SCIENCE HISTORY INSTITUTE

RONALD D. MACFARLANE

Transcript of an Interview
Conducted by

Michael A. Grayson

at

Texas A&M University
College Station, Texas

on

26 May 2011

(With Subsequent Corrections and Additions)

Ronald D. Macfarlane

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.

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RONALD D. MACFARLANE

1933 Born in Buffalo, New York, on 21 February

Education

1954 BA, University of Buffalo, Chemistry
1957 MS, Carnegie Institute of Technology, Chemistry
1959 PhD, Carnegie Institute of Technology, Chemistry

Professional Experience

University of California, Lawrence Berkeley Laboratory
1959-1962 Postdoctoral Fellow

McMaster University
1962-1965 Assistant Professor of Chemistry
1965-1967 Associate Professor of Chemistry

Texas A&M University
1967-2008 Professor of Chemistry
2008-present University Distinguished Professor

Honors

1969 J. Simon Guggenheim Fellow, Niels Bohr Institute, Copenhagen
1974 Visiting Faculty, Center for Nuclear Research, Strasbourg, France
1974 Visiting Faculty, Phillips University, Marburg, Germany
1981 Visiting Faculty, University of Uppsala, Sweden
1982 University of Paris, Orsay, France
1984 Texas A&M Faculty Distinguished Achievement Award for Research
1989 American Chemical Society Award in Nuclear Chemistry
1991 American Society for Mass Spectrometry Distinguished Achievement Award (Inaugural Award)

ABSTRACT

Ronald Macfarlane was born in Buffalo, New York, the oldest of three children. An excellent teacher in high school sparked his interest in chemistry, and Macfarlane attended the University of Buffalo, majoring in analytical chemistry. He found coursework rather boring, but relished exciting summer jobs in chemical industries. Nuclear chemistry was just getting started, and Macfarlane entered Carnegie Institute of Technology for a PhD. In Truman Kohman's lab, he researched natural radioactivity. He made a kind of giant Geiger counter, which he published to international praise. Next, he accepted a postdoctoral position at Lawrence Berkeley National Laboratory, working on alpha activity in rare earth elements. After accidentally creating a more efficient way to get ionized particles; he discovered new isotopes for years, saving his discoveries for later publication.

Macfarlane accepted a job at McMaster University. There, he named his accidental creation the "helium jet recoil method" and began publishing data he'd stored up. He visited the Soviet Union, where he met John McIntyre, a physics professor at Texas A&M University. Months later, Arthur Martell, chairman of the new chemistry department at Texas A&M, called to recruit Macfarlane, and he took up a full professorship there.

The Atomic Energy Commission funded Macfarlane's nuclear work for a while but ceased after an incidental discovery during one of his nuclear chemistry experiments led to what became known as ^{252}californium plasma desorption mass spectrometry. Macfarlane left the nuclear chemistry field to concentrate on mass spectrometry. He spent fifteen years developing the method that was the first to characterize the mass of large, fragile biomolecules—a method that quickly became well known and widely used to characterize a wide spectrum of biomolecules especially in the pharmacy and medicine fields. Early in the course of the discovery, he obtained National Institutes of Health funding to develop and expand the methodology. As one discovery led to another, his focus drilled down to another new field involving characterization of unusual lipids. He believed in "letting nature tell [a person] what is going on;" this approach has led to his interest in trying to determine who has cardiovascular disease and which components of his or her lipid profile contribute to the disease. One of the most important discoveries involved the characterization of an atherogenic type of the good cholesterol associated with APOC-1 (apolipoprotein C1), using both mass spectrometry and some of the novel platforms his lab developed to characterize lipoproteins.

At the time of this interview, Macfarlane, age seventy-eight, was still unready to retire. Having thrown out the textbook in favor of his own "commentaries," he continued to teach analytical chemistry his way, incorporating constructivism, conceptual learning, and other elements of educational psychology. Using blood samples from actual patients Macfarlane continued his work on cardiovascular disease. He believes that a person should contribute to the betterment of society, which he thinks he has done. His work, which has received nearly continuous funding, has straddled the boundary between applied and pure science, and he has always wished he could return to "real science." Macfarlane concludes the interview by saying that his colleagues over the years have been supportive and gracious; most of his collaborations have worked equitably; he has tried to mentor his students while fostering their own creativity. Macfarlane's advice to young scientists is to listen to nature and to pay attention to small details.

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.

ABOUT THIS TRANSCRIPT

This interview was conducted as part of the Mass Spectrometry Oral History project, a collaboration between the Science History Institute and the American Society for Mass Spectrometry. The Mass Spectrometry Oral History project records the human dimensions of the growth of mass spectrometry in academic, industrial, and governmental laboratories during the twentieth century.

The Center for Oral History, Science History Institute, is committed both to preserving the recording of each oral history interview in our collection and to enhancing research use of the interviews by preparing carefully edited transcripts of those recordings. The preparation of interview transcripts begins with the creation of a verbatim typescript of the recording and proceeds through review and editing by staff of the Center; interviewees also review the typescript and can request additions, deletions, or that sections be sealed for specified periods of time. We have established guidelines to help us maintain fidelity to the language and meaning of each recorded interview while making minor editorial adjustments for clarity and readability. Wherever possible, we supply the full names of people, organizations, or geographical locations mentioned during the interview. We add footnotes to the transcript to provide full citations for any publications that are discussed, to point to extant oral history interviews, and to clear up misstatements or provide context for ambiguous references in the transcript. We use brackets to indicate the addition of material that was not in the audio, and bracketed ellipses to indicate the deletion of recorded material. The transcript also includes time stamps at five-minute intervals. We omit without noting most instances of verbal crutches and all instances of nonlexical utterances. We also make small grammatical corrections where necessary to communicate interview participants' meaning. Finally, staff of the Center create the abstract, chronology, table of contents and index.

Audio quality, particularly of the interviewee as opposed to the interviewer, is noticeably poor overall, and some portions are inaudible.

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INTERVIEWER: **Michael A. Grayson**

LOCATION: **Texas A&M University, College Station, Texas**

DATE: **26 May 2011**

GRAYSON: So, I'm going to start the way we usually do by saying, my name is Mike Grayson, and I'm sitting in the office of Professor Ron Macfarlane in Texas A&M University in College Station, Texas. Today is 26 May 2011. A nice pleasant day, but it'll get warm before everything's over. So, we're going to do a little oral history interview of Ron's career. Normally, we like to start these back in the beginning of time, so do we have information on your birthdate and location? I don't think so.

MACFARLANE: No.

GRAYSON: So when were you born?

MACFARLANE: Nineteen thirty-three, 21 February, in Buffalo, New York.

GRAYSON: Okay. So you're a real transplant to this part of the country.

MACFARLANE: That's right.

GRAYSON: And your parents' names?

MACFARLANE: William Arthur MacFarlane and Margaret Ann Baker.

GRAYSON: Okay. Were there any other children in the family, or you were . . . ?

MACFARLANE: Yes. I was the oldest. I have a brother and a sister.

GRAYSON: In the beginning you obviously had developed an interest in science somewhere along the way . . .

MACFARLANE: [Yes], right.

GRAYSON: So, a little bit about your education—well, how about your parents' education? Were they very well educated?

MACFARLANE: No, they weren't. They came through the Depression.

GRAYSON: Ah, okay.

MACFARLANE: And so neither one of them had a college education. In fact, I think my dad went to high school. I'm not for sure about my mom. My mother was born in Virginia—Richmond, Virginia. My father was Canadian.

GRAYSON: Oh, okay.

MACFARLANE: He came down to Buffalo to look for work during the Depression. That's where they met, in Buffalo.

GRAYSON: I see.

MACFARLANE: They settled there, and that's where the family started. Then I went to a public school there, and then I went to high school—Kensington High School.

GRAYSON: Is that Kensington, did you say?

MACFARLANE: Kensington High School, [yes]. And in retrospect—I'll just put in some things that, in retrospect, had an influence on the direction of my career.

GRAYSON: [Yes].

MACFARLANE: When I was in grammar school, I was the weakling in the class. I was the—I didn't have a whole lot of self-confidence. I was physically not very strong, so I had a really bad image of myself. And even then what my mother said, "Ron, you are going to go to college. You don't have any options. You're not going to go through the kind of financial life that we've gone through, and so as soon as you reach the age of twelve, you're going to start getting a job and getting income."

GRAYSON: Oh, my, twelve. Child labor. [laughter]

MACFARLANE: And so the job I got was, I was a newspaper deliverer. And to start out, you get a relatively modest newspaper route, but it was on the fringe of Buffalo. That area actually grew to a point where it was now a major newspaper route, so very quickly I lost my timidity, and became self-confident, and did a lot of daydreaming. That's where I got used to daydreaming, because I had a lot of walking in the winter snows and all this sort of stuff. I had fantasy-type things—like, how could I make my job better? I was fascinated by what I saw in department stores, where they had these pneumatic tubes. If I had a set of pneumatic tubes, I could just put the newspapers in the pneumatic tubes. I said it'd make my life a lot easier. Those are the kinds of mental games I would play. But I found that this was something I was used to. I liked my brain. So when my parents got me a chemistry set for Christmas, for reasons I don't really know—

GRAYSON: Do you know how old you were at the time?

MACFARLANE: Well, I was probably in sixth grade or so. I would say probably around ten. It was their idea, because I didn't request it, but I thought it was very fascinating. I was really interested to the point where they actually set up a laboratory for me in the basement, complete with a Bunsen burner.

GRAYSON: That was pretty gutsy.

MACFARLANE: I know it. [laughter] Then furthermore, there was a chemical supply company in Buffalo. I could buy anything that I wanted. If I wanted ten pounds of sodium cyanide, I could get it. So <**T: 05 min**> my favorite thing was getting metallic sodium.

GRAYSON: Oh, [yes].

MACFARLANE: Boom. And I developed a circle of friends that also got interested in chemistry. We would get together and do weird things to the point where it's amazing we're still alive. We got into making pipe bombs.

GRAYSON: I can hardly imagine at that age being able to buy unlimited quantities of . . .

MACFARLANE: I know it. So, we made pipe bombs. We blew those things up, and except for one day, we were making a pipe bomb in the garage of one of my friends, and it fell off the table and exploded, and shrapnel all over the place, and not one of us with a scratch.

GRAYSON: Oh, wow.

MACFARLANE: We said, "Okay, that's a message." And we stopped that.

GRAYSON: You got the word there.

MACFARLANE: But then when I went to high school, I had a formal chemistry class, and a wonderful chemistry teacher by the name of Angelo Gianturco, and [I] brought my yearbook with me. That shows me in the chemistry class with another student. He really took a special interest in me.

GRAYSON: How do you spell the last name?

MACFARLANE: Gianturco, G-I-A-N-T-U-R-C-O. I can give you a copy of this if you want. But he was the one that actually, he put a face on chemistry. He made it a human thing. He encouraged me to continue with it, and do experiments outside the lab.

GRAYSON: See, I think that's kind of what we're trying to do with this oral history program is to, you know, get people down from their pedestals that they get put on by everybody else, because, oh, you know this guy is famous, he did all this wonderful stuff. But, you know, he used to be a human being, and has really interesting things going on . . . .

MACFARLANE: So then my love for chemistry really blossomed, and to the point where I actually started going to the library and getting chemistry books. I could understand inorganic chemistry. Organic chemistry didn't make any sense at all. You had the carbon, hydrogen doing all these things. So I remember going to the library to try to figure out, what is there about organic chemistry?

Then, when I graduated from high school, I went to the University of Buffalo and that was within walking distance of home, too. That was a big deal, because I—because of the financial situation, I could not afford to really think about that, so just I turned left, I turn right when I went to college.

GRAYSON: Is that a private school or public?

MACFARLANE: Private school at that time. Now it's a state university, University at Buffalo, The State University of New York [. . .] or something like that.

GRAYSON: So they charged tuition, I guess.

MACFARLANE: [Yes], but that was okay. By the time I graduated from high school, I had fifteen hundred dollars in the bank from being a paperboy.

GRAYSON: For how many years now? That must have been about . . . .

MACFARLANE: It was four years.

GRAYSON: Oh, wow, okay.

MACFARLANE: And so I applied for a scholarship, and they said, "Well, how much money do you have in the bank?" I said, "Fifteen hundred dollars." "Oh, you have too much money, you are not eligible."

GRAYSON: Even then?

MACFARLANE: I said, "I worked my butt off for four years." Somebody who went to play during high school, they were able to get a scholarship. So that was one lesson learned.

Anyway, I could control it . . . because in fact, I was looking at the bank book this morning, my parents gave it to me, and I could see where we started then. Two hundred fifty dollars a semester was the tuition. So I was disappointed though, with the chemistry courses, because there was a lot of memorization stuff, and it wasn't . . . the beauty of it that I got from Gianturco, was not there. It was just go to the blackboard, and textbook, and memorize the facts.

But fortunately, in the summer I had summer jobs, and they were always—the four times I did that, they were in companies that had a big chemistry department. The first one was in a company that converted coal into coke, and they'd recover the chemicals, the petrochemicals like pyridine, and benzene, and all that sort of stuff. I was in an analytical lab, but I was able to every once in a while visit the chemistry lab and see what was going on. That was my first exposure to chemistry outside the classroom. I said, "This is really what I want to do." Then the subsequent years, I worked at a company that made foam rubber, where the latex would come in on a tank car, and they convert that milk into foam rubber. That was in the analytical chemistry lab.

GRAYSON: Would this be like in early 1950s?

MACFARLANE: [Yes], early 1950s.

GRAYSON: Okay. What was the name of the first company that was . . . ?

MACFARLANE: The first company was the <**T: 10 min**> Donner Hanna—

GRAYSON: I'm sorry.

MACFARLANE: That's the company, coal company. Then [. . .] the second company made the foam rubber. I don't remember the name of that one. But then the third time, the third summer, I was at a company that was making plastics called Durez [Plastics]. It was part of the Union Carbide. There again, I was in the analytical lab and making polymers, and it was really fascinating. I said, "This is really what I want to do." My mother in particular was very excited about that, because she could see me getting a job in an industry after I graduated.

GRAYSON: So what were they making in this—

MACFARLANE: I think they were making—

GRAYSON: You said something resin.

MACFARLANE: Well, they were making [the] stuff telephones are made of. Bakelite.

GRAYSON: Ah, okay.

MACFARLANE: [Yes], phenolics.

GRAYSON: Phenolics of some kind, okay.

MACFARLANE: Okay, so I got more exposure to industrial chemistry. Then I became aware of who had the most interesting jobs, and who were the supervisors. They all had advanced degrees. I never even thought about taking anything beyond a bachelor's degree. So then I looked into this, and they said, "Well, yeah, if you really want to do more than being a technician, you have to have an advanced degree." I mentioned that to my mother, and she hit the roof. "No. Don't tell me this. Not four more years."

But I became convinced that—first of all, I was still very independent at that point. I knew I did not want any supervisor, and there weren't many jobs where you don't have a supervisor. I didn't know where I was going on this, but I knew I needed more time. So I told mom, I said, "I really want to go to graduate school. Plus they pay you . . ." "Okay, then, that's okay. We'll let them worry about that."

Now, the fourth year, I was really—and I was still at the University of Buffalo. I had pretty well soured on chemistry, because of the courses. There was a new professor came in in nuclear chemistry. I was fascinated by that, because it was the first time . . . I didn't even know the field existed. It was a field that mixed together chemistry, and physics, and instrumentation, and computers, even at that time. I thought this felt like this is going to be the future of science. So I applied to—the leading university at that time, was MIT [Massachusetts Institute of Technology]. A fellow nuclear chemist there by the name of Charles [D.] Coryell, and he came from the Manhattan Project. You know, at that time they were making the atomic bomb. And my grades weren't good enough. I didn't make it into MIT, but Carnegie Tech [now Carnegie Mellon University]—it was called Carnegie Institute of Technology at the time. They did accept me. Truman [P.] Kohman was a nuclear chemist at that time. So then I went to Carnegie Tech, [. . .] and I joined his group. His big deal was natural radioactivity. He was looking at meteorites and the radioactivity boost by cosmic rays. There was also some of the elements of the periodic table and isotopes that were radioactive. I thought that was pretty cool. Like gadolinium was one of them and hafnium is another one.

GRAYSON: What was that first one again?

MACFARLANE: Gadolinium. So he said, "Why don't you look at that?" I said okay. What you do is you take a small sample—a few micrograms of material. You put it on a photographic plate. You let it sit for a couple of months. Then after that, you develop it, and you see tracks through the alpha particles. You count the tracks. After a couple of months of that I thought, "This sucks." I said to Dr. Kohman, I said, "There's got to be a better way to do this." "What do you have in mind?" I thought about what the problem is: "There's not enough material there. I need to have a detector that I can put more material in." "What do you have in mind?" I said, "Well, a giant Geiger counter." I said, "Something this big." Here again, it was the daydreaming part. So to my amazement, he said, "Go for it."

GRAYSON: Oh, wow, okay.

MACFARLANE: "I'll fund it and you go into it." So I spent the next three years putting this together.

GRAYSON: So this was an improvement to the existing technology—

MACFARLANE: That's right—

GRAYSON: —for your particular problem. So I <**T: 15 min**> guess the disintegrations that were occurring were at such a slow rate—

MACFARLANE: That's right. The half-lives were like ten to fifteen years.

GRAYSON: Oh, okay.

MACFARLANE: So, I got the darn thing working, and I remember he had an electrical engineer in his group. He said, "I'd be willing to help you." I said, "I don't want any help." It was at a time where you didn't have electronics, you had to build your own electronics. So I did that. I learned how to do that. I built my own electronics. This engineer did it. He developed what's called pulse-height analyzer. I used that. I showed Dr. Kohman that the thing really works. He was very excited about that. He said, "Well, go for it." My thesis then was on that,

and I made some discoveries. So I got a thesis out of that. It was published in *Physical Review*.[1] He got all sorts of letters of congratulations from colleagues around the world. I never thought about science being international. I thought this is really cool. He showed it to me. So then I realized the instrument that I had, nobody else has. I had the whole field to myself.

GRAYSON: You had developed something that was unique.

MACFARLANE: [Yes].

GRAYSON: How did you [. . .] get the super Geiger counter? I mean, what's the secret to it?

MACFARLANE: Well, first of all, it was a big cylinder. It was about that long and about that diameter. I had sheets of copper that I could—I had a way of actually putting a solution of the sample on a trough. Then I would slowly rotate the sheet, while there was a heat lamp on it. So that way, I got a uniform distribution of that on the cylinder. In the literature there was a different kind of Geiger counter called a proportional counter—

GRAYSON: The what?

MACFARLANE: Proportional counter—

GRAYSON: Oh, proportional counter.

MACFARLANE: —which consisted of a cylinder with a wire going down the middle. So then in a vacuum an alpha particle—not a total vacuum. The alpha particle goes out, it ionizes the gas in the proportional counter, and the electrons are attracted to this wire, which is positively charged. [fingers snapping] It produces an electronic pulse. So I count them. Also the magnitude of the pulse is proportionate to the energy of the alpha particles. So I was able to use the spectrum—energy spectrum—of the alpha particles.

GRAYSON: And so this is just a really basic, scaled-up concept of a different, smaller version of—

[1] R. D. Macfarlane. "Natural Alpha Radioactivity in Medium-Heavy Elements," *Physical Review* 121 (1961): 1758-1769.

MACFARLANE: [Yes]. Right

GRAYSON: —that had been created by somebody. But it was good for you.

MACFARLANE: Right. But it not only counts the particles, it tells you what the energy of the alpha particles is. And so there was one isotope of samarium that was well known—samarium-147. I put that on there, and they just lit up. It was unbelievable. I counted the sensitivity of the [. . .] at that time.

I was also a TA. I got an exposure to actually doing some teaching. I realized this is something that it's a possibility that I want to stay in academia, and because I was reasonably good at it, but I need more time. So then I told Dr. Kohman, "I think I'd like to take a postdoctoral appointment. I need a little bit more time to figure out what I want to do."

GRAYSON: Well, did you tell your mother that too? [laughter]

MACFARLANE: Well, at this point, she was very happy, and particularly when I got my Ph.D. She was on a cloud. She sent an article to the Buffalo newspaper and a picture and all sorts of stuff. I didn't know this, but after she died I found a scrapbook with all of this in it.

GRAYSON: Oh, wow, okay.

MACFARLANE: I asked Dr. Kohman. I said, "Where should I go?" He said, "Well, the best place is [University of California] Berkeley. Lawrence [Berkeley National Laboratory] Radiation Laboratory. A good friend of mine is Glen [T.] Seaborg."

GRAYSON: Oh, wow.

MACFARLANE: He was a Nobel Laureate [Chemistry, 1951] and all that stuff. So I applied, and he sent a support letter, and I got accepted. So then I arrived at Lawrence Berkeley Laboratory, that's the mecca for nuclear chemistry. I arrived and I said to Dr. Seaborg, "Well, what do you want me to do?" <**T: 20 min**> He says, "Anything you want to. This is a lab . . . whatever you want to do." I did not anticipate this. [laughter]

GRAYSON: No. But I mean, you know, by this time you've got your PhD, so you should be able to come up with independent research.

MACFARLANE: That's right. But here again, I was driven by I don't want to have competition, so then I look at what they had, and they had just developed a new kind of accelerator that could accelerate heavy ions. So I said, now this is a possibility, because this is the only one in the world. It has that component. I don't have any competition. So I was able to get beam time, and that's also where they were doing stuff, that Dr. Seaborg was part of that.

I looked at what they were doing, and I said, "Well, I'll essentially copy that conceptually"—what they were doing, the nuclear development stuff—"because I want to continue looking at alpha activity in the rare earth elements". It's going to lower neutron deficient isotopes that I could than just for the natural occurring ones. So that meant developing a system that would allow me to measure short-lived active alpha activities. I more or less spun off from what Seaborg's group was doing, which involved actually a thin target where a beam would go through where the nuclear reaction would occur in products would come and they were helium. Then they had an electrode that would attract positive ions to the electrode, a detector that would look at that. So that's what I set up. So then the detector rotates. There's a thin film and I was able to put a negative voltage on that, then the detector—the vacuum occurred. I look through the thin film, and I could detect. And that started . . . didn't really work well, and I was focusing on the reverse. One day, in the middle of the night, I was watching my instruments, then all of a sudden the radioactive ray zoomed up—force of magnitude . . . I called the control. I said, "Stop the beam. I got to go and find out what happened." I went in, and I opened up the lid, and I looked. I saw a thin pinhole had developed. What happened is the helium was rushing through that pinhole and carrying with it these recoils and depositing it on the detector. I said, "Well, this may be a better, more efficient way to do it than using voltages. So I went back. I said, "Turn the beam back on." I had no voltage on, and still the radioactivity was coming through like mad. Positive voltage, negative voltage, it didn't matter.

GRAYSON: So the accidental development of the hole in the film created another, more efficient method of getting your ionized particles—

MACFARLANE: Right, right.

GRAYSON: —to be detected.

MACFARLANE: [Yes].

GRAYSON: Serendipity happens.

MACFARLANE: That's right. So then there's another postdoc [Roger D. Griffioen] that was with me on this, and I said, "Roger, let's push this." I mentioned this to Al [Albert] Ghiorso who was the head of the nuclear development program. I said, "I think we discovered a new way to measure these." He said, "I'm not interested in it. Anything you can do, I can do better."

GRAYSON: So let me get some names here, then. There's Roger's name is . . .

MACFARLANE: Roger Griffioen.

GRAYSON: [. . .] "Better than you," his name was . . . ?

MACFARLANE: Al Ghiorso.

GRAYSON: Oh, okay.

MACFARLANE: [Yes], he's a big wheel. You don't mess with this guy. [. . .] For the next couple of years, Roger and I just began discovering new isotopes left and right. I knew as a postdoc—I didn't even publish while I was there. I was saving up the data.

GRAYSON: So now, when you say you're discovering isotopes, that was because of the development of this new, more sensitive . . .

MACFARLANE: [Yes], we could actually detect and study isotopes that lived for a few milliseconds.

GRAYSON: Okay. Now, you've gone from looking at reactions that took 10^{15} seconds, you know, to things that were in the other end of the spectrum.

MACFARLANE: But, and we also discovered a new region of alpha activity, the fluorine region. We discovered a new form of radioactivity: beta-delayed proton decay. It was a gold mine. Here again, we had no competition. We had the accelerator and we had this instrument.

GRAYSON: And you were saving up this data.

MACFARLANE: [Yes], right <**T: 25 min**>. So, then I was told that—I was there now as a postdoc; I was there from 1959 to 1962. I was told, "You're here for three years, it's time for you to move on." I thought, "Well, I knew that was going to happen." At that time, my wife developed multiple sclerosis.

GRAYSON: Multiple sclerosis.

MACFARLANE: [Yes], that was a real blow to me. Here I am starting off on my career and my wife has this deadly illness. Also at that point, we had two children. So here I'm starting off, trying to find a new job, two young kids, and my wife with MS. I thought, "I've got to move back close to Buffalo. I need to have family support on this." But my mentor had said—at California—had said, "No, you've got to go to a major university. Look. You've done some major stuff here. You can't afford to go to a podunk university." "I'm sorry, but I have to." So I got a job at McMaster University in Hamilton, Ontario, which is fifty miles away from Buffalo. My dad was a Canadian, so I even had relatives in Canada.

GRAYSON: [Yes], I wanted to check about that. So he kept his Canadian citizenship.

MACFARLANE: Well, no, he very quickly became a citizen.

GRAYSON: Became a US citizen.

MACFARLANE: [Yes]. It was a very big thing for him.

GRAYSON: Oh, really?

MACFARLANE: He was so grateful for getting a job, and grateful to FDR [Franklin Delano Roosevelt]. You know, FDR was his savior.

GRAYSON: What kind of work did he end up doing when he . . .

MACFARLANE: Well, he was a bookkeeper.

GRAYSON: Oh, okay.

MACFARLANE: And he developed a new form of bookkeeping that was before computer stuff that they adopted and that, when he retired, they mention this in a plaque which I have. But he really wasn't that interested in higher education. It was my mother that was the driving force on this. He was supportive, but he had a bad feeling about people who had college degrees that he felt they were kind of snooty. He couldn't teach them anything. [laughter]

GRAYSON: [Yes]. Well, I mean, he obviously had some innovative concepts of his own, if he was able to develop this bookkeeping thing. I can see where there's a tendency for people with college degrees to be a little bit dismissive of—which is not good.

MACFARLANE: But anyway, so then I . . .

GRAYSON: So you went to—now you're an American citizen going to Canada.

MACFARLANE: [Yes], right.

GRAYSON: Kind of reflection.

MACFARLANE: And also my wife was welcomed with open arms, and socialized medicine kicked in.

GRAYSON: Ah, okay.

MACFARLANE: And they said, "Don't worry. You're covered for everything." My wife kept getting worse and worse.

GRAYSON: And her name was . . . ?

MACFARLANE: Beverly Frankie was her name. So then by that time, I had published what we called the helium jet recoil method.[2] It caught on big time, internationally. It was adopted by many laboratories. So I started to get invitations then to give talks at international meetings, international laboratories. That was kind of a hoot. Even though I was at McMaster University, the papers were flooding out now, because they were papers I had stored up. McMaster University was amazed I could be publishing and they were giving me peanuts for research, but I was getting papers out of it. They never figured out that that wasn't work that I'd . . . but they had a reactor, though. I started up a research program using a reactor, relatively modest stuff. But at that time, Yale University built a heavy ion accelerator. They invited me to start a research program continuing what I was doing at—

GRAYSON: Berkeley.

MACFARLANE: —Berkeley. But I could still stay as a McMaster faculty. So once a month I can commute with my group, between Yale and Hamilton. So then I . . .

GRAYSON: Did you ever get Ghiorso or whatever to figure out that you were doing something better than he could?

MACFARLANE: Well, let me get to that.

GRAYSON: Okay.

MACFARLANE: So then his major competition for the new element stuff was in Russia. There's a laboratory located in a town outside of Moscow [Russia] called Dubna [Russia]. [. . .] And the head of that program is a fellow by the name of [Georgy Nikolayevich] Flerov. [. . .]

I was invited to give a talk there and they had <**T: 30 min**> . . . this was through a translator. He said, "We have five Macfarlanes working in the group." I said, "What do you mean?" He said, "Well, that's what the instrument is. It's a Macfarlane." I said, "Well, that's kind of cool."

GRAYSON: These are the helium recoil thin film with the pinhole in it?

[2] R. D. Macfarlane, R. A. Gough, N. S. Oakey, and D. F. Torgerson. "The Helium-jet Recoil Transport Method." *Nuclear Instruments and Methods* 73, no. 3 (1969): 285-291.

MACFARLANE: [Yes].

GRAYSON: Wow. [laughter]

MACFARLANE: And by that time, they'd been converted. I don't know if I have examples here. So anyway, he said to me, "Why isn't Ghiorso using your method?" I said one word, "Politics." He understood that. He laughed. He laughed. He laughed. Eventually, Ghiorso got wind of it, and he figured out that, well, "This is what he was doing all the time." So then by that time, I was nominated for the American Chemical Society [Glenn T. Seaborg Award for] Nuclear Chemistry [in 1989]. So they asked me to write a citation. In the citation, I put in it, "that I had discovered the helium jet recoil method." They accepted that and I published it anyway. So eventually . . . he eventually came [around]. He accepted it. But still he, to this day, when people go to his lab, he says, "Well, this is the method I developed.

GRAYSON: So he was doing it all along, but didn't know it.

MACFARLANE: That's right. [Yes], that's what his story was. Well, it was pretty . . . he had it all set up. All you had to do was put a pinhole in the thing he had, so I could see where he was coming from, but the guy was a genius anyway.

So one of the times when I visited to the Soviet Union—

GRAYSON: There was—okay, this is where you were visiting the Soviet Union, probably in a not very pleasant time period.

MACFARLANE: [Yes]. It was during the Cold War.

GRAYSON: Nineteen sixty . . . late 1950s?

MACFARLANE: Let's see, I was still at McMaster. So that was . . .

GRAYSON: Late 1950s, early 1960s . . .

MACFARLANE: It was the early 1960s. So I remember going to the Kremlin and to a concert there and seeing officers from North Korea there.

GRAYSON: Oh, wow.

MACFARLANE: And it was really kind of a . . .

GRAYSON: So did the government give you any grief in doing this travel—the United States government?

MACFARLANE: No. None whatsoever. None whatsoever.

GRAYSON: So you weren't on their radar, in terms of . . . that's probably good.

MACFARLANE: And I was invited by the Soviet Union, so that wasn't a problem there, either.

GRAYSON: What was it like there, when you got—did you get a sense of there's a different, you know, something significantly different in the way people were dealing with their lives?

MACFARLANE: Well, no, because I was interacting with the scientists. I was very naïve. There was one fellow in particular that had been following what I was doing. In fact, his instruments were very similar to mine. I said, "What's it like living behind the Iron Curtain?" He said, "What's the Iron Curtain? I don't know that name."

GRAYSON: What's the Iron Curtain. [laughter]

MACFARLANE: Then I realized how naïve I was. Iron Curtain was a Western term. I couldn't really see anything that indicated there was a problem. They were happy. You know, they had nice stores and stuff. I was just totally—I couldn't really detect anything there was . . .

GRAYSON: So they were getting decent funding for their research?

MACFARLANE: Sure, [Yes]. Well, it was a national lab.

GRAYSON: But it would have been an interesting time to visit Russia, I'm sure.

MACFARLANE: [Yes]. Actually, the fellow that . . . we became good friends. We actually were able to talk philosophically about our different lives and our background, and what turns him on, and all that sort of stuff. So that was a really good thing to experience that. But at one of the talks I gave [in Russia], there was a physics professor from A&M there in the audience. Afterwards he said, "We're building an accelerator here at Texas A&M; would you be interested in joining?" I said, "Well, I don't know, probably not. I'm happy where I am." Then a few months later, I get a phone call from Art [Arthur E.] Martell, saying—this is now in January—he said, "I understand you mentioned to John McIntyre <**T: 35 min**> [you] might be interested in joining our group." I said, "Well, I don't know." "Would you be willing to come down for a visit, and give a talk?" I really wasn't all that interested in Texas. When you're from western New York, Texas—

GRAYSON: [Yes].

MACFARLANE: —is tumbleweeds. I said, "Probably not." But I said, "Well, what's the weather like?" "Well, it's beautiful blue sky, 75 degrees." I looked out, there's a blizzard blowing. I said, "Okay, I'll come down for a visit."

I went down. I spend three days here. I can see the possibility. So, it was really a cow college at that time. It was only men, and so I was not very impressed, but I felt there was a spirit here. Martell was hired by the university to build up a chemistry department like this. [fingers snapping] He had a reputation for this. So he wanted an instant nuclear chemistry. I could see possibilities then for the future. Then I went back and he called me. He said, "Well, are you interested?" I said, "Probably not." He said, "But what would it take to bring you down here?" I had just been promoted to associate professor. I want to get this guy off my back. I said, "Promote me to full professor, and double my salary." He said, "No problem." [laughter]

GRAYSON: There you go. Got to ask the impossible and it's no problem.

MACFARLANE: Then I said, "Well, let me just try it for a year." He said, "Well, that's the best news I've heard from you since I started talking with you." So he says, "Of all the people I've been talking to, you're the one I want the most, for reasons I do not know." But this has been a reoccurring thing that, people pick on something that I'm not aware of. I'm an oddball and they don't know it. To this day, people keep telling me that you're an oddball, but stick with it. I came down with my family . . .

GRAYSON: Nineteen . . . ?

MACFARLANE: This was . . . let's see, 1966, I came down.

GRAYSON: What did McMaster think? Did you ask them if you could go away for a year or something like that?

MACFARLANE: [Yes], leave of absence. Then they said, "[Yes], go for it." I had really close friends there and that was part of what was keeping me there. Academia in Canada is much softer—humane—than academia here in going for your tenure and all that. I came here. I spent a year. I realized that this is really where I wanted to be, and my wife was happy. Because she was getting worse and worse. She said that the temperate climate makes it more comfortable. So that's it. She was a major factor.

GRAYSON: [Yes]. The winters here are definitely . . .

MACFARLANE: [Yes]. And she definitely—she knew that she felt the worst when she was in the wintertime, so that aced it for me. And so then we settled here, and I got involved in the chemistry program. I set up my helium jet method here, and got going on that. Then it was developing into being a mass spectrometrist, because I was interested in measuring the masses and finding masses of these radioactive species, because from there you can get nuclear binding energy.

GRAYSON: So, your technique enabled you to come to the discovery of new isotopes, because you were able to get this very . . . well, they're very short-lived isotopes.

MACFARLANE: [Yes], right.

GRAYSON: But you could only speculate about their mass based on what you were seeing from loss of the particles. Now you're saying, "Well, in order to make it a real discovery, I need to determine the mass of the isotope."

MACFARLANE: Right. [. . .] The experiment was to have the helium jet take the radioactive species to a point where I could skim off the helium, and have a beam of the aerosols containing radioactive particles hit a <**T: 40 min**> thin film. This then in a high vacuum, so then when radioactivity occurs—and I had a detector in back of the thin film that would tell me

radioactivity has occurred—then the recoil from that would fly off, and it would accelerate it compared to the time of flight. The flight tube was very long, because you needed to have a lot of significant figures. This worked beautifully. I was able to get exactly what I wanted.

By then I had a graduate student and a postdoc from Canada working with me on this. Then I noticed in the mass spectra there were peaks that did not correspond to radioactive recoils. We speculated that they must be that the ionizing radiation is ionizing impurities on the surface, but they are being accelerated, and they have the same timing signal as the radioactive one.

GRAYSON: So this is an asynchronous-coincidence type of thing?

MACFARLANE: [Yes], that's right.

GRAYSON: And you knew pretty much from previous work what you would expect to see for peaks in the spectrum from isotopes.

MACFARLANE: Right.

GRAYSON: So when you get something that's not part of what you expect, then you've got to figure out where it's coming from, so you surmised that you were actually ionizing compounds—

MACFARLANE: On the surface.

GRAYSON: That were on the . . . essentially impurities or dirt or what have you.

MACFARLANE: [Yes], that's right.

GRAYSON: And they were behaving, you know, just like your decay particles.

MACFARLANE: [Yes], that's right. And so then what? So after this, I said to the guys, I said, "We got to figure out what's going on here, to prove this is the case." We had a californium source. It's a standard thing when you're nuclear chemists. They use it for calibrations. The

californium source has a neat aspect to it that 5 percent of the reactivity is through a spontaneous fission.

GRAYSON: Five percent?

MACFARLANE: [Yes]. The rest is alpha particles. So then there's a way of electronically distinguishing between alpha particles and fission fragments. When fission occurs, one fission fragment goes this direction, the other goes that direction, so I use that one to start the clock, and then this one to [. . .] ionize it. So then we tried it. The mass spectrum lit up, because the fission fragments are much more ionizing. So it was ionizing the heck out of anything that I put on the screen. So we had a bunch of inorganic things—rare earth oxides. We put that on. We saw mass spectra going for the thousands. I said, "What the devil's going on here?" I said, "We better go to the literature to find out what people are doing in mass spectrometry." [laughter] There was nothing about high-molecular-weight mass spectrometry. So there's still a curiosity that I thought, well . . .

GRAYSON: These experiments you're doing in the late 1960s?

MACFARLANE: [Yes], that's right, the late 1960s, and the early 1970s. So I said, "What happens if we put a biological molecule on the surface?" I said, "Well, amino acids, aren't they biologically active?" I said [to the graduate student], "Why don't you go to the biology storeroom and get some amino acids?" He came back. He said, "Well, they come in twenty-one different flavors."

GRAYSON: They got amino acids. There's a lot of them.

MACFARLANE: Right. So I said, "It doesn't really matter." He went back and got literally two, arginine and cystine. So we then we made a thin film of that, saw beautiful spectra of arginine, cystine, and I said, "Well, that's really nice, you know." So now it's time to go to the literature and find out what people are doing in mass spectrometry on amino acids. And a review article had just come out saying that all the amino acids can be studied by mass spectrometry except for two: cystine and arginine.

GRAYSON: Oh, wow.

MACFARLANE: Because they're too unstable. You try and heat them up and they decompose. [fingers snapping]

GRAYSON: So this was an era when people were officially using electron ionization as the . . .

MACFARLANE: [Yes]. And the field desorption was there as well, [and] the chemical ionization. They had to heat up the sample, and the lore was . . .

GRAYSON: To get it volatile.

MACFARLANE: [Yes]. But it's involatile and you try to heat it up and it decomposes.

GRAYSON: So, well, you just happened to pick the two that didn't work. [laughter]

MACFARLANE: I know. That's right. I mean, even then <**T: 45 min**> it was just a curiosity, because I spent my whole career being a nuclear chemist. This was a deviation. I did not want to be a mass spectroscopist, period. One of my undergraduate researchers went to Stanford [University]. He joined a group there doing natural product research. He mentioned to his professor that a new kind of mass spectrometer was developed at A&M and it was different. It involved radioactivity. He said, "Like what? What is it?" Californium. "Well, do you think he'd run a sample for me?" And so I said, "Yes, I would."

He sent me a sample of tetrodotoxin. It was a big deal on naturally occurring toxins. So we ran it and got a beautiful spectrum. It had mass three hundred and twenty and a little peak there. I sent the data back to him. He said, "We're inviting you to Stanford to give a talk."

GRAYSON: Oh, wow. So what did . . . the mass wasn't that high.

MACFARLANE: Three hundred-twenty . . .

GRAYSON: Okay, but it's . . .

MACFARLANE: It was one of these molecules, if you heat it up, it decomposes. He had tried many times—

GRAYSON: To try and get it to the vapor phase.

MACFARLANE: —using field desorption. [Yes], and so I—and Stanford and Berkeley were sort of like competition here. Berkeley is the mecca for nuclear chemistry. Therefore, Stanford doesn't want anything to do with nuclear chemistry, so here I am a nuclear chemist, going to Stanford to give a talk.

GRAYSON: Anybody show up? [laughter]

MACFARLANE: [Yes], they did. Afterwards, my host gave a party for me at his home, and so I really liked that. He took me aside, "Ron, I want to tell you something." He says, "I know you do nuclear chemistry, but I want to tell you something. You've hit on something. We need you. Forget the nuclear chemistry. We need you to develop this method for biomolecules." He had a name for it, a name that organic chemists can remember. I said, "Well, there's field desorption, which to me is the number one thing. Well, what about plasma desorption?" "Okay by me. Can you make it a little bit more interesting?" I said, "What about californium plasma desorption?" Oh, that's fine, great . . .

GRAYSON: There you go, yeah, californium.

MACFARLANE: Californium . . . Stanford. So I said, "Okay." But still, I went back and I said to him that [. . .] when I went to graduate school, I was going to be a nuclear chemist. I really wanted to go to another field, totally unknown, that I don't know anything about it.

GRAYSON: So you were, at this time, what about fifteen years from your PhD?

MACFARLANE: [Yes].

GRAYSON: You already made some significant contributions in your field.

MACFARLANE: That's right, I was already a leader in the field.

GRAYSON: People acknowledged you. I mean, you got enough name recognition that, you know—

MACFARLANE: I was funded by the Atomic Energy Commission.

GRAYSON: —got you here to come to A&M in the middle of nowhere. I mean, how big is that field in terms of . . . it's a new concept to me—nuclear chemistry. Does it have a very large group of people involved in it?

MACFARLANE: Not a whole lot. We have nuclear chemists here. They're struggling, because the nuclear chemists actually were accepted by the nuclear community, because nuclear physicists need to have chemists to separate stuff. That's, again, partly going back to the Manhattan Project, they need to perform chemical separations. The physicists would take the—

GRAYSON: Was that with Otto Hahn? Wasn't he a chemist? [. . .]

MACFARLANE: [Yes], he discovered nuclear fission. Hahn and [Fritz] Strassmann. But then the nuclear chemistry has always been on the fringe, you know, because . . . even here, there's a problem with nuclear chemistry being identified as really being a part of the department. There's a separate building. They don't really, really come to chemistry seminars. They spend most of their time with nuclear physicists.

GRAYSON: Chemistry's becoming biology.

MACFARLANE: [Yes], right. I said, well, if I get funded then maybe then I can do it.

GRAYSON: So most of your funding was probably coming from the Nuclear Atomic Energy Commission, yeah?

MACFARLANE: And so I wrote a proposal to NIH [National Institutes of Health] and NSF [National Science Foundation], thinking maybe one of them might pick it up. I <**T: 50 min**> wasn't even tuned in on the system of the NIH proposals, of their ranking rate from one hundred to five hundred. I just assumed, since they don't know any mass spectrometrists, I'm going to get the lowest score possible, which is one hundred. Sure enough, when the guy called me, he said, "Well, we got your score, you got a hundred." I said I'm not surprised. He said, "What do you mean? That's the best score you can get!" [laughter] "What?" "[Yes], nobody can get any better than that."

GRAYSON: [Yes], the upside down scoring system.

MACFARLANE: That's right. And so then I read the critiques—

GRAYSON: [Yes]. This was NIH, right?

MACFARLANE: —and I remember one of them saying, this guy doesn't know any mass spectrometry, but he's doing stuff that nobody else can do. So, that's what started it. The NSF funded me as well. So now I had two grants. Then the Atomic Energy Commission decided not to fund me anymore, because I wasn't doing nuclear chemistry. But what Seaborg . . . Seaborg, I mentioned him as one of my mentors, because he was very excited that I found a use for californium-252, his baby.

GRAYSON: Oh, okay.

MACFARLANE: What he did was, he actually . . . he became head of the Atomic Energy Commission. One of his presentations to [US] Congress for financial support, he mentioned our project as an example of peaceful uses of atomic energy. Then he was actually . . . behind the scenes had a lot to do with my getting the Guggenheim Fellowship, for example, and promoting my efforts and the use of californium-252 in mass spectrometry. I thought that was a really cool thing to do. [. . .]

GRAYSON: Now, you submitted these proposals, and within the appropriate length of time, they said, "Okay, here's the money."

MACFARLANE: [Yes].

GRAYSON: Wow, that's good.

MACFARLANE: [Yes]. That meant I had to be serious about it, but I didn't . . . it just meant that I was no longer the cyclotron. Then when the word got out, I began publishing stuff, we got flooded by requests from drug companies and from people in natural products. This is now the early 1970s, and for the next fifteen years that was our major activity, running samples for people, which wasn't exactly something that I was happy about. But the feedback I was getting like, "You're the eyes of our research." The drug companies saying, "We can't market anything. The FDA says we have to know the molecular weight of these things before we can market it. And now you're giving it to us."

But at the same time, the mass spectroscopy people didn't really know what to do with me, and so in fact I had a little bit of trouble getting published. I remember the first paper.[3] We wrote a paper on the mass spectrometry of insulin, and it got rejected by the reviewer but accepted by the editor saying, "Our reviewer's wrong." There were a couple of papers that I felt that—well, in retrospect I was rocking the boat. Here's a well-established field. The more important you are, the bigger your magnet is. So the magnetic mass spectrometer was the true . . . if you're really, really serious that was your mass spectrometer.

GRAYSON: Oh, yeah, magnetic sectors ruled.

MACFARLANE: [Yes]. So here we [are], coming along with time-of-flight, which had a bad reputation.

GRAYSON: Oh, yes, definitely.

MACFARLANE: You remember those days? [laughter]

GRAYSON: Oh, [yes]. My first instrument that I worked on when I was on my own was time-of-flight—the Bendix.

MACFARLANE: Bendix, yeah, had a bad reputation, so that was strike one. User inactivity was number two strike, and so the fact that I had to abide by all this work that had been done like, at MIT, derivatizing molecules to make them volatile was no . . .

GRAYSON: [Klaus] Biemann.[4]

MACFARLANE: [Yes], Biemann's group was now not relevant. They took that very badly. But there was a component of the Mass Spectrometry Society [American Society for Mass Spectrometry] that welcomed you with open arms. And I remember shortly after we published <**T: 55 min**> our first paper, *Biochem Biophys Research* column, the president of the Society was a Texan . . .

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[3] P. Haakansson, I. Kamensky, B. Sundqvist, J. Fohlman, P. Peterson, C. J. McNeal, and R. D. Macfarlane, "Iodine-127-plasma Desorption Mass Spectrometry of Insulin," *Journal of the American Chemical Society* 104, no. 10 (1982): 2948-2949.

[4] Klaus Biemann, interview by Michael A. Grayson at Alton Bay, New Hampshire, 29 August 2006 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0279).

GRAYSON: [Yes].

MACFARLANE: Not [Fred W.] McLafferty.[5]

GRAYSON: ASMS?

MACFARLANE: [James A.] McCloskey.[6] He came to visit A&M, and he heard about this weird kind of mass spectrometer and wanted to see it. He said, "You know, our next meeting is in Houston [Texas], in about a month. I'd like you to give a paper there, even though it's past the deadline." I said, well, okay. I went to the meeting and I saw where the field was, and Biemann was there. He'd given an invited paper using field desorption. I asked him, I said, "Is field desorption really the way to go?" He said, "It's the only way. It does everything." Okay. That means there's really no room for anything new.

So my paper was the last paper on the last day, and it was five people in the audience. The only reason they were there is they were waiting for their plane. One of the people was McCloskey. [There's] McLafferty, and Hank Fales. And they were totally silent. They couldn't believe what they were seeing, because I was showing Vitamin B_{12}, and all these complicated molecules. And we didn't think it would ever happen. And Hank Fales said, "Will you build a mass spectrometer for me at NIH?" Which I did. Later on at an ASMS meeting McLafferty took me aside. He says, "Ron." He says, "I was not sure that the californium thing is the way to do it, but you proved it could be done. You broke the psychological barrier." So it was nice to hear that from a guy who was actually the big person in the field. Those guys actually carried the ball for me. They gave me the support—the psychological support—to continue.

GRAYSON: [Yes], well, they were all tuned into the requirement or the necessity of getting larger and more difficult molecules ionized. And it's just . . . I mean, I was living through that period too, at the meetings, and people were trying everything under the sun. Field desorption seemed to me, my recollection is that it was so technique-y. You know, a lab technician could do it, every day. The next guy . . . they couldn't do for love nor money. [laughter]

MACFARLANE: Right. But here again, I didn't really have my heart in it, because I still really wanted to do stuff that was relating to nuclear stuff, or whatever. But I was not happy being essentially a technician.

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[5] Fred W. McLafferty, interview by Michael A. Grayson at Cornell University, Ithaca, New York, 22 and 23 January 2007 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0352).
[6] James A. McCloskey, Jr., interview by Michael A. Grayson at the McCloskeys' Home, Helotes, Texas, 19 and 20 March 2012 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0702).

GRAYSON: [Yes], well, you were running samples for all these people, and they were very grateful, but it's not exactly what you'd planned.

MACFARLANE: But what had happened was that my nuclear physics colleagues caught on to what I was doing. They had all the same instrumentation I had. They had accelerators, and so a whole field grew up where if you got the physics of a process, the electronic excitation . . . So, there were several laboratories in Europe, in particular, that really this became a major thing for them. That instead of looking at inorganic targets, all they were putting proteins and amino acids in front of the beam and accelerators. That field is actually continuing. It's blossomed now, to where they're accelerating ion clusters and getting huge yields of molecular ions, including the proteins. So that's an ongoing field that we would meet once every two years, and discuss the physics of the desorption process.

GRAYSON: So, is this like an informal group meeting of people who are in the . . .

MACFARLANE: Well, it's actually turned out to be . . . it became something that began to grow, because some of the mass spectroscopy people got wind of it, and they began to be part of the audience. Particularly the MALDI [matrix-assisted laser desorption ionization] guys . . .

GRAYSON: [Franz] Hillenkamp.[7] [Michael] Karas . . . .

MACFARLANE: [Yes]. They started coming to the meetings. I said, <**T: 60 min**> "It seems like laser desorption's the way to do this. Why aren't they successful?" They would report results on their negative view. It's not working, blah, blah, blah.

GRAYSON: The whole theory of the paper that they published, where they tried different things.[8] You can see them working their way through the problem.

MACFARLANE: [Yes]. But every time we had a meeting, I was anticipating they were going to come up with [it] and say, "We got it now," that I could back off and get back to my other life.

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

[8] M. Karas, F. Hillenkamp, "Laser Desorption Ionization of Proteins with Molecular Mass Exceeding 10,000 Daltons," A*nalytical Chemistry*, 60, no. 20 (1988): 2299-2301.

GRAYSON: So now this was a sub-meeting of the ASMS?

MACFARLANE: No. ASMS, in fact, they did not like this—these satellite meetings. In fact, [R.] Graham Cooks came down on me once. He said, "Ron, you're competing with us."

GRAYSON: Yes. Was it you that had set up the separate kind of [meeting]?

MACFARLANE: Well, it was because the physicists were uncomfortable with the chemists. The chemists could [not] figure out what the physicists were doing. So there's this natural gap between them, and . . .

GRAYSON: But you needed . . . the information the physicists were developing was useful for you, for . . .

MACFARLANE: For me, but not for the chemists or not for the mass spectrometrists. They could not care less about that.

GRAYSON: [Yes]. But then the mass spec people started coming to the meeting too, because they wanted to see some of the physics going on.

MACFARLANE: [Yes], right.

GRAYSON: The guys were doing that laser work.

MACFARLANE: Right. So that was a weird time. In fact, we had several symposia here. I think I brought in one of our—

GRAYSON: I know ASMS is sensitive to other people messing in the ASMS by or mass spec by . . .

MACFARLANE: [Yes]. But I brought in—

GRAYSON: So these were probably fairly small, informal type of meetings, that you had?

MACFARLANE: Well, but they in interesting places. There'd probably be no more than, I'd say, a hundred people.

GRAYSON: Oh, a hundred, okay.

MACFARLANE: [Yes]. They were held in places like in Brazil—Rio de Janeiro, there was a group there.

GRAYSON: Oh, wow.

MACFARLANE: In Germany, we had several meetings there and they had it in interesting places like castles. We had several meetings here, called the Texas Symposium [on Mass Spectrometry], and there's a series of books that came out of that.[9] My wife, Catherine [J.] McNeal, was organizing those. It was very well attended, people like Cathy [Catherine E.] Costello became part of it. We had a Texas thing that they would . . . there's a little town called Round Top here We'd go there and we had, essentially, the whole town to ourselves. Country line dancing in the streets. I remember that Frank [H.] Field was there with another fellow who was also a violinist from Europe.[10] They were going to put on a concert. So they were worried about, well, how do you . . . what level of sophistication was your technique? They didn't want to be showed up by the other person. Anyway, the human part was there. And Frank Field was very much a part of the this at that time, because he had actually . . . he built a californium system, and he hired one of the nuclear physicists [Brian Chait] to actually set it up and run it. He became a well-known person in his own right.

GRAYSON: Oh, [yes].

MACFARLANE: So that's the way the field evolved.

GRAYSON: But you're still kind of ambivalent about it.

MACFARLANE: [Yes]. Well, because it was not something that was intellectually satisfying for me. Also the field was getting too busy .

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[9] Catherine J. McNeal, ed., *Mass Spectrometry in the Analysis of Large Molecules*, John Wiley & Sons, 1986.
[10] Frank H. Field, interview by Michael A. Grayson at Durham, North Carolina, 9 and 10 December 2009 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0636).

GRAYSON: Did you have graduate students working?

MACFARLANE: Oh, [yes]. We had a whole bunch of papers there that we found little things that we could improve on, and kind of relate to the chemistry of the process, particularly in making the samples and working in the matrices.

GRAYSON: Is it very much a matrix-dependent process?

MACFARLANE: Not really. We thought that when MALDI came along, we had to play with that idea of working in a matrix. We did get some enhancement. There's a very strong group in Uppsala [Sweden] that picked up on the californium stuff, and also they were in accelerated, because they were both. They discovered nitrocellulose was a good matrix for that and you just put a drop of this stuff on, spin it off, and nitrocellulose was a good matrix for that. So that would have been calculated there <**T: 65 min**>.

But then when MALDI and electrospray ionization came along, then I knew that the handwriting was on the wall. I remember when FAB [fast atom bombardment]—FAB was part of it too. I remember when Mickey [Michael] Barber gave one of his first talks, he started off by saying, "I'm going to tell you about a mass spectrometry method that analyzes biomolecules with a *real* mass spectrometer."

GRAYSON: Gotcha. [laughter]

MACFARLANE: [Yes]. So but that was the way that people looked at it. You had to have a magnet, otherwise you weren't part of the club.

GRAYSON: [Yes], right. You weren't a member of the group.

MACFARLANE: So, some years later, I had a chance . . . I was invited to his laboratory. So I said to Mickey, I said, "Now, did our californium stuff have any impact on you?" He says, "Did it ever! It was the carrot that kept us going." He said, "We had a picture of you with a mass spectrum of vitamin B_{12} on our bulletin board."

GRAYSON: Oh, my.

MACFARLANE: "And every day we looked at it, and said, 'Why can't we do that?'" So he played around with matrices and finally figured out how to do it. So I was glad to hear that there was some impact, but nobody would publicly admit to the fact that there was.

GRAYSON: Well, in that original paper that they put out, you know, they showed this ton of compounds that you could do with FAB that, I think, blew everybody away at the time, because like you say, they were using the mass spectrometer.

MACFARLANE: Right, right.

GRAYSON: But the thing is that, you know, I mean he had mass range issues, too. [. . .] I mean they had mass range issues. But at any rate . . .

MACFARLANE: But anyway, I did not like competition. By that time, I said, "What do we do next? I'm too far removed from nuclear chemistry now." Too many things . . .

GRAYSON: [Yes]. Well, you kind of got sidetracked.

MACFARLANE: Right. So, but I was fascinated by the enthusiasm of people that asked for what we were doing from the medical point of view. My wife—my second wife . . . my first wife died when she was thirty-nine years old.

GRAYSON: Oh, my.

MACFARLANE: My second wife, actually, was in my research group before we got married. She's twenty years younger than I am. So by that time, we were married, I said, "Cathy, I think we've got to do something in the spirit of not having any competition." I liked the idea of getting involved with medical research. That was just something that is of obvious benefit to people. "Do you see any possibility that maybe we could . . . all these methods that we have of mass spectrometry, and all the capillary electrophoresis, and all this sort of stuff. What about if we get into medical research as chemists, not as people coming from biology and have a different slant on it?" She thought, "Well, let's talk with some people." This is the dean of the medical school, at UT Galveston and tried talking us out of it as if it's a dumb idea. "You chemists have the right answers to which you have no questions." So it was the fundamental stuff versus the application. He says, "Well, what you've got [to have] in your team, is an MD.

GRAYSON: Is what?

MACFARLANE: MD. So on the way back to Galveston . . . we, now at this point, we had a two-year old daughter and she got sick when we were in Quebec and was hospitalized there and hardly anyone would speak English with us so we were pretty frightened. Cathy said, "I'm never going to be in this situation again and I'm tired of not understanding the medical part of the projects we're working on so I want to go to medical school." I said, "What?" "Well, I know I'm too old. I probably won't get in." I said, "Well, go for it." She applied and was accepted.

GRAYSON: Oh, really. Wow.

MACFARLANE: So that set the stage for the next chapter. She went to medical school. So now, the first thing we've got to do is to is to figure out now—if we still have the californium system—is to figure out where we fit in, and within two months she came home. She said, "[I found the project: my biochem prof said there is this very complex lipoprotein called lipoprotein-a that is very difficult to characterize molecularly and it's important to atherosclerosis." She figured if anyone could characterize large, complex biomolecules, it could be our group.] <**T: 70 min**> I said, "Okay. Let's give it a whirl."

She gave me a few articles, and I looked at it. I quickly figured out that if we could get funded by NIH, who was funding our mass spectrometry part . . . let's see what happens. So I sent a proposal in to NIH, with a thing about applying modern methods of analytical chemistry to [characterize complex lipoproteins], and it got accepted—got funded. So then at that time, I said, "Well, the first thing we do is get rid of our mass spectrometer. I don't want to have it. It's too tough, to fall back." So we dismantled our californium system, totally. I have a table, and there's a hole in it, and that's where the pump was. So then we picked a set of [novel] analytical methods to [characterize lipoproteins] that would give information rich, lend itself to . . .

GRAYSON: I'm sorry, lend itself . . . what . . . ?

MACFARLANE: To clinical testing, if it ever got that far. [Our new tools included density-gradient ultracentrifugation and capillary electrophoresis just to name a few, but ultimately we also circled back to add mass spectrometry.]

GRAYSON: Clinical . . .

MACFARLANE: People. And so now this is where we're at. And the . . .

GRAYSON: This decision to . . . when did you destroy your instrument, what year?

MACFARLANE: It would have been about 1994. But then mass spectrometry came back into the picture, because that was one of the methods we were using to characterize the lipoproteins of serum. The gold standard for characterization of lipoproteins is measuring the density, the distribution of particles, the LDL, HDL, VLDL. We looked at what they were using, and it was a method that was built in the 1960s that involved preparing a sodium bromide solutions layer and then you put the serum in that, and what . . . it might have what they call sequential layering. You can get a distribution of the lipoproteins as a function of their density. It's still a gold standard. It takes forty hours, and stay at room temperature, and there's questions to whether the lipoprotein particle is stable or not. But anyway, that's still the gold standard . . . today it is.

So we said, "That's our first thing to do is to try to improve that." Instead of using sodium bromide, we wanted to use a solute that had a high enough molecular weight that we could actually get a homogeneous solution, spin it, and get a naturally developing gradient. We want it to be something that was of a compact molecule. It was not viscous, because they were using this thing, use sugars for this. So we decided the EDTA [ethylenediaminetetraacetic acid] complexes of metal ions was exactly what we needed. You control the molecular weight of the EDTA complex with metal ions by the counterions.

I came up with that idea that, I asked the student working with sucrose if he'd be willing to check it out. I had to go to a meeting in Washington for that critical time, I said, but if it works just send me an email. The next morning, I checked my email box, and there were two words, "It works." So that's what got us into where we are right now. [. . .] We started publishing in the medical journals. But very, very cautiously, because if I think of the politics of mass spectrometry, it's a capital P, Politics. And there are gurus that whatever they say, is law. If you're not doing what they're doing, you're wasting your time. <**T: 75 min**> We have published some papers. We now have enough that we've been funded again now, a couple of cycles by NIH. I have planned out for the rest of my career—hopefully, there's at least five more years—is to work on developing an accurate screening method [that can be used to characterize lipoproteins, especially unusual atherogenic lipoproteins that's going to be the cause for a person] to develop atherosclerosis. I have posters that I can show.

At the same time, we have a method that from the ultracentrifugation tube, we can slice out fractions, and do chemistry out of like the mass spectrometer. This is an example of a recent article that we feel is a kind of breakthrough in the field. What we want to have now is a way that we can take out the sample of blood, and do tests on it that tell you . . . well, it tells you two things. And again, we're approaching as chemists. So this is something that does not go over well at all with MD's. They tell you that you have to . . . HDL is good, LDL is bad. We took the position now that, again, it's a carryover from our basic philosophy that started when I was in Carnegie. You have an instrument. You have a set of protocols that nobody else has. You have

access to patients. Let nature tell you. I think it really . . . the hypothesis is let nature tell you what's going on.

So, when we started running these [lipoprotein] density profiles, and we got the head of the statistics department here involved. Cathy now is an MD at Scott & White [Healthcare] in the [Division of Cardiology so she had access to patients and] serum samples of people who have known heart disease [as well as the patients who had an angiogram and were free of disease. She selected the patients she was most perplexed by who had heart disease without many conventional risk factors. Using the advanced statistical approaches and our new method for lipoprotein density measurements we could distinguish those with and without atherosclerosis with almost 100 percent accuracy.] Cathy's seeing patients that have normal lipids, normal LDL, normal HDL, yet they have heart disease. Why is that? [It turned out in many of these cases, they had a very unusual HDL that was actually discovered in newborn infants—literature Cathy was familiar with since she also was a pediatrician and internist—that was very atherogenic.]

GRAYSON: Well, [yes].

MACFARLANE: So now we have a study. We're just in the process of starting to prepare manuscripts, where we could actually—with the statistical analysis—we could not only distinguish [with] 100 percent accuracy, who has CVD [cardiovascular disease], who does not have it, we can tell what components of lipoprotein density profile are contributing to it. What nature is telling us is not the LDL, or the HDL, it's that whole system of lipoprotein subclasses that's working in concert. There are so many factors that go into it, like heredity, your lifestyle, probably things that are unknowns, and there's no way you can unravel it.

So that's our story here. What we're doing now, is we're publishing a set of papers that I talked with the guy who is the editor at *Analytical Chemistry*. He says lots of you are in this boat. You're chemists doing translational research and the medical community's turned its back on you. We will accept all this—the translational research stuff.

GRAYSON: Translational research?

MACFARLANE: [Yes].

GRAYSON: That's like getting outside of your box.

MACFARLANE: Or no . . . you're mixing. You're mixing your box with other people's boxes.

GRAYSON: Oh, that's bad. [laughter]

MACFARLANE: And so that all of our fundamental stuff is being published there, like your EDTA complexes . . .

GRAYSON: In *Analytical Chemistry*?

MACFARLANE: [Yes]. Then this one, we're preparing right now, we've got . . . there was the precision method.

GRAYSON: Well, that would be interesting, you know, to have some medical breakthrough show up in *Analytical Chemistry*. But you know, this fellow at Yale, Sandy [Seymour R.] Lipsky used to publish a lot of stuff in *Analytical Chemistry*.

MACFARLANE: [Yes].

GRAYSON: He was, I think, one of the first people to use . . . I mean, he was an MD, but he was trying to use analytical—modern analytical techniques, chromatography, mass spectrometry to shed some light on . . .

MACFARLANE: Same mindset.

GRAYSON: And they even named part of the laboratory after him . . .

MACFARLANE: [Yes], I remember.

GRAYSON: He published at least a dozen papers in *Analytical Chemistry*.

MACFARLANE: [Yes].

GRAYSON: But he has an MD, you know.

MACFARLANE: Right. Well, because you publish there, then the MD's come and they criticize you, your method, say, "Well here it is, all in print." You want to criticize all you want. It's your choice. That still is our strategy.

GRAYSON: When did your wife get her MD degree?

MACFARLANE: It was . . . let's see, she got her MD degree . . . I'll have to use our daughter's age as the—she got it ten years ago [in 1996 and finished her residency in Internal Medicine and Pediatrics in 2000]. <**T: 80 min**>

GRAYSON: So that must have been an interesting slog for her to undertake after you know . . .

MACFARLANE: I know. Well, it was. Right now, she actually has her mind more in the MD world than in the chemistry world, but that's okay, because I have a built-in critiquer, and she tells me that. I'll come up with some theory that she says, "That's garbage. It's a piece of shit." [laughter] But I filter and say okay, because that's not part of the way MD's are thinking, so I don't mind that.

GRAYSON: It's an interesting way to do some research and attack a problem.

MACFARLANE: So with that then I had a lot of confidence, [that we] really are onto something here. Our story is then is the system of lipoproteins are working in concert and it's more than one pattern that is a healthy pattern, and more than one pattern is unhealthy, so it's just a matter of getting our library big enough, we can cover all bases.

GRAYSON: You say the HDL, LDL is a supersimplification?

MACFARLANE: That's right.

GRAYSON: Of, I mean in many cases it helps provide—

MACFARLANE: They are working as a team.

GRAYSON: —some guidance, but it's really just not . . . you know, there's more to it than that, and we need to get the rest of it.

MACFARLANE: The idea here is that [. . .] we had the age of these people as potential parameter, but statistics say that's not a factor. Age is not a factor. Then we read the literature, now it's saying that people who do autopsies of young people, they find that they already have developed . . .

GRAYSON: [Yes]. That's, I recall seeing something like that, where the people who "shouldn't" be getting . . .

MACFARLANE: All that.

GRAYSON: [Yes].

MACFARLANE: So then our model now is that the chemistry of your blood is not right as manifested by the distribution of lipoproteins, then you are beginning to form domains on your arteries that are the precursors of developing coronary heart disease. Then it only becomes a manifestation when you have something that a doctor can detect. That's our line on this. Now, the other part of it, we had a feeling that these lipoprotein density profiles are transferred. But then we did not really want to get into this so much. The vet school here got wind of what we were doing, and it turns out there are some animals that also have cardiovascular disease.

GRAYSON: So in the veterinary school . . .

MACFARLANE: [Yes]. So we have one study involved with parrots, another one involving miniature schnauzers. We have two schnauzers at home. And so the miniature schnauzer one . . . they had some schnauzers develop pancreatitis and others don't. They had the cohort of, I think, sixty schnauzers that we got profile on, tested profiles on, and we were able with 100 percent accuracy to distinguish those that have pancreatitis and those that didn't. So then the next thing they did was, the ones that had pancreatitis, they put them on a special diet and half of those dogs would go over to the healthy side.

GRAYSON: Go to what?

MACFARLANE: Half of those that were on the unhealthy side, would go over to the—

GRAYSON: Healthy side.

MACFARLANE: —healthy side—their profile. So that meant then that the lipoprotein profiles are dynamic. You can change them by changing lifestyle. And so that's part of our equation. One of my students actually is using his own blood. He's overweight. He's following his profile as he's working out and changing his . . .

GRAYSON: Interesting.

MACFARLANE: [Yes]. But all that was based on the density distribution. But I want to have other things in there, particularly mass spectrometry.

GRAYSON: Somehow this density distribution method is something that you devised?

MACFARLANE: [Yes].

GRAYSON: With the layering of the EDTA . . .

MACFARLANE: The layering . . . no. We take a homogeneous solution. I'll show you on our poster. We take a homogeneous solution, and we expose it to the ultra-centrifugation, high speed for six hours, not four days.

GRAYSON: Oh, wow.

MACFARLANE: At 4° centigrade. So that preserves, <**T: 85 min**>as far as we know, the integrity of lipoprotein particles. So, that's our first piece of data is the parameterization of the individual lipoprotein. The density distribution is that it's seeing where it lies on the statistics axis. [. . .] Now, what the analysis showed us was that there were certain classes of the HDL, subclasses, that seemed to be correlated with people who have heart disease. [As I mentioned above, Cathy noted that their profiles looked a lot like the profiles we analyzed as part of a collaboration with Pete Kwiterovich, a pediatric lipid specialist at Johns Hopkins who wondered why some low-birth-weight babies develop atherosclerosis. Working with that group, we were part of a vascular biology team led by Subroto Chatterjee that characterized a new type of HDL

enriched in APOC-1 [apolipoprotein C1] which had really atherogenic properties. No one had ever shown that type of HDL persisted in adults so Cathy reached out to Dr. Chatterjee and said she thought our lab may have detected it in her adult patients and could they confirm if they thought it was the same type of HDL.]

So we began to look at the subclasses, and now I told the student, this is Deva [V.] Moore—this was last May—I said, "Now, Deva, you know that we have an unusual distribution of methods here. We have an unusual distribution of people. We're going to now look at MALDI mass spectrometry of the proteins that are HDL subclasses. Keep your eyes open for surprises, okay?"

She came to me about three weeks later. She said, "Dr. Macfarlane, there's one protein that is an HDL. It's actually a minor protein, but because it is, it has lots of basic groups . . . it's a major peak in the MALDI spectrum, APOC1." [And independently, the Chatterjee group confirmed that the HDL fractions we isolated from these adults behaved just like that from low-birth-weight infants that had APOC-I-enriched HDL.] This is actually part of the density profile. We've eliminated the LDL. This is showing the HDL subclasses there. Then we were looking at it, so what Deva did was take a sample of this, and sample of that. Get rid of the lipids and do MALDI on those two subclasses. About six or seven years ago, we had a student from Russia, Pavel [V.] Bondarenko, who did our first MALDI experiments with these. It was the first time anybody had ever tried MALDI on these lipoproteins. I remember seeing new isoforms all over the place. One of them actually was a truncated form of this APOC1. I said, "Well, that's molecular weight of sixty, sixty, two hundred. But it had with a two amino acids, how they had terminus were truncated off. We don't know why. But there are other . . . it's rich information.

But anyway, but Deva came to me and said, "Dr. Macfarlane, there's something weird about this APOC1." What is that? This is now a MALDI [spectrum], that region [. . .] these were molecular weights that agree in literature. Then once you look at the MALDI spectrum for people that we knew had CAD [coronary artery disease], the masses were shifted.

GRAYSON: They were shifted . . .

MACFARLANE: By ninety mass units. For every one of them. Every one of those—I think there were fifteen in the group—had shifted by ninety mass units.. None of the controls had had that. Okay, what's going on here? At first, I didn't believe it. "Deva, check your mass calibration." Right on. Had another student do it. He had the same answer. Then we went further into this, and we had found that there were some of these people with CAD that were even more complex than this. So then it was a variable. This is the HDL2, that's the HDL3, just something's going on here. Our current hypothesis is that the HDL particle . . . first of all, the only reasonable explanation is that it's a genetic mutation. It's an all or nothing thing, which is a total surprise.

GRAYSON: [Yes]. It's not like it's a little bit of each.

MACFARLANE: I know it.

GRAYSON: But it's all one or the other.

MACFARLANE: And that's one of the mysteries. Then seeing this implies that the . . . and then you look at it from the standpoint of a chemist. Now assume the artery being artery and all this stuff, look at it as a chemist, like capillary chromatography. We have a stationary phase, all the artery, and a mobile phase, the blood. If there are patches on the stationary phase that are highly reactive, as they are when you have plaque, there are all sorts of enzymes there that can do more stuff. This would explain why <**T: 90 min**>—these have been chemically modified; and that's our hypothesis. Deva has about fifteen other [samples from Cathy's patients] that show there's a big variety here. So what this implies is that not only do we have mutations, but also it implies that HDL particles [can be an] internal probe of the chemistry of our arterial wall. The HDL only lasts for two days. [fingers snapping] Then it gets recycled, gets picked up by the liver, and then new HDL is formed, and then it goes into a cycle.

GRAYSON: So now, this is a pretty recent paper?[11]

MACFARLANE: [Yes]. It just came out.

GRAYSON: Two thousand eleven. It's probably not in your bibliography then.

MACFARLANE: Oh, it is. You have it in the top here, at that point, that time, I did . . . it was accepted right away.

GRAYSON: Okay.

MACFARLANE: And with even a comment by the editors that this is a very exciting paper. It was accepted right away, and a month later, it was already posted then. Within one week, it was posted on their web.

[11] D. V. Moore, C. J. McNeal, R. D. Macfarlane, "Isoforms of Apolipoprotein C-1 Associated with Individuals with Coronary Artery Disease," *Biochemical Biophysical Research Communications*, 404 (2011): 1034-1038.

GRAYSON: And what journal?

MACFARLANE: *Biochem Biophys* [*Biochemical and Biophysical*] *Research Communications*. So then they received 17 December, available online [. . .] 25 December. Available online. It was in January issue of *Biochem Biophys Research* . . .

GRAYSON: That's good. So you're still back to using mass spectrometry?

MACFARLANE: [Yes]. Well, that's part of why I was telling you this . . .

GRAYSON: [Yes]. You're not using the old californium system?

MACFARLANE: That's right. I felt that it was important to tell you that I'm back in the fold. In fact, we have a poster for ASMS on the subject.

GRAYSON: Okay. What do you think about the . . . I know that sometimes it's called particle desorption mass spectrometry. Other people are doing it still, right?

MACFARLANE: Right.

GRAYSON: Has it kind of fallen off somewhat?

MACFARLANE: Well, it's actually become quite specialized. I mean, you have to have an accelerator. Actually, one of my colleague [at A&M], Emile [A.] Schweikert, looks into this. He has his own californium system as well. Then we've always had a strong collaboration with people who were at Orsay [Institut de Physique Nucléaire d'Orsay]. I've known them since the nuclear chemistry days. When they saw this, they picked up on it, and they were using the californium mass spectrometer as well, having performed a service for those that . . . they always said they were doing the biological stuff.

GRAYSON: So basically, it's still—I mean, the only source is the californium. That's the one that . . .

MACFARLANE: Well, no, [. . .] they've gotten more sophisticated. They have found that they could actually take gold and put it on a filament and heat it up and get giant gold clusters coming off. They can accelerate those and they're charged. They can accelerate those to a pretty high energy, and this is what Emile is doing. They blast it into a target. They get enormous yields of biomolecules, also of things that are of interest to people in solid state chemistry and surface science. Apparently that part, particularly the surface side part is a growing field, because there's a lot of interest now in the nanoparticles and what's going on in surfaces. So Emile has quite a few collaborations. [. . .]

GRAYSON: [Yes]. I think he gave a talk at Washington U, at a discussion group a few years back.

MACFARLANE: Right. He has close ties too, with Orsay, and [. . .] was the major PI on the Orsay project. He's since retired. His first lieutenant has taken over and has continued collaborations, so that he comes quite often, back and forth. Most of the R&D ion source was done at <**T: 95 min**> Orsay. They transferred that technology to Schweikert's laboratory.

GRAYSON: Okay. So it's like it's morphed in its own subspeciality of plasma desorption, particle desorption mass spec, and people are using it still, but in other ways, and . . .

MACFARLANE: Right, in fact, I guess the way that they talk, there's still an offshoot from the PDMS days. It's evolution, you know. As the chemistry field is locked into MALDI, electrospray is now an ongoing project that has roots in the californium stuff.

GRAYSON: [Yes]. Well, those techniques have really pushed the biological side of things tremendously in the last...ever since they came on the scene, probably fifteen years now. They're getting more powerful with time. [Yes], I was looking at this shop that [Dave] Russell has over there with all that stuff he's got is amazing. He really likes this Waters system. It's got this kind of strange ion mobility sector thing that he . . .

MACFARLANE: They locked into that early on.

GRAYSON: So I think you could say that Bartlett's . . . it's Bartlett, right? The fellow that brought you here, Bartel?

MACFARLANE: Martell.

GRAYSON: Martell?

MACFARLANE: Right.

GRAYSON: His vision is being realized here at A&M because what is it? What would you say the chemistry department is compared to . . . well, you came here as a nuclear chemist. But he was a chemist.

MACFARLANE: [Yes]. He was an organic chemist.

GRAYSON: So when you came here the chemistry department was, what?

MACFARLANE: He hired fourteen people that year.

GRAYSON: Fourteen people in a year.

MACFARLANE: [Yes]. He'd do it on his own.

GRAYSON: Oh, wow.

MACFARLANE: He didn't have any committees, so they really gave a free hand. He brought in some high visibility people like Cotton, Al [F. Albert] Cotton.

GRAYSON: Who is that?

MACFARLANE: Albert Cotton. [. . .] Brought him from [MIT]. [. . .] He brought in a famous natural product chemist, [Ian Scott]. My brain is starting to get a little tired here, I'm forgetting names. But he attracted these people, really because first of all, they both had some political baggage at Yale and at Harvard or MIT, I forget which one of them, it was. Then he came here. Al Cotton, well, actually was into horses, and he had a ranch. He was a big kid on the block. So then he attracted a lot of younger people . . .

GRAYSON: Cotton?

MACFARLANE: Because he and this other fellow—Scott, he and Ian Scott. They both attracted some of the younger faculty. I think it grew from there. [. . .] Once he got funded, it just kind of grew on its own.

GRAYSON: So where does the funding for this University come from? Is it state funded?

MACFARLANE: Well, you know, partly, [yes]. And also outside grants: the NSF and NIH, and a little bit comes in from oil industry.

GRAYSON: So the A&M school, is that a land-grant school that were . . .

MACFARLANE: Agriculture and mechanical

GRAYSON: [Yes].

MACFARLANE: And we had no humanities. Now they have a token humanities group here. All that stuff was related to the University of Texas [at Austin]. Still, there's a special feeling at A&M that's truly a family-type university. There's a lot of cohesion. [I want to take advantage of that.] My game plan is to actually incorporate the university population as subjects for the development of screenings. I already have half a dozen undergraduate pre-meds actually making the measurements, and I'm going to have them be involved in actually setting up the strategy. The administration is very excited about it <**T: 100 min**>, because we can take advantage of the Aggie spirit of the fact that there are [Aggie] families here—generations of people that we can get data for. That's a reason I'm about to pull off an NIH grant renewal to convince NIH that we deserve funding for the next five years.

GRAYSON: Well, it's clear—I've been in Austin, and one of my kids went through the UT system in various degrees, so I'm aware of the unique competition that exists between UT and A&M, and it's definitely . . . there's nothing here but A&M. I mean, this defines the area, that's for sure.

MACFARLANE: I went to a baseball game last Saturday with my son. Right now they're in championship game. I have a UT shirt that says, "UT Dad," but underneath I have a maroon shirt, so when A&M won, I took it off. [laughter]

GRAYSON: Well, we kind of covered a lot of turf. I think we need to make sure that we go back and check out some—

MACFARLANE: You know, I wrote a lot of stuff. [. . .] You could take a copy of this, if you want, as well.

GRAYSON: Sure, that would be good. But is there anything in there that you want to talk about that we didn't get a chance to get, you know, a quick pass through?

MACFARLANE: So then the philosophy of education.

GRAYSON: I mean, it's apparent that your mother was an influence on you in terms of making sure that you got an education.

MACFARLANE: [Yes]. In fact—

GRAYSON: —at least the bachelor's degree. You had to have a bachelor's degree at a minimum.

MACFARLANE: Right, but then when I went to McMaster in Hamilton she was very excited about having us back, and her grandchildren back. Then when I told her that I was being offered a job in Texas, she was very unhappy about it. You can't do that. [sobbing noises]. "How much are they offering you?" I told her and she said, "Dad says to take it." That was my father.

GRAYSON: They're paying you enough, huh?

MACFARLANE: Right. So when I got the ASMS award, the first one [the 1990 ASMS Distinguished Contribution in Mass Spectrometry Award], that was really very emotional for me, because I knew that there were people that had been in it for a long time, and I felt uncomfortable. I was an outsider. They give you the first award. And I remember I said, "I wish my mother were here." But she'd already died. I said somehow I have to honor her someplace, I don't think it . . . I dedicated my talk to my mother. You know, I saw Mike three weeks ago, at the Hank Fales thing. He said, "Ron, remember the talk that you gave?" I said, "[Yes]." "I was really moved by the fact that you mentioned your mother." I said, "Really? Oh, Mike, you

made my day," because that was nervousness showing. It was worth it, you know. Here again is something that surprised me, that when [she thought] things were going so well, she was very excited. She has all these articles about me that she had saved. The last time I saw her, although I didn't know it was the last time. "Why is that, Mom?" "So I could be your mother. Oh, that's all I needed." But I thought, geez, what better thing could a mother say to a child?

GRAYSON: I read your ASMS write-up. That is kind of cute, when she says, "You're giving away your secrets." [laughter]

MACFARLANE: Right. "They'll steal your thunder."

GRAYSON: [Yes], right. That's really good. That's typical. Sounds like your typical mother, you know.

MACFARLANE: Right. [Yes]. So we have a question about philosophy of education there. Career selection, why I did what I did. Early career. What's your career evolving, mentor, manager, funding issues . . .

GRAYSON: Apparently now, it seems like you've been having pretty good luck with the funding in your career.

MACFARLANE: [Yes], almost continuous. Little burps here and there, but it was almost . . .

GRAYSON: [Yes]. I don't know the way things are going, that may be changing, because of <**T: 105 min**> the . . .

MACFARLANE: [Yes]. I worried about that.

GRAYSON: These budgets are going to be tightening.

MACFARLANE: And my age too, you know, with these young people coming up. I've had my day in the sun.

GRAYSON: Well, that was John Fenn's commentary. He was unhappy that he wasn't able to get funding for some of his projects, but he acknowledged the fact that they had to fund some of the new, upcoming people; that he felt like he got shortchanged, because he came up with a really unique concept and then got it going. Then when he went to funding it just, well, you know, we'll give it to these other people. But, particularly now, the government . . . I mean, I don't know. At one time, companies would fund research, but it seems like that's not being done much anymore.

MACFARLANE: Well, I worry about this. My wife is having a hell of a time getting funding, because she's [one] of the lump of MD's. If you write a proposal, all they see is: is it hard-core science? They said it's irrelevant. Then in my particular case, I know there's some problems at NIH, that there's not good communication. We had a visitor from NIH come and give a talk about funding at NIH. I had a chance to talk with her one on one. I said, "I'm getting mixed signals from NIH." I said the upper administration says that they want to actually have more scientists be involved in medical research involving people. I said it's not the way reviewers are looking at [it]. She said, "Is that obvious to people outside of NIH?" It was obvious to me, right? Upper administration has all these great ideas, and even now, [Francis S.] Collins is saying, "We are the National Institutes of Health, not National Institutes of Research." But yet, it's nice to say that, but the people at the other level, the funding level, are relying on their reviewers to evaluate the proposals. The reviewers are for the most part for pure science.

GRAYSON: [Yes].

MACFARLANE: But they said this is application—applied science. So they're only looking at pure science. And so what I have to do now, and what I'm doing, is being sensitive to this and trying to get the pure scientists excited about what we're doing, as a pure scientist. Then switching over to, I want to apply this now to people. I'm hoping that this particular paper . . . it's kind of a bridge. Here, we have people. I can tell what their age is by looking at a mass spectrum of blood. But it's a gamble. But fortunately, what NIH did was develop a new type of a study section called EBT, Emerging Biotechnology. That's where my proposals are going. It seems to be a mix of people who aren't totally in the pure science part, but they have an ear for the emerging biotechnology. That's my hope. Now, I don't know. My age is going to be really . . .

GRAYSON: [Yes]. Let's see. You're looking at what?

MACFARLANE: I'm seventy-eight, right now.

GRAYSON: Seventy-eight, [Yes]. Well, let's see, Fenn was getting funded into his eighties. Late eighties.

MACFARLANE: [Yes]. And the fact that I have access to patients and I'm not going to work with mice is a plus, but again, it's a big question mark. If I don't get funded . . .

GRAYSON: But you're saying even your wife's having troubles on her side.

MACFARLANE: In fact, she sent a proposal to the American Heart Association. She called yesterday and said, "It wasn't funded, but at least I got a score." Up until that, it didn't even get to where you get a score. They're picking on stuff like how this paper . . . they said, "Well, it's nice that this APOC1 with a mass of ninety is as it is, but you don't know what that difference is. Until you find out why, what's cause for that, it's worthless." <**T: 110 min**> That's the mindset. That's the idea that there's something wrong, that there's something there that by itself is a marker. In fact, both the A&M and Scott & White were excited about it; they have already submitted a patent application.

GRAYSON: But, I mean, you said that the journal it was submitted to, that accepted it right away and posted online immediately—

MACFARLANE: [Yes], right.

GRAYSON: Well, the whole reviewing issue is fraught with difficulties, and people you know agree trying to figure out what's good and what's not.

MACFARLANE: Some of the early things in here, like my desire—innate desire—to think out of the box and not have any competition.

GRAYSON: I mean, this was a game plan on your part. I mean, you [. . .] kind of evolved into the game plan.

MACFARLANE: I realized it [was] my first mentor, Truman Kohman, [who] was the one that really triggered it. He gave me the freedom to build this giant detector, so when I got this professor thing, I wanted to call him and thank him. Well, I did have a chance to thank him. I said, "You gave me the freedom to do what I wanted to do. You accepted my ideas." He said, "You know, of all the graduate students I've had, you're the only one that agreed with me,

followed up on my suggestions." I thought that was kind of a neat thing. But it was he that actually made it possible for me to go that next step. Then Seaborg coming up and kind of continuing that, reinforced that. I was very fortunate.

GRAYSON: Well, yeah, you can't much better mentor than Glen Seaborg.

MACFARLANE: I know. And he came here quite frequently, because he was associated with The Welch Foundation.

GRAYSON: Okay, so The Welch Foundation is a source of funding, big funding.

MACFARLANE: It was. It was until I got into this, and then they dropped it.

GRAYSON: Oh, okay.

MACFARLANE: They only fund pure research. But if Seaborg would come here, as a member of that committee, we would always talk. One time we were talking and the department head came in. And Seaborg stopped and he says, "You know Ron." He says, "Ron is one of us." [And the department head said,] "[Yes], I know that. I know that." I knew what he was talking about. I'm still part of the perfect family.

GRAYSON: Ah, okay.

MACFARLANE: That made me feel good that that's the way he . . . well, he perceived I was.

GRAYSON: Well, at least if you want to have somebody pulling strings for you, that's definitely somebody—

MACFARLANE: Oh, I know it.

GRAYSON: —you want back there pulling strings.

MACFARLANE: But he was excited that one of his isotopes, californium-252 was being used this way. And let's see, what other things? My first wife's illness really got me a chance to leave McMaster and to try to springboard my career here.

GRAYSON: So now, let's talk about Seaborg a little bit. I mean, obviously he was a big man. Was he pretty generous with himself with people or was he one of these . . .

MACFARLANE: I think he was.

GRAYSON: Because you know, a lot of these guys get kind of snooty, when they get up in the upper levels.

MACFARLANE: But he was [generous]. There was another one of my colleagues [Rand L.] Watson, who is now retired; he was one of the nuclear—there were three nuclear chemists. I was one of them. Then Watson was another one. I knew Rand Watson, when I was a postdoc at Berkeley; then Watson was a graduate student. When he came here to interview he said, "What are you doing here?" He thought I was competing. But anyway, Rand told me that Seaborg helped him a lot too, in terms of behind the scenes, pulling some strings without really saying it, but when I talked with him, I was aware of the fact that he knew what I was doing.

GRAYSON: So he was keeping tabs on his people, and seeing . . .

MACFARLANE: In fact, I think even at The Welch Foundation. After he died, I lost my funding. There's another person that's on the committee, that's one of these gurus in medical research, except I'm not doing what he's doing. That's my interpretation.

GRAYSON: So Welch [Foundation] is supposed to fund pure research.

MACFARLANE: [Yes]. Even though [Robert A.] Welch gave them money because he felt that chemistry was providing a lot of benefit to society. Anyway. <**T: 115 min**>

GRAYSON: So he [Seaborg] was obviously a good mentor to have. Then by the time, that time, though, you're starting to mentor people yourself. So you're . . .

MACFARLANE: That's right.

GRAYSON: Do you do the same kind of things: follow up on your troops and keep an eye on them, and make sure that they're . . .

MACFARLANE: Well, I tell them when they're deciding whether to work for me or not, I say, "This is my style here. I can come up with new ideas. I can try to get funding for the new ideas, been pretty successful at this. But then you're on your own. I can serve as a resource person when you call on me, but I'm not going to micromanage you." Some people don't like that. They want to be hand-held, and I don't want that. So, mostly the people I get are people who are independent, self-confident, that run with the ball. If you don't fit into that, pitch it or leave the group. It doesn't happen very often. So my mentoring is that I'm a mentor, but I'm not one that's going to actually steer you; it has to be your ideas. My feeling is that's what having an advanced degree is all about.

GRAYSON: [Yes], sure. [Yes], creating new knowledge.

MACFARLANE: [Yes]. And coming up with ideas on your own and thinking out of the box. For the most part they've done this, from what I can see.

GRAYSON: So let's see. Obviously, you haven't had any . . . well, everybody has some difficulties in publishing. Like your reviewers didn't . . .

MACFARLANE: [Yes], but it's been great. I've really been very successful. Took a little bit of time in the beginning, say just the mass spectrometry. I had some trouble with mass spec people, because I was too far off the wall. But then I persevered and didn't really have that trouble; only one paper that should have been published that I never did. But I now know what it takes to get published. There are a lot of PR parts that I have to address and make sure I'm aware of what people have done in the past in connection with what I'm doing.

I've been a little bit lax in my publishing. My sloppiness that the articles that I have that has . . . and I stopped writing. When I went through my bibliography that I sent you, geez, I feel like some other stuff was completely missing here. [Yes]. I did not have any backup until I got what you sent to me. What you did was a very important thing for me to have.

GRAYSON: Good. Well, I say I try to get the publication record as best I can, because it tells a lot about someone's career, and so out of that list of papers, obviously, there's a handful or couple that you were going to rank as more significant than others.

MACFARLANE: [Yes]. Well, I think that the helium jet method was the first one where I reported on some of the helium jet for transporting short-lived nuclei from the place where they're produced in the laboratory to flow back.[12] That really caught on and got me some international exposure and also led to several important discoveries. One thing that's always bothered me is that I'm not aware of what makes me different.

GRAYSON: Like what?

MACFARLANE: What makes me different. My colleagues joking would call me an oddball. I remember I spent this year with the [Niels] Bohr Institute in Copenhagen [Denmark] that—I was asked to give a talk there about what I was doing. It was on the short-lived radioactivities. [. . .] I was looking at the peaks of the alpha particles in the mass spectrum and saw that there [were] two peaks in there. I knew where their origin was, and I realized that I was actually seeing the influence of <**T: 120 min**> beta-neutrino correlation, which is part of the conservation of parity. So I included that in my talk and which is a bit . . . it's an off-the-wall, out-of-the box type experiment. Afterward, Niels Bohr's son Aage [Bohr] came up to my office and thanked me for that, and says, "You keep doing and thinking the way you're doing and making contributions to society." "What am I doing?" But again, the fact that I went out of my way to think out of the box, just so as to avoid having competition, turned out to be a hallmark of my style.

GRAYSON: And fortunately, it's far enough outside the box that no one else realizes it's a good box to get into. [laughter]

MACFARLANE: That's right. I keep on telling people, I say, "I don't mind being in a race if I'm the only one in the race; then I always come in first."

GRAYSON: [Yes], right. So what was his first name? Aage Bohr? [. . .]

MACFARLANE: [Yes]. So that was a nice experience too.

GRAYSON: That was a sabbatical that you took when . . . ?

[12] Macfarlane, Gough, Oakey, and Torgerson, "Helium-jet Recoil."

MACFARLANE: Well, it was actually a sabbatical one year after I came here, because I told Martell, I said, "Look, I'm about one year before I go on a sabbatical. Are you going to let me go on sabbatical after one year?" "[Yes], no problem."

GRAYSON: So there—

MACFARLANE: Nineteen sixty-nine. There I was. And I applied for this Guggenheim Fellowship and got it like that. [fingers snapping] Because of Seaborg, as I found out later. And there I went, to spend a year in Copenhagen.

GRAYSON: Well, that's nice.

MACFARLANE: It was to the walls of all the people from those days of Niels Bohr and Albert Einstein, and all those guys. And that same room where they gave talks, I gave my talk. So it was a real upper.

GRAYSON: How do the hardcore physics types think of nuclear chemists? They tolerate you guys?

MACFARLANE: Well, they don't take us seriously, but they like to have their research be clean and to have it be relatively simple system, so they can do fundamental theory on it. Anything that looks like it's complex, they call it chemistry. So to them, even my colleagues in Uppsala, amino acid is a complex molecule versus cesium iodide. They thought [they were doing] something really significant, when they were bombarding an amino acid. I said, "Well, you've got to do something more than that." They said an amino acid is complicated enough. I finally convinced them, the months that I was there, to put insulin into the mass spectrometer. [In front of their beam—they had an iodine beam.] And they immediately got a mass spectrum. [fingers snapping] That's what we submitted to *JACS* [*Journal of the American Chemical Society*].[13] Initially, it got turfed. So that got them to thinking about larger molecules. But for the most part, the physics community remains that way. They want to keep the systems simple enough that they can apply fundamental laws to it. That anything that's complicated, like a benzene molecule: out of their realm. So in nuclear chemistry, where we've got our niche is in areas of nuclear physics that are more complicated systems. For example, the compound nucleus, which is the whole liquid drop model, which was originally introduced by Niels Bohr.

[13] P. Haakansson, I. Kamensky, B. Sundqvist, J. Fohlman, P. Peterson, C.J. McNeal, R. D. Macfarlane, "Iodine-127-plasma Desorption Mass Spectrometry of Insulin," *Journal of the American Chemical Society***,** 104, no. 10 (1982): 2948-2949.

GRAYSON: [Yes], that's what I was thinking. Bohr introduced that concept.

MACFARLANE: [Yes]. The fact that you excite the nucleus, it acts like a liquid drop, and you have these neutrons. The neutron spectrum has a Maxwell-Boltzmann distribution of energy, and so a liquid drop bottle <**T: 125 min**> is part of it, but then the nuclear chemists picked up on that. That's why heavy ion and heavy ion nuclear physics actually was in the realm of nuclear chemistry, because they had the heavy ion that was too complicated versus a proton. So it's still that way. When I think even now about nuclear chemists here, Joe [Joseph B.] Natowitz is one of them. He was big on the nuclear liquid drop model and the compound nucleus dynamics. Then the other—there are two other nuclear chemists. One is in the transuranic elements and chemistry of it, but they're not part of the mainstream nuclear physics.

GRAYSON: There's a group at Washington University that's doing—they call it radiochemistry.

MACFARLANE: That's right. They give talks to nuclear chemists. I forget their names, so I'll try to come up with it.

GRAYSON: I should know them, because I was there not that long ago.

MACFARLANE: Tell Mike Gross, because I knew these guys. They were part of what I was in and that's what I really . . . I knew nothing about Washington University in St. Louis. But I went there, I was amazed at, first of all, the lovely parks, essentially. It sits on a hill or something.

GRAYSON: They call it the Hilltop Campus.

MACFARLANE: [Yes]. But it was a very, very congenial thing. What they were doing was very similar to what I was doing. I got involved in beta-neutrino correlations and alpha emissions. They were involved in some of that as well. But the . . .

GRAYSON: Well, the building that the mass spec facility [is in] used to have a cyclotron in it.

MACFARLANE: [Yes], that's right.

GRAYSON: That was the, I think, one of the early—

MACFARLANE: That's right, exactly.

GRAYSON: — small cyclotrons, and so I always thought it was something with some horrendous politics to get that wrestled away from the physics department to convert it to a mass spec lab for Mike Gross. But I mean, obviously, in terms of cyclotrons, Washington University at one time might have been a little bit of a force, but not anymore.

MACFARLANE: Well, they were [into] the low-energy nuclear physics. Whereas the high-energy part that then became part of the nuclear chemistry.

GRAYSON: The nice thing about that arrangement is that there was a shop in that building, and they kept the shop there, so if you needed anything built then there it was really convenient.

MACFARLANE: Similar situation here, except with the relation between chemistry and the cyclotron was so bad that, once I moved over here, I was the only one who had access to the machine shop.

GRAYSON: What department are you in?

MACFARLANE: Chemistry.

GRAYSON: You're in the chemistry department?

MACFARLANE: [Yes].

GRAYSON: But you're doing cardiovascular research.

MACFARLANE: [Yes].

GRAYSON: Okay. [laughter]

MACFARLANE: [Yes]. That's another thing that, because I'm not part of the club, [Texas A&M University] Health Science Center doesn't recognize me, even though we get medical students coming to do a summer project here. We're kind of tolerated, even though we have a key laboratory for cardiovascular chemistry; but that may change.

GRAYSON: So, the medical side of the school doesn't think much of you, and the chemistry side of the school doesn't think much of you.

MACFARLANE: Right, right.

GRAYSON: You're an oddball.

MACFARLANE: An oddball. If I don't push it, and one . . . now that I really want to get the pre-meds. There's a lot of interest in pre-meds doing some medical research, because they can put that in their CV.

GRAYSON: Oh, [yes].

MACFARLANE: And so the head of the undergraduate honors research program—I had a long conversation with her about a month ago—she asked me, "Well, why isn't the Health Science Center involved?" I said, "Because politics," and she understood that. The reason for that is that when the Health Science Center—

GRAYSON: I'm sorry this is the "L?" You call it the "L" Science Center?

MACFARLANE: "Health"—Health Science Center.

GRAYSON: Health Science Center, okay.

MACFARLANE: The state legislature had to approve it, and there was an item in the budget for A&M to support that and A&M took it for themselves. They said, "To heck with you," so there was a polarization that began there. But what the Health Science Center did, they went to Austin and complained. They got a line item in the budget that says it's for you guys. Since then on both sides, if I tell the dean <**T: 130 min**> or vice president of research that I'm interacting

with the Health Science Center, well forget it. They don't want you to do it if it involves the Health Science Center. That feeling is still there to a point where I think the Health Science Center's moving off campus.

GRAYSON: Great.

MACFARLANE: Towards Bryan [Texas], whereas most of the [elite] universities, the health science centers and the hardcore science are together.

GRAYSON: [Yes].

MACFARLANE: So anyway, my wife is actually on the senate of the Health Science Center, even though she's at Scott & White. There's a branch of the Health Science Center that's in Temple [Texas]. If I don't push it, it becomes their idea and that's where you get it, but it has to be their idea.

GRAYSON: You have a secret operative.

MACFARLANE: [Yes], right. Lie low and I've had my day in the sun, and whatever way it goes, I can still do my thing, as long as I get funded by NIH. But now I should not have all my eggs in one basket. I haven't figured out how to solve that problem yet.

GRAYSON: That's a very interesting nonlinear career. It's an interesting model for a career.

MACFARLANE: Well, actually, one of the guys you've been interacting with recently, Frank Field, he came around and he says, "Ron, the secret to your success is that you follow your nose."[14] It's right on; a very succinct description of myself. I follow my nose.

GRAYSON: Well, it certainly has worked, it would seem. It's interesting that having a paper route when you're a kid changes your world view.

[14] Frank Field, Oral History Transcript #0636.

MACFARLANE: [Yes], in retrospect, I asked myself, "Why am I so different?" Because I actually do a lot of daydreaming, still. That's why I don't like a cell phone. Well, I even put something in here about the . . . I'm worried about . . . [flipping through papers]

GRAYSON: Well, everyone's connected, that's for sure. Maybe overly connected.

MACFARLANE: So this is something that is a continuation. Okay. So then continuing with . . . I lost some funding and gained other funding to compensate. The funding issue's a question of pure science versus applied science. The experience inside my organization, [. . .] outside funding for research . . .

GRAYSON: Now, were you obliged to teach courses?

MACFARLANE: [Yes], but I wanted to anyway.

GRAYSON: Okay. So what did you teach?

MACFARLANE: Well, at first I taught p-chem. Then when I switched from nuclear chemistry to mass spectrometry that was in the realm of analytical chemistry. I could have stayed in p-chem, but I thought, no, the analytical chemists are really where I should be. So the physical chemistry people said, "You don't want to do that," because analytical chemistry is a bad word.

GRAYSON: It seems like analytical chemistry has a bad reputation on it.

MACFARLANE: That's right. So I knew that, because even at ACS [American Chemical Society] meetings, analytical chemistry is usually in another building. The analytical chemistry is what you do if you can't do p-chem. So anyway, I thought what the heck. They said, "Well, we'll have you teaching analytical chemistry, but you'll come back running." [. . .] I said, "Well, let me see what happens." Then I realized what the problem was: it was too superficial. There was no p-chem in it, even though physical chemistry is really underlying, so I took that out as a charge. I was going to convert that quasi-vanilla analysis course into one that's actually a physical chemistry with an applied physical chemistry.

GRAYSON: Applied physical chemistry.

MACFARLANE: [Yes]. And so <**T: 135 min**> I worked on that, and also it turns out that half of the class there were from some other departments. You had to take an elective, science elective. So that in itself became a parallel challenge for me, to not only get involved in medical research, but also to try to develop a course that was relevant to this generation of students. Now my daughter at that time helped me, because even when she was in grammar school I said, "Caitlin, would you let me go to sit in some of your classes? I want to see what the teachers are doing."

GRAYSON: Oh, wow.

MACFARLANE: For a while she let me do it.

GRAYSON: What'd the teacher say about that?

MACFARLANE: Well, I got to get permission to go. I want to learn about it, because I don't have a degree in teaching—none of us do. It's assumed if you get a PhD, you can teach, right?

GRAYSON: [Yes].

MACFARLANE: She knew that, and she welcomed me. I said now, "Well I see that you had them in groups, yet, every fifteen minutes, you're changing what you're doing. Why is that?" That's the time between commercials. [laughter] That means they've got to be synced with their clock. So I'm aware of the fact that every fifteen minutes, I ought to be shifting the topic to keep them up and I still do that, if I can keep my wits about me.

As I became aware of this, I realized that there was an emerging force to try to improve higher education. And then I began to talk with people in education psychology, and all the people there, and realized that there's a whole field out there that was relevant. I asked my colleagues. I said, "Why aren't we talking to people in educational psychology about how to teach?" "Well, they know how to teach, but they don't know what to teach." That was the end of that. But then I developed a relationship with one of the profs there, we went to lunch together. He introduced me to the field, and the key topics; constructivism is one. I began to incorporate that into my teaching, and realized I was doing as much research in the theory of learning as I was with the analytical chemistry stuff. So I have these two things going, and fortunately, the teaching part is more financially stable than the research part. And this is where I am right now. I'm having a ball.

GRAYSON: Oh, okay.

MACFARLANE: And I'm very excited about it, and—

GRAYSON: This is an undergraduate p-chem?

MACFARLANE: Applied analytical chemistry.

GRAYSON: Applied analytical chem, applied p-chem.

MACFARLANE: [Yes]. And I have constructivism, conceptual learning, and then students tell me the conceptual learning is something new to them that they apply to other fields, in the other courses, and I've made lots of strokes on that.

GRAYSON: Are they getting the message that you're actually teaching them some p-chem to boot, or do they know . . .

MACFARLANE: [Yes]. Well, they realize it. Well, one thing. I get feedback. Well, I realized that one of the problems with quantitative analysis was that the textbook hadn't really changed. [. . .] So I began to move more and more away from that, and more and more giving what they call commentaries. They would involve a mix of my own understanding of physical chemistry applied to analytical stuff that's in the literature. At some point last year, I bit the bullet and I got rid of the textbook.

GRAYSON: Oh, wow.

MACFARLANE: Relying on the internet and my handouts. And then combine that with what I'm learning about the theory of learning has being very effective. From what I hear—

GRAYSON: How large are these classes?

MACFARLANE: Thirty-five, thirty-six.

GRAYSON: So they're not too big.

MACFARLANE: Right.

GRAYSON: They're not these huge sections of organic and that kind of thing.

MACFARLANE: No. But anyway, some of them don't like it. Some of them like to memorize. They're going to have trouble, because I tell them if you memorize, you've got trouble. I'm giving you problems that give you experience in problem-solving, so you have strategy [for] solving problems. Some of them don't like that. They've gotten this far memorizing . . .

GRAYSON: Oh, [yes]. Got to use their brains.

MACFARLANE: [Yes]. So anyway, it's a mixed bag.

GRAYSON: That's interesting. But you're teaching that now.

MACFARLANE: [Yes], and part of my daily schedule is to devote one or two hours to improving on the handouts. We have a website they go to and to pick up stuff, and then I <**T: 140 min**> get a lot of feedback from them. I drop [the students] in to small groups of six. They call them cells and they compete against each other for . . . we have major exams, and the one with the highest grade, I invite to have lunch with me at the faculty club. While I have them there, I interrogate them about what I am doing right, doing wrong, give me some ideas. So a lot of what I'm going on now is input from them.

GRAYSON: Oh, wow. So this is not exactly what you think a seventy-eight-year-old professor would be doing. [laughter]

MACFARLANE: But once they realize I'm real, that I'm serious about it, they give me all sorts of ideas. For example, if you can relate the subject to something in my life, I'm going to learn it. They have to make presentations to the class at the end of the semester on a topic of their choice. They make big PowerPoint presentations, and it'll involve anything from drug abuse, to how the breathalyzer works, to applications of medical care, pharmacology, the environment, and they have to apply what they've learned in class with something that . . . they have to have articles, they have to analyze the article, tell me what was their strategy in

developing the analysis. What were the fundamentals of it from the p-chem point of view? They do it. And I have a nice collection of PowerPoint presentations.

GRAYSON: That's neat.

MACFARLANE: [Yes]. This will be just one example: measure the sugar content . . .

GRAYSON: Okay. [Yes].

MACFARLANE: This was their PowerPoint presentation. They give a little skit beforehand. Why is analysis important? They have to take that from the textbook. Then this particular one involves actually a touch pH meter that you put on the tooth to get the pH of the plaque. But they present this to the class, and here's the Nernst equation, and the fundamentals behind it all. And there's the statistics that go with it. And then here I tell them that there are two questions on the final exam that relate to the presentations. So you have to find out from the cells what you need to know about what are the fundamentals and what are the strategies.

GRAYSON: Gives these guys a little bit of a buzz, I guess, huh?

MACFARLANE: [What]?

GRAYSON: That gives them a little bit of a buzz to do something like that.

MACFARLANE: [Yes], it does. Well, when I tried this, I was worried had I gone too far? I sit back there, I'm almost nervous. They come up with these skits that last, like, five or six minutes to get the thing going, ranging from somebody that is picked up by the cops and given a breathalyzer. That one they're lying on the table, and they're delivering a baby, because they worried about . . . anyway. So one of them actually had a small rock group, guitar and all sorts of stuff. They were doing something . . . it literally had something to do with vocabulary. They look forward to this and there's lots of good feelings.

GRAYSON: I can imagine they'll remember this course long after they've left. [laughter]

MACFARLANE: My colleagues think it was screwball; that you really are an oddball.

GRAYSON: But they're learning something.

MACFARLANE: The word gets out, and I had even at one point . . . anyway.

GRAYSON: Take Macfarlane's class. It's a gas.

MACFARLANE: Well, it fills up like that. [fingers snapping]

GRAYSON: Oh, really?

MACFARLANE: [Yes]. Two sections and it's already filled up for the fall.

GRAYSON: I love it. This is interesting. My one son teaches organic at Tulane [University] and he's going to get saddled with organic [lab]. We were out on a float down the Guadalupe [River] a couple of weekends ago. I've still got some effects of that. But, my son was—the other son—was talking about all the chemical ingredients [listed] on the back of the sunblock [bottle], and so Scott got his camera and took a picture of it. I said, "What's that for?" "Well, I thought I'd show it to my organic chemistry class, and you know have them explain all these organic compounds and why would you have this in sunblock." So he's got this trying to connect it to the real-world aspect of things.

MACFARLANE: Sunblock is a favorite topic of theirs [the students].

GRAYSON: Oh, [yes].

MACFARLANE: Because that involves the spectroscopy part, so that's interesting to other guys. I know other guys are doing this. They're realizing that it beats . . . the old-fashioned way's not going to cut it.

GRAYSON: Well, <**T: 145 min**>, I don't know. It was kind of left over from another world. But the only input that is out there today is impossible. It doesn't really work. I mean if you want to go to the memorization thing . . .

MACFARLANE: [Yes].

GRAYSON: Who wants to do that?

MACFARLANE: They will. They love to surf the internet and I take advantage of that. So when they find a hot website, that's exactly what we're talking about, they'll share it with me.

GRAYSON: Oh, good.

MACFARLANE: Then I'll scan the website and I could email that website to the class. So it's very dynamic. The discovery part of science. They can get that feeling for did we discover something that's relevant. That's why I feel now my teaching and my research, it's the same mindset to come up with new ideas, thinking out of the box about the . . .

GRAYSON: Now you teach two sections?

MACFARLANE: I only teach one section. Another person teaches another section, which I'd say the traditional way you know, a textbook and . . .

GRAYSON: But then quantitative analysis has a lab associated with it too, doesn't it?

MACFARLANE: [Yes]. And that's something that I'm working at, and the lady that runs that, she knows what I'm doing. She's heard feedback from them. It's not traditionally . . . it's been treated like a totally separate course.

GRAYSON: The lab course?

MACFARLANE: I see the virtue of having it linked with my lectures. Now for example, she knows that there's one example, that Kjeldahl nitrogen analysis. I use the Kjeldahl analysis as a paradigm for titration. You can get into what the nitrogen analysis involves. Is it connected with proteins? And the proteins are something that's important for Third World nutrition, and then we're continuing and developing new agriculture products that are high in protein. That's a big deal, is the protein analysis. Then we're actually making beef that's been raised on a particular diet that's supposed to be rich in protein and low in fat. I don't know where I'm going on that. But then . . . okay, so I lost my train of thought on that one.

GRAYSON: Well, using Kjeldahl as a model for—

MACFARLANE: [Yes], right. [. . .] Right. But then the other things like the marijuana detection in urine, and analysis of the sunscreen, and there was a really neat application of Beer's Law using the sun as a light source to measure the ozone content in the upper atmosphere. The students found an article on that, and they made their presentation on the use of the Beer's Law.

GRAYSON: That's neat.

MACFARLANE: [Yes]. I would never have thought of that, but they have a whole collection now of really interesting PowerPoint presentations.

GRAYSON: You know, the idea that the subject that you're learning is connected in many ways to the real world, and they're giving you real-time information about the world, just makes it a heck of a lot better than just . . .

MACFARLANE: Well, that's the word I get from the students. "We're willing to do that, if you can relate to our lives". And I remember one time I had a student come to me, it was very close to the beginning of class last semester. He had failed the first exam. Said, "I've never failed an exam in my life and this could be devastating to me, because I want to go to med school."

GRAYSON: Oh, yes, the old med school problem.

MACFARLANE: And so I said, "Well, just show me how you're studying." He said—and it was obvious he was memorizing. I said, "That's your problem." He said, "What? There's no other way." I said, "Yes, conceptual understanding." "What's that mean?" I gave him an example. "I never thought of that." I noticed that all the rest of the semester he got As, but he never, he never came back to me to visit me here <**T: 150 min**> except six years later, he came back to my office—

GRAYSON: So this is six years ago?

MACFARLANE: Six years later.

GRAYSON: Later, [yes].

MACFARLANE: And he said, "Remember me?" I said, "Vaguely." He said, "Well, I came to your office and I failed my exam. I was upset about it. You told me what conceptual learning is." I said, "Oh, I remember now." "Well, today I graduated from med school, and you are the reason I made it." Well, that made a good day.

GRAYSON: [Yes].

MACFARLANE: Because I learned what conceptual learning means, because conceptual understanding of theory comes . . . [fingers snapping]

GRAYSON: [Yes]. [Yes], and besides, I think you would want your MD to learn that way.

MACFARLANE: That's right. Well, they do actually, because my wife has been through that now. And the medical school's actually realized this. In fact, the first complaint they get from their students is they're memorizers. It's something; you cannot be a memorizer and be an MD. The way that the medical school has developed [now] is there is lots of shadowing and hands-on stuff. So that's another way of getting reality to us. So you spend years in med school and as a resident to get practical experience, but that's another way of . . .

GRAYSON: Definitely, [yes].

MACFARLANE: [Yes]. So now, I'm amazed that that stuff my wife comes up with. Oh, but some little detail. "How do you remember that?" "Well, we learned that in med school; when we see some patients that have that, it kind of sinks in."

GRAYSON: [Yes]. I'm sure they've seen a lot of patients with that condition.

MACFARLANE: So medical research is very, very well designed and works really well.

GRAYSON: What do you think about a break for lunch?

MACFARLANE: Okay. I have an interesting place to go to, if you want to.

GRAYSON: Yes.

MACFARLANE: We can walk to it, if you're up to that. [. . .]

[END OF AUDIO, FILE #1.1]

GRAYSON: Looks like we're ready to go again after a very pleasant lunch at [Café] Eccell. [. . .] Okay, very good. One of the things that occurred to me while we were having lunch is the fact that you were a senior faculty member, but you're still here doing research. A lot of institutions have this, you know, retirement, or push you out the door, or tell you it's time to hang it up, and beat it. Is A&M pretty generous that way?

MACFARLANE: I think it's very much dependent on the individual, because I'm worried about this. Right now, federally, they can't fire me because of my age, but they can make life difficult for you if you're not producing. And by not producing, it means that you don't have research grants, and that you're not teaching an undergraduate course. The two of us that are at this advanced age both are aware of this and are both very active in our research and our teaching. So any time, if there is an attempt to suggest I leave, I said put it in writing. And so that's my game plan.

So far, Dave [David H.] Russell has been kind to me. I think he's kind of ambivalent. I know he was the one that [offered me] distinguished professor. A lot of things that he did were kind of unusual. We had a collaboration with Johns Hopkins [University] that involved them preparing some cell cultures for which we were to send them some samples of our HDL, and the timing was critical. And I don't know if I should even tell you this, because it's not really relevant to the . . . but I'll give you the example of what happens around here all the time. At that time, they decided—there was too much mold in the buildings and there was a mold remediation scheduled for the day that we were supposed to be preparing the samples. So, that meant that we couldn't send the samples, even though the cell culture was ready. So, I mentioned this to the dean—there was some sort of a social event. I said, "I got a problem here." He says, "I don't see what the problem is. I'll just tell the remediation to delay a week, that's no big deal."

Well, Dave got wind of this, and shit hit the fan. "You're doing this behind my back, and it's a bust! They have a schedule, and they have to do the remediation that day, period." And he was pissed off at the dean. The dean got all nervous about it, because he—the dean—did not

want to upset Dave. So that's what happened. It was several thousand dollars' worth of cell cultures that went down the drain. So they had quite a fight about it. So is Dave really on my side? My bottom line right now is he is, you know, with some reservations. When I told him I was funded again: "Oh, really?" Instead of saying, "Wow, congratulations;" "Oh, really," because I think that's probably, the natural exit is I lose my funding, and then it's . . .

GRAYSON: [Yes]. Well, that's kind of like the gold standard of whether you can hang in here. So now, Dave is the chair of the department of chemistry?

MACFARLANE: [Yes].

GRAYSON: So he's the guy that was sitting in that office over in 107?

MACFARLANE: Not really. He spends more time, I think, in the other building.

GRAYSON: [Yes], he does. But I mean that's his office over in Room 107.

MACFARLANE: Right.

GRAYSON: Well, in this school, it's probably a very important position. A lot of schools . . .

MACFARLANE: I can't read Dave very well, because I get two readings from him, one that is supporting me, and one that is neutral. The sooner that I leave, the sooner he can hand that position to someone younger. My feeling is that, as long as I'm productive and now I have a website, and it's a chat room for other faculty who want to get ideas for teaching, he went along with that. So I'm just kind of being neutral on it, and just kind of moving with the flow, and keep my antennae up.

GRAYSON: I mean, you want to stay in this environment as long as you can? <**T: 05 min**>

MACFARLANE: That's right.

GRAYSON: [Yes]. Well, it's challenging intellectually and sounds like it's a lot of fun. I mean that's what it's really about in the final analysis.

MACFARLANE: [Yes]. But I think that it has a survival aspect, I have to be aware that I'm vulnerable. My other colleague, who is a couple years older than I am, feels the same way. You're talking about contributing to the department

GRAYSON: So the chemistry department's a bit far-flung, because the building here is with cardiovascular disease, was it? What's the title again?

MACFARLANE: Laboratory for Cardiovascular Chemistry.

GRAYSON: Cardiovascular chemistry. [Yes], we got the chemistry in there. [Yes]. Well, that's an interesting mixture of concepts. Okay. Well, I just wanted to . . . because I know this is an issue that John Fenn faced at Yale—issues with them trying to . . . well, I guess, they did eventually kind of push him out.

MACFARLANE: [Yes], right.

GRAYSON: But it's interesting. Winning Nobel Prize [Chemistry, 2002] gets you back in, [Yes]. Let's see . . . how we doing with this little outline. What've we gone through? Well, now, you do have a couple of patents. How does the school treat patents? Is that . . .

MACFARLANE: [Yes], very well.

GRAYSON: Very well.

MACFARLANE: They are kind of novices at it. The first time this became an issue was when we had a collaboration with Johns Hopkins. And they were looking at the cord blood of newborns and wanted to know if our method would distinguish between newborns born smaller than they should be and newborns born normal size. And their data showed that if you're prematurely born, your chances of getting premature heart disease is a lot higher. They wanted to know why. Is there anything in their blood, when they're newborns—the cord blood—that would distinguish that. We agreed to run some samples for them. We didn't know which is which and our results was that there are two populations, one population is this, one population is that, and they were dumbfounded, because we separated the smaller than they should be from the normal.

GRAYSON: This is looking at cord blood?

MACFARLANE: Cord blood.

GRAYSON: Analyzing it by what method . . .

MACFARLANE: Lipoprotein method . . .

GRAYSON: Which is the . . . okay.

MACFARLANE: Density profile. And so there's a bump in the HDL that was there for some but not for the others. That bump was due to being born more small than they should be. They get all excited about that, and we have actually been able to get a *JAMA* [*Journal of the American Medical Association*] article on it.[15] That was a bit of a tour de force, because they never before—this was based on something they initiated. We had to put in language that an MD would understand. So that was a bit of a challenge. We did it, and it got published. And so then I said to our collaborator, I said, "This looks like something that should be patented." "Well, we've been thinking about that." Nothing happened. Nothing happened. Then I mentioned it to our technology transfer people, and they said, "Well let's look into it." He emailed back and said they've already filed a patent and your name is not on it. They contacted the patent office at Hopkins and they said, "Sue us."

GRAYSON: Oh, wow.

MACFARLANE: I tell you the story because it means that our office, technology transfer, was weak. And so they admit this. They just don't have the power that Johns Hopkins has. So then more issues came up and then there was another discovery that we made for which we got a patent. Then one of our alumni ran a business that was pretty good. He sold it, and he had some money that he wanted to invest, so he came to department and says, "Is there anything ongoing that looks like it might have some financial traction?" And he <**T: 10 min**> mentioned our project.

[15] P. O. Kwiterovich, S. L. Cockrill, D. G. Virgil, E. S. Garrett, J. Otvos, C. Knight-Gibson, P. Alaupovic, T. Forte, L. Zhang, Z. N. Farwig, and R. D. Macfarlane, "A Large High-density Lipoprotein Enriched in Apolipoprotein C1: A Novel Biochemical Marker in Infants of Lower Birth Weight and Younger Gestational Age." *JAMA* 293, no. 15 (2005): 1891-1899.

He got in contact with me. He's a good friend of mine actually, from when he was a student. So he had his company based out of Houston [Texas]. And he bought the license for the technology and started to pay fees for this, we got a little bit of income from that. So then we told him exactly how we were doing it. He sat in our group meetings, that we had nondisclosure agreement between us. So he got the business going [. . .] and he found a loophole in the patent. So he got around it, and said, "Bye. I'm on my own." Then I said to patent officer, "What are we going to do about it?" He said, "We don't have the tools to fight it, and we can't do anything about it." So he used our name in his advertisement and all that sort of stuff. Then he started to file other patents based on stuff that we shared with him in our group meetings. So therefore, I said, "This is not going to work." [We] just don't have a patent office with any teeth in it. We still got some patents out of it. Now, the latest thing is this.

GRAYSON: [Yes]. I was thinking that should be patentable.

MACFARLANE: [Yes]. So then the patent office at A&M asked Scott & White because they provided the serum. And my wife was on it. They got their teeth into it, and said this is something that's big time. So then they hired lawyers out of Boston [Massachusetts], high profile, big time lawyers that—

GRAYSON: The Boston lawyers?

MACFARLANE: That's right. So they looked at it. He got very excited about it. Actually, when he reviewed it, and commented on it, it's like he was one of the group. He understood what we were doing. He spoke in glowing terms, this is really a hot issue here. So out of that the patent application was filed with A&M and Scott & White on it and so that's a done deal. It's now at the patent office. We just got an acknowledgement that they've gotten it. So I know that NIH is excited about it, because it's evidence that research they're funding actually has some possibility of being part of being, of having access to public . . . . So anyway, that's where we are on this.

GRAYSON: So that's in process?

MACFARLANE: Well, it's been accepted by the patent applications. By the patent office in Washington. It's going up the international thing as well.

GRAYSON: Normally, the originator doesn't get a whole lot in terms of financial remuneration from a patent. I guess you don't get much of anything, do you? Or . . .

MACFARLANE: On the other ones, why, like, when [inaudible] license we're getting, every three months I get a five hundred dollar check.

GRAYSON: Oh, okay.

MACFARLANE: And my rule is that if there's any student that was involved in it they're on the patent as well. It's a given. And so Deva's on this patent.

GRAYSON: Oh, okay.

MACFARLANE: And so they realize that. So they get a check every once in a while as well. It's not big money, but it's residual. The driving force is to have access to the public.

GRAYSON: At least there are some patents going forward and these are actually realize something . . .

MACFARLANE: Four of five. In fact, I have one plaque that . . .

GRAYSON: Oh, [Yes]. [. . .]

MACFARLANE: So my dream was that . . . we actually had a meeting on this a couple days ago. They were talking about a new research park, and [. . .] and the purpose of the research park was to find a mechanism to take academic research [coming out of A&M] and they would take care of the business end of it. I'm really excited about that, because I thought that what we did in the lab here, we would be the research and development part, and then over there would be the laboratory that would actually <**T: 15 min**> run samples for us. And unfortunately, that didn't come to pass.

There was some politics that was . . . but that was the game plan. I think that what reactivated it is the business of academic research being commercialized is important, as the big companies realized how they cannot support having in-house research and development. There's a company in Richmond, Virginia, that's interested in our technology. And from what I see now with A&M and Scott & White Hospital. So this is a meal ticket, where they want to get a patent on it, and license it to a company, and get income from the license. They could care less about the altruistic part.

I've realized it's the reality of life. Hopefully, at some point that won't always be the case, because there's a lab in Minnesota, it's a model for an academic—well, a commercial lab running [in an] academic setting. That particular lab gets a reputation. My feeling and my hope is that we could establish a lab based on our technology that's unique, that I'd be able to send them blood samples and we'd be able to tell them whether they already have [. . .] or whether the particular measurement they're working on is effective or not.

And because the little we've done so far, the patients—Cathy's patients—as soon as they see that they are on the CVD side, they immediately want to check the kids to see if they have inherited it. So I think this is probably where all the action is going to be, but as a prevention part and the fact that there's [some] evidence that if you catch it early, you can actually reverse it, change the chemistry, the level of proteins, and you can actually have these plaques, re-dissolve off of that. There's a couple people who are in the field say this is where the future is. Keep at it.

GRAYSON: Well, it sounds like—

MACFARLANE: Did I answer your question?

GRAYSON: [Yes]. But it reflects the present state of your research and the importance of what you're doing. The fact that it has immediate impact on life as we know it, what it is that the Wash. U tries to promote some as lab bench to bedside, you know.

MACFARLANE: Right, [yes].

GRAYSON: What you do in a lab has a direct connection to bedside patient treatment? [. . .]

Okay. So your decision to go into academia really just kind of evolved out of your continued interest in doing fun things and not having a boss.

MACFARLANE: [Yes].

GRAYSON: You feel like you don't have a boss, or . . . ?

MACFARLANE: [Yes], I feel like I have a boss. [inaudible] It was really motivated by my summer jobs in industry seeing the administrative structure. [. . .] Where are you on [your list]?

GRAYSON: I was looking at the scientific innovation, what it means to you. It's right after your experience [in the outline].

MACFARLANE: [. . .] I tell my students to keep their eyes open. If you're surprised, let nature tell us what no one has ever seen before. That's how I approach it, the innovation question. <**T: 20 min**> We'll do this in three different fields, nuclear chemistry, mass spectrometry, and cardiovascular research.

Professional network with peers. [Professional] network has been more in the clinical studies, where my wife is kind of like the catalyst for this, because what she has done is she established a network. In fact, she's very successful at this, at a national level. One thing that the HMOs are doing is, they're starting to unite to develop [this kind of] network, where they can communicate with each other electronically. And the NIH and Francis Collins in particular, is very excited about this. They have more of a community-type interaction.

So, I see this as a potential source of patients, if we get our act together, that it's become a viable clinical procedures that we would actualize to thirty HMOs that are in the network right now. Cathy, at a national level, is a leader in this, because she speaks the language of the MD as well as the scientist. Which is what is catching on. There are very few people that have a foot in both fields.

GRAYSON: [Yes]. So what is her specialty in the MD side?

MACFARLANE: Her specialty is actually . . . they kind of made a position for her. She's in cardiology, and what they call lipid management. What she has a license now for that. She's got a fellowship with the National Lipid Association, so she gets referrals from the cardiologists. Typically a patient comes to them, they have documented coronary artery disease and no risk factors. So why the devil do they have it and what do I do for the treatment? That's where the sort of thing that she does that are relatively new. But then she sends the samples to us, get a profile for these people to get some insight as to what's going on.

GRAYSON: So, I guess all the appropriate protocols and what-not are taken care of in terms of samples that patient's given.

MACFARLANE: Oh, big time. I have two IRB [Institutional Review Board] groups that I have to address . . .

GRAYSON: So IRB?

MACFARLANE: Institutional Review Board. To make sure that they maintain patient confidentiality, the patient safety. Actually, the IRB rules are more stringent here at A&M than they are at Scott & White. Lots of groups have to go through all this and to prove that I have covered all the bases. I think that's one thing why not very many people are in the physical science field get involved with people. If you work with mice, you don't have to do that.

GRAYSON: Oh, [yes].

MACFARLANE: You don't have to do that. But I thought here again, if I want to separate myself from the masses, I'm willing to take the—

GRAYSON: Put up with the extra paperwork.

MACFARLANE: —and get my IRB approval. So then the NIH demands that if I have human subjects, I have to follow the rules, and get the certification. So I don't mind that.

GRAYSON: No. It's a highly bureaucratic kind of thing.

MACFARLANE: Extremely. But on the other hand, I have to say that it makes sense. I had to take an online course. It took three days for me to do it, and it was really very informative. It was back to the Nuremberg Trials, Nazis and what they did. It builds up to some of the stuff that we did in the US that, with the blacks at Tuskegee that, using the blacks as mice for human studies. So it's very informative. It's not a waste of time, although it took a lot of time to get approved. But I learned a lot from it. And the pre-meds who are involved in the group, they have to take that as well. They have to know, if you're going to work with humans, these are the things you're going to worry about. So I'm comfortable with that, and I want everything aboveboard. NIH has helped me a lot with this, because at first I was nervous about it. Initially, they determined that I was not subject to these restrictions, because I didn't know who the people were. Anonymous samples. But then they changed the definition of anonymous.

GRAYSON: Oh, my. How do you do that?

MACFARLANE: They did. They said <**T: 25 min**> we have determined that you're [not] exempt from this because you really are not exempt the way that your proposal reads. This is like six years after—

GRAYSON: Oh, great.

MACFARLANE: —doing it. But you don't argue with these guys. They said, "This is what you got to do, and this is what you got to do," and [. . .] they walked me through it, and I realized that I could do it. But NIH was tremendously helpful. They weren't bureaucratic at all, they said, "Just be calm, careful, and keep your cool." So it all worked out. So that part, I had to address it. Now whenever I'm developing these studies that involve the college student, it's a sure thing that I will be protecting them with IRB rules.

GRAYSON: All part of the game.

MACFARLANE: So I did innovation. The professional network is through . . . what we have right now is that we get a blood sample from Cathy—from her patients. We have a bubble sheet that tells the details of that medical history of that patient. We don't know who the patient is—a serial number. Then we do our thing. And then then we prepare these HDL2, HDL3 fractions for the rest of the collaborations. There is one collaboration that does cell culture studies, another collaboration does animal model stuff. Another collaboration with expert on lipoproteins [. . .]

GRAYSON: So you're kind of doing sample work up for various collaborators in this stage, but you're going to need to work the sample up for what you're going to do anyway.

MACFARLANE: Right. That's right. It's just a matter of purifying the sample, and quantifying how much is there. And that's a part of the contribution to the . . .

GRAYSON: So you end up with the serum sample, then to work with . . .

MACFARLANE: [Yes]. And right now, we can actually do the measurement—our measurement—on a drop of blood. Other methods need a lot more blood. At some point, we were thinking about a finger stick as a possibility for what we're doing, which would actually be very attractive for the dissemination of the method. What we're learning from these collaborations is . . . . There's a particular group at Tufts University that's key to our field. The head of that group is one of the old-timers that's set in his ways, but he has young faculty who are not set in their ways, [and we are interacting] with them. There was a meeting in Vancouver [Canada] last year where we linked up with these people. We had a poster there, and this fellow came over and he studied the poster and studied it. He introduced himself and looked to be a

guy in his thirties. He says this is the direction that we should be going. He said, "Well I'm working with gel plates, but what you're seeing and what I'm seeing are compatible. We're coming to the same conclusions with regard to it being a system."

So we immediately began to establish a dialogue using the same language. This is growing, he said, so we sent him the samples recently, and he was so excited about the results he got, he said to Cathy, "You can only tell these results to Ron, but nobody else."

GRAYSON: Oh, wow.

MACFARLANE: I want us to put together a proposal just based on this. If this gets pulled off then his boss will add some certification what we're doing is real. It's the sort of thing that we needed, when we had mass spectrometry.

GRAYSON: [Yes]. You get some . . .

MACFARLANE: When Hank Fales and all those guys said, "This is real," all of a sudden, people took notice; otherwise, it's just . . .

GRAYSON: Get some validation.

MACFARLANE: [Yes]. So it looks like we're on the verge of getting validation from some of the bigwigs, if we play our game right and don't oversay . . .

GRAYSON: So you mentioned Hank Fales. I was working with Sandy [Sanford P.] Markey—

MACFARLANE: Sandy Markey, [yes].

GRAYSON: —to put together this poster <**T: 30 min**> that's going to be at ASMS that, you know, we mentioned the fact that you had gone to NIH to put together an instrument. That sounded like that was a fun event. And I was—

MACFARLANE: It was strange.

GRAYSON: Well, first off, Hank saw what you were doing and said, "I want to have one of these."

MACFARLANE: Right, right.

GRAYSON: [Yes]. And so he obviously, had some experiments in mind for it.

MACFARLANE: Well, actually this was part of my talk at the [NIH Mass Spectrometry in Biological Systems:] Hank Fales Symposium. In fact, [the title of] my talk was "Hank Fales: The Guardian Angel of Biomedical Mass Spectrometry," because when I first met him, I didn't know who he was but I knew he was associated with Frank Field and Burnaby Munson and was big on chemical ionization.[16] I could understand why here's a guy who was a physical scientist, rather than a NIH laboratory. It was applied. As the years went by, I realized that he had a vision that mass spectrometry was something that was going to be a major player in biomedical research. He didn't really know why or how, or what it was, but he pushed it without even saying it.

GRAYSON: [Yes].

MACFARLANE: So he picked up on chemical ionization, and then when he saw our stuff, he added that to his list of things he wanted. And then later on they built it. And so this is where I think he had a vision that mass spectrometry someday was going to mature to a point where it was going to be part of the mainstream of biomedical research. So, that was my message in my talk.

GRAYSON: So you've essentially built the instrument here?

MACFARLANE: Well, I built it. It was weird because he says NIH will provide you the money for it. I get a budget, and so I actually, all this stuff . . . we assembled it here. I got it working to make sure it was going to work.

GRAYSON: [Yes]. Now, was this fairly early in . . .

[16] Frank Field, Oral History Transcript #0636; Burnaby Munson, interview by Michael A. Grayson, at the University of Delaware, Newark, Delaware, 9 April 2010 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0688).

MACFARLANE: [Yes], it was early. Like, it was maybe 1975, or so. Then he hired a nuclear physicist out of Ken [Kenneth G.] Standing's lab—Ken, who was a nuclear person—to get the thing running.[17] I brought my group there, my electronics tech, and brought the regular tech, he's a Texan. He'd never been in a big city before. A lot of [time he spent] looking out the window of the hotel room at the traffic. I remember we were filling the vacuum pumps, and he kept asking the technician, say I want some "awl". So he said they don't understand what I'm saying, because "awl"—oil . . .

GRAYSON: Oil.

MACFARLANE: Oil.

GRAYSON: Oil. He repeated that, so he made that word sound silly, oil.

MACFARLANE: Oil. This is an example of this meeting of two different cultures, the Washington [DC] culture, and the College Station culture. It's basically a week. We actually got the thing working. We stayed at Hank's house, Cathy and I, and this is part of my talk, as well. I said one night we came home, and Cathy said—and we had our pet schnauzer with us. Cathy said, "Didn't they have curtains on the front window?" I said, "Yes." "They're not there anymore." I said, "No, don't tell me." The dog had taken down the curtains and shredded the curtains.

GRAYSON: Oh, no.

MACFARLANE: It was part of my talk, because it brought out Hank's personality. There was a guy [. . .] in the audience. He was shaking his head like he knew the story. So Hank came home and I said, "Hank." He said, "Don't worry about it, we needed new curtains anyway." [laughter] That was Hank Fales. Nothing fazed him. So that incident really broke the ice. We became really close after that.

GRAYSON: Oh, [yes]. I mean, I never was close to Hank. I know, the only time I really ran into him was the conferences, but he just seemed like such a wonderful guy, and so laid back, and so interested in trying to promote whatever would make it better, you know, whatever he could see to . . . for the field. <**T: 35 min**>

[17] Kenneth G. Standing, interview by Michael A. Grayson at University of Manitoba, Winnipeg, Manitoba, Canada, 29 October 2014 (Philadelphia: Science History Institute, Oral History Transcript # 0922).

MACFARLANE: Well, there was more to it that came out at this Symposium, because he actually been involved in other fields. The bottom line was applying mass spectrometry to other fields. So it was a lot of stuff relating to the snakes research, for example, that showed that mass spectrometry could actually give you some new insights into the chemistry of snakes. There [were] some other fields that were totally off the wall, that he brought mass spectrometry into it, and it elevated it to our level. That was his theme of life. That mass spectrometry was so powerful that no matter what area you applied it to, it was going to greatly accelerate the development of that field.

GRAYSON: [Yes]. This, well, you know, it's too bad he's no longer with us. But I was hoping to interview him, you know, but unfortunately his name was on the list. But I didn't get the word soon enough to get it done. So he's definitely an important person to mass spectrometry in so many ways. That's what we're trying to convey in this poster that'll be at ASMS in Denver [Colorado]. There's so many new people in the field that don't understand the significance of some of these names. We're just trying to get that [. . .] through to the new people.

We were having a little discussion at lunch about this outfit called [Texas] Public Policy Foundation. Historically, it might be good to just get a concept of what that's about, and where you are, and where Texas is, and where A&M is in regard to that. In an effort . . . when some people, when they see the idea they think it's good, but then when they see the embodiment of it, they say it's not so good.

MACFARLANE: Well, I give a lot of thought to it [. . .] The basic idea, as you can see, is the fact that our bureaucracy, for example, has too many assistants and associates, so that part I think it could be streamlined. A lot of our resources go into administration and not the academic part. Then when it comes to cutting back, they don't cut back on administration, they cut back on the teaching and all this sort of stuff. So there's a problem there, administratively, that's something that's a political part in that. The basic idea with what they call these seven breakthrough things is that the university—public universities [. . .] they want to also have something that's not really cost effective, because it's not going to be a cost expense for the average family. They see that the tuition's going up and up and up. They want to control that.

This is what the governor has been doing. They had this think tank look into the economic thing and saw that it was run inefficiently and that they had evidence that there were some professors that weren't pulling their weight and didn't have any research grants. They had TAs running their lectures. And that's true. They just, they really it's a soft . . . going to be lots of time off, summers off, if you want to. So we're looking at a few people that have that, they give a bad mark for everybody.

There are professors that are not going to change their lectures from one year to the next. It was definitely a problem. So when I talk about innovation in teaching, I tell them, "These kids are different." "No, they're not. They're lazy. They're always on their cell phone, blah, blah,

blah, they just don't want to work." So, a lot of them are like that, and a lot of us are just the opposite. So what this group has done is stir the pot. So <**T: 40 min**> consequently, the majority of the faculty feel threatened by this. And the people who are in this think tank, they're very conservative, looking at stuff like the forty-hour week. They even rank us in terms of the money we bring in. It's our research money, plus the money that we get from the state in terms of how many students we teach. So if we teach a big freshman class, then you're in the black. If you teach an upper division class like me, I'm in the red. [I'm not bringing in as much.] They're kind of naïve on that part, but I think their strategy for the first step was to create a shock to actually give some publicity to the fact that higher education needs to change. I'm interested in this for quite some time, wondering if we're really relevant.

We have a lot of collaboration with other companies—the department does. They provide some money. So I asked them one time if we were doing a good job in teaching the young people about industry. He says, "Not really." "Oh, what are we doing wrong?" He said, "Well, they're very good at solving problems already solved and not at problems that haven't been solved. They don't know how to do it." So, okay, I can see that. I was on a committee that was in charge of the relationship between the chemistry department and industry. The chairman of that committee asked me for ideas. I said, "Well, I think one thing we ought to do is, we ought to talk to these companies and ask them if we're doing a good job." He said, "I'm not interested in that."

GRAYSON: They don't want any feedback.

MACFARLANE: [Yes], end of story. So that's why I think the reason we are missing them . . . . There's a sickness, and that sickness is being brought out in a rather dramatic way. I have fifty new emails on my computer right now that have come in since a few hours ago, related to the dialogue as to what to do today. I was talking to that fellow that said you're talking about the board of regents. There's a bunch of us that are in there to provide some input. But I think that what might come out of this is ideally two things. That we should pay more attention to the research that we're doing, not just say we're doing research because we don't want to do it. Something you've got to learn when you're in graduate school. At least pick a topic that's a possibility that it could have some benefit to society, if we're a public university. Private university, I think you have more flexibility.

GRAYSON: [Yes].

MACFARLANE: I think if you're a public university, you're obligated to do something, at least has some possibility of bettering society, if there's public money in it. Here again, there's going to be a lot of flak on it's pure research that's something you don't touch. The other thing is what we're teaching and the way we teach it. If we're preparing these young people for the outside world—and for the first time yesterday, I got an email that said we ought to be focusing

on that—jobs. I think that after all the dust has settled and we look at these issues to see whether we can definitely improve higher education to be receptive to the needs of society, because things have changed. We have to change. We can't be doing things the way we were doing before.

GRAYSON: Yes. Well, change is not always met with great enthusiasm.

MACFARLANE: Right.

GRAYSON: Well, I think we got a pretty good sense of your current work and interests which are being an innovative teacher and getting into cardiovascular chemistry.

MACFARLANE: Read what I wrote. Surely improving health care, prevention, and early detection; influencing and inspiring young people to be creative and recognize the real nature. It's kind of like what your son is doing, and so anyway, that's <**T: 45 min**> . . . the dog sniffing is an example of using nature as the ultimate professor.

GRAYSON: Just for the benefit of those people who weren't privy to our previous conversation, it was about the fact that animals, particularly dogs, can be trained to detect the presence of colorectal cancers in people. There's something going on there that we, as humans need to tune in to and try and pick up on. If the dog can sniff it, then there's a small molecule involved. If there's a small molecule involved in [then if] we get the sensitivity high enough, we can find out what it is, and that'll further our diagnostic capabilities. The thing about these is if you can get it early on—I mean, it's a big problem with cancer is the sooner you know it, the better off you are.

MACFARLANE: I have a personal example of that. I have prostate cancer.

GRAYSON: Oh, really? Okay.

MACFARLANE: [Yes]. I caught it early and barely—

GRAYSON: Okay. So how are we doing here? [. . .]

MACFARLANE: I have a statement on that.

GRAYSON: Okay.

MACFARLANE: Pay more attention to higher education developing young people to be creative problem solvers, to put more emphasis on serving others, less on financial rewards. It kind of falls . . .

GRAYSON: [Yes], [yes]. I think it's something that should be done in the educational process. To some degree, I think some of our young incoming people, kids, this generation are a little bit more sensitive to the environment than maybe previous generations. I don't know if you've sensed that or seen it?

MACFARLANE: It's a mix. But right now, as I indicated to you from the profiles that I get, more and more of them are in it to serve the society and make a positive impact. I think a lot of the negative stuff has been turned off. So we say, "Well, our generation can do better than my parents."

GRAYSON: Okay. So you've got a series of people that you collaborated with over the years. I went and did an analysis of your work. I don't know if you . . . . This is your publication record as a function of time, at least from what I have. [. . .] If you'd like to go over the principles in the publication list. Obviously, you collaborated with some people more than others over your career. I'd just like to kind of get your insight into that collaboration and . . .

MACFARLANE: Oh, [yes]. Cathy's my wife.

GRAYSON: Okay.

MACFARLANE: Dave Torgerson was my postdoc from Canada, and came down with me.

GRAYSON: So he actually came down to A&M. Wow.

MACFARLANE: And Neil Oakey, he's another Canadian. He didn't come down, but he was a major student when I was at McMaster. Dave actually was having this PhD stuff. He was the one that actually . . . . Also part of the Yale experiments back and forth, back and forth, as a

nuclear chemist. Then he was in my group, when we discovered the californium desorption. He's first author of that first paper.[18]

[. . .] We printed two of them. They generated two hundred californium mass spectrometers. But at the time, it was Bondarenko was there. Pavel was in that with the company. So he came here to continue this, and then [. . .] he was involved more in mass spectrometry, californium stuff. But when Pavel came here, we'd already made the decision to shut down the californium system, and got involved in MALDI—[Dave Russell's operation]. So the first thesis that actually involved mass spectrometry—MALDI mass spectrometry—was his. He's the one that discovered several new isoforms. He set the stage for the whole thing. Then these other people were graduate students for the most part. [A.] Benninghoven, he's a SIMS [surface ionization mass spectrometry] man. We had some interaction there with him.

GRAYSON: Was that through just collaboration at a distance?

MACFARLANE: [Yes], although he came to visit the lab to see what we were doing, because he was a guru for SIMS. What we were doing that could not be done by SIMS and realized that his SIMS was more or less concentrating in inorganic systems—the crystals and surfaces.

GRAYSON: [Yes].

MACFARLANE: Then all of this other stuff was—the organic stuff was background he didn't want. Then he realized the background is really—

GRAYSON: [Yes], it's more important than—

MACFARLANE: Well, that actually is another dimension. Then being a physicist . . . . Chemistry and physics, again we see that at the Tandem Accelerator Laboratory, our collaborator in Uppsala. All these other people are . . .

GRAYSON: Well, it kind of entails now just a couple of publications, but the ones where you've had, obviously, a long . . .

[18] D. F. Torgerson, R. P. Skowronski, and R. D. Macfarlane, "New Approach to the Mass Spectroscopy of Nonvolatile Compounds," *Biochemical and Biophysical Research Communications*, 60, no. 2 (1974), 616-21.

MACFARLANE: [inaudible] for example, is one of the people that was just totally . . . . I think he's in Israel—an Israeli natural product chemist. He was enamored with it. He's the one that said we were the eyes of his laboratory.

GRAYSON: Did you ever have any collaborations that blew up in your face?

MACFARLANE: No.

GRAYSON: Most of them were pretty . . .

MACFARLANE: Well, except the Uppsala people. They were a strange bunch. They came and they spent a lot of time in our lab. They want to know everything. Then we visit Uppsala. They want to keep stuff away from us that they had developed. Was that a fair thing? At some point, I got irritated with them and they wanted to know what we were doing, and they were keeping what they were doing [close] to the vest. I didn't think that was very . . . I didn't understand . . .

GRAYSON: [Yes], that you were open and aboveboard with them. It seemed like they would reciprocate.

MACFARLANE: Like, they're the ones that used nitrocellulose as a matrix. They said, "We have a new matrix that gives higher yields." What is it? So that kind of soured that relationship to a point where we really weren't doing so much sharing. But they were doing that. There are other laboratories who were just the opposite. You know the laboratories in France and Germany, a lot of sharing was going on, and synergistic stuff. But the Uppsala group they just . . . it's everybody. They kind of said, "Just stay away from us," kind of thing. But that was the only time that collaborations were a little bit sour.

GRAYSON: Well, it could be that the general mentality of the area, or group leader, or the head person would have some kind of . . . some people were very protective of their research and didn't want anybody else to know what they were doing trying to understand it.

MACFARLANE: Right. [Yes]. Well, I think Bo Sundqvist was actually the leader of that group and was very frustrated that he wasn't getting the recognition that he was in the field. It was because he was standoffish in part. He was not really considered to be part of that inner family. I think he sensed this and that might have been part of it. But that was the only sour part of collaboration. <**T: 55 min**>

GRAYSON: Okay. Well, we covered funding and that good stuff.

MACFARLANE: Special topics. Where are you?

GRAYSON: [Yes]. Well, I think we finished your current work interests and that kind of thing. I think we're just at the special topics related to your own career. I think we covered some of these items . . .

MACFARLANE: [. . .] I told you about the nuclear chemistry, the phases of the chemistry as rotation. The mass spectrometry, not my choice. I don't want to get into it, but that it was something . . . we had fifteen years we had the whole field to ourselves.

GRAYSON: Fifteen years?

MACFARLANE: I had the whole field to myself. It took that long for the MALDI and the ESI to really take hold, and be something that was a continuation.

GRAYSON: See. I don't know. In my mind—and you can correct me, if you think I'm wrong, or have a different perspective on it—but I see the rising of time-of-flight mass spectrometry rising from the ashes beginning with your work.

MACFARLANE: [Yes], that's right.

GRAYSON: I mean, obviously the reflectron was necessary.

MACFARLANE: That's right. It was a nice addition.

GRAYSON: But the fact that you use TOF as an analyzer, and were getting results with it, got people to think about, well, can that analyzer concept be proved to the point . . . you know, let's go back and revisit it, because obviously, I know Bendix struggled with trying to improve the resolving power of their basic instrument. They didn't have—their mindset was too rigid in it.

MACFARLANE: [Yes].

GRAYSON: I mean, they had some ideas that . . . . I mean, they had time-lag focusing, which was so . . .

MACFARLANE: Right, right.

GRAYSON: Which helped some. Then they had the idea you really had to get these pulses sharpened up. It was never going to . . . . You had to come up with something more than that.

MACFARLANE: Right. A lot of prejudice against that. In fact, when McLafferty first visited our lab to give a talk, he wouldn't even talk to me.[19] He said, "You're using time-of-flight, forget it." It wasn't until later when he saw me doing it, okay. The big prejudice against that is that I don't have control over that. I didn't have a magnet. I didn't really want to say that these three sector magnets were going to be dinosaurs, because I was not in the position. I just wanted to blend in. Whatever fell, fell. I didn't really care. I figured, you can always go back to nuclear chemistry if it doesn't turn out. But the drug companies, all these people were sending me samples. There were some interesting stories there, because they . . . well, there was a well-known natural-product industry initiative of Colombia.

GRAYSON: Do you know how to spell?

MACFARLANE: It was in my . . . I think it was in . . .

GRAYSON: Okay, I'll dig them out of . . .

MACFARLANE: Anyway, he sent me a sample. He says, "You've got the wrong answer, so I'm going to send it off to McCloskey.[20] I'll derivatize it, and maybe I'll get the right answer." So there were a few other situations. Well, one of the most dramatic was Al Cotton, for example. He had a very complicated molecular cluster that he wanted to have the molecular weight on. So we got a very nice mass spectrum of it. I said, "You're off by two mass units."

GRAYSON: Two mass units?

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[19] Fred McLafferty, Oral History Transcript #0352.
[20] James McCloskey, Oral History Transcript #0702.

MACFARLANE: Two mass units, [higher than expected.] So therefore your method is not very accurate.

GRAYSON: But, I mean, by that time you knew that it should be accurate to the . . .

MACFARLANE: Well, I didn't know.

GRAYSON: Oh, you were—

MACFARLANE: I never thought of a complicated little thing. I had no idea, or even what the mechanism of the ionization was. So two years later I ran into Cotton and he said, "Do you remember that you ran that particular molecule?" I said [yes]. He said, "You had the right answer." Cotton had realized there's a hydride molecule. It's in their crystal, and it's a major discovery. I said, "Well, that's nice to hear." It would have been nice to hear from Cotton earlier.

GRAYSON: [Yes].

MACFARLANE: He's a big guy. So there were other—lots of examples like that for the time, where I got the wrong answer and the right answer . . .

GRAYSON: Well, I think the technique was so different from what—you know, mass spectrometry—they say, "Well, then that's such a weird technique, if we're not getting what we expected, it must be a problem with the technique."

MACFARLANE: Well, [yes]. For some reason, in retrospect . . . . I mean, you asked me to do all this stuff, really brought back what was happening at the time. I was not emotionally reacting to that, because I did my job. I just felt like I didn't have any control over what . . . . The result I get is what I get, and you're probably right that I'm wrong. I did my best.

GRAYSON: [Yes]. So you didn't . . .

MACFARLANE: It wasn't an issue of my ego. Ego was not ever part of what I was doing, in part because I wanted to get out of the field. I wanted to get back to doing real science.

GRAYSON: [Yes]. But now you were getting paid for doing these analyses, I assume.

MACFARLANE: For a small fraction. Most of it was gratis.

GRAYSON: Oh, wow.

MACFARLANE: The companies . . . . I was able to establish a consulting agreement with a lot of companies. The other ones were all pro bono. A lot of the articles in there are due to these collaborations. Some of them, I didn't even know that they had published.

GRAYSON: Oh. Well, that's what I was wondering. I mean, as we've been working by email, your publication record from what I was able to—

MACFARLANE: I had no idea they had published particular result. Getting a publication is nice, but it would have been nice if they had told me.

GRAYSON: So your name was—yeah, I was thinking your name must have be on a whole bunch of publications that you never knew it was on.

MACFARLANE: Right.

GRAYSON: Because you never knew they were . . .

MACFARLANE: I would have liked to have known that, because I could have added it to my list on my annual report to NIH.

GRAYSON: [Yes]. Now you can report an extra fifty publications in the last year. [laughter]

MACFARLANE: [Yes], right. That'd be kind of weird. Anyway, it was a period of at least fifteen years that that was a lot of our material. A lot of the people in mass spectrometry did not

even know we were doing this. So later on, when the MALDI came up and these other things that, people like McCloskey that would do a lot of work with DNA fragments, from the literature found out that we had already done a lot of this stuff. I said, "[Yes], we did." He had no idea that the californium analysis had been done.

GRAYSON: Now you published that article in *Analytical Chemistry,* that eight-page article. That was what, 1983?[21]

MACFARLANE: [Yes], something . . . yeah, right.

GRAYSON: And that, but so did that get a buzz from that from the community?

MACFARLANE: No. The biggest buzz came from the *Science* article.[22]

GRAYSON: Oh, okay. That was earlier . . .

MACFARLANE: Nineteen seventy-six or something.

GRAYSON: [Yes], okay.

MACFARLANE: I was invited to do that. Again, Al Cotton—

GRAYSON: Oh, okay.

MACFARLANE: —was responsible for getting me the invitation.

GRAYSON: That's nice.

[21] R. D. Macfarlane, "Californium-252 Plasma Desorption Mass Spectrometry," *Analytical Chemistry*, 55 no. 12 (1983): 1247A-1250A.
[22] R. D. Macfarlane, D. F. Torgerson, "Californium-252 Plasma Desorption Mass Spectroscopy," *Science* 191 (1976): 920-925.

MACFARLANE: [Yes], it was. I mean, that's where the publicity really came out, the *Science* [article].

GRAYSON: Well, there's something about *Science*. Publications in *Science* get a lot of attention.

MACFARLANE: [Yes].

GRAYSON: Then the eight-page article was a little bit later in the *Analytical Chem*. [. . .] So you were saying, basically, the *Science* article is the one that got people to come to you. Well, I guess it probably gets spread out to a group of people that are a little bit more . . .

MACFARLANE: [Yes], that's right, outside of chemistry.

GRAYSON: [Yes], more than the *Analytical*. And into the bio and medical side of things, which is obviously where the technique has applications. So let's see., where are we on . . .

MACFARLANE: Impact the field on . . . let's see, biomedical research. [Yes]. I got into biomedical part, right now. Then just the impact of the field of particle desorption ionization. That's where I wasn't sure that there was an impact at all <**T: 65 min**>, because of the fact that there was such a strange method. The ASMS treated me very well. I gave an invited paper very early in the game. I was very nervous about that, and the audience was full. Here I am a stranger in front of all these people at the ASMS. I start off by saying that I was nervous about this, and the fact that I don't really know who the gurus are in the field. At that point, the door opened in back of me, and I had the guy from—

GRAYSON: MIT. Klaus Biemann.[23]

MACFARLANE: [Yes], Biemann, and the audience just broke up and laughed. I looked at him. I didn't know who he was. Then afterward, somebody said, "Do you know why there was all this laughter?" "I have no idea." That's Klaus Biemann. He's one of the . . .

GRAYSON: He's the guru of the gurus.

[23] Klaus Biemann, Oral History Transcript #0279.

MACFARLANE: Right. So I got off to a shaky start on that one. But afterwards, Robert Finnigan, for example said, "This is the most important development that's occurred in mass spectrometry in quite a while, and you made a real contribution."[24] They were real positive about it. The ASMS treated me extremely well, extremely well. People like . . . geez, my mind is getting tired now. Your colleague at Washington University.

GRAYSON: Ah, Gross. Mike Gross.

MACFARLANE: And the other guy that works with Mike on the *Journal* [*of Mass Spectrometry*]. He's at Vanderbilt [University].

GRAYSON: Ah, [yes]. [Richard M.] Caprioli.

MACFARLANE: [Yes], Caprioli. They were examples of a younger generation that took me under their wing and gave me lots of . . . . Because people like the big gurus, that's one thing to know. But to know that the younger generation has enough self-confidence to accept these for what they are—they really are contributions. I learned that psychologically there are people that are comfortable in their skin and people that are not comfortable in their skin. The people that are comfortable in their skin are able to take on some new development that may look to be something that they're doing, but they can accommodate it and pick it up. There are other people that can't handle it.

GRAYSON: Definitely. In a sense, it's a little bit understandable because, I mean, the guy has been pursuing a path that where he thinks this is going to be the way of the future, and he's been plowing away at it for a couple of years.

MACFARLANE: Like Biemann, for example.

GRAYSON: He's making progress, and it's—

MACFARLANE: He's the guru of derivatization.

[24] Robert E. Finnigan, interview by David C. Brock at Los Altos, California, 4 December 2001 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0227).

GRAYSON: [Yes]. Then somebody else comes along and does something that's totally off the wall, and totally unrelated, but is getting good answers, it's kind of hard to accommodate that new input.

MACFARLANE: So there is this bipolar aspect of the mass spec community that you're either in one camp or the other camp.

GRAYSON: I think there was an attempt by the Society or by the people that led the Society to try and cultivate the "young Turks," so to speak and try and—

MACFARLANE: [Yes], they use that term in fact, even early on.

GRAYSON: —give them a voice and get them involved, because I think they see it's a very dynamic field.

MACFARLANE: Oh, when I got into it, the ASMS was in trouble. These are the people that were like presidents. They weren't sure there was any future for ASMS, because they weren't attracting young people into it. As soon as it became apparent that mass spec actually played a role in the emerging proteomics, all of a sudden young people started to be attracted to mass spectrometry.

I think that was the spinoff that I could connect to. I had some sort of indirect influence on it. Now I feel also that the field is very dynamic, has a very bright future, and there are lots of wonderful ideas coming out of it. That's one reason why I went to the meetings. I probably will go to all the meetings from now on, just for old time's sake, and just . . . yeah, remembering that I really was part of it. I remember we had a visitor one time, one of Dave Russell's friends that he invited here to give a talk. He introduced me. This is Ron Macfarlane. [His friend] said, "The Macfarlane." Wow, the legend. [laughter]

GRAYSON: It's nice to know somebody thinks you did something useful.

MACFARLANE: Right. Then the SIMS people, they reacted to this, because they realized this was under their nose, they could have done it early on, if there had been some chemists doing SIMS, realized you can use SIMS in organic molecules. This is where Ken Standing came into the picture, because he was a nuclear person.

GRAYSON: Oh, he was?

MACFARLANE: [Yes], I knew of him from nuclear days. Manitoba.

GRAYSON: Okay.

MACFARLANE: So, he's familiar with all of the nuclear techniques. So his focus was on improving SIMS to where it could be competitive with PDMS. He really pushed it in terms of the physics behind it and the way that the energy was deposited. The idea of having a short energy burst was the secret to it, and you could simulate that with SIMS, if you do it right. So then the FAB came along, and I told you that there was influence there from my learning from Mickey [Michael] Barber.

GRAYSON: [Yes]. FAB was in, what, 1981? Somewhere in there.

MACFARLANE: [Yes]. I heard the first time—I was actually in England at a meeting where he had the first talk. It was the last talk of the session. This weak little voice came up and showed [this data and I thought "Gee whiz, we may have some competition here."]

Development of analyzers. We already talked about the fact that time-of-flight became legitimate after a while.

GRAYSON: [Yes]. A in Biemann's lab, you know, they had a Bendix machine, but they used it as a test bed. If it was a strange thing that they were going to try, and if it looked like it was going to work, then they'd put it on their "real" machine.

MACFARLANE: [Yes], right. I visited his lab, but I'll tell you his mass spectrometer looked like a nuclear laboratory. It was big, a three-sector instrument.

GRAYSON: [Yes].

MACFARLANE: It was big time.

GRAYSON: So personal interactions. Maybe people were competing with you but maybe you didn't know it, or you didn't feel like they were competing?

MACFARLANE: My colleagues in mass spectrometry were very wonderful, gracious and supportive. I had the opportunity to give invited talks. I was given the Distinguished Contribution Award by ASMS. [. . .] I never really felt like I had a competitor. I guess by the time I was doing all this stuff, there was nobody else to compete with. When the competition did come up, I was ready for it. I was tired of running samples. Then my mentor—I just mentioned Kohman and Seaborg. I can give you a copy of this.

GRAYSON: [Yes], that's probably a good idea. We can use that.

MACFARLANE: And my students, I see them at the ASMS meetings, and they're all doing well.

GRAYSON: Do you have a feeling for how many students ended up overall in the . . .

MACFARLANE: Well, there must have been at least thirty, not a whole lot. But they were all of this type that they were the thinking out of the box. They're not just looking for something with a rubber stamp. They wanted something new. For the most part, they went to the pharmaceutical industry working with biological samples. It's a big plus from what I am told. [. . .]

GRAYSON: [Yes]. We talked about one of them.

MACFARLANE: The first publication announcing the californium system.[25] I was worried about that, because it was really a mass spectrometry article about being a mass spectroscopist.

GRAYSON: What journal did you submit that to?

MACFARLANE: That was in [*Biochemical and Biophysical Research Communications*], same journal as that. But I was nervous that the . . . let's see <**T: 75 min**>, this is your . . .

GRAYSON: "A new approach to mass spec of nonvolatile compounds and . . ."

[25] Torgerson, Skowronski, and Macfarlane, "New Approach."

MACFARLANE: [Yes].

GRAYSON: Excuse me. [Number] seventy-four, that's in *Biochemical and Biophysical Research Communications*.

MACFARLANE: [Yes]. So then in 1971 we were doing work with radioactive [nucleotides, doing high] mass analysis. There was a forerunner of that.

GRAYSON: So that set the stage then as a primary . . .

MACFARLANE: [. . .] At that time, we had the results from this tetrodotoxin. I still wasn't convinced that we wanted to get into. And Dave Torgerson said, "You've got to publish this. This is something that we just can't let it die on the vine." I said, "If you're willing to write the article, go for it." So that's how that went.

And okay, so now I was . . . just the way I look at the field now when I see how proteomics is taking off, and I look back on the days when you couldn't do most amino acids, I said, "I think I made a contribution to the field." That's enough, I can't give any more than that. So then the year the Nobel Prizes came out, and I heard that Fenn had gotten it, I thought that's good. I [knew] a little bit about the politics part of it. Then a Dane [Peter Roepstorff] was also on that committee, and he was very unhappy with the results they got. It's to the point where he resigned from the committee [. . .].

So then I found out I was on the list, but that I didn't make it, and that was okay, too, because I didn't really . . . . It wasn't anything that was a big thing for me anyway. But then I got a communication from the Nobel Committee. So I'm on their mailing list. [Macfarlane hands a document to Grayson.]

GRAYSON: Interesting. So you're invited to submit a proposal for [why your research should be considered for a Nobel Prize].

MACFARLANE: [Yes].

GRAYSON: How do you respond to something like that?

MACFARLANE: Ah, I didn't. Probably this is something of an honor just to be asked. [. . .] I see what other fields are evolving as a part of my work, that's enough for me, to be satisfied with everything.

GRAYSON: [Yes]. So is this the way they worked? They end up actually inviting nominees to—

MACFARLANE: I guess so, [yes].

GRAYSON: —to submit a package, so to speak, for . . . I like the signatures. They mail <**T: 80 min**> this out to you. How much time do you have to do this, when you get it? It's got to be submitted by . . .

MACFARLANE: That one's already past.

GRAYSON: [Yes]. But, I mean, they have a deadline. So they sent it to you in 2008 and you have until January of 2009.

MACFARLANE: Right.

GRAYSON: That's a couple of months. [. . .] Well, it's a nice letter to have in your file.

MACFARLANE: I know. That's why I keep it.

GRAYSON: Can I get a copy of that for the—

MACFARLANE: [Yes].

GRAYSON: —file, for the records, and we can . . . it's nice you have everything here you need. That's it. My battery's shot. Oh, crud. I don't think I brought my . . . maybe I can do that tomorrow. Do you have a few minutes tomorrow when I can come in and do a short video?

MACFARLANE: [Yes].

GRAYSON: I thought I had this thing charged, but apparently it's not. I need to keep my wits about me in some of these things. Thank you, sir. Put that in the file. So if there's anything else you want to mention, I think we're getting . . .

MACFARLANE: I had some comments about the Philosophic interview.

GRAYSON: [Yes]. I'd like to do that with the video.

MACFARLANE: Okay.

GRAYSON: And just a short one. So I have to come back tomorrow and do that first thing in the morning, if you're amenable. Then we can pack up and get out of your hair. If you want, you can keep these guys, if you want to. I've got electronic files on those. I think it's fun to look at, you know, the different levels of productivity in terms of papers and so on, you know.

MACFARLANE: [Yes]. I have to work on this part, and I need to have . . . . I went all out and tried to get a bunch of papers out in the next couple of months.

GRAYSON: Did you finally get out all of those papers on the work that you did at Berkeley that you were—

MACFARLANE: Yes, I did.

GRAYSON: —letting pile up?

MACFARLANE: [Yes]. It was—

GRAYSON: The whole series of alpha or whatever . . .

MACFARLANE: Nineteen sixty-three. See, I left Berkeley in 1962. So all this stuff about 1962 was when I was at McMaster then. This is the one that Kohman . . . based on the thesis back in 1961 that he got all of these letters congratulating . . .

GRAYSON: Oh, the *Nature* paper?[26]

MACFARLANE: [Yes]. No, this one [fingers tapping].

GRAYSON: Oh, oh. I'm sorry, the [. . .] like I say the disconnect between what you had for your publication record, and what I was able to dig up what was going on was in the database thing out there.

MACFARLANE: So I guess what I'm going to do is I'm going to update my . . .

GRAYSON: [Yes]. Well, you have the electronic versions of . . .

MACFARLANE: Of what you sent me.

GRAYSON: [Yes]. But so is that good enough? Do you need any . . . I can send you the Endnote file, or whatever.

MACFARLANE: No. I'll just cut and paste and put it together.

GRAYSON: The other thing is I can change the format of the . . . I notice your, the way you name . . . in other words, the citation formats is different than what I was using when I ran mine <**T: 85 min**> . If you want to . . . what I'd like to do is include in the most up-to-date publication, bibliography we can in the transcript. I think that's important to have that as part of the record for the historical . . .

MACFARLANE: Some of these things bring back good memories here, like this one.[27]

GRAYSON: Memories . . . [old publications bring back] good memories?

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[26] Ronald D. Macfarlane, "Natural Occurrence of Samarium-146," *Nature* 188 (1960), 1180-1181.
[27] R. D. Macfarlane, "Alpha-Decay Properties of Some Thulium and Ytterbium Isotopes Near the 82-Neutron Closed Shell." *Physical Review* 136, no. 4B (1964): B941.

MACFARLANE: [Yes]. Well, this one in particular was an example of paying attention to detail. I was doing an all-night run, and I was looking at the alpha emitters of ytterbium, with a four-hour half-life. I saw a peak and thought, "This isn't the right place." I just for some reason, ten minutes later, I said, "Let me just get another measurement of that four-hour half-life." It turned out, and there was something weird about ytterbium-149. People who were doing nuclear reactions at the time said this does not match the rest of the getting in terms of changing the energy of the beam, and there was just something weird about it. So it turned out that there was an isomer of this—a high spin isomer—that's only made if you have a heavy ion accelerator. Nobody picked up on that, the spin nucleus, and the manufacture of that was connected . . . .

GRAYSON: It's kind of like an artifact of the production of the—

MACFARLANE: Well, in a way, but it was like the . . . . They found out that, actually, in heavy ions' reactions there's a lot of angular momentum that's involved. It picks out the nuclear states that have high spin. So, here's ytterbium-149, a high-spin isomer, and rarely . . . . And you don't normally excite it, but heavy ion reaction you do excite it. When I told my colleagues that I think I have the answer to this anomaly ytterbium-149 high spin isomer, they couldn't believe it. They verified it, and that opened up a whole new field of heavy ion reactions involving the influence of spin.

GRAYSON: And this was just because you made a random observation that you wouldn't normally have made.

MACFARLANE: [Yes]. Why would I have repeated results that I had got, do it again, ten minutes later? I wouldn't have done it, because the energy difference was, like, very small.

GRAYSON: [Yes].

MACFARLANE: And the fact that it disappeared is like, what's going on here? But then it's an example of paying attention to detail. Of letting nature tell you that, if you're sensitive to it. Give nature a chance to tell you something, and it's over and over again, I have—

GRAYSON: Don't let your preconceived ideas get in the way of reality.

MACFARLANE: That's right, [yes]. It's a hard lesson to learn.

GRAYSON: [Yes]. Well, particularly, people have invested so much in their preconceived ideas . . .

MACFARLANE: Well, [yes], the heavy ion accelerator is something that nobody—hardly anybody—had at that time. Here is an example of what can happen when you have a unique instrument.

GRAYSON: This was an experiment, where you're taking these large . . . you said they were the part of the rare earth elements?

MACFARLANE: Right.

GRAYSON: Most people were looking at banging protons, and alpha particles, and that kind of stuff.

MACFARLANE: But I was using carbon ions, oxygen ions.

GRAYSON: Whereas this was working with things like the molecular weight or atomic number 150, and that kind of thing.

MACFARLANE: That was the target, but the projectiles were heavy ions like carbon ions, oxygen ions, those were the projectiles.

GRAYSON: Okay.

MACFARLANE: And the feature of the heavy ion reaction versus a proton reaction was the fact that angular momentum plays a big role. But this was something that was just beginning to become appreciated. They couldn't figure out what's going on. This played right into it. Fortunately, I had some colleagues there who were into the nuclear reaction part. They picked up on this, and said this is exactly what we need to understand what we're doing here.

GRAYSON: I don't know, but I think there's a certain amount of fortuitousness to your career.

MACFARLANE: Well, [yes]. I realize I'm lucky. And but here again, this is like what Frank [Field] said that I use my nose to lead the way.[28] That's what's <**T: 90 min**> made it so exciting for me, the way my career went. It all goes back to my graduate days with Dr. Kohman and doing things that are out of the box. And when you're in the box, you're a little too sheltered.

GRAYSON: [Yes], and, you know, there's other people in the box with you. [laughter]

MACFARLANE: [Yes], that's right. That's right, [yes].

GRAYSON: Okay. Well, I'll see if you have any other things you want to say at this particular point in time. I think we can say we pretty well covered the turf. Invariably something will come to mind after the fact.

[END OF AUDIO, FILE #1.2]

[END OF INTERVIEW]

[28] Frank Field, Oral History Transcript #0352.

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