbers in the cluster distributions. But that was a different story. So it was just by happenstance that we saw these signals and we didn't [label] them. So it's only later on that I think they must have been buckyballs.

GRAYSON: Must have been buckyballs, well sure.

HILLENKAMP: [Yes]. What else could it have been? [Yes]. Okay. You remember that for the development of LAMMA, one of the most critical parameters was sensitivity, because you have a very small [volume] that you desorb, or evaporate or ablate, whatever you want to call it, so there were only a few ions. So sensitivity was a key issue and the reviewer actually had pointed out that the sensitivity would most probably not be reached. The idea was there are not enough ions.

It turned out that this was not true. Our limitation was not the number of ions of the elements. The limitation was the background signal in the mass spec. There was a grass, you know, on every single mass spectrum, the resolution wasn't good enough. It was just a shift of baseline. So that limited our sensitivity, because the, let's say, the calcium signal got lost in the background signal that was [there.] When we realized that we began, of course, to think of what is this background? Where does it come from?

Now we saw that there was some regularity in there, in the intensity of the peaks. It was a signal on every mass, but, you know, it was small here then became larger and smaller again. So there was some pattern there. That, but just looking at this spectrum you would immediately pick it up. So that was one thing we knew. Something you must know is that for electron microscopy, you embed your tissue in epoxy resin. Otherwise, you couldn't cut it on the microtome. So the major material in the sections that we had was epoxy. It didn't take us too long to realize maybe these are fragment ions of the organic matrix that our cell is embedded in. We did a very simple experiment. We just changed the resin from one more tough to a more soft

resin, and sure enough, the pattern changed. So that was our first recognition <**T: 170 min**> that there could be even molecular organic ions and that it may be worth pursuing them.

This was still in Munich. When I left for Frankfurt, this I knew, and my decision was to put my major effort in Frankfurt on looking at laser desorption of bioorganic ions. So we spent about a year looking at every single amino acid. We found that, yes, you could get molecular signals of the amino acid, but you also got fragments, and the degree of fragmentation depended apparently somewhat on the laser parameters which we had [available.]

GRAYSON: Sure.

HILLENKAMP: At that time [we] could, to some extent, change [the wavelength] around. We had a neodymium-YAG laser already by that time. So we could use a tripled [or] quadrupled neodymium-YAG laser. Of course, my background in laser-tissue interaction, and bio-optics, let's say, from that I knew that there were amino acids that absorb in the UVC at about 280 nanometers. Those are the aromatic ones, tryptophan, tyrosine and phenylalanine, and there were . . . most of the others are aliphatic and they don't absorb at all [in the accessible wavelength range.]

Also, when we went to the tripled YAG laser at 355 nanometers . . . oh, this we investigated at the quadrupled YAG laser, wavelengths at 266 nanometers. When we went to 355 nanometers, we didn't . . . there's no absorption of any of the amino acids. We got much stronger fragmentation and needed quite a bit of higher laser irradiance.

GRAYSON: But so you're looking at the individual amino acid . . .

HILLENKAMP: Oh, we just dissolved amino acids in water or water/alcohol or . . .

GRAYSON: And put them on . . .

HILLENKAMP: Then just dripped it onto the grid and let it dry. So preparation was extremely simple.

GRAYSON: Then, but you were able . . . depending upon the wavelength, you were able to get spectra out, mass spectra . . .

HILLENKAMP: Mass spectra, but they were . . . you know, there were apparently differences, and the wavelengths was important, whereas for the LAMMA, it didn't seem to be so important a parameter. But for the amino acid, it was.

So and now comes a little story again. I wrote a proposal and sent it in to the German National Science Foundation. I was asking for an excimer pumped dye laser, excimer pumped and frequency-doubled dye laser. That would allow us continuously to change the frequency from 266 all the way to the visible. That was an expensive setup. You know, I don't remember how much it was, but it was certainly something like two hundred fifty thousand Deutschmarks or so.

So I turned it in, and a few months later, I got the reply. [Yes]. It sounded kind of interesting, but the risk was pretty high. The reviewers felt that you should do some more preliminary experiments. They just gave us money for one grad student for one year, so we did some more preliminary experiments along the same lines. Nothing revolutionary new came out of that. The year afterwards, I resubmitted the proposal with the results we had gotten in between. Same story, I got a letter back. There is still . . . the reviewer was not convinced that this was a useful project to pursue. We should do more preliminary experiments, [and got the] salary for a grad student for one year <**T: 175 min**>.

After this second year, I turned in the proposal a third time, and got the same answer, so at that time, I was so angry. I was really mad, because I thought they didn't know what they were talking about. I first thought to just reject the whole thing and not even take the salary. But then my situation in Frankfurt in terms of funding was very critical, so I couldn't really afford to do that. After sitting at my desk for an hour and contemplating the whole thing, I just picked up the phone, called the National Science Foundation, and said I wanted to talk to the president.

For reasons that I still don't know, I was put through to the president. I said I was very angry. This has happened a third time, and if the reviewer had good arguments that would be all right with me, but I was never told any [details of the argument], only his conclusion, but never his arguments. I said, "This is not fair. Besides that, you are giving out tax money, and if I don't get the reviewer's reasoning, I will sue you." All this, you know [was not realistic. So, his response was]: "Oh, young man, don't be so [angry]."

But in the end, [after] maybe ten minutes' phone conversation, he said, "I'll talk to the officer and ask him to send you the arguments, because I understand you want to go on. If there are arguments against this project, then you should know." [Yes]. It took about a week, and I got a letter from the officer that was responsible. It was that long. It said, "Reviewer Two said that the applicants haven't read the literature, because it can be read from the literature that the wavelengths is not an important parameter in laser desorption." Okay.

That I must say the reviewer was at least fair. He gave a reference. Okay. The DFG [*Deutsche Forschungsgemeinschaft*] officer gave me the reference as well. I looked at this, and

it was a review paper by David [M.] Hercules.[11] I'm sure you know who . . .

GRAYSON: Oh, [yes]. I know who that is.

HILLENKAMP: David Hercules.

GRAYSON: [Yes].

HILLENKAMP: We had . . . on the LAMMA thing we had chosen to collaborate with David, and he also spent a year here as a [Alexander von] Humboldt [Foundation] Fellow, with [Alfred] Benninghoven. I couldn't remember in that review article, that there was anything said about the wavelengths. So I immediately went to the library, pulled out that review article. Sure enough there was a statement. The statement said something like, "The wavelengths is not an important parameter for these applications."

Now first of all, this was LAMMA [not MALDI of organic ions.] Secondly, he was quoting a reference again. So this reference was another very well-known review paper at that time, written by [Robert J.] Conzemius and [Harry J.] Svec.[12] Remember . . .

GRAYSON: [Yes].

HILLENKAMP: So they were at . . . which National Laboratory? Somewhere in the north, Harry Svec was the senior . . .

GRAYSON: [Yes]. That was Iowa, wasn't it? Iowa State [University]?

HILLENKAMP: Iowa, right. Right. But it was a National Laboratory [Ames Laboratory]. It was not the University. Again, I knew that review very well, and I couldn't remember ever having read it in there. I pulled it out, looked at it. In there it said, "So far, laser wavelengths [have] not turned out to be an important parameter," and gave a reference. The reference was

[11] David M. Hercules, R. J. Day1, K. Balasanmugam, Tuan A. Dang, and C. P. Li. "Laser Microprobe Mass Spectrometry 2: Applications to Structural Analysis." *Analytical Chemistry* 54, no. 2 (1982): 280A-305A.
[12] R.J. Conzemius and H.J. Svec. "Scanning Laser Mass Spectrometer Milliprobe," *Analytical Chemistry* 50, no. 13 (1978): 1854-1860.

one of our first papers we ever wrote on the LAMMA thing.[13] I mean, sometimes you have to be lucky. So you know, I wrote up the whole story, sent it to the program officer, and a copy to the president. Within a month, I had my laser.

GRAYSON: [Yes].

HILLENKAMP: So then we <**T: 180 min**> began to systematically investigate the wavelength as an important parameter. What we learned from these experiments was that at 266 nanometers . . . let me restrict my discussion to the 266 nanometers. What we then called threshold fluence—that is, the minimum laser energy per area that was needed to see clearly identifiable parent molecular ions of the amino acids—for the aromatic amino acids was about a factor of twelve lower than what was needed for the aliphatic amino acids. I mean, it makes sense, but we had done it in a systematic fashion and we knew even a number, you know. We knew it was an order of magnitude difference that there was [between the two groups of amino acids.]

GRAYSON: Interesting.

HILLENKAMP: Because, of course, the aromatic amino acids absorb some at the wavelength 266, it's not right at the center, but it is quite a good match. . . .

GRAYSON: Much better than aliphatic.

HILLENKAMP: [Yes]. And in 1983 Michael Karas joined my group as a postdoc. So what I'm going to tell now was already done together with Michael. I will come to Michael later on.

GRAYSON: Okay.

HILLENKAMP: We then went on and looked at dipeptides. When we analyzed some of the dipeptides spectra, we were very surprised that we got signals of both amino acids reconstituted. You know, in the peptide bond you lose one molecule of water. So you can reconstruct the amino acid on the . . . let me see, on the carboxyl side, but the amino acid, the signal that you get on the amino side of the dipeptide should be minus water.

[13] E. Unsöld, F. Hillenkamp and R. Nitsche, "Laser Microprobe-Mass Analysis of Biological Tissues," Analysis 4 (1976): 115. Presented at XVIII Colloquium Spectroscopicum Internationale, Grenoble, France, September 15-19, 1975.

GRAYSON: Right.

HILLENKAMP: But we saw both there, and we . . .

GRAYSON: You saw the dipeptide as well.

HILLENKAMP: We saw the dipeptide, of course; we saw the dipeptide and we saw both amino acids. We tried different combinations of amino acids in the dipeptides and so on. It was a regular pattern. Since it didn't seem to make any sense, we went two floors down. There was the department of biochemistry and talked to the biochemists and said, "You know, this is what we see. We can't make any sense. What do you think?" He looked at it and said, "Oh, that's very simple. When you buy dipeptides, it's never pure. There is always some leftovers of the single amino acids. It's as simple as that."

[Yes]. That sounded reasonable. We were at least satisfied that we understand what we were seeing. But we thought we better put that on a more firm basis. We began to mix amino acids in with the dipeptides, and took mixtures only of amino acids. All right. Not dipeptides, but mixtures, and compared.

I can [still] see the day in my office when Michael came in with this spectrum and said, "Look at this. You see anything?" I said, "[Yes]. It looks okay, but what sample was it?" He said, "Well, this was a sample of a mixture of alanine and tryptophan. Mixture." I said, "It can't be." "Yes," he said, "That's what it is." So within minutes we had the concept of matrix desorption that at . . . oh, the spectrum was taken at the laser fluence where we should only have seen tryptophan and not the alanine. We saw the alanine signal, almost same strength as the tryptophan. It was a one-to-one mixture. So the alanine came riding piggyback on the tryptophan, and <**T: 185 min**> that's when MALDI was really born.

GRAYSON: Because you saw the effect of having that absorber.

HILLENKAMP: [Yes], right. And then we . . . of course, then we immediately started to fiddle around with the system. We found out that it was advantageous to have the absorbing component, the tryptophan, in much higher concentration than the co-desorbed analyte. But there were limitations to this. It wasn't really good enough for any analytical method, but the concept of matrix was certainly there.

By the way, one should say it was in discussion in various aspects at that time. There's a paper by [R] Graham Cooks.[14] Have you interviewed him?

GRAYSON: No.

HILLENKAMP: No. You must. You must absolutely.

GRAYSON: Yes. Well, tell it to ASMS.

HILLENKAMP: [Yes]. Graham is actually a great guy.

GRAYSON: He's a crazy guy.

HILLENKAMP: [Yes]. [Yes], not really crazy.

GRAYSON: He was a . . .

HILLENKAMP: Very, very inventive . . .

GRAYSON: He wants a mass spectrometer in every garage, or . . .

HILLENKAMP: [Yes], [yes]. Sure. Sure. No, he's driven by mass spectrometry, and mass spectrometers, for sure, but I respect him very much . . .

[Yes], he had added, I think, sodium chloride to some samples for SIMS spectra, and had also [seen a matrix effect]. There was a sentence in that paper saying that a matrix may be important. Let me try to remember when that came up. I think FAB came in later. Of course, that's when the glycerol matrix . . .

GRAYSON: [Yes].

[14] Lilian K. Liu, Kenneth L. Busch, and R. G. Cooks. "Matrix-assisted Secondary Ion Mass Spectra of Biological Compounds." *Analytical Chemistry* 53, no. 1 (1981): 109-113.

HILLENKAMP: It was . . . you know these were all just called the matrix. It was certainly different in our case. But the matrix, we thought was a proper term to be used in that case.

GRAYSON: So what time frame was this, when Karas came in and showed you his . . .

HILLENKAMP: Karas joined my group in 1983, and this must have happened in 1984. You know, I'm not sure. It happened in 1984, and we published the basic paper in 1985, in *Analytical Chemistry*.[15] So that's the sequence of events.

By the way, how late is it?

GRAYSON: [Yes]. I think we should probably take a break for lunch. Is this a good place to . . .

HILLENKAMP: Right, right. So let me quickly finish this, and then we'll break for lunch.

GRAYSON: Okay.

HILLENKAMP: What we did, we were not satisfied with the analytical performance of the system, so we started to look for different matrices. It was sort of a random search. It would have to be a small organic molecule that was aromatic and had strong absorption at 266 nanometers [and was vacuum stable]. We pretty quickly by chance or so found nicotinic acid to be a very functional matrix. We got our first really good spectra with nicotinic acid as a matrix. As I said, these results were published in *Analytical Chemistry* in 1985, and already in there, we coined the term "matrix-assisted laser desorption."

GRAYSON: Okay.

HILLENKAMP: It's as a headline of one of the paragraphs.

[15] Michael Karas, Doris Bachmann, and Franz Hillenkamp. "Influence of the Wavelength in High-irradiance Ultraviolet Laser Desorption Mass Spectrometry of Organic Molecules." *Analytical Chemistry* 57, no. 14 (1985): 2935-2939.

GRAYSON: Okay, 1985, [. . .] "Influence of Wavelength in High-irradiance . . . "[16]

HILLENKAMP: [Yes]. I think that's what it . . .

GRAYSON: Okay.

HILLENKAMP: I mean, is it in *Analytical Chemistry*?

GRAYSON: [. . .] So this is a 1985, *Anal. Chem.* paper, there's a fellow by [the name of] . . . Bachmann? <**T: 190 min**>. Is he . . .

HILLENKAMP: [Yes, Doris Bachmann] was an undergraduate student.

GRAYSON: Okay, *et al.*, so . . .

HILLENKAMP: [Yes]. This is the basic paper, which essentially describes all of the features of matrix-assisted desorption. From there on, it was perfectionating the whole thing. But the principles were established at that point, I think.

GRAYSON: Very good.

HILLENKAMP: So let's have a break now. [. . .]

[END OF AUDIO, FILE 1.1]

HILLENKAMP: This was our first laser microscope, set up for micromanipulation of cells. This, actually, the guy with the glasses, is Leon Goldman . . . [Fig. 14]

[16] M. Karas., D. Bachmann, and F. Hillenkamp. The Influence of the Wavelength in High Irradiance Ultraviolet Laser Desorption Mass Spectrometry of Organic Molecules, *Analytical Chemistry* 57: 2935-2939.

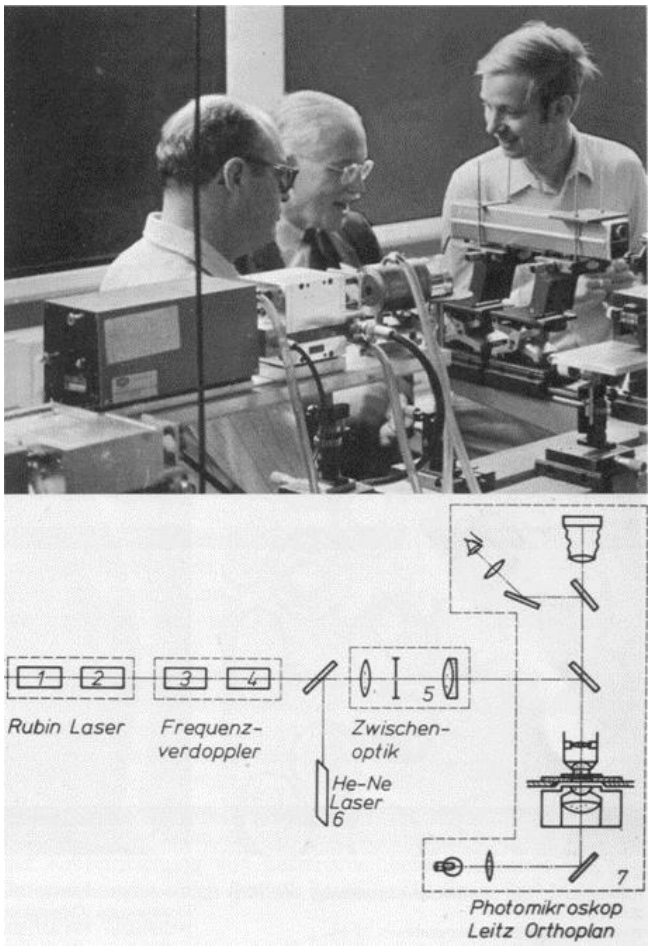


Figure 14. Dr. Hillenkamp's first laser microscope. Pictured with Dr. Hillenkamp (at left) are Dr. D. Glick and Dr. L. Goldman

GRAYSON: The one in the middle?

HILLENKAMP: [Yes], the middle one. [. . .] Leon Goldman, he was a dermatologist in Cincinnati [Ohio] and is considered the father of laser medicine.

GRAYSON: Oh, okay.

HILLENKAMP: He was trying almost everything with any laser, and did a few very good things, a very nice man. I've corresponded with him, which he signed "Leon without Gold, Man." So this man [on the left], I've never met later on. I don't even remember where he came from, from somewhere in California. [At the right], that's me, of course.

GRAYSON: So you're a little bit younger there.

HILLENKAMP: [Yes], a little bit. [Yes], just a little bit younger.

GRAYSON: So you're focusing the . . .

HILLENKAMP: The frequency-doubled ruby laser with intermediate optics onto the sample here. This is just a photomicroscope. Here's the camera, and here's the visual observation. Okay.

This . . . a little [dim], unfortunately. That was my first laboratory at the GSF, with my mechanic and my assistant. [Fig. 15] This was the laser housing I brought from Siemens. So this is all about 1972. I don't know whether that's of interest for you.

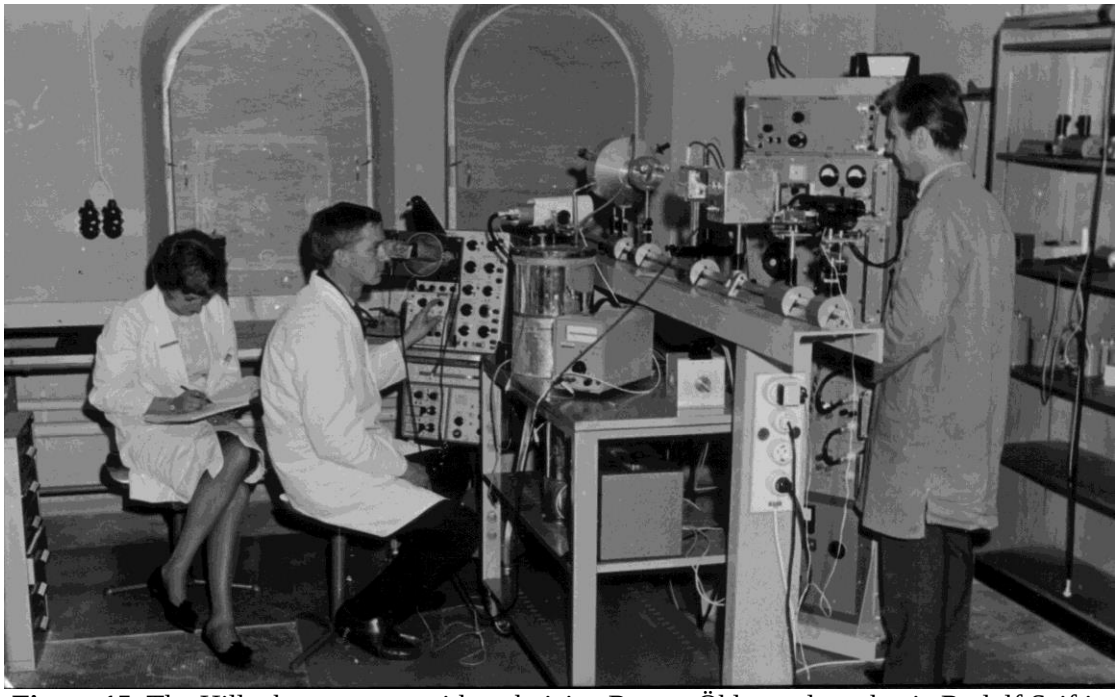


Figure 15. The Hillenkamp group with technician Renate Öhler and mechanic Rudolf Seif in the lab around 1966

GRAYSON: Oh, [yes].

HILLENKAMP: I pulled that out. Okay.

GRAYSON: So this is a home . . . well, not home built, I guess. But . . .

HILLENKAMP: [Yes], the laser was home built. [Yes], as I said, including polishing the ruby rods.

GRAYSON: Oh, wow. That must have been fun.

HILLENKAMP: [Yes]. Tedious. Now let's look. We have looked already at the LAMMA pictures. Oh, we'll come back to that in a moment. Oops, no, this is not what I wanted.

This is already my Münster group and we went for a week, we had a seminar and hiking in the Bavarian Mountains. [Fig. 16] That's in front of the hut where we stayed for that. I wanted to . . .

GRAYSON: So this was all people working in your area . . .

Figure 16. The Hillenkamp group with his Münster research group around 1998

HILLENKAMP: Work in my group, [Yes]. There was . . . let me see. Oh, Michael had already left at that time. Michael is not on it. Okay.

Then this was another mountain hike that the whole group did. [Fig. 17] I don't know what year that was, but I would guess in mid 1990s, or so.

Figure 17. Dr. Hillenkamp's group on a hiking trip

GRAYSON: So is this . . .

HILLENKAMP: [Standing up,] that's me. [Yes].

Figure 18. Hillenkamp "at work"

GRAYSON: That's you [as well?] Okay.

HILLENKAMP: [Yes]. It says, "the group at work."

GRAYSON: [Yes], right. Some "Arbeit!"

HILLENKAMP: [Yes]. Then this is the prototype of the LAMMA 1000 that we used to develop the MALDI [on its way to the Deutsches Museum in Munich]. Not this year, three years ago . . . you know the Deutsches Museum in Munich? They opened a new section on nano and biotechnology, [where it is now on exhibition.]

[. . .] You can see here. So, there will be a few more [points of] interest about that instrument. After we thought it was only occupying space, but we didn't use it anymore, we were about to dismantle it. Then I got an inquiry from the Academy of Sciences whether they could have it to put it on exhibition in the building in Düsseldorf [Germany]. It stayed there for a few years. Then the Deutsches Museum came, and I thought it was much better to have it there to educate students and the populace.

So this was when it was . . . the whole thing was mounted on a huge granite slab. It's very heavy, more than a ton. So there was a special crane that took it out of that building, and shipped it to Munich. [Fig. 19]

Figure 19. LAMMA 1000 on its way to the Deutsches Museum

This is the same instrument again, front view. [Fig. 20]

Figure 20. LAMMA 1000 prototype in the Münster lab

That's Michael. [Fig. 21] Apparently <**T: 05 min**> I took these from slides, 1997 at ASMS [American Society for Mass Spectrometry]. This, we may come back later to the question of the Nobel Prize.

Figure 21. Dr. Michael Karas

This is something that . . . this slide was made by Cathy [Catherine E.] Costello on my [birthday]. This is my birthday cake. [Fig. 22] That was in . . .

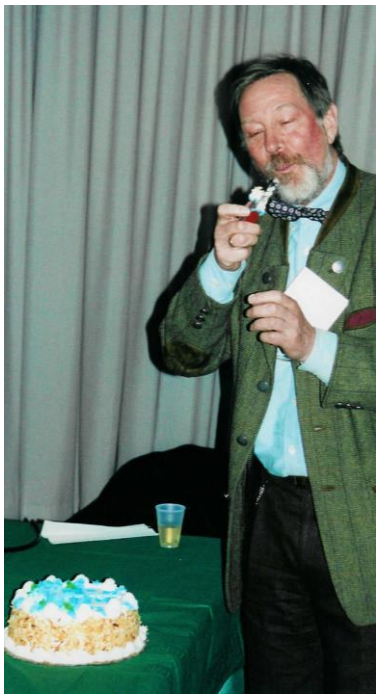


Figure 22. Dr. Hillenkamp at Cathy Costello's lab at Boston University enjoying his birthday cake

And these are several of my students. I mean, this is a group of my students. [Fig. 23] Actually, I should have also taken that photograph that . . . with Cathy on it. She took it when she was in Münster.

Figure 23. Group of Dr. Hillenkamp's students. Photo taken by Prof. Costello at one of her many visits to Münster

This is Bernd Stahl. [Fig. 24]

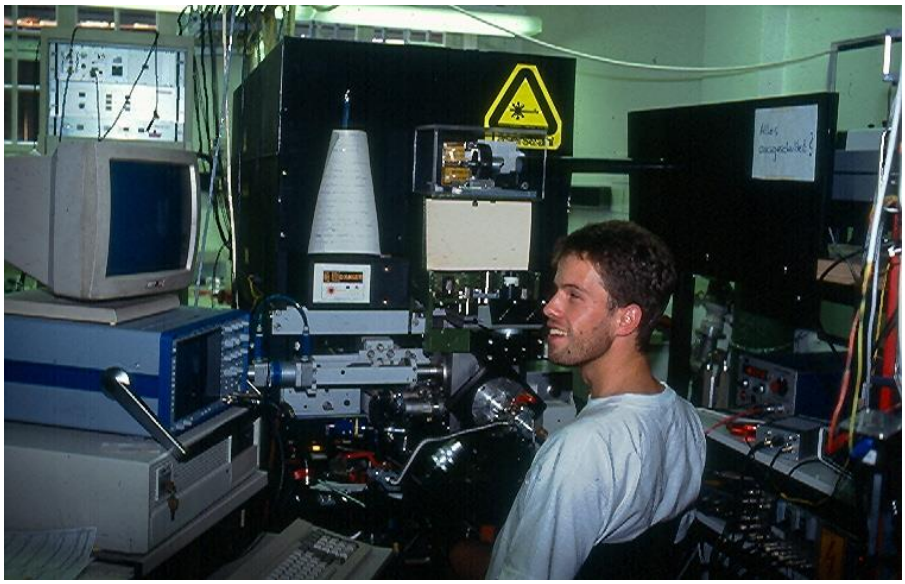


Figure 24. Bernd Stahl

This is Kerstin Strupat. [Fig. 25]

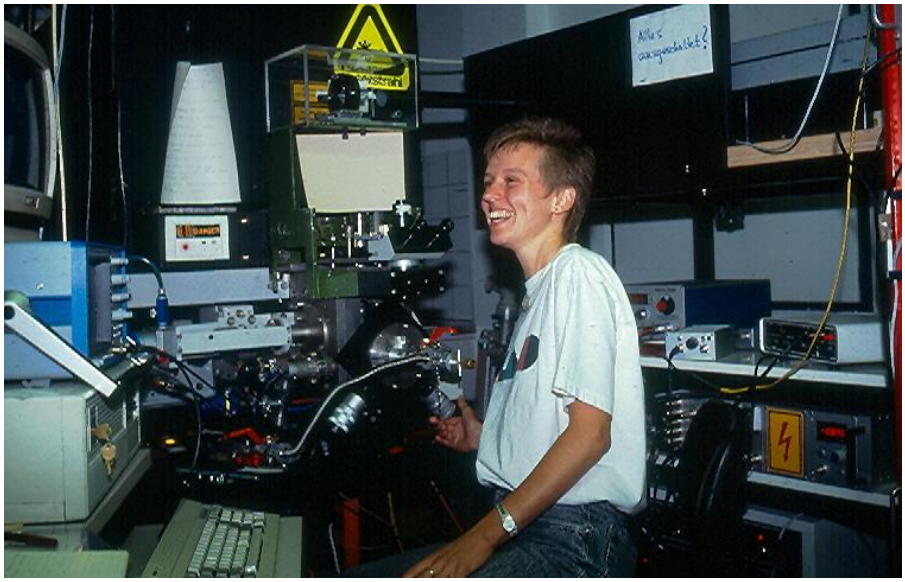


Figure 25. Kerstin Strupat

This is . . . oh, who is this? Anne Hassenbürger, [Yes].

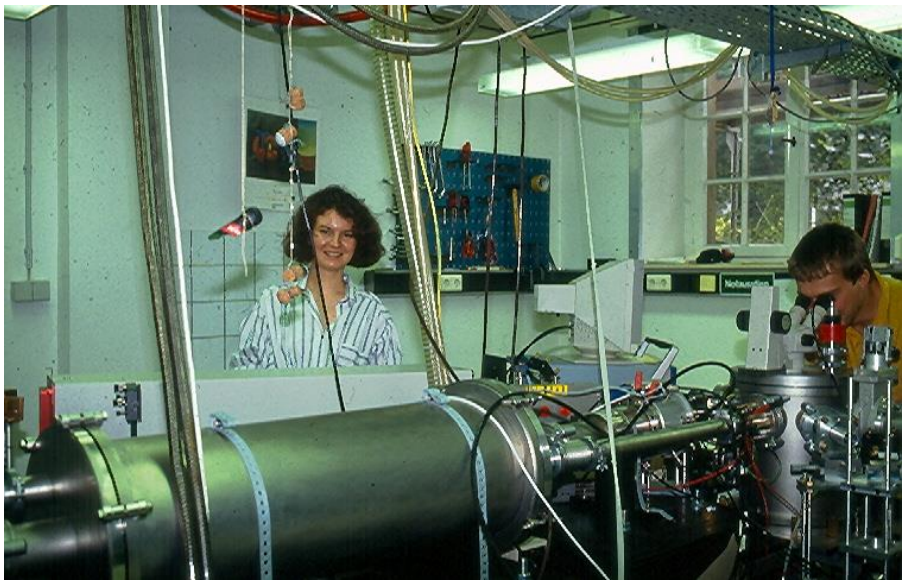


Figure 26. Anne(liese) Hassenbürger

[She is standing behind] another mass spec that we built as a prototype. [Fig. 26]

This is in Japan. This is my wife and me, also around 1995 or so. [Fig. 27]

Figure 27. Dr. Hillenkamp and his wife, Annemarie, in Japan

This is again at the birthday party, Cathy had invited this lady. She plays what's called the glass organ. [Fig. 28]

Figure 28. Dr. Hillenkamp celebrating his birthday at Cathy Costello's lab at BU

And this is . . .

Figure 29. Dr. Richard Caprioli, Dr. Victor Talrose and Dr. Hillenkamp at the award of the Thomson Medal by the International Society for Mass Spectrometry, 2003

GRAYSON: Ah, there's [Richard] Caprioli . . .

HILLENKAMP: [Yes], Caprioli and Victor Talrose . . .

GRAYSON: Oh, yes.

HILLENKAMP: When we got the Thomson Medal at the International Conference in Edinburgh [Scotland]. That was it. [Fig. 29] Then there are some more. Let me see.

I think I sent you the file of the selected publications, right.

GRAYSON: Yes.

HILLENKAMP: Yes, you have that. So we can . . . you have questions about it, you can ask. Then I have a few just photos, digital photos. Let's just quickly go through. This was at the ABRF Award. [Fig. 30]

Figure 30. Michael Karas and Dr. Hillenkamp receiving the Association of Bioanalytical Research Facilities Award in 2003

This is Michael, again, and me, and . . . [Yes], same situation with Ute Bahr, you see, is the life companion of Michael, and that's my wife. [Fig. 31]

Figure 31. Michael Karas, Ute Bahr, Mrs. Hillenkamp and Dr. Hillenkamp at the ABRF award ceremony in 2003

Then we went skiing afterwards in the Rockies for a week [to burn the award money]. [Fig. 32]

Figure 32. Dr. Hillenkamp, Ute Bahr and Mrs. Hillenkamp on a skiing trip in 2003

This is another of the award of bioanalytics that we got in 2000 . . . let me see, [yes], that's same. [Fig. 33]

Figure 33. Dr. Michael Karas and Dr. Hillenkamp receving the 2000 Award for "Molecular Bioanalytics" of the Deutsche Gesellschaft für Biochemie und Molekularbiologie

That's something else. But first, let me get something here. Oh, no. Don't have that here. I thought I put that in. Maybe there will be one more. This was at Desorption Conference in Brazil. [Fig. 34] Dancing there. [There is Peter Roepstorff in the right panel and I in the left.]

Figure 34. At the 1998 Desorption Conference in Brazil. Dr. Hillenkamp (left panel) and Prof. Peter Roepstorff, right panel Samba dancing

This is in St. Petersburg, [Russia]. [Fig. 35] That's [Boris A.] Mamyrin, the reflectron person.

Figure 35. Dr. Hillenkamp with Boris Mamyrin in St. Petersburg, 2004

This was when I retired. [Fig. 36] I sent this picture around.

Figure 36. Dr. Hillenkamp on his way to retirement

Now that was taken in our seminar room. I don't know when, sometime. It was of my birthday. They gave me this [tape measure], and we fixed it up at this column. It's supposed to be a new mass scale, totally new mass scale. [Fig. 37]

Figure 37. Dr. Hillenkamp with the new mass scale

GRAYSON: Oh, okay.

HILLENKAMP: This is [Koichi] Tanaka. [Fig. 38]

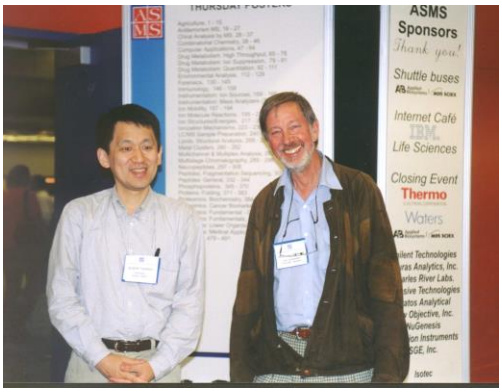


Figure 38. Mr. Koichi Tanaka and Dr. Hillenkamp at ASMS 2003

[. . .] This picture I was looking for. This is at another awards ceremony. [Fig. 39] I don't know what we are laughing at, but something . . . we were sitting on stage, and something was projected and we found it funny. So I was talking to Michael.

Figure 39. Dr. Michael Karas and Dr. Hillenkamp

GRAYSON: That's . . . [Yes], I like that picture. It's very interesting.

HILLENKAMP: [Yes], right. I like it too. This is again the LAMMA 1000 with Michael and me. [Fig. 40] That was taken 2005, or something like that.

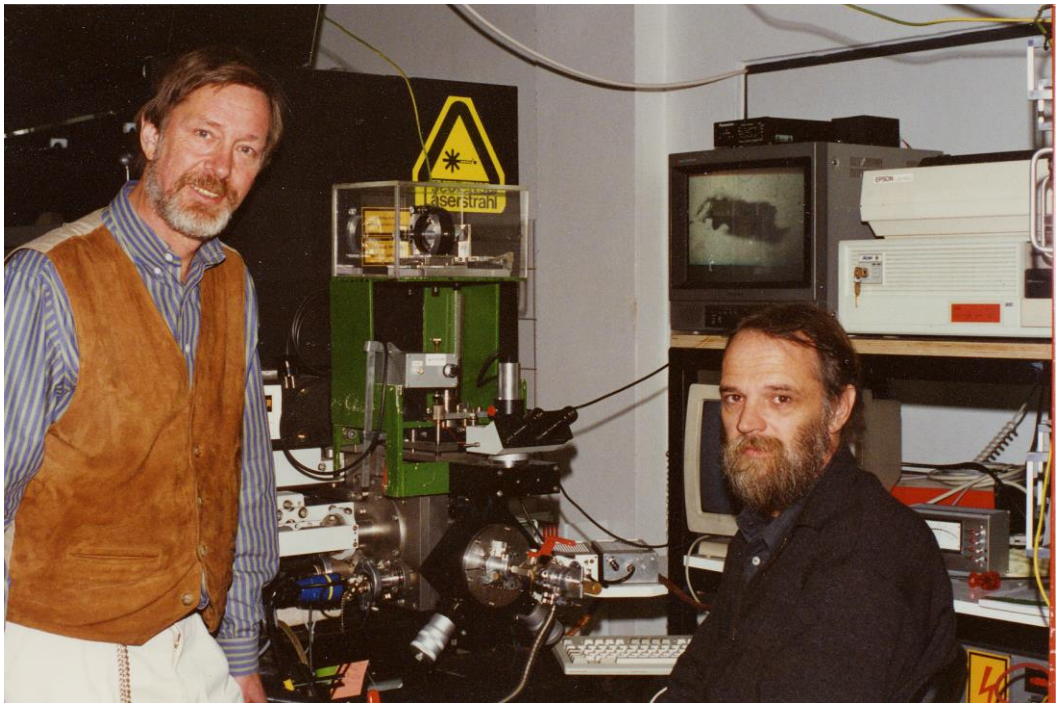


Figure 40. Drs. Hillenkamp and Karas with the LAMMA 1000 prototype

This is again, one where they <**T: 10 min**> . . . it was transported to Munich. [Yes], see Deutsches Museum. [Fig. 41 and 42]

Figure 41 and 42. Transporting the LAMMA 2000 to the Deutsches Museum

Oh, this is something . . . when I was still in Munich, and we were doing this work, among others, on laser safety. And one day we got called by some city agency. They asked us to come over to the Munich Opera House, because they were practicing a ballet which they called "Laser." So this is the announcement of the ballet, actually. [Fig. 43]

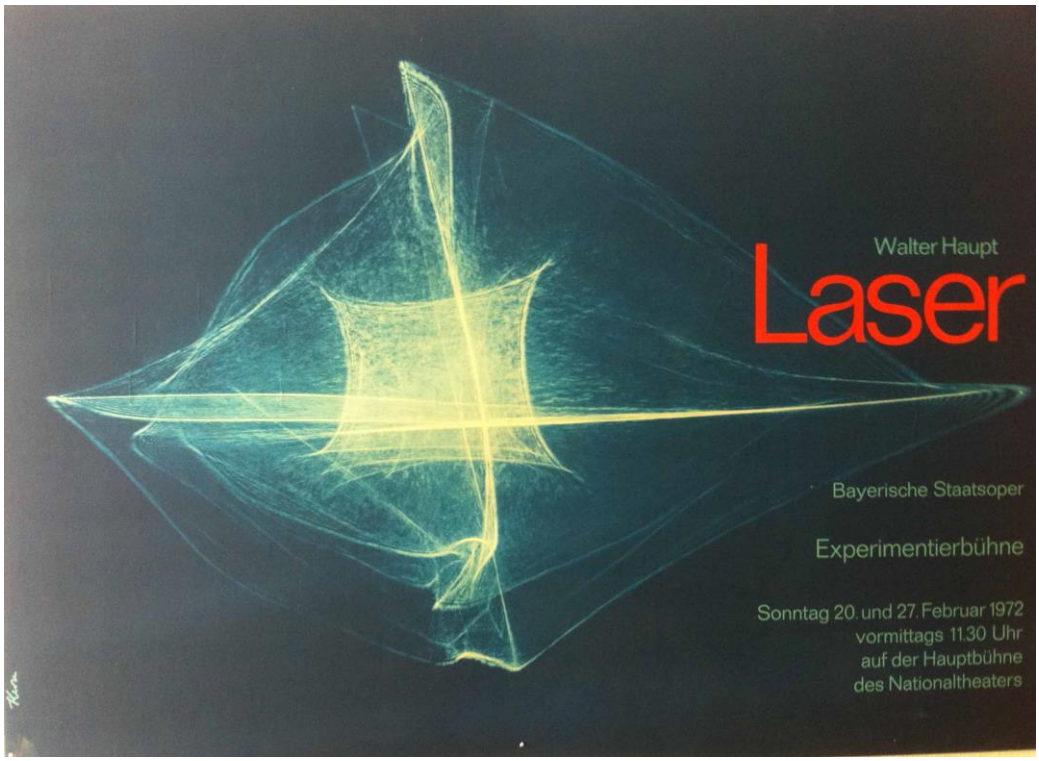


Figure 43. Laser Ballet Poster

Because the guy from this agency was not sure that the way they were operating the laser was safe. So we went there, and they were in the midst of rehearsal. We went into the center . . . what's a *loge* in English? The place where the king in the old days would sit . . .

GRAYSON: Throne.

HILLENKAMP: Huh?

GRAYSON: Throne.

HILLENKAMP: No, no. It's a separate place on the balcony.

GRAYSON: Oh, okay.

HILLENKAMP: You know, how do we call that?

GRAYSON: Presidential suite . . .

HILLENKAMP: Suite. [Yes]. Maybe a suite. So, we went in there and it was actually Peter Gabel and myself. We were watching it, and it was immediately clear that they were jeopardizing the dancers' eyesight. But after a while, when we were watching, Peter just [said], "Look at the dancer." I said, "[Yes], why? What is it?" "Don't you realize something?" I said, "No." "There is something special about the dancer." I said, "No, I don't see anything." He said, "I bet he's one-eyed."

So it turned out he had played with a steam engine as a child and lost one eye. Peter as an ophthalmologist saw that. So they were chasing this guy with a naked argon laser. I mean, one wrong movement and the guy would have been blind. Unbelievable. This is some . . .

GRAYSON: He was able to recognize the fact . . .

HILLENKAMP: [Yes]. And then . . .

GRAYSON: That's remarkable . . .

HILLENKAMP: The question was what to do. We talked to the manager, or how do we call the guy who . . .

GRAYSON: Producer . . .

HILLENKAMP: Producer, [Yes]. We said this is really dangerous. You can't do that. That's too dangerous. He said, "No. But I want to do it." I said, "Well, we have to tell the agency that this cannot be done." He said, "[Yes]. Well, what do you suggest?" I said, "Well, they have to . . . the dancer has to . . . "—actually there were several dancers—"they have to wear safety goggles." He said, "No way." No way that they would wear safety goggles. "I think, maybe you wait. We'll bring some tomorrow and show." You know, these were the old type goggles which were really big. He looked at it and said, "Oh, this fantastic."

GRAYSON: Yes, I was thinking you know . . .

HILLENKAMP: Right. So that was about this laser ballet.

This was for my seventy-fifth birthday. My students gave me as a gift a parachute jump. [Fig. 44 and 45]

Figure 44 and 45. Dr. Hillenkamp on his seventy-fifth birthday

GRAYSON: Oh, wow.

HILLENKAMP: [Yes]. Of course, you do it with an experienced one, is what you do. This is when we left the plane. You leave . . .

GRAYSON: The photography . . .

HILLENKAMP: [Yes]. [Yes]. It's . . .

GRAYSON: Oh, wow.

HILLENKAMP: That was another parachuter going around us taking pictures.

GRAYSON: Oh, neat.

HILLENKAMP: [Yes]. They told me afterwards . . . they asked me, how old are you? I said, "Seventy-five." He said, "We have never had a jumper of that age." Actually, I wouldn't want to do it more often, because it takes so long to get up there. It's noisy, and polluting the air. Then you jump out, and the free-fall takes just two, three minutes. Before you can realize what's going on, they have to open the 'chute.

GRAYSON: [Yes]. Neat.

HILLENKAMP: You know, my colleague now, [Jasna] Peter-Katalinic who actually came out of the door this morning. She and I edited the MALDI book five years ago and we're right now in the midst of <**T: 15 min**> of editing a second edition, improved edition.[17]

[17] F. Hillenkamp and J. Peter-Katalinic, editors. *MALDI MS.* Weinheim, Germany:WILEY-VCH Verlag GmbH & Company, 2007.

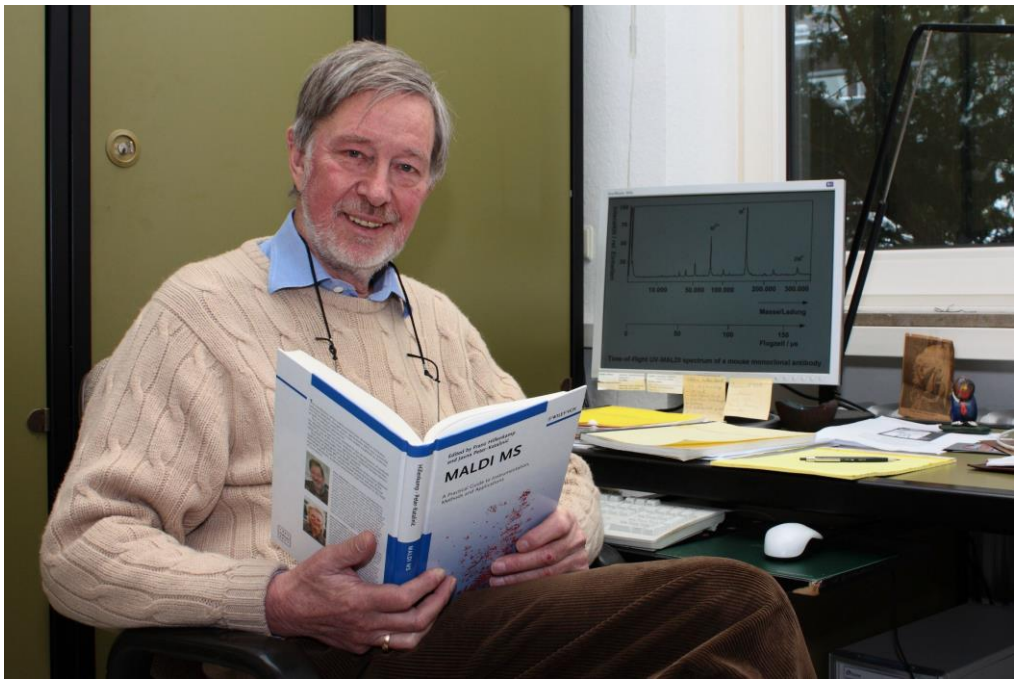


Figure 46. Dr. Hillenkamp with the MALDI textbook he co-edited

So those are the photographs that I've collected. [Fig. 46]

GRAYSON: Oh, they're good.

HILLENKAMP: And we can see later on, what to do with them, right?

GRAYSON: [Yes]. Those are very good.

HILLENKAMP: [Yes]. So coming back to the development of MALDI, and was it all by chance, or was there some guiding principle behind it? I think it's important to realize that in the 1970s and 1980s, biochemistry made huge advances over the 1960s. When I started out with my LAMMA research, it wasn't even known . . . the exact structure of proteins were not known. Whether it was a branched polymer or linear polymer, it was not known.

During the next three or so decades, it became more and more obvious that biology and biochemistry needed a more sensitive method for analysis that would also allow it to give structure information. Not just identification, but also structure information. So there was different work going on [in mass spectrometry] in that direction. There were certainly quite a number of people who realized that demand. But not many that really took up work in this direction. Not all of them were really in the end, very successful. You know, there was static

SIMS developed by Benninghoven here. Then came FAB [fast atom bombardment]. Then californium fragment plasma desorption. Then one was laser desorption.

It turned out around the mid-1980s or so, that several methods could in principle generate ions of these biomacromolecules. But the quality of the spectra was poor, but more importantly even the sensitivity wasn't there, okay. If you are in biochemistry or biology it may take you weeks to isolate a protein out of a tissue, and then you wind up with picomoles. You want to do some functional tests with picomoles, so you can afford only a few femtomoles for the analysis.

So our work was not decoupled or independent of these different activities going on. As I said, it was known that we needed better methods, but nobody knew how to do it. Certainly there was a common notion that most probably it would be impossible to isolate these huge molecules, which were stabilized by their solvation shell out of a biological system or just their aqueous environment, and bring them into a vacuum. Then on top, ionize them and detect them. So there was really great skepticism.

Let me . . . I put them away. Let me get one of the photos again. I just want to give you a citation of that time.

Okay. This was in 1986, and it's from a publication of Frank [H.] Field's.[18] [Fig. 47] "The mass region of real interest for proteins is 40,000–100,000, and one can only speculate as to whether such monster gaseous ions can be produced. My personal feeling is that to do so may well require the discovery of some new technique." So that was real foresight.

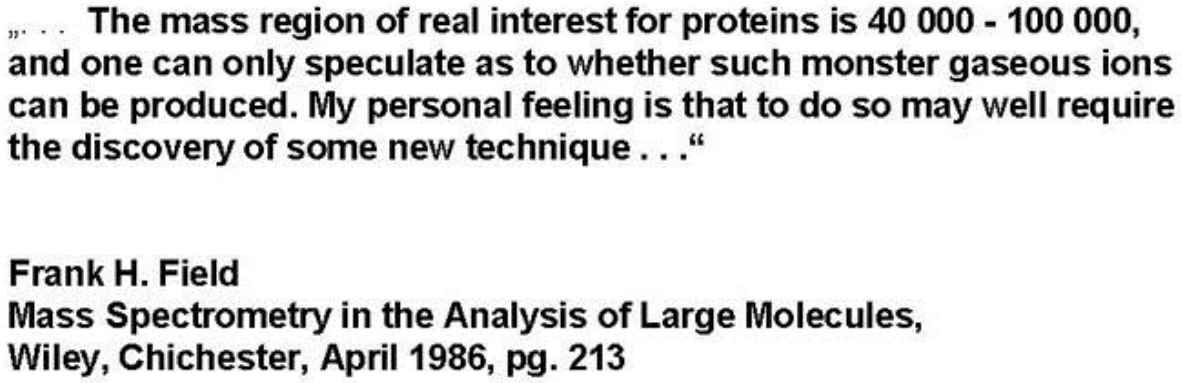


Figure 47. Frank Field's Citation

[18] Frank H. Field, "Epilogue" in: C.J. MacNeal (editor). *Mass Spectrometry in the Analysis of Large Molecules*, Chichester, England: J. Wiley & Sons Ltd., 1986, p. 214.

It turned out to be true, of course, for electrospray, which nobody <**T: 20 min**> had thought about originally. It was true for laser desorption as well. Actually, worldwide there were only three or four groups seriously looking into laser desorption. We were the only one using UV. All the others used infrared, CO2 lasers mostly, because the idea was you want to do something thermal. The infrared you just heat up the rovibrational transitions in molecules.

From our work in laser medicine, you see, we knew quite a bit about the behavior of these molecules in the UV. So, [yes]. It was in a way a combination of systematic analysis, because we looked at all of the different amino acids. We saw what the difference was in desorption for the different amino acids. But then, this observation of the mixture of alanine and tryptophan was . . . that was serendipity, of course.

GRAYSON: Yes.

HILLENKAMP: But when it came, we knew how to read it, interpret it.

GRAYSON: Better than the cluster ion and the carbon spectrum.

HILLENKAMP: [Yes], [yes], right.

GRAYSON: You knew how to make sense of what was going on . . .

HILLENKAMP: [Yes]. In this case, we knew what to do, and how to make sense of it. Whereas, with the buckminsterfullerenes we had no clue, whatsoever . . .

GRAYSON: No idea . . .

HILLENKAMP: And it just passed by, and then was lost again. So I think that is important to realize that in a way the time was ripe for some new techniques. We just lucked out to find the right one. What else did I want to say?

Oh, a few words more about my relationship with Michael Karas. Of course, first of all, when I hired him, he was recommended by a colleague in Bonn, where Michael had just gotten his PhD. I absolutely wanted a chemist, because I thought I knew the physics reasonably well, but from school days on chemistry wasn't my game, so I absolutely wanted someone who was an expert in chemistry. This complementary knowledge and experience was very important.

Also I'm more the person who would do systematic experiments. Michael is more intuitive. You know, he has some idea, he doesn't know exactly why he thinks it's so, but he would very often be on the right track. Or . . . every once in a while we had to repair the laser. When I would repair the laser it would take at least a full day, but then it was perfectly aligned. Michael—and the same is true for Kaufmann by the way—he would just turn the wheels and the knobs, and it wasn't quite as perfect as my solution, but he did it in an hour. So we were quite different in our attitudes.

But the most important thing was that we were both very curious. We kept debating every day for hours, sometimes very loud so that our students would think we would jump at each other. Several visitors came to the lab and later on said, "You know, we don't understand how you guys can get along with each other. You shout at each other. You never agree on [anything]." In reality, this was the most important feature for the success, because we didn't [give up]. Neither he nor I gave up until we had arrived at some solution that we could both live with.

GRAYSON: Now, he was junior to you by a number of years in age, right.

HILLENKAMP: Oh, [Yes], sure. Sure, twenty years . . .

GRAYSON: But, I mean, that's not traditional for the junior person to argue with the senior person in this academic realm in Germany . . .

HILLENKAMP: Right.

GRAYSON: Right. That's unusual. Usually the senior person says <**T: 25 min**> "Go away . . . "

HILLENKAMP: Right. Right. At least traditionally it is not very common in Germany, but I told him at the very beginning, when I hired him. I said, "I don't know enough about chemistry that I can give you advice. So you have to be on your own, and I want to learn from you. I'll teach you the laser physics, but I want to learn from you the chemistry." From the very first day, our relationship was that of two equals.

GRAYSON: Okay, I mean, that's . . .

HILLENKAMP: I mean, I made a little more money. I had a lifelong position, and he had only three-year position originally, which was then extended later on. [Yes], there were some differences, but in the way we dealt with each other there was absolutely zero difference.

GRAYSON: Okay.

HILLENKAMP: Then he left in 1998, I think, and immediately got a chair in chemistry at the University of Frankfurt. So he bypassed, so to speak, the assistant and associate professorship level, because he matured very quickly. So since he's in Frankfurt, we both from time to time call each other. We miss these debates. It was fun. It was real fun. You know, sometimes I was more right. Sometimes he was more right. It didn't matter. We wanted . . .

GRAYSON: Whatever was right.

HILLENKAMP: Whatever the best solution was, [yes] . . .

GRAYSON: [Yes]. So how long . . . how many years was in your collaboration?

HILLENKAMP: Let me check, so I don't want to give you the wrong numbers. Where is it?

GRAYSON: Now, he wasn't with you at Munich was he, or was he?

HILLENKAMP: He came in 1983, early in 1983, and he left in 1995.

GRAYSON: So he came . . . you were in Frankfurt then, at the time in 1983.

HILLENKAMP: Oh, [yes], [yes]. Actually, when he moved back to Frankfurt, he took the chair of chemistry for the medical students, which was in the same building. So he returned to the same building. From 1983 to 1986, he worked with me in Frankfurt. Then in 1986, we both—and Ute Bahr, and Bernhard Spengler—we moved here. He stayed until 1995, and then went back to Frankfurt. [Yes]. That's right. Sometimes the obvious things you don't think to mention.

GRAYSON: So that collaboration essentially was the continued development, evolution, perfection of MALDI as a tool for ionization of biological compounds. We've . . .

HILLENKAMP: Well, he was as important as I was for the original development of MALDI. You know looking at the spectra of the amino acids and the dipeptides and so on, that happened while he was already in my group, so I think we both take equal credit for inventing MALDI. Then here in Münster, there was somewhat of a break of our work, because we had to transfer the instruments and build them back up again. So for a half year, I commuted back and forth. So the work slowed a little bit down around 1986. Now you look at the list of publications . . .

GRAYSON: Well, let me . . . at this graph, which shows that there was a little dip down there about the time you moved . . .

HILLENKAMP: [Yes], I think it's more statistical to be honest . . .

GRAYSON: [Yes]. But . . .

HILLENKAMP: Sometimes happens.

GRAYSON: So why did you come to Frankfurt then? I mean, what . . . why did you come to Münster from Frankfurt?

HILLENKAMP: Oh, because [in Münster] I was offered the chair and directorship of the department of medical physics and biophysics. This was a step ahead in my career, one thing. Secondly, Münster was a center of mass spectrometry in Germany because of [Alfred] Benninghoven. Okay. Thirdly, my predecessor, the one who had the chair before me, [Gerhardt Pfefferkorn], was actually in electron microscopy but he <**T: 30 min**> did a lot of electron microanalysis, so he got one of the first prototype LAMMA 500 instruments from Leybold that was here already [when I came]. So there was some bias for coming to Münster.

GRAYSON: Okay. I was just kind of curious why all of a sudden you end up going . . . you know you left Frankfurt to come here.

HILLENKAMP: [Yes]. But . . .

GRAYSON: But that means moving all of the equipment, and you . . .

HILLENKAMP: And several of the people that were in my group.

GRAYSON: Did you have problems . . . I mean, say the school wanted to keep the equipment? Or you know a lot of times there is an issue with who gets to keep the goodies.

HILLENKAMP: Yes. Yes. That was a business . . . a difficulty. But unfortunately . . . no, fortunately, the chancellor of the University of Frankfurt . . . I mean, the chancellor in Germany is the main administrator. The rector is the president.

GRAYSON: Oh, okay.

HILLENKAMP: So the chancellor who is, of course, responsible for the gear, the money, and all of that, I went to see him. He said, "You know, formally all of these instruments belong to the University of Frankfurt, and according to the rules, we would have to offer [it, if] we don't know what to do with it anymore, because the one who will take your position in the physics department will do different research. But we have to offer it to all other [Hessian] universities. My experience is that they always find someone who claims the instrument and then will never use it. So why don't you talk to your colleagues at the physics department and get their consent that you get it as a loan?" That's what happened.

So in the Deutsches Museum actually, where the LAMMA [1000] now is, it says it's a gift from the University of Münster. But in reality the University of Münster never had a title to that instrument. It is still officially the property of the University of Frankfurt.

GRAYSON: Crazy.

HILLENKAMP: [Yes]. It's certainly crazy.

GRAYSON: But once again, this person was willing to work with you to have a good outcome.

HILLENKAMP: [Yes].

GRAYSON: You know as opposed to . . .

HILLENKAMP: Right. Right. [Yes], he was reasonable. He wanted this instrument to be used and not to sit around somewhere. There was in the whole state of Hessia nobody who would do even similar work. Remember, 1986, that was before the first publication of larger protein [came out.] So later on, of course, many people jumped the bandwagon, but not at that time, yet, I may say.

So what did we do here in Münster, when the whole thing was up and running again? Well, first of all, after we discovered the matrix-assisted desorption, we still were working on the project for the National Science Foundation. We had to produce some systematic results. They were not interested, really, in the macromolecular desorption. So before I left Frankfurt, the biggest molecule we looked at was mellitin which is about mass 2600 or so. We had already insulin in the fridge, but we didn't get to measure it, as I said, because I was on the run to Münster.

When we were . . . when the instruments and Michael and all the others came up here, one of the first things we did was look at insulin and got results, quite interesting spectrum, almost right away. "Almost right away" meant he went down to the laboratory in the morning and around 11 o'clock or so, he came upstairs with the spectrum. I have to retrieve that spectrum. I don't remember where I left that. I'm sure I pulled it out. This insulin spectrum is very funny, because <**T: 35 min**> you have a baseline, and then you see it goes up. Then there is a spike, and then it slowly comes down. We published this as insulin spectrum sometime later, maybe a year or so later.

We were wondering about the spikes sitting on this hump. We looked at . . . we spread the spectrum, and there was a spike. It was a spike, and it stayed a spike. So it turned out that this spike, which really looked nice as a spectrum, was a noise peak sitting on that hump which was definitely insulin, so it was an insulin spectrum, but that spike there was, it was noise. [Fig. 48] You know the electromultiplier sometimes produces noise peaks.

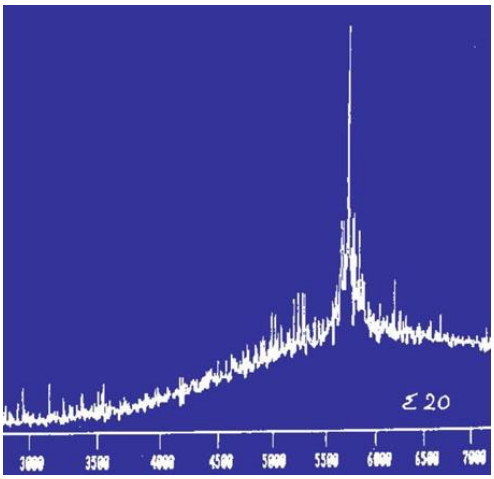


Figure 48. First spectrum of insulin

Unfortunately, we have lost that original spectrum, because I wanted to go back and show it to someone, and we couldn't find it again. I hope I can retrieve it later and give you that, because it's, sort of, interesting side aspect.

Then we submitted an abstract to the conference of the International Mass Spectrometry Society meeting in Bordeaux [France] in 1988. The abstract said something, "laser desorption of biomolecules with mass above ten thousand." That was submitted, I guess, around late in 1987, or early 1988, you know, at least half a year prior to the conference. When we presented our results in Bordeaux, we had already a spectrum of mass 160,000.[19] You know, it went within a half year, we went up from . . .

GRAYSON: Well, insulin's about what five fifty . . .

HILLENKAMP: Insulin and a lot of material prepared, and very poor resolution, to something that was much better than that. Excuse me, but it seems I've lost something here, in my files, because . . .

GRAYSON: It's always fun to try and find something that you've lost, that's for sure.

HILLENKAMP: Uh-oh. Let me . . . can you switch it off for a moment, because I have to take my stick here and see whether . . .

[pause in the recording]

. . . showed how the spectra evolved over that half year, you know. As I said, within a half year, we were up at way above 100,000 in mass. We went down from 10 picomoles or so, to just a few femtomoles. [Fig. 49]

[19] M. Karas and F. Hillenkamp. "Ultraviolet Laser Desorption of Proteins up to 120,000 Daltons." In: *Bordeaux Mass Spect. Conference Report A*, vol. 11 (1988): pp. 416-417.

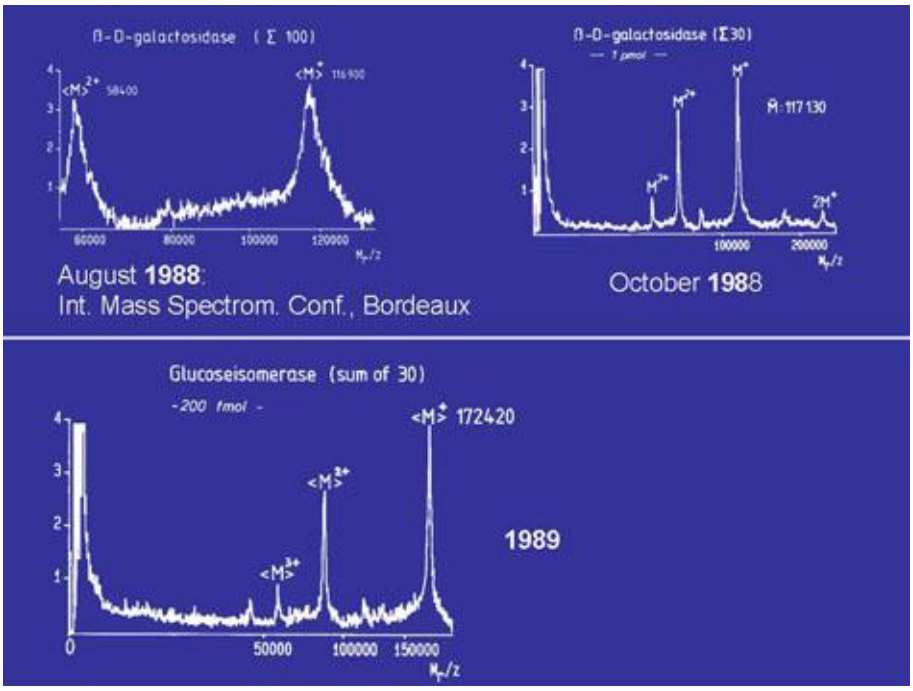


Figure 49. Evolution of spectra quality in 1988/1989

Looking back, I think it is clear that while the high mass range was spectacular at that time, because nobody had believed that one could ever generate ions of that size and put them into vacuum and analyze them. But the feature which made it so useful was the sensitivity, because that's what biologists needed. I think it's fair to say that this was the most important aspect of the MALDI technique.

Well, then at the Bordeaux conference—actually, the next morning after we had presented our results—I was coming to the conference site and there was Frank Field sitting, having coffee, and he called me over and said, "You know, you have dropped quite a bomb yesterday." So that was sort of the acknowledgement after he first said in this publication that it needed a new technique. I immediately sat down with him and we agreed that we would start a cooperation. He said, "I must try that. I must have that at Rockefeller [University]." I said, "Look. You have Brian [T.] Chait <**T: 40 min**>, and Ron [Ronald C.] Beavis and I have Michael Karas, why don't we bring the younger ones together and let them try to find out what can be done."

This is another experience that I would like to share with you. That is, if you are lucky in your professional life, you have a good combination between competition and, maybe not necessarily friendship, but good personal relationships. We were extremely lucky in our field, that we had this combination with X number of groups. One was Brian and Ron.

To tell you how that went, then, of course, the next year . . . was this next year? I think so. The next year, ASMS, we had a presentation.[20] By that time, the Rockefeller group had set up their instrument and they had some results. After the session, which was the last one in the afternoon, Brian and I went on the boardwalk—this was Miami [Florida], I think—and just chatted, you know: what would we think should be done next, and what would be a useful way to go?

We both agreed that it would most probably be advantageous to move from the 266 nanometer wavelengths into the UVA at [337 or 355] nanometers, because there was no absorption of literally any biomolecule and therefore, there would be less fragmentation. So we discussed that and we confided to each other that that would be our next goal. We also agreed that we weren't sure whether going to longer wavelengths would work at all. But it would be worth a trial.

We also exchanged information that they were looking . . . they were waiting for the frequency tripler of their YAG laser to get to 355 [nm]. We were waiting for our nitrogen laser at 337 [nm]. That both they and we had already thought of some matrices if things would work, then we would find them first with these new lasers.

Now ASMS is usually end of May, right? End of May, early June. So we were told by the company who made the nitrogen laser that there was some delay, and they kept telling us the laser would come in a week, or in a month, and it didn't come. So by August or so, I was getting nervous, because I knew that we were in this competition, and I had no idea when they would get their frequency tripler.

So I sat down with Ute Bahr, who was operating one of the MALDI machines. I said, "What do you know? I know it takes about a week to set the whole thing up. But let's use our excimer-pumped dye laser, frequency double it to 337, and see whether we can get spectra." [Yes]. It took her about a week to get the whole thing to work. And we got beautiful spectra right away.

We first had as a matrix amino benzoic acid. That worked so-so. But then, we tried 2,5-DHB [dihydroxybenzoic acid], and that worked very well. The Rockefeller group had been thinking of the cinnamic acid derivatives. Actually, it turned out we beat them by two weeks or so. That fall there was a conference organized by Al [Alma L.] Burlingame in San Francisco [California]. He was <**T: 45 min**> there, and I was there. I presented the results. He came up to me and said, "Ach, you guys have beaten me. We just didn't get our frequency tripler."

But you know, [yes], it was a competition, but it was a friendly competition. We have stayed in good contact ever since. In fact, what happened was that they tried the benzoic acid matrix, and we tried the cinnamic acid matrix. They kept claiming the alpha-cyanocinnamic acid

[20] F. Hillenkamp and M. Karas, "Ultraviolet Laser Desorption of Biomolecules in the High Mass Range." *Proceedings of the 37th ASMS Conference on Mass Spectrometry and Allied Topics*, Miami Beach, Florida, May 21-26, 1989, p1168.

was better than DHB. We claimed that DHB was better than alpha-cyano. The question was, why would that be so? We didn't know what the reason was.

So the next summer, when I went over to Boston, I took some of our matrices, the stuff that we bought from the chemical company. I took them along. I measured the solid-state absorption by the diffuse reflection in a Beckman spectrophotometer at the Wellman laboratory. Brian sent me some of his stuff, and we couldn't see any difference. So at the end of my stay in Boston, I went down to New York. We just took spectra.

All of a sudden it occurred to both of us: it had nothing to do with the matrix. They were using a linear TOF [time-of-flight] and we were using a reflectron TOF. And alpha-cyano generates more fragments; it's a hotter matrix than DHB. In a reflectron TOF that's no good, because that deteriorates mass resolution. In the linear TOF, you don't see that. The fragments arrive at the same time as does the parent molecule. So that was the reason. But we both wanted to know.

A similar situation happened with the Manitoba [Canada] group, Ken [Kenneth G.] Standing and Werner Ens. I have been there many times. We did some development, instrumental development, together. At some point, the Manitoba group had published a paper claiming that if you plot the ion yield as a function of fluence that if the fluence gets too low there is what they called "a precipitous drop of the ion signal."[21]

When I read that paper, I sent an email and said, "Can you give me any reason, any physical process that would lead to a full drop-off all of a sudden, as would be true for photo electrons," you know, that [Albert] Einstein got the Nobel Prize for. They said no, but that's what they observed. I said, "But we don't really see that."

So Werner Ens came over here for a couple of weeks. With his detector, they used ion counting. We used analog signals and we sorted that out. In fact, he stayed overnight on the air mattress in the laboratory, because at low fluences, it takes you a long time to do ion counting to get decent signal.

So and the same was also true for Cathy Costello and the Boston group, and with several others in Europe. So except for one or two exceptions, there was always a fruitful and good exchange of information. At the same time, we did not always disclose to the other group what we were working on at the moment. But it made the research, and life, very pleasant.

GRAYSON: Sounds like a cooperative competition.

[21] W. Ens, Y. Mao, F. Mayer, and K. G. Standing. "Properties of Matrix-assisted Laser Desorption. Measurements with a Time-to-Digital Converter." *Rapid Communications in Mass Spectrometry* 5, no. 3 (1991): 117-123.

HILLENKAMP: [Yes], right. [Yes], that's what we might call it. So what else? Then already in 1988, we started some collaboration with Finnigan Company [Finnigan Instrument Corporation], and as a result of that, the Vision 2000 instrument was <**T: 50 min**> developed, and marketed by Finnigan.

GRAYSON: What was that, they called . . .

HILLENKAMP: Vision 2000. [. . .] Actually, again this is an interesting story. Because Finnigan had all this experience with ion optics—I mean, they were really masters in ion optics—this Vision 2000 had the best ion optics of any MALDI instrument I have ever looked at or used. At the same time, however, the person that was responsible at Finnigan for this development, Uli [Ulrich] Giessmann, he wanted this to be a nice-looking instrument, something special, because he said, "Even if it performs well, if it looks good that is very helpful in promotion of the instrument."

So it was a reflectron instrument, but the linear path, and the reflective paths were both drilled in the same aluminum block, about this size times this size. The reflector was sitting at the end of it. I must admit it was a very appealing instrument to just look at. But I had these debates with Uli and said, "You know, I am concerned that everything is so narrow and crammed in, and that makes it look good, but it gives you very little freedom to change things later on, if it turns out that changes would be desirable."

It wasn't more than a year after the Vision 2000 instrument was on the market that Marvin [L.] Vestal [and some others] rediscovered the delayed extraction. I mean, it was already in the very old . . . what are the two guys who built the very first time-of-flight?

GRAYSON: [Yes]. I should know the names off the top of my . . . [W.C.] Wiley and [I.H.] McLaren.

HILLENKAMP: [Yes], Wiley and McLaren. It was already in their theory. But we didn't, we hadn't realized that that was an important option. The reason actually was—and that was also the difference between the instrument that the Rockefeller people built, and us—we were coming from the LAMMA. In the LAMMA instrument, because the sample had to be [at a] low potential. The time-of-flight tube had to be at high potential. We never went beyond 3,000 volts, three kilovolts, in our time-of-flights, whereas the Rockefeller people, they actually used parts that they had already prepared for plasma desorption instrument, and that was operated at 20 kV. When Marvin visited the Rockefeller people and . . . oh, no. Sorry. I have to backtrack. Again, this is history, right?

GRAYSON: Oh, [yes].

HILLENKAMP: Okay. In Bordeaux, we had a fantastic conference dinner at one of these caves, you know, these caves where they keep the Bordeaux wine. On the way there, I was sitting next to Marvin in the bus. Marvin said, "Really interesting, what you have done." I said, "[Yes], we like it." He said, "Do you think it's of commercial value?" I said, "Marvin, I'm not sure. If I would be you, I would wait, because the mass resolution isn't as good as one would like it to have. There are some other open questions." He said, "[Yes], that's what I figured as well." So we left it there.

Then after the Rockefeller people had their instrument up and running, Marvin visited them for other reasons. He was visiting Frank Field actually. He saw that, and said, "Oh, this can't be. This is so simple." He was the first one to build a commercial instrument, the Vestec instrument, right?

GRAYSON: [Yes].

HILLENKAMP: What he didn't realize was that it was so important to have visual observation of the sample, because the samples are very heterogeneous <**T: 55 min**>. Us, coming from the LAMMA, the microscopic arrangement, we knew that visual observation of the sample was very useful. So, you know, everyone comes from a different direction and then you combine things.

So, the Vision 2000 and the Vestec were commercialized about the same time. For a while they were the standard instruments that people used, until Marvin then sold his company to ABI [Applied Biosystems Inc.] and they developed a new instrument.

But it's part . . . you asked me earlier today whether my engineering background was of any use. Yes. In these sorts of developments together with companies, be it Leybold for the LAMMA or the Vision 2000 for Finnigan . . . yes, that was useful. I knew what are easy ways to mill something, or drill something. Until I retired I never operated a commercial instrument. I mean, the only commercial instruments, so to speak, were the prototypes of the LAMMAs and the Vision. But they were very different from the final industrial products. Many of the projects that I pursued, or my students pursued, could not have been done on commercial instruments, except for the Vision, we always kept things big and open so that you could add things . . .

GRAYSON: Sure, modify it.

HILLENKAMP: Modify. Oh, another thing that happened around 1990, I think, was that . . . wait, when was ASMS in Tucson, [Arizona]? Do you remember?

GRAYSON: I don't remember, but I can get the date. Probably would have been . . .

HILLENKAMP: [Yes].

GRAYSON: Oh, my. Let's . . .

HILLENKAMP: 1989.

GRAYSON: 1989?

HILLENKAMP: 1989, [Yes]. I had . . . no, we had an excimer laser that could also be operated with CO2 gas.

GRAYSON: Ah, okay.

HILLENKAMP: We had tried this laser for desorption, but we couldn't get any spectra. Now, there is something to be learned here. We were convinced that the ionization process in MALDI was photoionization, a two-photon photoionization process, and at the CO2 laser wavelength [of 10.6 µm], you would have needed something like 30 photons or so in one molecule to get to the ionization limit, so I was sort of convinced that laser desorption with CO2 lasers would not lead to ions and could not be used for MALDI.

But we were still pursuing some laser medical work. So did Kaufmann in Düsseldorf. He had money for an erbium YAG laser. Erbium YAG emits at about three micrometer wavelengths. These early erbium YAG lasers were very difficult to operate, but I had used one in Boston, so I had some experience with it. We agreed that the laser would get delivered to Münster. I would first check it out and get it up and running, [and] then we would transfer [it] to Düsseldorf and he would use it for other laser medical work.

So the laser came. I got it up and running. Then I said to one of my students, "How about . . . you know, let's at least give it one more trial of infrared desorption." I had a couple of visitors that morning. I don't remember who it was. We were sitting in my office and debating. Around 10 o'clock the student stuck his head through the door and said, "Do you want to see something?" I said, "Yes <**T: 60 min**>." He showed me [a] beautiful, I think, some protein spectrum. He said, "Erbium YAG."

So this remains as a challenge. Are the ionization mechanisms similar or the same for UV or infrared? Are they different? If so, what is the difference? It is still an open question. But it turned out that infrared MALDI works as well as UV. The main difference is that the penetration depth of the irradiation into the sample is ten to hundred times more, and that means you take off per shot about ten to hundred times more material. If you have very little sample, then this is not desirable.

GRAYSON: But this is still MALDI or matrix . . .

HILLENKAMP: It still . . . well, of course, the matrix has to absorb at the laser wavelengths, but that is simple in this particular case with the erbium YAG at three micrometers. Three micrometers is the OH stretch bond. There's almost no biomolecule which doesn't have hydroxyls, or NH, also. Still, the maximum absorption of pure water which is the strongest absorber at that wavelength that it can have is only about a tenth of the UV absorption at all the other matrices.

So I think infrared MALDI is still interesting from the basic point of view of what are the processes going on, but for practical purposes, people always use, rightly so, the UV wavelengths.

Something else that we have discussed at times and which I have no answer to is 2,5-dihydroxybenzoic acid and alpha-cyanocinammic acid are by far the most used matrices still. Now in the meantime, several groups have taken off looking at other compounds for useful matrices. I would assume that at least several hundred different compounds have been tested.

GRAYSON: I'm sure of that.

HILLENKAMP: [Yes]. There are certain special cases. Let's say for synthetic polymers, you would mostly . . . certainly not alpha-cyano, sometimes DHB, sometimes some other matrices. The same is true for some carbohydrates, and so on. But if you ask, what is the best universal matrix, so to speak? It is these two. These were the two ones that were first discovered, totally independently by two groups, not knowing [of] each other. You know, how and why?

GRAYSON: [Yes].

HILLENKAMP: I don't know. I don't know. But it's certainly an interesting question.

GRAYSON: With good planning or good thought on the selection of the original matrices.

HILLENKAMP: No, I think it was good luck. To be honest, I think it was good luck. Because just went through a [Sigma Chemical Company] catalogue, and looked for small aromatic molecules that looked promising. Just this Thursday one of Michael's students from Frankfurt, [Thorsten Jaskolla], will come here. He's a very good theoretical and experimental chemist. He has looked at the proton affinities of different matrices. So we have some clue at least for DHB, why it is a good matrix. But it's still partly guessing, partly knowing. Still, I think it was luck, on both sides.

There was something else, by the way. I forgot to mention that earlier. When Brian and I were on that boardwalk <**T: 65 min**> in Miami at the ASMS, and we talked about the next steps, and we decided that it would be useful to go to longer wavelengths. We both had that opinion, because we felt that if there's no absorption of the biomolecule, there's less fragmentation. You know, photofragmentation, after all, was quite a well-known process at that time already. So that's why we did it. It is not true, at all.

Now these other wavelengths are more used because it's easier to build lasers for those wavelengths. But certainly, desorption with nicotinic acid at two 266 nanometers is softer than even DHB at 337 nanometers. So we did the right thing again, for the wrong reason.

So in the end, it is always the experiment that wins over . . .

GRAYSON: [Yes].

HILLENKAMP: [Yes]. You have to check it out. If you're lucky, your negative result does you some good. [Yes].

During those years then, what we did here actually were three major directions of research. Students from chemistry and biology and biochemistry in particular were mostly applying MALDI for certain of their projects or just trying to find out which biological molecules did lend themselves to a MALDI analysis.

So we were the first ones to look at proteins and peptides anyway, but then the first ones to do DNA, the first ones to do carbohydrates, the first ones to do synthetic polymers. None of that we pursued to any extent. We just wanted to know which group of molecules it was good for, and then we left it to specialists in, let's say, synthetic polymers to pursue it further. So that was one direction.

The other direction was to try to understand mechanisms that lead to the formation of the MALDI ions. Actually, we were not very successful. The question is why is that so? Well, there is a reason for that, I think. Others have tried, of course, you know. Like Bob [Robert J.] Cotter, the husband of Catherine Fenselau, at . . .

GRAYSON: Hopkins . . .

HILLENKAMP: . . . at Johns Hopkins [University]. Certainly the Manitoba group, and Brian Chait, and Ron Beavis didn't do that much of it but did some, and some others, some of the younger mass spectrometrists looked into the mechanism. Why is it so difficult?

Well, if you come to think of it, you generate these ions on a time scale of nanoseconds in volume of nanoliters. To do good spectroscopy on such samples—you know, that's optical spectroscopy—is extremely difficult. So we made some progress, but not nearly as much as I would have liked to see it or had hoped that we would get.

There's one thing that we did find out about, and did sort out, was the incorporation of the analyte into the matrix. While we had discovered 2,5-DHB, and Michael and I both for whatever reason were visiting Brian Chait and Ron Beavis at the Rockefeller, we got a fax from one of my students here. She had set out to grow larger crystals of matrix <**T: 70 min**>, millimeter size crystals. You know, the growing of organic crystals is not easy. But she was successful and she sent us some pictures of that, so that was good. We put it . . . we came back, we put it in the instrument, and we kept banging the same location for a thousand times or so, drilling millimeter deep holes into the crystal, and got quite good spectra. Sometimes they were a little weaker, and then they came back up again. But clearly there was always some signal, which made us believe that the analytes were really incorporated into the matrix crystals, but couldn't make much sense of it. Then we cleaved the crystals, looked at the cleaved interface, and got good spectra, so we convinced ourselves that the analytes, the proteins, were sitting in these crystals.

At that time, the chemistry department had invited—I don't want to mention the name—a very famous German physical chemist, actually a Nobel Laureate, who got a Nobel Prize for crystallization [of a cell organelle.] Because I was wondering whether we were on the right track, I asked the head of chemistry department whether I could sit next to this person during coffee before he gave his lecture.

[Yes]. He was nice, and I sat next to him. I told him about our results. He said, "No way. Absolutely no way. These small molecule crystals, they cannot accommodate proteins." Because I told him we did, of course, crystallography. It looked absolutely perfect, and I showed him the defractogram. He said, "No, no. You know, you physicists, you must be more clean. You're just . . . what you see is just a contamination from your sample plate or from wherever. So, no, no, no."

So I was a little bit disappointed. He did not convince me. I kept—in my presentations wherever—I kept saying, "We believe that the analyte gets incorporated into these crystals." About, maybe now, eight years ago or so, I was scanning literature. My eye was caught by a title of a paper. It was—and I don't know why—it was on electron microscopy of sea urchin

teeth. Would you believe it? I thought that was a funny field of research. So I pulled up the paper and scanned through it. Guess what it said. It said the sea urchin's teeth—and meanwhile I've seen another paper on whale teeth—they are calcites. They are inorganic calcite crystals. Calcites crystalize . . . even in physics everyone knows can be a very easy to cleave. So the teeth of the sea urchins and the whales would be very fragile. What holds it together are proteins that are incorporated into these crystals. They cross the border you know, these plains in the crystal. So it tells you that nature is very, very clever. I mean, we ran into that by accident. Nature developed this on purpose in evolution. I think it's very, very funny.

GRAYSON: I think that's the same mechanism that gets this mother-of-pearl feature in the shells, it's the nacre, or they call it nacre [. . .].

HILLENKAMP: [Yes]. It could be. Then . . .

GRAYSON: Where you get the inorganic crystal-type stuff . . .

HILLENKAMP: [Yes], [yes].

GRAYSON: But the proteins are incorporated in there to help make that tougher.

HILLENKAMP: [Yes]. [Yes], that I haven't come across yet, not in the . . .

GRAYSON: I think if you check in the literature, I think I saw something recently about that. So it's . . .

HILLENKAMP: [Yes]. That could well be. I mean, it's the inorganic factor in organic life. Yes, if you want to have something very hard <**T: 75 min**>, you need inorganic substances. You can't . . . organics, they have all these non-covalent interactions. You know, the organic world is basically soft, even polymers are . . . there is . . . if you want to have something very hard, you better go for the inorganic crystals.

So you also asked . . . I think one of your questions, did we have difficulties to publish things? Yes. Yes. It was on and off we had difficulties. Early on, we could publish, but not in very high-ranking journals, you know.

GRAYSON: So what were you trying to publish at that time, in your early . . .

HILLENKAMP: Well, the first concept of LAMMA, for example, we got into *Nature*.[22] That was . . . but that was a real exception. Okay.

But what I wanted to tell you about this incorporation business. Later on, three separate groups, independent of each other, developed a different method. One is at ETH [Eidgenössische Technische Hochschule] in Zürich, in Switzerland, that's [Renato] Zenobi. One is at the Max Planck Institute for Polymer Sciences in Mainz [Germany]. And us. We figured that sometimes it was advantageous to not mix the analyte solutions and the matrix solutions together and rather have matrix crystals. Then add the analyte [as a solid powder.]

It's not by chance that the Mainz people were after that, because there are some polymers where you don't have good solvent. If you do try to dissolve them, you extract certain low-mass polymers of the distribution and the bigger ones don't come out. There are lots of problems with solubility of polymers, and therefore, the standard MALDI preparation is not the way to do it.

So, the question was, can one add, for example, the matrix solution [to the solid analyte sample] afterwards? [Yes]. The matrix solution afterwards and then let it dry [because the analyte does not dissolve, it stays at the surface of the matrix crystals.] It works, but it doesn't work nearly as softly as it does when the analyte gets incorporated, when it's sitting at the surface.

Also we found out by using special fluorescence techniques that if the analyte gets only physisorbed at the face of the crystal, of the matrix crystal, then you cannot get any MALDI spectra. No way. But if it gets chemisorbed then all of a sudden you get very good spectra, but in this case you get no fluorescence. You know there are fluorochromes that, if they transfer a proton, go from the dark state to the fluorescent state. We could . . . this would monitor the proton transfer, which is the basic process behind chemisorption between the two phases.

When we tried to publish that, then we got a very harsh review, and I battled back, of course, and so on. It went back and forth, I think, three times. In the end, the reviewer—I think I know who it is, but doesn't matter—the reviewer said . . . oh, no. One of our arguments had been that if you take the polymer and matrix, and then you grind them in the mortar and pestle, or in a ball mill, the longer you grind, the longer you use the ball mill, the better the spectra [you] get.

I had just written [that], off the top of my head, because it was obvious that the longer <**T: 80 min**> grinding made smaller particles. Smaller particles have a larger surface area per volume, and therefore, it's not a surprise that the spectra got better. The reviewer insisted that

[22] F. Hillenkamp, E. Unsöld, R. Kaufmann, and R. Nitsche. "Laser Microprobe Mass Analysis of Organic Materials." *Nature* 256, no. 5513 (1975): 119.

we provide an electron microscopic picture, or a micrograph, of ten minutes grinding and twenty minutes grinding. You know, this was one of the, in the end, more funny arguments by a reviewer.

I cannot say that the papers that I think were the most important ones were the easiest to be accepted . . . not at all. There's no correlation actually.

[Yes]. We kept also having some funding problems, you know. Looking back now it's all easy, but at times, I had to pay my students here. It wasn't all that easy, I must admit. We also looked, by the way . . . as far as the properties go, an important question of the non-covalent complexes. Actually, one of my students [Kerstin Strupat] got her *habilitation* with that work. By and large, MALDI is . . . or MALDI mass spectrometry on non-covalent complexes is very difficult to do.

One more trivial reason is actually, interestingly enough, in the first spectra that Koichi Tanaka published. He used lysozyme, tons of lysozyme, and he claimed he had seen masses above 100,000. In reality, these were non-specific complexes of the lysozymes. You know, lysozyme one, two, three, four, five.

This is something that is negative of laser desorption, because you never know whether it will have a real, biologically important covalent complex or whether it's unspecific complex formation at the gas phase. So by and large, if someone wants to analyze non-covalent complexes by MALDI, he has to be very careful, or she. It has to be done with great care. You have to add non-specific partners to see how the peaks vary with this addition and things like that. It's difficult. However, in a way it's also complementary to other techniques because, for example, protein-protein interaction, which is sometimes difficult [to analyze] by ESI [electrospray ionization] or other techniques, works relatively well in MALDI because you have a large contact face usually between the proteins.

The interaction between receptor and target molecule is almost impossible to do by MALDI, because during the MALDI process the proteins no doubt lose some of their quaternary structure. In this interaction of—what do you have to say?—a receptor ligand, it's usually a very small area where, the affinity area between the receptor and the ligand. That easily gets lost in MALDI preparation.

GRAYSON: [Yes].

HILLENKAMP: So [yes], we tried to do as much work as we could on clarifying the mechanisms, but it's still not finally solved . . .

GRAYSON: But it seems to me that is a conundrum in all of the newer . . . like, FAB. I think there's still a lot of uncertainty as to exactly how it works. The same with electrospray. I think there's at least some debate about the two different . . . several mechanisms . . .

HILLENKAMP: [Yes]. I think it's clear now that both of them are active. We have a similar thing in MALDI by the way of preformed ions in the matrix crystal already versus protonation in the gas phase. We had a tremendous . . . that was really a fight with Richard Knochenmuss, who started out to work with Renato Zenobi in Zürich, then left. They couldn't get along with each other. He kept insisting that it's all gas phase. Michael had a different hypothesis [the "lucky survivors"]. I think that we have sorted out seeing that both are active. You know. No one is only right or only wrong, which in nature is not so rare a situation.

GRAYSON: Well, how about light as a wave and light as a particle?

HILLENKAMP: [Yes], right. So we are dealing with very complex systems. You know, a protein is a very, very complex system. We shouldn't be surprised that the methods turned out to be successful for their analysis are not simple methods, as well. The notion that you start out with a concept and you develop that concept, and you wind up with a perfectly functional system is . . . in very, very rare cases it may be right. But mostly it is not.

GRAYSON: I think that's what is taught after the fact, when everything has been worked out, and you know how it [came] about. Then you teach it as though it's a straightforward system, when in fact it's a very difficult, tortuous path you have to go through.

HILLENKAMP: Something I also wanted to mention, because it was a question on one of your papers there, was about mentoring students.

GRAYSON: Now you had a fairly decent number of students, I would assume.

HILLENKAMP: Right. Well actually, in Munich I had no students, because it was a National Laboratory. In Frankfurt, I had relatively few students, maybe for the ten years there were a total of twenty, certainly no more than that. But here in Münster, I had a pretty large group as you saw from one of the pictures. In Frankfurt, I just didn't have the money to pay them, and things improved here. Certainly when you apply for funds, it does matter whether you're a full professor or an associate professor. The method became popular soon enough that it was soon easier to get money.

Besides realizing this matrix-assisted desorption, that was truly Michael Karas's and my work. The rest, I could not have done without my students. I think I have . . . I was gifted with X number of very, very good students. I wouldn't want to name any of them, specially. [Yes], a few of them did standard work. None of them was lazy by the way. But it was, sort of . . . I usually came in at 9:00 in the morning, and I left at 10:00 at night. There was . . . certainly in the early days, there was a real enthusiasm in the group of what could be done and so on. That transpired to the students. They were exceptionally good, that's all I can say.

I always tried to form subgroups. Let's say, one biology student, one physics student, and one chemistry student. They learned a lot from each other, and I watched that going on. [Yes]. They had to learn that the first time after a half year, into their thesis work, let's say. They had to give a seminar, and that there would be a discussion. We would take their hypotheses or results apart. It wasn't easy for them.

But at the same time, I think they realized that they had learned something. I realized that without these students, work wouldn't have progressed, at least, nearly as fast as it did. I'm very indebted to ...

GRAYSON: So they come primarily from any one discipline to your group? Biology, chemistry, physics, medicine . . .

HILLENKAMP: You know, that's something that's still typical German. The Department of Medical Physics and Biophysics is part of the medical school. When I came . . . in Frankfurt, I was part of the physics department. I was a member of the physics department <**T: 90 min**> and I had a secondary membership at the medical school, because the laboratories were actually located in the medical school, and not in the physics department.

Here, this department is part of the medical school. I applied to the physics department for secondary membership because otherwise, I could not mentor PhD students that were physics students, and they declined.

GRAYSON: Oh, my.

HILLENKAMP: I never got that. Despite of Benninghoven, who was very helpful because then I got stuck. So I needed two mentors from physics and he was always [one of them.] In reality, I wrote the review. He just changed a few words and then did it, because I didn't want to put that much of a load on him. But they didn't grant me a secondary membership and certainly not the chemists and the biologists.

So one of my very good students was Bernd Stahl, who did the first work on carbohydrates, actually; on sugars in milk actually. He finished his PhD. Then there was

commencement ceremony, and I went there. He was there, of course. He got an award for the best thesis of that year in biology. It was mentioned he was the student of Professor X and Professor Y. My name wasn't even mentioned. I didn't care much, except that it was not always easy to recruit students.

GRAYSON: [Yes], [yes]. So let me get this straight. You got your PhD in statistical communications from an engineering department.

HILLENKAMP: Right. No. My PhD in laser energy measurement . . .

GRAYSON: Laser energy measurement.

HILLENKAMP: Laser energy measurement from an engineering department.

GRAYSON: Engineering department.

HILLENKAMP: Correct.

GRAYSON: So now, when you were at Münster . . .

HILLENKAMP: No, I was in the physics department in Frankfurt.

GRAYSON: Frankfurt. Now . . .

HILLENKAMP: Now I'm in the medical school . . .

GRAYSON: Medical school . . .

HILLENKAMP: Right.

GRAYSON: So here you are an engineer in the medical school . . .

HILLENKAMP: Right.

GRAYSON: Who cannot get approval from the physics department to . . . okay.

HILLENKAMP: Yes. This is ridiculous.

GRAYSON: Yes. It's interesting.

HILLENKAMP: Actually, I don't know whether you have read about it. We had this, what's called the Excellence Initiative in Germany. The federal government has put aside a very decent amount of money, 700 billion euros, to support special research projects at universities which are interdisciplinary. They must be interdisciplinary. They must have some new ideas in it. There were two rounds of request for proposals. In the first round we, the University of Münster, failed 100 percent.

The second round, a proposal from the medical school together actually with biology, the two departments together, failed by a very small margin, but we got awarded another project on religion and politics. Münster is traditionally strong in the liberal arts. This is a fantastic project, really. There is so much in it.

Then it was the third round. It was known there would be a third round. But between the different rounds, there was five years in between. So our rector, the president of the University, is a woman. She got together a scientific advisory board with the . . . not the only, but the main purpose to help come up with proposals for the Excellence Initiative. I was very [strongly involved] . . . and I'm a member of that committee. I spent a lot of time in mentoring or counseling [. . .] of an extended <**T: 95 min**> project that originally was just medicine and biology, it's now medicine, biology, physics, chemistry and mathematics. It's called Cells in Motion. It had nothing to do with mass spectrometry. [Yes]. But it has a lot to do with optical spectroscopy, and optical techniques because 50 percent of it is imagining, of course in biology and in biology systems optical imaging . . . I mean, there is the macro imaging of PET [positron emission tomography] and NMR [nuclear magnetic resonance], and so on. But all the micro imaging is optics actually.

So I'm not part of the group, because I have been retired for twelve years now, but I helped them a lot to formulate it and it made it. That just happened a couple of weeks ago.

GRAYSON: Congratulations.

HILLENKAMP: It's 40 million euros, for five years.

GRAYSON: Whoa, that's very good.

HILLENKAMP: It's big money. We're now really looking forward to these projects.

GRAYSON: All right. Now, you just mentioned something that's interesting. You've been retired for ten years. Now, is there a mandatory retirement for the academic community here? Or . . .

HILLENKAMP: Yes. It is age sixty-five. I retired at age sixty-five.

GRAYSON: But you're still around.

HILLENKAMP: [Yes]. But it's a question of people like me to be around or not. So now, I mean, I have this position of being a member of the advisory committee, which really has adopted a lot of, I wouldn't say power, but involvement in restructuring the university. For example, we want to get rid of these strict borders between physics and chemistry and biology, and so on, and organize research more on topics rather than on fields. So, you know, that kept me quite busy the last two or three years or so.

GRAYSON: No. But I mean are you compensated for that, or you just do that for the goodness of your heart?

HILLENKAMP: Yes, I get compensated for . . . let me try to remember how much it is. It is 5,000 euros a year. It's peanuts.

GRAYSON: [Yes], right.

HILLENKAMP: It's peanuts.

GRAYSON: That's for sure.

HILLENKAMP: No, no. Actually there are three of the seven members are now retired. Originally, I was the only retiree. Then two more retired over the last ten years. We do it as a service to our university, and because it's interesting.

GRAYSON: Oh, [yes].

HILLENKAMP: You know, I don't think that I could still go down to the laboratory and do experiments. The tactile ability is not there anymore, and maybe the patience also. I think . . . and that's all true by the way for the Wellman Center in Boston. I think it is much more . . . a much better use of my time if I act as a mentor and help people to think things through, formulate. You know, after you have written twenty or thirty or whatever number of proposals, you know a bit about the to-do's and the not-to-do's. So that's actually my function here.

The medical school, as you can imagine, is interested in surgery, and maybe oncology, which brings in the big money. They're not interested at all in mass spectrometry, so they couldn't . . . they didn't replace me by someone else for seven full years. That was not good for the field, and was not good for some of the people who stayed, were younger than I and stayed. My concept when I retired, actually, was different anyway. The department had four professorships: my own, and I was the director, then there were three associate professors, one in optical spectroscopy, one in electron microscopy, and then Jasna Peter-Katalinic in mass spectrometry of carbohydrates.

I thought when I retired that it would be very useful to get together <**T: 100 min**> with the physics department and the chemistry department and start a new initiative on structure-function analysis. My chair would have gone to crystallization, and there is the accelerator in Hamburg, which is reachable in two hours by train. Chemistry would contribute the [macromolecular] NMR. Then physics and we together would do the mass spectrometry. But I couldn't convince enough people that that would be a useful concept.

I think if we would have been successful with that, we would most probably have been successful already in the first round of the Excellence Initiative because it's putting a roof above all of these different fields, and really, those are the methods that keep adding knowledge to our understanding of molecular processes, and so on. So after seven years, they finally hired someone for optical spectroscopy. I told you, actually he's more of a physiologist. He works on the brain synapses and does super resolution microscopy, very good work.

I had no objections to hiring in my succession someone who would do something else, because only when the professorship changes has the university the chance to go from one field to another or add something new. But the original arrangement would have been that when Jasna, the mass spectrometrist, would retire that then they would hire a mass spectrometrist, and build up that group again. It hasn't happened so far, and I'm not sure it will ever happen.

In fact, we're now trying to work on a concept where one of my former PhD students, [Rainer Cramer] who actually did his [PhD thesis] work at Vanderbilt [University] with the free-electron laser and now has a chair in analytical chemistry at Reading, in England, but maybe we can get him back here. But I'm not sure it will work. So . . .

GRAYSON: So you're retired, but you're not retired.

HILLENKAMP: No. I'm . . . that's right. Yes. I'm retired, and . . .

GRAYSON: As Al [Alfred O.C.] Nier used to say, his wife accused him the only thing he retired from was his salary.

HILLENKAMP: [Yes], right. [Yes].

GRAYSON: Because he would apparently . . . well, you know, I interviewed Al Nier many long years ago. He was . . .

HILLENKAMP: I beg your pardon?

GRAYSON: Al Nier, University of Minnesota.

HILLENKAMP: [Yes], right.

GRAYSON: [Yes]. I interviewed him in 1989 or whatever. He said he went in every day. Then he retired, I mean, he was *emeritus*, but he went into work every day and weekends, Sundays included.

HILLENKAMP: Well, I complained recently to the rector and our dean of the medical school. We were just standing together discussing this and that. There were some decisions that had been made about a research proposal which was somewhat controversial. I said, "You know, actually what you are doing is not right. You have need of my expertise opinion here."

It's open. People know that I was against that proposal for certain reasons. At the same time, I have absolutely no official function in the medical school. This is going on a rope

without a net underneath. They said, "[Yes], you are right, actually right." So now they plan to make me "senior professor."

GRAYSON: Ah, there you go.

HILLENKAMP: So I get a title. But that has to go through the faculty meeting and so on, so it has some official touch to it. So maybe sometime in fall, they will appoint me . . .

GRAYSON: It's obvious you're not ready to abandon the intellectual . . .

HILLENKAMP: No. I would get bored . . .

GRAYSON: Activity that's associated with the university.

HILLENKAMP: But you know, I don't work nearly as hard anymore as I used to. I told you we have a second home in Munich. For times, we just go there. This summer it didn't work out, because my wife got sick. But otherwise, we spend some time down there, and we go to music festivals <**T: 105 min**>. You know, we go on biking tours . . .

GRAYSON: It's a lovely city.

HILLENKAMP: [Yes]. Oh, [Yes]. Munich is just great. Since I lived there for fifteen years, you know it's . . .

GRAYSON: You go hiking in the Alps and all this.

HILLENKAMP: [Yes]. [Yes]. Well actually, you know this Feb . . . , no March it was, we went skiing again. For as long I can think back, two weeks of skiing in winter was an absolute must. I developed this myeloma last summer, and this attacks the bones, so the bones get somewhat fragile. My oncologist said, "You know skiing, I don't know. Maybe you should abstain, and not go." I said, "But I want to." So they took an MRI [magnetic resonance imaging] of the whole spine. It mainly goes into the vertebrae, the whole spine. It looked good. You know there were no fragile places, or so. But they did not look at my . . . how do you call these bones here?

GRAYSON: Hip bone.

HILLENKAMP: Hip bones, [yes]. On the day three or so of skiing it was beautiful weather and great snow. It was in Arlberg [Austria]. I was standing at the top of a run, and was looking down, and [my wife] was behind me. There was a woman, and she passed by me pretty close. Then she got scared, I guess, because it was steep. She stumbled, and fell and slid down half of that slope.

But her one ski stayed up there. So just intuitively, as I would always have done, I bent over and grabbed the ski to bring it to her. On the last turn, when I wanted to get to her, my poles, which were just dangling down, caught, or one of the skis caught the poles, and I went over a couple of times and broke two fractures in my pelvic bone. So if you would have come earlier, then I would have been on crutches. [Yes]. So sometimes you have to pay attention to . . .

GRAYSON: What the man says.

HILLENKAMP: To age.

GRAYSON: [Yes], right.

HILLENKAMP: So I guess my skiing career is over for now. I'm so sad about it, because I just love it.

GRAYSON: I think that comes from, I guess, doing it as a child. I imagine that you skied quite a bit. Well, didn't you say you had to ski to school in winter?

HILLENKAMP: [Yes]. As a student, we didn't have money for any of the lifts so we were going . . . we were hiking the mountains on skis with skins underneath, you know, sealskins underneath. So you could walk up and then, take the sealskins off and then you ski down. Oh, I have so good memories of many of these. But our boys ski, and all our grandchildren know how to ski already, without . . . except for the two ones in Lyon [France], which are too small. One, just born.

So I don't know. This was in our more private life. But you can strike that out . . .

GRAYSON: Well, it's mostly . . . it's up to you. I mean, you'll get a chance to see the transcript of everything we said here, so you can decide what you want to leave in and what you want take out. But, I mean, I think it's . . . part of what we're about is trying to humanize the person to show that they have interests that are greater than their scientific career, and that those interests actually can contribute to their career in ways, and they're more complex than just somebody who did some sterling, important work.

HILLENKAMP: Well, we were jumping back and forth quite a bit . . .

GRAYSON: Well, that's okay. I mean, it's not supposed to be, well, super organized. They'll fix it up. They have . . . what they usually will do is have, in the beginning, a section that summarizes, like, an abstract that tells the different parts . . .

HILLENKAMP: But who writes the abstract?

GRAYSON: They will do the abstract.

HILLENKAMP: [Yes]. It's good that it's done by someone who is not that involved . . .

GRAYSON: [Yes]. So there's actually several oral histories that you can actually look at online that ASMS has on their website. You can kind of get an idea of how they end up <**T: 110 min**> when they're completed.

HILLENKAMP: Okay.

GRAYSON: It will take some time, because all of our conversation is transcribed. Then they edit it and look at it to clean it up. Either one or both of us will look at it. So . . .

HILLENKAMP: [Yes]. Well, you have seen many of these interviews. So I would appreciate if you would first go through it and maybe clean it up a little bit here and there.

For example, right now, I remember that I forgot to say that within my own professional career, I made three of my best friends. Kaufmann was the first one. Then Reginald Birngruber is the second one. Actually, he became the director of the Laser Medical Institute of University of Lübeck, and retired last year. So my first grad student already retired. And Mike Karas is

number three. So that's something important. If you look at . . . I can give you a few hints about these names.

Klaus Dreisewerd is still here. He's in mass spectrometry.

GRAYSON: Now, he's at Münster.

HILLENKAMP: He's at Münster. He is still here, and he is publishing quite regularly. But he's still mostly in MALDI mechanisms.

GRAYSON: They have so many different computers and the keyboards . . .

HILLENKAMP: [Yes], right. [Yes]. Then Reginald Birngruber is in laser medicine.

GRAYSON: And do you interact with these individuals?

HILLENKAMP: Oh, [yes]. I mean I see Klaus almost daily. Michael Karas, we phone from time to time. Reginald, actually, is now . . . he's originally from Munich. He's moving back to Munich, and he's retired, as I told you. We share a lot of interest in music, so besides laser medicine, of course. He also spent some time in Boston at the Massachusetts Eye and Ear Infirmary and the Massachusetts General Hospital and at the Wellman laboratory.

Kerstin Strupat is one of my very good students. She is now working for Finnigan.

GRAYSON: Oh, okay.

HILLENKAMP: [Yes]. She developed the MALDI source for the Orbitrap.

GRAYSON: Oh, okay. So she's fairly young then.

HILLENKAMP: Oh, well, she's now . . . let me see. Her children are now ten, twelve, or so. So she would be close to forty, something like that.

Ute Bahr is the life companion of Michael.

GRAYSON: Okay.

HILLENKAMP: Also a chemist. I hired her when I hired Michael. Actually, I had another opening. We had a few interviews, and neither Michael nor I were satisfied with the students who were applying for the job. Then one day he came up and said, "You know, I would know of someone else, but I'm not sure you want to hire her. She's my life companion." As long as he was with me, she was with me. She's very good. She's much more mature, of course, than the other students. She was a PhD also.

GRAYSON: So she worked in the lab along with Michael and you . . .

HILLENKAMP: No. Actually, Michael and I saw to it that she was more independent and that she would neither work for me, nor for him. You know, she was a postdoc anyway. She had worked for the industry before.

Okay, Peter Gabel is the ophthalmologist. He's also a very good friend by now. He has just recently moved back to Munich <**T: 115 min**>.

GRAYSON: Everybody's moving back to Munich.

HILLENKAMP: [Yes]. Well, you know this was our laser gang at that time.

Raimund Kaufmann, also a very good friend. He unfortunately died in 1998 of a brain tumor.

GRAYSON: So he was kind of the guy that kind of got you started a little bit . . .

HILLENKAMP: Well, he . . . [Yes]. In a way, because he had the right problem to . . .

GRAYSON: For which you had a tool.

HILLENKAMP: Right, had the tool. [Yes]. Certainly, he was very important in that phase of my life.

GRAYSON: So a chance meeting at a party.

HILLENKAMP: [Yes]. Actually, the sort of final concept of LAMMA we developed in a public pool. It was summer, like today. There was a lot of sun. We went there and we lie on the lawn, and scribbled things down. He was a very unusual man, incredible womanizer, incredible womanizer. He was also married then and had a daughter. But that didn't keep him from chasing. We would say he was chasing every apron.

But he was very good. His father actually, that's interesting. His father was a professor of physics in Freiburg. His father had done an experiment, an early experiment, that was . . . actually is now considered the earliest proof of Einstein's theory of relativity.

GRAYSON: Oh, wow.

HILLENKAMP: But . . . but, he was very conservative man, apparently. I never met him. He was long dead, because Raimund was a very late child of his. He spent the rest of his life trying to find a classical explanation to that experiment, and had huge controversies with Einstein. Raimund had a letter from Max Planck. Max Planck was then president of the German Physical Society. Max Planck . . . it was then called Emperor Wilhelm Society.

Apparently Kaufmann had written him a letter that he was annoyed about this Einstein, with his strange theory of relativity, and so on. The letter by Max Planck reads about, "you know I have my reservations about Einstein's theory, as well. But I would recommend to you to be a little bit more careful with your arguments, because he's really a very bright guy."

GRAYSON: Oh, wow. You know there's this old tradition in the German physics community that if you can't demonstrate it with an experiment . . . the theoretical stuff is okay, but if you can't demonstrate it with an experiment, then it's no good for anything. You know, I mean it was to be experimentally based. So . . .

HILLENKAMP: You don't think that's right?

GRAYSON: Well, but I mean, the whole idea of any theoretical thought was really, it was just, you know, pure speculation.

HILLENKAMP: [Yes]. [Yes]. You should not stand up and say, "This is all nonsense because there is no experiment" . . .

GRAYSON: Because there hasn't been an experiment performed yet . . .

HILLENKAMP: But . . . [Yes], right. But it should be a challenge for the experimental physicists to do the experiment. The best example is the recent last myon that they . . . no, not myon, what was it?

GRAYSON: Large Hadron Collider at CERN . . .

HILLENKAMP: Right, right, in CERN. So, I mean, it took billions of dollars, and hundreds and hundreds of researchers to hopefully, finally prove that the Higgs particle . . .

GRAYSON: Yes, the Higgs boson

HILLENKAMP: And [Peter] Higgs is still alive, I don't know whether you knew that.

GRAYSON: [Yes]. I think . . .

HILLENKAMP: He went to the ceremony when they presented the results to the public. I think that's fantastic, if you . . .

GRAYSON: So they really think they found it? Because it seems like they've only gotten evidence for, like, two or three. My understanding is that they really have only the slightest evidence.

HILLENKAMP: I think the . . . say, the uncertainty about the evaluation of all of these detector signals is less than a percent or so. But there <**T: 120 min**> is a little doubt left, but the main doubt came from the people in Chicago [Illinois], I think it is, right? Because they had claimed the Higgs particle before and it was clearly shown that it wasn't. There is a real tough competition. There's a lot of money in that. Okay.

GRAYSON: [Yes]. [Yes].

HILLENKAMP: So, that was then. Stefan Berkenkamp is one of my grad students. He actually, he's also a very good student, very unusual.

What did you say about Graham Cooks? He's . . .

GRAYSON: Crazy?

HILLENKAMP: Crazy.

GRAYSON: Imaginative.

HILLENKAMP: [Yes], to some extent Stefan is crazy. He was brought up in a very liberal school. He only does what he wants to do. But he was . . . he and Finn Kirpekar, which here he is, they found out that with glycerol as a matrix in infrared desorption, you can get ions of several hundred thousand dalton of DNA.[23]

GRAYSON: Glycerol with infrared.

HILLENKAMP: With infrared, right. But with UV, you know, typically you can analyze a fifty-mer as a maximum, which is fifteen kilodalton. But with infrared MALDI and the erbium YAG and glycerol as the matrix, they went up to 250,000 or so. Again, it's sort of a mystery why this is so. That made it into *Science*. That was a *Science* paper.

GRAYSON: Oh, very good.

HILLENKAMP: He was very proud of course, as a grad student to be first author on a *Science* paper.

GRAYSON: Oh, sure. A lot of people would love to be on *Science* papers.

[23] Stefan Berkenkamp, Finn Kirpekar, and Franz Hillenkamp. "Infrared MALDI Mass Spectrometry of Large Nucleic Acids." *Science* 281, no. 5374 (1998): 260-262.

HILLENKAMP: Right. He is now mass spectrometrist at a company in San Diego [California] called Sequenom [Inc.]. [. . .] They are the only company actually that market a MALDI mass spectrometer for DNA analysis, mainly SNP [single nucleotide polymorphism] analysis. He actually designed and supervised the construction of a relatively simple and cheap mass spectrometry for these applications. The company actually now is off to something else. They thought they could use MALDI to analyze the DNA in the bloodstream of the mother-child DNA, and be able to show whether or not there was some genetic disorder. It turned out that MALDI was good enough for about 80 percent of all samples, but the rest of the twenty samples, there was not a clear answer. That was . . . you can't market a system like that, so they now do it by regular sequencing. It's an ethical question now, and it's not clear whether that will be allowed to be done in many countries.

In Germany, for example, there are strong resentments because they essentially, now that they . . . when they tried to do it by MALDI, they had to choose maybe twenty or thirty SNPs and they would look only at these SNPs. The only information they would get would be what the distribution of these SNPs were, you know, single nucleotide polymorphism, and then they could conclude back on trisomy as a genetic disorder. But now that they go to sequencing, they can essentially sequence the whole genome of the baby, so they could certainly, easily, find out whether this it's a boy or girl early on <**T: 125 min**>. The whole thing happens during the first few weeks. So they still market these instruments for other applications, and that is MALDI. So it's another company that is in MALDI business.

Rainer Nitsche was actually a grad student of Kaufmann and myself in the LAMMA development. At some time, the Heraeus Company, not Leybold-Heraeus but Heraeus, went into the business of medical lasers. He worked for Heraeus to develop and market mainly infrared lasers for laser surgery. I don't . . . honestly, I don't know where he is now.

GRAYSON: Okay. So here you have a laser, following up on lasers. Here you have a fellow that's following up on MS MALDI, eye doctor, chemist, following up on MALDI . . .

HILLENKAMP: You know what? If you reorder that, bring Kaufmann up to the top, above Michael . . .

GRAYSON: Where is Kaufmann? Here he is. See if I can grab him here.

HILLENKAMP: That will make things a little easier. Okay. Then bring Rainer Nitsche up there, right below Kaufmann.

GRAYSON: Wrong button.

HILLENKAMP: Okay. Then who else is here? Bring Gabel up. We reorder Birngruber below Gabel.

GRAYSON: Let me put this guy back.

HILLENKAMP: Okay. Then [Reiner] Wechsung under Nitsche. Okay. Then there was another side where . . . okay, [Henning] Vogt. [Yes], above Gabel. No.

GRAYSON: Let's see above here. [Yes].

HILLENKAMP: Okay.

GRAYSON: Let me put this guy . . . okay.

HILLENKAMP: Okay. Now let's look at the other side whether there's someone else. Where would I put Giessmann? Let's leave it there at the moment. Let's go back up here.

All right. Now, these are the LAMMA people. Wechsung and Vogt are the . . . Wechsung was the head of the development section of Leybold-Heraeus. So he was essentially responsible for the design and construction of the LAMMA instruments.

GRAYSON: A-E-U-S, right.

HILLENKAMP: Right. Vogt, he worked for him, for Wechsung. Nitsche was formerly a grad student of Kaufmann, because Kaufmann at that time was already a professor and I wasn't. But he, Nitsche, actually worked in my laboratory, because Kaufmann was first in Freiburg and then in Düsseldorf. So he only came to visit once in a while.

GRAYSON: So these . . .

HILLENKAMP: So Kaufmann, Nitsche, and . . .

GRAYSON: And the Vogt . . .

HILLENKAMP: [Yes]. No, where is Wechsung?

GRAYSON: Oh, Wechsung . . .

HILLENKAMP: And Vogt. So these are the LAMMA people.

GRAYSON: All right, this <**T: 130 min**> . . .

HILLENKAMP: Maybe you put a blank line in between.

GRAYSON: [Yes]. Let me do . . . I'll make those guys red. So why don't I go up here and say, "LAMMA people"?

HILLENKAMP: All right.

Then these are the ophthalmology people, you know, that started out as laser interaction with the eye, and then went onto other organs.

GRAYSON: Okay.

HILLENKAMP: Ophthalmology people in Munich.

GRAYSON: Okay.

HILLENKAMP: Okay. So then after that, I think Michael Karas is . . . the rest are all the MALDI.

GRAYSON: Okay. So just these two are in the ophthalmology . . .

HILLENKAMP: Oh, there were more people, but . . .

GRAYSON: But they weren't . . .

HILLENKAMP: [Yes]. It's ...

GRAYSON: All right.

HILLENKAMP: Those represent the group quite well. Okay.

GRAYSON: Okay. So from here on is MALDI . . .

HILLENKAMP: MALDI, [Yes]. Okay. So let's go. We talked about Kerstin, Ute Bahr, we talked about. Stefan, we were there that just when we left. So he did essentially the infrared MALDI of DNA.

GRAYSON: So this is Stefan, or . . .

HILLENKAMP: Stefan, [Yes].

GRAYSON: Okay, MALDI DNA.

HILLENKAMP: [. . .] Okay. Now, Eckie [Eckhard] Nordhoff did the early work on the sequencing of peptides and DNA. So he was my . . . the rest, I think all of them are my grad students, or postdocs. Okay. Bernd Stahl was a biology student. He did the first work on carbohydrates. Arndt Ingendoh was a physics student, and he did quite a bit of instrument development. He optimized the reflectron, for example, for our purposes.

GRAYSON: Okay.

HILLENKAMP: Stephanie Hahner . . . oh, let me just see. He [Bernd Stahl] works now for a company that . . . the name of which I don't know because there have been too many changes of names, and being bought up. It's a food company, and they make baby food. So he does the carbohydrates, actually milk sugars. He's the world's expert, I think on milk sugars as ingredients in baby food.

GRAYSON: In baby food, and mother's milk.

HILLENKAMP: An interesting observation there by the way, when Germany got reunited in 1989, it turned out that for whatever reason, the government in East Germany had accumulated a huge amount of human milk. His company bought that up. (It was, of course, lyophylized.) So his company became aware of it, and bought it. He analyzed that all, and that went into the recipes of <**T: 135 min**> the baby food, because the carbohydrates in human milk have a very strong immunologic function. So he's . . . and did it all by MALDI. So . . .

GRAYSON: Why would they do baby . . . collect all that mother's milk?

HILLENKAMP: I don't remember why they did it, but I guess their social system was such that babies were taken away from the mother at a very early age. The mothers would just pump off the milk, and then give it to the organization which took care of the children, like kindergartens and very small ones. Obviously, that was surplus.

GRAYSON: So there was a separation of the infants from their mothers in East Germany?

HILLENKAMP: Not always, and not necessarily, but the Communist system, certainly part of it was that the children should be educated not by the parents, but by the society, first of all. They had solved the gender issue much earlier than we even became aware of it. That is, women should work.

GRAYSON: Ah. So they have no responsibility to have the child . . .

HILLENKAMP: Right. Even if they were not productive, what they did, they had to work. So it must have something to do with . . . I don't know. I just know there was all this human milk.

So Stephanie Hahner did the late work on the DNA analysis, and maybe . . . [Yes]. Okay. She worked for Bruker [Daltonics GmbH] until not so long ago. Then she got a child and I don't know exactly where she is now. But she was in Bremen [Germany]. [She has become a school teacher now.]

GRAYSON: Ah, okay.

HILLENKAMP: But I should . . . at this point in time, and when you reshuffle the whole thing, you may move that forward. I should say that during the years here in Münster, I did not do much work, or my group did not do much work, on proteins and peptides because everyone jumped on that field. I thought that wasn't interesting enough. We concentrated on nucleic acids, DNA, and RNA.

GRAYSON: Which I think are more difficult, aren't they?

HILLENKAMP: [Yes], they are substantially more difficult and for a very simple reason. If you think of the double helix, you have these phosphate groups. Then you have the sugar ring. Then you have the base. Under natural conditions, the proton of the phosphate group jumps over to the base, if the base is a base, at least temporarily resides with the base. If the base on the top nitrogen is protonated, that draws electrons from the N-glycosidic bond and the base falls off. Once the base falls off you have an asymmetric molecule. It just falls apart.

So part of Julia Gross's work was exactly to clarify that mechanism, because I had discussed it with Michael Gross (they had nothing to do with each other, not relatives, even though they have the same name) and we did . . . Julia did a lot of HD exchange experiments to prove where the protons were going or coming from. So that's why DNA is so much more difficult.

Actually, Stephanie Hahner's work—we were just at her name here—was to see whether one could derivatize DNA to stabilize the N-glycocidic bond, for example, by replacing the hydrogen in RNA by fluorine in the 2' position. The basic result of her work I would summarize to say <**T: 140 min**> that, yes, this can be done, and then it's good for mass spectrometry. But all of the enzymatic chemistry, which precedes the MALDI analysis doesn't work well. These enzymes, they just don't like fluorine or CH3 in that position. So that was Stephanie Hahner.

Finn Kirpekar was a postdoc from Peter Roepstorff's group . . . no, from Peter Roepstorff . . . no. He came here for a year as a postdoc. He had gotten his PhD from Peter or a colleague from Peter, who was in DNA. Peter was always in proteins.

GRAYSON: Did I get that spelling, okay?

HILLENKAMP: Roepstorff is okay. It's okay. You could also write University of Southern Denmark, [Odense]. Okay. Here, I made a mistake. Eberhard Unsöld is LAMMA man. So we have to move him up.

GRAYSON: All right. We'll do that.

HILLENKAMP: He was a postdoc.

GRAYSON: So let's get him here.

HILLENKAMP: Oh, no. These are the company people. Put him up here, because he was like Nitsche. He was actually my postdoc in [Munich.] Okay. Actually, his father [Albrecht Unsöld] was a very famous physicist. There was a question of whether he should have gotten the Nobel Prize for the energy cycle of the sun. He wrote very early a very famous book, *Physics of the Stars*.[24] He was made full professor at the age of twenty-five. He lived to celebrate his fiftieth anniversary as a full professor.

GRAYSON: Wow.

HILLENKAMP: [Yes]. Very—I met him a couple of times—very interesting man.

Okay. So let's go down here. [Hans-]Christian Lüdemann actually did almost all of his PhD work in Boston, but on MALDI. He proved experimentally that . . . I have to go backtrack a little bit, and tell you a little bit more about the ionization mechanism. The quantum energy of a photon at 337 nanometers or 355 or so, is less than half the ionization potential of any of the [matrices as well as] peptides or proteins, or any of the biological molecules. So with one photon you cannot generate ions.

GRAYSON: At what . . . what was the 350 nanometers . . .

HILLENKAMP: Oh. It's about 3.5 or so eV. I don't remember the numbers now. It's too long that I have been kicking these numbers around. But it's about . . .

GRAYSON: It's not a very . . . one photon is not enough to get the job done.

HILLENKAMP: Not even enough for half of it. Okay. Of course, in lasers you can drive the laser irradiance to a point where a molecule is already in the excited state, absorbs the second

[24] Albrecht Unsöld, *Physik der Sternatmosphären, mit besonderer Berücksichtigung der Sonne*. Berlin: Springer, 1955.

photon resonantly, and goes . . . and then you have the energy of two photons. With a little bit of help by thermal energy or so, that could be enough for the ionization. But if you calculate that, and that was in one of my early papers already, you find out that there's not enough photons in the beam.[25] If you have enough photons for a sizable excited state absorption, then you destroy your sample. You know, we discussed before that you have to be very careful to not exceed certain limiting laser fluence or laser irradiance. So that doesn't work. We then postulated in an early paper that there are mobile excitons <**T: 145 min**> in these crystals. That is, you have an excited state of one, let's say, DHB molecule. This excitation energy can migrate through the crystal.

GRAYSON: Exciton.

HILLENKAMP: Exciton. [Yes], they're called excitons, excited molecules.

GRAYSON: Like a phonon?

HILLENKAMP: [Yes]. It's a little bit like a phonon. But it's much higher energy. You know, it's UV. Phonons are usually lower energy . . .

GRAYSON: [Yes], okay. So it's a hot . . .

HILLENKAMP: [Yes]. They are called excitons.

GRAYSON: Okay, exciton.

HILLENKAMP: So there are mobile excitons. The notion was that two excitons would combine in one place, and one molecule would go up to twice the energy, and the other one would fall down to the ground state. Okay. This is . . . we didn't invent this idea, because physicists knew about the excitons, and about Frenkel excitons which are localized and then non-localized, or mobile excitons. So you can take that from a book in solid-state physics. Okay. So we postulated that that was the mechanism . . .

[25] H. Ehring, M. Karas and F. Hillenkamp, "Role of Photoionization and Photochemistry in Ionization Processes of Organic Molecules and Relevance for Matrix-assisted Laser Desorption Ionization Mass Spectrometry." *Organic Mass Spectrometry*, 27 (1992): 472-480.

GRAYSON: So you got one photon, but with the excitons in there that . . .

HILLENKAMP: Well, one photon gets absorbed. So it turns the molecule that absorbs it into an exciton, into an excited molecule. Okay. Then it passes its energy to the neighboring molecule. Then on and on and on. It's like in semiconductors. The excitation energy jumps. This can happen at some reasonable efficiency only if it's a well-ordered crystal. In amorphous systems this is not very probable.

At any rate, you can predict if that's a mechanism that if you look at the fluorescent yield, because all of these molecules have low, but have some fluorescence. If you plot the fluorescent yield as a function of the laser fluence, then you lose . . . at higher fluences you lose some of the fluorescence. In other words, when you start at very low fluence and you begin to increase, the fluence increases in proportion to the excitation. The more photons you put in, the more photons you get out. But then all of a sudden this curve levels off, because the photons are not available anymore for fluorescence, or the excitons for fluorescence, but they go into an ionization process, so that's a different process. [. . .] So that is a very tricky . . . are very tricky experiments to be done, Christian Lüdemann did that in Boston, exciton migration.

[. . .] After he finished his PhD, he went to Harvard Business School, and he's working for a bank now.

GRAYSON: Oh.

HILLENKAMP: When I last saw him, he said it was so boring he wants to go back to physics.

GRAYSON: Ahh, boo. I have a friend of mine, who did that. He was in science, got his M.B.A.

HILLENKAMP: Yes.

GRAYSON: Makes a ton of much more money.

HILLENKAMP: Of course, you make much more money . . .

GRAYSON: Get money coming out of your ears, you know.

HILLENKAMP: Right.

GRAYSON: All right.

HILLENKAMP: Right. Chris [Christoph] Menzel did also the . . . much of the design work in infrared MALDI. He's now working for Qiagen [. . .]. [Yes], I think that's right. [Yes]. I have to check it, but I think that's okay. Which is a company that makes assays for medicine and for chemistry, and so on. So even though he was a physicist, he deserted <**T: 150 min**> . . . how do you say that? He went off to chemistry.

GRAYSON: He was a deserter.

HILLENKAMP: [Yes]. Martin Schürenberg is another interesting . . . is also one of my grad students. He is my nephew, actually. He's the son of my sister. He absolutely wanted to do graduate work in laser medicine. He came here, and I said, "Okay, if that's what you want, we can try it, but I don't have good partners for medical laser work here in Münster. The good partners I have are all in Boston." He was already married and had a child, so it would have been very difficult for him to go to Boston, so he started a project on laser surgery here, but after about a year, it was clear it wasn't . . .

GRAYSON: Wasn't going to work?

HILLENKAMP: It wasn't going to work. You know, it wasn't getting him anywhere. So I had a long discussion with him and said, "Look. I can . . . you see the others doing the work on the MALDI, that's a sure thing. I mean, if you do good work, then you can certainly get your PhD for that. Why don't you switch?" So he switched. He worked pretty closely with Klaus Dreisewerd, who's on the list.

Klaus Dreisewerd got his PhD and Martin hadn't gotten good results yet, so he was about to quit because I had asked him to see whether one could also do MALDI with wavelengths in the visible. Other people had tried that and claimed some success, but I was not sure that those were real results. But I told him, you know, it may well be that it doesn't work. If it doesn't, you can get a PhD no matter whether it works or it doesn't work. But you have to make good experiments, and prove . . .

GRAYSON: One way or another.

HILLENKAMP: So he was at that point in time somewhat desperate. Then we changed the topic a little bit around and within a half year, he had tons of results, really very good results. He, for example, showed that you could irradiate the sample from behind and still get good ion signals.

What else? Actually now, I . . .

GRAYSON: But this was using . . .

HILLENKAMP: UV MALDI.

GRAYSON: UV MALDI, I thought . . . he started out in the visible but the visible didn't work . . .

HILLENKAMP: [Yes]. Those experiments were done pretty soon. He was done with them, and it was clear . . .

GRAYSON: The visible wasn't going to work.

HILLENKAMP: We did not find any molecule that would work as a matrix in the visible.

GRAYSON: Oh, okay.

HILLENKAMP: This question isn't finally answered yet. In fact, I hope that Klaus Dreisewerd, together with this student [Thorsten Jaskolla] from Michael, who will be coming on Thursday. They will use their OPO laser to go from the UV continuously into the visible and see what happens there. My suspicion is that one can get it to work in the visible and it will be similar to infrared MALDI, less sensitive. But we don't know yet. He [Martin Schürenberg] could not find any matrix that would give results anywhere nearly as good as in infrared or UV. We gave that up. But . . . oh, I then put him to something else. That was . . . are you familiar with Tanaka's work?

GRAYSON: Yes, a little bit.

HILLENKAMP: Okay. So in the Tanaka system, you have glycerol like in FAB. You use metal particles that are suspended in there. In all likelihood the ionization process is similar to FAB, okay. It's thermal, but it's modulated by the glycerol, which takes away from the molecule some of the thermal energy. The question was, can one prove this as a system <**T: 155 min**>?

Martin looked at about a dozen different particles, carbon and metal particles, polymer particles which were covered with some fluorescent molecules and so on. In particular he looked at the results as a function of the particle size. It is absolutely clear, if you have particles that are small enough that the laser beam will penetrate them, and do a bulk heating of the particle, this is very different from the situation when you have a larger particle and the laser radiation penetrates only superficial layer, and you get a lot of cooling, immediate cooling to the surrounding. So that was also published, I think in *Analytical Chemistry*.[26] It's a very nice paper, because it really proves what the mechanisms are.

GRAYSON: So this is . . . he followed up on Tanaka's work.

HILLENKAMP: [Yes]. Well you see, Tanaka never did any . . . ever any systematic work . . .

GRAYSON: [Yes]. [Yes].

HILLENKAMP: In fact, he never used it.

GRAYSON: Well, did anybody else?

HILLENKAMP: No. No. I mean, he . . . I visited in his lab where he was using MALDI, or electrospray. [. . .] There was Ulrich Giessmann, I think. There was Giessmann.

GRAYSON: Is that right?

HILLENKAMP: [Yes]. [. . .] Giessmann was head of development at Finnigan for the Vision 2000. So it's MALDI. [. . .] At some point in time, Finnigan decided to not make any MALDI

[26] Martin Schürenberg, Klaus Dreisewerd, and Franz Hillenkamp. "Laser Desorption/Ionization Mass Spectrometry of Peptides and Proteins with Particle Suspension Matrixes." *Analytical Chemistry* 71, no. 1 (1999): 221-229.

mass spectrometers anymore. Then he moved on to some other company, and he's now with Bruker in Billerica [Massachusetts].

GRAYSON: That's in Massachusetts.

HILLENKAMP: Massachusetts, right. It's close to Boston.

GRAYSON: Okay, then Peter Roepstorff.

HILLENKAMP: Okay, both Giessmann and Peter Roepstorff are good friends. At some point in time, Peter and I had joined a project on DNA analysis, actually, financed by the European Union. Peter is just a great guy.

GRAYSON: That kind of gives a rough idea of how these various characters fit into your research environment . . .

HILLENKAMP: Right.

GRAYSON: Which I think is a good thing. I mean, this list was derived primarily by my search of the SciFinder to how many different people you had published many papers with, so they're . . . and be . . .

HILLENKAMP: That list is not complete, but I don't think that needs to be . . .

GRAYSON: No. I know there are many, many, many more . . .

HILLENKAMP: Many, many, right.

GRAYSON: It goes on forever.

HILLENKAMP: [Yes].

GRAYSON: I think I've got the complete list here somewhere, but I don't . . .

HILLENKAMP: No. This is okay. In one of your emails you also said you wanted to talk a little bit about patents . . .

GRAYSON: [Yes].

HILLENKAMP: And IP.

GRAYSON: [Yes].

HILLENKAMP: That is not a simple topic. First of all, I must tell you that until shortly after I retired, there was a law in Germany that professors at a university, and it was a privilege only professors at the university . . . only full professors at a university would have the full rights to their patents.

GRAYSON: Oh, wow.

HILLENKAMP: So the patent was not owned by the university, but it was owned by the <**T: 160 min**> professor.

GRAYSON: But, I mean, if you weren't a full professor, the university owned it.

HILLENKAMP: Yes.

GRAYSON: And you had nothing. I mean . . .

HILLENKAMP: No, no. If there was some revenue coming from the patents, then the university would have to share that with the inventors, and the percentage was . . . you know, there was a long list of criteria, like in the US. It's very, very similar to . . .

GRAYSON: But the full professor . . .

HILLENKAMP: The full professor . . . so and in . . . no, not the full professor, the professor who had a life position. Okay. So in Frankfurt, I was already owning my own IP, and in Münster, as well. At the National Laboratory, the Laboratory owned it, but when I left the Laboratory for Frankfurt, sort of as a compensation for the fact that I had been treated very poorly by the head of my department, they gave me the title to the patents that I had filed before I left for Frankfurt.

This sounds great. But in reality, it mostly prevented IP from being patented at all, because in the old days, you would at most file for a patent—as a German professor—file for a patent in Germany. Nowadays if you want to get anything out of it, you have to file for patents at least in Europe, in the US, in Japan, now, I guess, China.

GRAYSON: [Yes].

HILLENKAMP: [Yes]. This gets so outrageously expensive that most of the IP never made it to a patent. While I was at the National Laboratory, they had a patent lawyer. He did most of the work, and the National Laboratory paid for the patent, for the early patents, let's say. They never made any revenue and so they lost . . . they didn't lose much money either. They were only German patents.

When we began with Raimund Kaufmann, he was also a very clever businessman. When we began the work on the LAMMA, we immediately filed . . . before we published, we filed a couple of patents. We filed them in Germany first. Then we began to talk to Leybold-Heraeus about building the instruments. So they took them over, and they saw to it that there were international patents. There are about a half dozen patents on the way you arrange the laser and in what fluence range you work.

You know, I learned a lot what's important in a patent to make it difficult to get around a patent. For these, about fifty to seventy, I don't remember the number of LAMMA instruments that Leybold sold, they paid us revenue fee. I don't remember how much money we made, because that was never part of my personal income. I used it . . . for example, I was not permitted to send students to conferences. They didn't have a fulltime position, so they couldn't get refunded for their travel expenses.

So I always paid their . . . let's say, in Bordeaux, I think there were twelve of us, because we really wanted to see people get excited about it. I paid for almost all of that, those travel expenses. But it was . . . it didn't make us rich, but it was sizable money. It was something like half a million Deutschmarks, or something, all together. But it was split actually between Raimund Kaufmann and Eberhard Unsöld and Rainer Nitsche and myself, so there were already four. Okay.

When we started the MALDI development and started to work with Finnigan, we made a different arrangement. I said, you know, even if . . . by that time the University would have supported <**T: 165 min**> me with the patenting procedure. But I said, even if that would happen, the likelihood that the University can find a company that would use the patents is relatively low. I mean, some of the patent and IP offices in Boston that I have been dealing with, particularly Mass General Hospital, they are extremely good now. They make a lot of money out of their patents. But they are pros.

That was not the case here. I said, well, on the one hand, all this research that resulted in this IP was paid for by public money, this was tax money. So actually, the patent, if you have a patent should belong to all of society. On the other hand . . . and then the patent isn't very useful. On the other hand, if you have something good and it's not patented, you won't find a company to take it over, because they wouldn't have any protection. So I felt that the most reasonable thing would be that Finnigan would file the patents, but would name us as the . . .

GRAYSON: Inventors.

HILLENKAMP: Inventors. And we had a license agreement with Finnigan which said that they would pay us royalties, and a certain amount, 3 percent of the sales price or something like that. Importantly later it turned out, it had a paragraph saying that if they would stop selling MALDI instruments, the patents with all the rights and without any fee would go back to us. It sounded like a good arrangement for the reasons we discussed before.

The Vision instrument wasn't a great success because—I think we got off that topic, by the way. But let me then, put it in here—for the reason that this delayed extraction which tremendously increases the mass resolution of the time-of-flight mass spectrometer, this works only at high acceleration potentials. Down at three thousand [volts], you can hardly pick it up. We had only instruments with three kV; so with the Vision instrument. Because everything was so narrow, built-in, even with . . . we had then Teflon sheets we wrapped around the reflectron, we always got sparking. So there was no way . . . and then, the same happened in the ion source. You know, if you have potential differences of ten kV between different electrodes, that's not a simple thing to do.

GRAYSON: [Yes]. That can be . . .

HILLENKAMP: [Yes]. All attempts to bring that to speed didn't work, and therefore, Finnigan didn't sell many of them. So we got a relatively small amount of royalties and that was it. Then the rights of the patents should have gone back to us, but that requires a change in the [role] of the patent office in every country that you have filed a patent for. Finnigan just didn't do it. You know, can you . . . [Yes]. Of course, you take a company like Finnigan to court, but I would be a very poor man before I got anywhere.

GRAYSON: [Yes].

HILLENKAMP: So they sat on the patent until about ten years ago. By the time they gave them back to us . . . actually, what had happened was someone in the development of quadrupole mass specs in San [Jose], in California. Finnigan there, he also was involved in trying whether these instruments could be used with MALDI, which they did. Actually, they developed a source for that, and later he became of chief of development at Finnigan.

I met him at an ASMS and I complained. I said, "You know, this is really not fair, because you know exactly how things went." There is . . . okay. He said, "I will look into it." A couple of weeks later, he came to Germany, so he visited me in my office <**T: 170 min**>. We struck a deal that they would be allowed to use these patents without any royalties in the future if they wanted, but the patents would go back to us. But at that time, they were almost expired.

GRAYSON: [Yes].

HILLENKAMP: So we really didn't make sizable money with our MALDI patents. Actually, we had foreseen when we filed the patent, we had foreseen that there might be something in the infrared, so it said, "Every wavelength longer than three hundred nanometers." So it wasn't a bad patent, but we didn't get anything out of it.

I think that for the acceptance of MALDI, as an analytical technique, it was good, because there wasn't a single company that could dominate the field. In fact, before Marvin Vestal started to build his Vestec instrument, he called me and said, "Do you have patents that can keep me from marketing such an instrument?" I said, "No, you can go ahead." So it . . .

GRAYSON: It's nice, at least, he called you.

HILLENKAMP: [Yes]. For the distribution of the technique, it was good. [Yes]. We could have made some more money, but I could have stayed with Siemens to begin with, if I had wanted to . . .

GRAYSON: If you wanted to make money.

HILLENKAMP: Make more money. I never regretted this, I must say.

GRAYSON: So you've at least a lot of experience with patents, and . . .

HILLENKAMP: Oh, [Yes]. I find it very hard to spend the time writing patents or just reading them, correcting mistakes that the patent lawyer makes. It has never been one of my favorite jobs. Particularly, now with Sequenom, they have a lot of patents, and I'm on some of them. In this field, and maybe it's not only in this field, patents have something like two hundred claims or so.

GRAYSON: Oh, yes.

HILLENKAMP: Oh, it's awful. It's awful. So I think there is no golden rule how to go about it.

GRAYSON: I think it's a lot of work for any person, and a few, very small number, actually benefit to a large degree. That's the sense that I've gotten. But for most people, it's just really not worth the effort. It's just . . .

HILLENKAMP: [Yes], right. [Yes]. I would agree with that. [Yes].

GRAYSON: The problem is you don't know which is going to be the one that turns into the big producer of gold.

HILLENKAMP: Right. But to the best of my knowledge, almost no university, not in Germany, not in the US that, they own the patents, make a breakeven between the people they employ to take care of the patents, and the royalties they have as an income. On the other hand, I mean, it is a valid argument that if you want something important for society to be available to society, you have to find a commercial partner. And a commercial partner needs protection.

So it's not just that people are after the money. That's the way, at least, I rationalize that even though all the money I ever had for my research was tax money. I did give something back to society by inventing a method that was useful.

GRAYSON: [Yes], very useful. I think everyone's pretty much in agreement with that. I don't know . . .

HILLENKAMP: Is there anything else that we . . .

GRAYSON: Well, I think we've covered everything on my list. I mean, we talked about quite a bit of this. Funding issues, and talked about a lot about your collaborators.

Obviously I think . . . it's my impression—I don't know how you feel about this—but it's my impression that many people in the mass spec community feel that the work that was done for MALDI was more . . . should have been more recognized by the Nobel committee than the work that was done by Tanaka.

HILLENKAMP: [Yes]. I mean, this is, of course, a difficult issue. I forgot about it. [Yes]. We mentioned Tanaka one or two times.

GRAYSON: [Yes]. <**T: 175 min**>

HILLENKAMP: Let me first of all say, Tanaka and I are not friends, but we are colleagues that respect each other. Certainly, the decision of the Nobel committee wasn't Tanaka's fault.

GRAYSON: No.

HILLENKAMP: We just were lucky enough to be considered. That's number one. Number two, it is true for publications and research proposals as well, there is a certain point to which you can drive your own work, and be responsible for the negatives and positives of it.

In other words, to be considered by the Nobel Committee—and I know that we were in the game, of course—that is a fruit of our work. But the final decision or the final review by reviewers is something else. There are other factors that go in that you have no influence on. I think we got as far as we could get based on our work. Then the Nobel committee, of course, made a decision that most people in mass spectrometry actually found very hard to understand. In fact, I would rather than talk about it myself, this is a letter that Peter Roepstorff wrote to the Nobel committee. He was invited to the ceremony.

GRAYSON: So it was chemistry that . . .

HILLENKAMP: It was chemistry.

GRAYSON: Okay.

HILLENKAMP: It was chemistry. Oh, yes.

GRAYSON: So the Nobel Committee receives nominations, is that correct?

HILLENKAMP: The Nobel Committee receives nominations. Then, I think the whole group of the Swedish Royal Academy of Sciences decides early on on a general field.

GRAYSON: Okay.

HILLENKAMP: So in that year, analytical methods in chemistry were decided a field because half of the prize went for NMR.

GRAYSON: Right.

HILLENKAMP: As you remember. Then, there's a small committee of six people or so, who really looks into the situation and suggests a list of names to the plenary session of the Royal Academy. So that's the way it goes. This [Peter Roepstoff's letter] was sent to the chairman of this eight-person committee or so. [Astrid] Gräslund and some other people.

They, of course, once they narrow their search on a few people, then they ask experts for their opinion. Peter was one of the ones who was asked and you can read that from this letter.

GRAYSON: I see we had something that's left out.

HILLENKAMP: [Yes], [Yes]. That was a bit too confidential and we won't share that with you.

GRAYSON: [Yes], sure.

HILLENKAMP: Which I think is very proper.

GRAYSON: [Yes]. That's . . . you know, I agree <**T: 180 min**>. So he actually did not go to the 2002 Nobel ceremony.

HILLENKAMP: No. He didn't go. Someone, and there's good reason to believe that it was one from the inner circle of the Nobel organization, slipped this letter to the *Aftonbladet*, the main daily newspaper in Sweden. This created a huge response all over the world. [Yes]. I mean, that didn't give us the Nobel Prize and the million euros. It would have been nice to have over half a million . . .

GRAYSON: [Yes].

HILLENKAMP: I don't know. But well, there's an email I want to show to you. This is from one of my friends at Wellman. It's very short. [Yes].

e-mail of Dr. Rob Webb, a colleague at the Wellman Center for Photomedicine, Boston.

Franz,

I can only say that you join a distinguished group of scientists who "ought to have gotten the prize". I won't list them (too long), but I think it perhaps better to be among them than among those who "ought not to have gotten the prize". of course, it would be best to be among those who deserved it and got it!

I am honored to have known you before this event, and to continue to benefit from your advice to all of us.

And I'm sorry.

Rob

GRAYSON: [Yes]. Are these for my file, these letters?

HILLENKAMP: [Yes], if you want them.

GRAYSON: [Yes].

HILLENKAMP: [Yes], sure.

GRAYSON: That's great.

HILLENKAMP: Of course, Peter's letter is confidential.

GRAYSON: Sure, okay.

HILLENKAMP: That should not anywhere appear in public.

GRAYSON: Okay. [Yes]. CHF is very sensitive to making sure that materials . . . nothing that is said here will be . . . the only people that will know about it are the two of us, the transcriber, the person who actually types it. They have no clue as to what's on it.

HILLENKAMP: Right. No, no. I understand that. But with particular, I don't want . . .

GRAYSON: [Yes]. I think for the record, I'll . . . it would be good to have it in the CHF file.

HILLENKAMP: Okay. You can imagine, I got tons of emails in that time. I couldn't answer every one of them separately, so I had a general letter that you can also have in your files.

GRAYSON: Very good.

HILLENKAMP: You know, I have known two people who felt that they should have gotten the Nobel Prize and didn't get it. Both of them wound up as alcoholics, and both of them died at a relatively early age. I lucked out. It didn't really touch me so much. Honestly, I didn't expect that this would make, the MALDI, to the Nobel Prize. Though I must say that, afterwards, when I looked at the list of Nobel Prizes more prizes were awarded to methods than, like PCR, or the solid phase synthesis method [Robert Bruce Merrifield, Chemistry, 1984] to make peptides, than to basic principles.

So it wasn't . . . later on when I thought about it, but before then I didn't think it was . . . I didn't expect it. Later on, I thought if you take electrospray and MALDI together, what impact this has on our society, on medicine, on biology, on our understanding of the world it is . . .

GRAYSON: Significant.

HILLENKAMP: A big . . . it is a significant impact. So I think that they nominated this field, it was quite okay. Why they gave it to Tanaka, nobody <**T: 185 min**> has a clue. There are theories about it that I don't want to go into. None of them is very pleasant, let's say. I met Gräslund at a conference once and she made sure she didn't bump into me. It was at a summer school actually in Croatia. I think it's fair to say, it was a wrong decision.

GRAYSON: I think so.

HILLENKAMP: I mean, you know, we published earlier by two years. The whole principle . . . it's true. If we would have tried trypsin, let say, at that time, we surely would have gotten a spectrum, and that would most probably have done it. But you know that wasn't my approach to science. I was interested in the mechanisms, and we looked at that.

GRAYSON: Sure. You were following a logical . . .

HILLENKAMP: [Yes], a logical . . .

GRAYSON: Research agenda to try to understand what was going on. The whole idea of just kind of waving this big flag, like the *New York Times* guy, you know . . .

HILLENKAMP: Right. So of course, one reason is that they have never, never, ever divided the Nobel Prize up among more than three people. So that may have been . . . but you know, then they should have left it out. You can't pick the wrong one only because he's a single person.

GRAYSON: Well, I mean, obviously, as you say there's a number of people . . . a number of instances where people think that they really made a mistake. I mean, there's that classic case of the woman astronomer [Jocelyn Bell Burnell] who did all this work . . .

HILLENKAMP: [Yes], and the DNA double helix, all the crystallography, which was the basis for [James] Watson and [Francis] Crick to think up the structure, who I always forget her name [Rosalind Franklin]. But by the time that they got the Nobel Prize, she was already dead. She died of cancer. But it's . . .

GRAYSON: Those people are known. Whether they get the Prize or not, they're known.

HILLENKAMP: Right.

GRAYSON: Okay, and most . . .

HILLENKAMP: No. It didn't bother me all that much. After a couple of months it was over, and I went on with my job and enjoyed life, and enjoyed science.

GRAYSON: So you've met Tanaka, obviously.

HILLENKAMP: Oh, [yes]. I met him four or five times, at ASMS, for example, and we certainly chatted with each other then. When I was at the meeting of the Japanese Mass Spectrometry Society a couple, few years ago, he invited me to his laboratory. That's when we went to see the geisha house, and had some fun there.

As I said, we are colleagues. We respect each other. We are not friends, but even if the Nobel thing wouldn't have happened, we would never have been friends, because he's a very different character. He's very introverted. [. . .]

GRAYSON: [Yes].

HILLENKAMP: So it's not a major issue . . .

GRAYSON: It's something that has happened, and it's an interesting part of reality, of the real world. I think your attitude is a good attitude. I assume Michael Karas feels the same way . . .

HILLENKAMP: Well, for him it was worse, because he was much younger, and he still had much more of a career in front of him. There, of course, the Nobel Prize would help a lot.

GRAYSON: Oh, [yes].

HILLENKAMP: That is certainly true. It was certainly worse for him. But what can you do? What I at times have been wondering about is whether the committee, like, the Nobel Committee, why don't they have the grandeur to later on admit that they made a mistake. It's . . . we all make mistakes at times.

GRAYSON: Oh, yes. [Yes].

HILLENKAMP: I told you several things happened in my career where we did something, and sometimes it turns out to be wrong <**T: 190 min**>. My hopes for the role of MALDI in DNA, RNA, analysis didn't really, come true for good reasons. Sometimes we did the right thing, for the wrong argument. Why can't a committee like that admit. It was . . . Peter Roepstorff wrote a letter, but several others, like Cathy Costello, who was at that time president of the ASMS, wrote a letter to the Nobel Committee, as a result of which she had a very difficult time with Catherine Fenselau and Bob Cotter. [. . .] I don't think that it was proper that the Nobel Prize committee asked them for a review. That was just not proper. But then, Catherine blamed Cathy for writing this letter in the name of ASMS and not having asked them.

So it's gone and over.

GRAYSON: Okay. Well, I think it's something that we . . . as long as you're comfortable discussing it, I think it's something that should be part of our discussion.

HILLENKAMP: [Yes], it's okay. [Yes]. No, no. I'm perfectly at ease . . .

GRAYSON: You'll get a chance to look through his and decide if you want to strike anything you've said, and that's perfectly fine and up to you.

[END OF AUDIO, FILE 1.2]

[END OF INTERVIEW]

INDEX