MATTHEW TIRRELL

An Interview Conducted by

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IEEE History Center

7 December 2000

Interview #410

For the

IEEE History Center

The Institute of Electrical and Electronics Engineering, Inc.

and

Rutgers, The State University of New Jersey

It is recommended that this oral history be cited as follows:

Matthew Tirrell, Electrical Engineer, an oral history conducted in 2000 by Frederik Nebeker, IEEE History Center, Rutgers University, New Brunswick, NJ, USA.

Interview: Matthew Tirrell
Interviewer: Frederik Nebeker
Date: 7 December 2000
Place: Santa Barbara, California

Nebeker: Let's start with where and when you were born and a little about the family you came from.

Tirrell: I was born September 5, 1950, in Phillipsburg, New Jersey. I was the oldest of three children. I have a brother who is two years younger than me and who is also involved in a field very close to mine. He's in biomaterials and is a chemist, and he is Chairman of the Division of Chemistry and Chemical Engineering at Caltech. We have a sister who is another two years younger who went to several colleges , graduated from none and became a terrific full-time mom. She is now a staff person for a Pennsylvania congressman.

Nebeker: What did your father do?

Tirrell: My father was educated as a mechanical engineer and worked with his father in their own silk weaving business until I was about fifteen. They sold their business and my father became an engineer for New Jersey Power and Light Company, where he worked for quite some time. Then my parents divorced and my father moved to the Midwest and worked in Milwaukee for a long time until he retired. I cannot remember the name of the organization, but it had to do with pollution control.

Nebeker: Do you think it was his influence that made you interested in science and engineering?

Tirrell: No, not particularly, it was kind of neutral. My brother and I had a terrific high school chemistry teacher, and I think that really sparked a lot of interest in us both, not only in science but particularly in chemical sciences.

Nebeker: One of you went into chemistry and the other into chemical engineering?

Tirrell: Yes. That's where my father was an influence. I told my father I was going to study chemistry. He said, "Well, why don't you at least study chemical engineering, then you'll get a job." That's honestly true. I went to high school full time in New Jersey, and then I went to Northwestern.

Nebeker: How did you choose Northwestern?

Tirrell: I participated in a summer program between my junior and senior year in high school, and that was almost at random. I applied to a lot of colleges. My parents were very supportive of the idea that it might be nice to go off and try some kind of college environment rather than have a summer job. Northwestern had a good program, but I didn't realize it at that time. So I applied to five or six of colleges, and Northwestern just kind of looked the best to me. But after I did that, I really decided that I wanted to go there.

Nebeker: Had you decided already that you wanted to go into chemistry or chemical engineering?

Tirrell: Not at that time. That was something that I decided in my senior year in high school. I don't actually remember the exact sequence of things, but I don't think I was 100 percent sure. Even after I was in college and studying chemical engineering, I took the law board exams. Everybody I lived with in an apartment became a lawyer, and I kind of wanted to show that I could do it on their terms too. It was a little bit of an unusual time.

I went to undergraduate school during the last stages of the Vietnam War. Northwestern, like lots of places, went on strike during the Spring of ‘71. The funny thing is that I was very politically active and interested, but I came back from a lot of political activity and a summer job feeling very serious about school.

Nebeker: I think that’s unusual for that to happen.

Tirrell: Yes.

Nebeker: At Northwestern, when did you decide to major in engineering?

Tirrell: I majored in chemical engineering. Yes.

Nebeker: Was that an early decision?

Tirrell: It was a pretty early decision because I went in with an interest in chemistry, so the switch to engineering was an easy one to make. But what I was talking about before with law and so on were just the kind of youthful threads that came along with a certain amount of indecision that kept my options open.

Nebeker: Had you thought about going into industry, or were you thinking of an academic career?

Tirrell: In my freshman year, I didn’t think about it very much. I went in there not thinking about it. After that, I had a couple of what I consider to be very influential professors. They are guys who are friends of mine now, who I thought were very good teachers.

Nebeker: Who are they?

Tirrell: One is still an active faculty member at Northwestern; he must have been very young when I was there. His name is Joshua Dranoff. I thought he was way older than me, but he must have been something like ten years older than me. I don't really remember. He was a very easygoing, humane guy who paid a lot of attention to how he explained things, and that revealed to me a kind of clarity of thinking that really appealed to me.

So after that, the way I always tried to teach myself was to often pose the question, "How would I explain what I'm hearing to somebody else? Do I know it well enough to explain it to somebody?" The other was that Northwestern had a very good and well organized co-op program, and I decided very early on to participate in that. You didn't have to. It wasn't compulsory at all, but I thought, "Why not?" It takes five years and I didn't necessarily want to get out of there soon, and they really helped to line up a job very well.

Nebeker: How did that work there? Did you take a semester off?

Tirrell: There were quarters, just like we have here, so it didn't require that.

Nebeker: You told me that you took part in the cooperative education program at Northwestern.

Tirrell: That's right. I don't think it was a factor in me going there, but after I did go there and learned about it, I decided it was really for me.

Nebeker: A lot of people through the years have told me that was very important for them. They felt they learned a lot and got a lot out of getting to experience the workplace while they were getting their education.

Tirrell: Yes, no question about it. And for me, too. It probably had the opposite effect on me, as with most people. This might sound like my co-op experience was unpleasant, but after I co-opped, I was absolutely convinced that I didn't really want to have a real job as an engineer—I wanted to go to graduate school. It helped me understand the difference between an engineer being involved in day to day engineering problems, production, manufacturing, and research. I was fortunate enough to get an exposure to a research environment during my co-op experience, and it really intrigued me, and I went right back to Northwestern. The company that I worked for at the time was called Advance Chemicals and Stabilizers. It was a part of a big company that still exists called Cincinnati Milling Machine Company (now Cincinnati Milicron). Advance was located on 500 Jersey Avenue in New Brunswick. They made additives for polyvinyl chloride and paint to prevent oxidative or thermal degradation. These were things that preferentially oxidized instead of the plastic. So I learned about plastics, and that was really the influential thing. I went back to Northwestern and tried to find a professor that knew something about that, and I did.

Nebeker: And you got a Bachelor's in chemical engineering there?

Tirrell: That's right.

Nebeker: Did you go straight to graduate school?

Tirrell: Yes. I did. When I said I went back to Northwestern and tried to find a professor there who was interested in polymers and plastics, I hooked up with a fellow named Bill Graessley, who later on left Northwestern and went to Exxon and then to Princeton in chemical engineering, and he retired from Princeton just a few years ago. I worked in his lab for two years. While I was going back and forth and co-opping, I really had a chance to do some of this.

Nebeker: You did part-time work in his lab?

Tirrell: That's right. So naturally, I asked him about where to go to graduate school, and he said that if I was interested in polymers and polymer science, which is what I had defined as what I was interested in, there's two kinds of places that I could go. One of them was a good chemical engineering program where they do polymers. The other is that there are some graduate departments that focus almost exclusively on polymers, and among those he recommended the University of Massachusetts. That's where I went. I went directly to graduate school. So I had a year and a half of engineering experience as an undergraduate in the co-op, and I shifted around from research, to production, to maintenance, and I actually worked as a chemical operator.

Nebeker: That sounds ideal for a cooperative program.

Tirrell: It was very good.

Nebeker: I need to ask you if you were influenced by the movie "The Graduate."

Tirrell: Yes. Well, I wasn't influenced by it.

Nebeker: The whispering in the classes.

Tirrell: No, I know what you mean. Believe me, it's come up. Honestly, no. It was a little bit too early. "The Graduate" was a 1967 or 1968 movie, and I was still in high school then.

Nebeker: It didn't get you thinking about plastics.

Tirrell: Not at that time. No. I got interested a few years later.

Nebeker: Tell me a little bit about your experience at the University of Massachusetts.

Tirrell: Well, you said that you looked over the things that I've done, and not all of what I've done, in fact a large fraction of what I've done, was not biomedical. But I was very attracted to that, even when I started at Massachusetts in the polymer science field. So, the thesis project that I chose was to look at the effect of mechanical stresses on enzymes. It just appealed to me a lot. The person who became my thesis advisor was Stan Middleman, who just retired from UC San Diego. Shu Chien knows him quite well, actually. In fact, he retired a few years ago, too, and Shu came to his retirement party where I spoke.

Middleman had this idea that enzymes are three-dimensional macro molecules that function as catalysts because they have a precisely defined pocket in them that functions as a catalytic site, and if you applied force or stress to them you would distort that and you would probably see a change in the enzyme activity. This could be relevant to a lot of biotechnology situations where you're pumping or mixing solutions that have enzymes in them. So, the problem he set to me was to find out if that's true or not.

Nebeker: That must have been quite challenging to somehow see what's going on with that.

Tirrell: That's right. The easy things to measure were the macroscopic results, so what I did a lot of was to do enzyme catalyzed reactions in a high shear viscometer, where instead of just having a quiescent solution, you would try to subject the solution to a high and relatively uniform shear stress and see if you could see a change in the catalytic reactions. You can, but still, your point is very pertinent. To attribute that to a particular mechanism is very hard because in order to create high shear stress, you have to make viscometers that have a very narrow gap so that when you shear the two surfaces, you get a high gradient of velocity. When you do that, you have a huge surface to volume ratio, and lots of other things can happen to the enzyme molecule at the surface.

Nebeker: Or happen to the reaction to slow down the reaction.

Tirrell: That’s right. What I found was that in these situations, there are actually very drastic effects on the enzyme kinetics, but it is unlikely that any of them had to do with the direct distortion of the enzyme molecule. Let’s put it that way. There are other effects, the surface effects, that might have existed almost without shearing. Even though you could see some shear rate dependence, still other things happened.

I don’t think that my thesis project proved much, but it was a fantastic educational experience. It was a very interesting idea to start with. I think I did careful experimental work. It was a complex situation, but it certainly prepared me for future complex situations. There was nothing wrong with the initial idea of the problem, and the thesis project was kind of a “no lose” proposition because the answer to the question was interesting no matter how it turned out.

Nebeker: You were getting some definite effects and you could throw some light on things.

Tirrell: Yes, on what happens under these circumstances. It didn’t happen to be the clear effect we were looking at, but I certainly was able to provide a lot of useful documented information about what happens when you conduct an enzyme reaction under high stress. So I found it a little frustrating when I was doing it, but I think that also goes with the territory.

Nebeker: So, I see you completed your Ph.D. in 1977.

Tirrell: Yes. Back to a subject we were talking about before, besides posing this interesting research problem and guiding me through it and being a good sounding board, my thesis advisor, from whom I took several classes, was a superb teacher. Because I was more mature and was a little closer to knowing what I wanted to do, he was even more influential than Josh Dranoff in guiding my career toward teaching.

Nebeker: I take it that that's been something important to you, the teaching aspect of university life.

Tirrell: It has. I teach the undergraduate fluid mechanics class and chemical engineering here now. It's a lot of fun.

Nebeker: There are many people who do that only because it's part of the job, but it sounds like you take an interest in teaching.

Tirrell: Well, for better or for worse, it's not actually a required part of my job right now. Teaching is very time consuming with the job that I have now, and I honestly don't know if I'll keep it up. I was doing this sort of as an experiment. I didn't teach the first year I was here, which was last year. So this is actually the first class that I taught. I have tentatively signed up to do it for a while, but I'm not trying to prove anything to anybody. I like to do it. So I'm trying to find out if I think it's really compatible with my job now. It would be a shame to me if it wasn't, but you move on. I've done teaching.

Nebeker: We'll return to the chronology, but while we're on this topic, I wondered if I could ask you about how you've liked administration. You've been involved for quite some time as head at Minnesota and then director of the Biomedical Engineering Institute and now as dean.

Tirrell: Well, there's a lot of things that I really like about it and some things that I don't like about it. I think there are some things that I'm good at about it and other things I'm not good at. I'm good at and I like the things that you saw today: the mobilization of people to do interesting things. I really like to do that, and I think that I can gain a feel for what kind of collection of talent is necessary to pursue an interesting job, to pursue an interesting new research or teaching activity, and then put enough energy and insight into it to mobilize people to make it happen. I'm not particularly good or fond of (and this might sound like I like the glamorous stuff and not the routine stuff), but I wouldn't characterize myself as a particularly well-organized person. So I don't handle the routine administration things all that easily. I like to talk to people. I like to talk about ideas

Nebeker: How has being a dean cut into your research time?

Tirrell: Well, it certainly has done that. There's no question that you have to put that first and you have to take that job a little more seriously than anything else, but one of the things that really clenched my interest in this job is that it was understood from the beginning that I would still do research. I was talked to as a potential dean, but I was also talked to simultaneously as a potential faculty member, and that made a difference.

Nebeker: You've been here about a year and a half now, and you've gotten graduate students?

Tirrell: Yes. The new graduate students for this year haven't made up their mind. Last year I took two graduate students. I came from Minnesota with a group of seven students.

Nebeker: That came out with you?

Tirrell: Yes. Two of them became UCSB graduate students. Three students have graduated this year, so I'm down to four students from Minnesota: two new ones, three post-docs here, and then still two Minnesota students who couldn't pull through for some reason.

Nebeker: Wow. You've got quite a group.

Tirrell: I've had twelve. Different people handle things differently. I have had a much bigger group, and I think that much bigger would be a stretch to handle and would not be a service to the students. I will probably take another student or two this year. I've talked to all of them, but the ball is in their court to decide whether they want to pick me as a potential advisor.

Nebeker: Your thesis work back at Massachusetts was this study of enzymes under stress.

Tirrell: Right.

Nebeker: I guess you did some teaching there at Massachusetts.

Tirrell: Just regular teaching assistant duties. Nothing out of the ordinary for a graduate student, although I guess I did put it on my resume.

Nebeker: Then on graduation, you got a job at Minnesota.

Tirrell: That's right.

Nebeker: How did your research evolve?

Tirrell: I actually started in three main areas. One was an attempted outgrowth of my Ph.D. thesis, in which I really tried to get an early start in bioengineering. I had a very significant colleague at Minnesota named Ken Keller who, at the time that I went there, was the department chair of chemical engineering and material science. Later on he became President of the University of Minnesota. He's a fellow of AIMBE American Institute of Medical and Biological Engineers. He was very influential in my accepting the job at Minnesota. I wrote three, four, or five NIH proposals with him that were all declined. The idea that we were pursuing was related to his own work, but we just couldn't seem to get it together here. It was on shear flow damage to blood cells.

Nebeker: Sure. That must happen in open heart surgery when the heart-lung machines pump the blood.

Tirrell: So what are the mechanisms of cell breakdown? We did some things. We had a joint student together. In fact, she's very successful now. She's a vice president of Medtronic named Becky Bergman. We never were able to attract good funding for it. We limped along and did things that weren't so expensive.

Nebeker: What do you think was the problem: your definition of the research or the failure of people to recognize that this was important? In other words, when you look back on it, are you angry at those reviewers?

Tirrell: No. I don't think there was anything particularly wrong with the definition of the research, although at the time there was a very strong premium in NIH funding decisions—as decided by study sections and things like that—on connection with clinical work at the same time. We really didn't have that. Ours was a scientific proposal to look at this and we didn't have that element that was viewed as important.

However, I was trained in polymer science, not in biomedical engineering in graduate school, and another outgrowth of my thesis project was all of this surface interaction. It was clear to me that the enzymes could adsorb and denature on the surfaces, and so the other area that I started to look at was polymer adsorption on surfaces.

There was another activity at Minnesota that also attracted me. We're talking now about 1977 and 1978, and the price of gasoline and oil was enormous. There was a group of people at Minnesota that worked on what used to be called enhanced oil recovery. The idea was that oil, when you pump it out of the ground, is not just sitting down there in big lakes; it's mostly permeating porous rock. So when you put a suction on it by pumping, you get some of it out, but a huge amount is left behind. If the price of oil is high enough, you can do some expensive things to try to get the rest of it out. One of the things you can do is pump polymers, surfactant, and soap down there to try to scrub the oil out of the rock.

Nebeker: So pumping some other fluid down there won't release the oil.

Tirrell: That's another interesting piece that is part of this research. The obvious fluid to pump down there is water, however water has too low of a viscosity. If you are trying to push oil, which is very viscous, with water that is not so viscous, the front between the two is unstable, and the water just pushes through the oil and leaves the oil behind.

So, the idea of putting polymers and surfactants in was two-fold. One was to up the viscosity of the water, like the polymers that are in your shampoo and salad dressing, and the other was to put surfactants in that scrub the rock and emulsified the oil and carried it out. My interest in polymers near surfaces was peaked at that time, and there were a lot of interesting things to do that involved both proteins and synthetic polymers. I realized at the time that, in some ways, synthetic polymers are easier to study than proteins. You can synthesize new ones that have the size and molecular weight and so on, and each protein has such a specific and intricate structure that it's hard to generalize. If you want to know how proteins adsorb at interfaces, you have to do fifty experiments, or fifty complete studies, to understand fifty proteins. With synthetic polymers, you can kind of get generic behavior. That really appealed to me.

So, we started studying polymer adsorption and polymer surfaces. That's where I spent an enormous amount of my career. We looked for new techniques to do this. We developed some ways of measuring how much polymer was adsorbed and was sequestered in porous media in pores that are not much bigger than the macro molecules themselves.

Nebeker: So your work was overall directed by this particular application, is that right, of recovering more oil?

Tirrell: In the '70s and early '80s, yes.

Nebeker: And the size of the pores that you were considering?

Tirrell: It was similar to sandstone. That's right. But it also had applications to chromatography. We were thinking about those at the same time, and we sometimes used chromatographic columns as model porous media.

Nebeker: But you're approaching this in a more scientific way. It's not the strictly engineering approach of trying different things and trying to see what kind of recovery you could get, but you're trying to understand what's actually going on?

Tirrell: In my own lab, we did very little work on actual recovery. I was kind of an adjunct member of a larger group that consisted of three or four other faculty members that really were focusing on recovery, and I was kind of a polymer expert.

In the course of this, I also got interested in two other areas of technology that ultimately come back to some implications for biology. One was adhesion. What is it that makes things stick? Why do polymers stick to surfaces and how can they augment and enhance the adhesion between surfaces? We started to tackle that problem to develop some methods to measure and actually predict adhesion a little better.

Nebeker: Predicted on the basis of the actual molecular configurations?

Tirrell: That's right. If you look at some of the publications early on my list we did some of these things that we called, "Calculations of the Healing Process." What we were talking about there is kind of a leap from what I was just saying, but it's another problem in this spirit. If you takes two chunks of plastic and you stick them together and supply enough thermal energy, how fast does it take them to weld just because the polymer molecules diffuse across the interface to the point where you can't tell where the interface was anymore. It's recovered the same strength as the virgin polymer,and so on.

The other area of technology I became interested in is sometimes called colloidal stabilization, where particles are in suspension. If the particles were there, they would clump together because of Van der Waals forces. Applying a polymeric coating or adsorbed layer is a very effective way to keep the particles apart, and this is an extremely important technology in paint.

Nebeker: I know there are a lot of substances that are emulsions, and you want to keep them that way for certain applications.

Tirrell: That's right. It's a form of stabilizing, or in loose terminology, emulsifying solid particles. Another simple way to talk about it would be to compare it to putting rubber bumpers between particles so that they can't really touch each other. The reason it is important in paints, pigments, and Xerox toner is that you want to have very finely divided particles so that you get high resolution printing instead of lumpy coatings.

Nebeker: In photographic film also?

Tirrell: Photographic film is extremely important. My interests in how polymers stuck to surfaces, which stemmed from my thesis work on how proteins stuck to surfaces, led to these interests in adhesion and colloidal stabilization.

Nebeker: Was that a new idea to try provide some coating for these?

Tirrell: It was a new idea at about the time I started on the problem. I can tell you exactly what my new idea was. It wasn't just to put polymers on the surface, because that had already been done for about five years. What I would say I realized, or at least focused on and tried to emphasize earlier than most people, was the fact that if you have a polymer molecule on this surface of a particle and another particle of the same type comes in the neighborhood, then the segments of the polymer molecule that adsorb on this surface can also adsorb on this one.

So, there are circumstances which were well recognized, but the answer to it was that there are a lot of situations where the same polymer molecule could get adsorbed simultaneously on both particles, and thereby create aggregation that it was supposed to prevent. It's called bridging Flocculation and that's a problem. Colloidal suspensions stabilized by polymers in the way I just described are inherently less stable than they might be. It's an easy, well known, but somewhat augmented synthetic challenge, but our idea was to make block co-polymers. So instead of getting a homopolymer with all one kind of segment on the surface, make a block co-polymer where you have a block of one thing and a block of another thing, usually one big and one small.

Nebeker: Now are these linear?

Tirrell: That's right. There will be a junction and it switches. There are ways of doing this that are very well controlled and very well understood. You make the short part love the surface and hate the solvent, and you make the part that sticks out not even stick to the surface, but it's anchored by the block co-polymer. So that's what we did. We showed that these were tremendously better than homopolymers to stabilize colloidal dispersions. It's a sticker. We call them stickers.

Some of this technology was adopted by Xerox, some by DuPont. We never patented any of it, and I do not want to give the wrong impression. We had some of these ideas early, but it was a very active field, and lots of people had their own independent ideas. They picked up on ours and we picked up on theirs. We were not totally unique, but I would say that it would not be too self congratulatory to claim that we were virtually the first to point out the possibilities of using block co-polymers in this way.

To keep the connection to our bio topic, I'll say that cells have a form of polymer layer like this on them, too. They're covered with polysaccharide molecules, and the purpose of the polysaccharide molecule is to create generic repulsion between the cells and a kind of a cushion into which the cells want to adhere to form a tissue. Specific receptors stick out and they form ligand receptor interactions. But before you can have specific binding, you have to block all the non-specific binding, and to some extent, that's what we were doing with the colloidal particles: blocking the non-specific binding.

Nebeker: That's how nature works, is that it first blocks the non-specific and then puts in the specific.

Tirrell: Because if anything stuck to anything, we'd look a little different. We'd be kind of blobs of cells or something. So in the back of my mind, there was always a learning process and a fermentation of some of the things that we were learning and how to apply it to biology. But I also had in my mind my distinct lack of success in attracting NIH support, whereas I was as successful as I needed to be in attracting NSF and industrial support. I kind of figured that the federal government knew what they wanted me to do. At first it wasn't biomedical engineering, it was something else.

Nebeker: You've drawn a couple of parallels between what you were doing and the biological situation. Do you think you ever kind of got the idea from biology? I know there's been this biomimetics, or this idea that nature is a great engineer. Let's look at how nature does it and try to copy that. Was that going on at all?

Tirrell: Not then. I can't honestly say that. It goes on a little bit more now in my own work and in my own mind. It was sort of the other way.

Nebeker: First do this and then realize that nature is doing something similar.

Tirrell: Yes. I have to say that later on when I actively and aggressively, and then somewhat successfully, turned my attention to some bio-surface, bio-adhesion problems, it was more with the intent to apply what I knew for colloid science to biology than the other way around. In talking about biological things it's very important and something that comes into my career in the '93, '94, '95 period. So now I'm jumping back to the '83 period. That was the time that I really set aside my specific efforts to attract NIH funding and turned to these other adhesion and colloidal problems.

Nebeker: You were very prolific. I've seen the list of your publications in those years.

Tirrell: There's a whole other line of research that I didn't really mention.

Nebeker: Well, let's at least get on the record what that was.

Tirrell: I had another very influential mentor in graduate school who was not my thesis advisor but just became a friend. I played rugby for the UMS rugby club, and another faculty member in the polymer science department there was the coach.

We were friendly. His interest was in polymerization reactions and I spent a lot of time with him. After a long effort, we ultimately published a book together on polymerization modeling that stemmed from a book that he was writing when I was a graduate student.

So, really as a parallel thing this has fed into my bioengineering interest in one way, and that is that we do new material synthesis in my lab. The ability to make your own materials is a tremendous asset in the biomaterials area. If you have to get stuff from other people and try it out, the time scale is slow, the creative cycling is slow. We have done a lot of things on studying, optimizing, and just performing polymerization reactions better that have led to an ability to make our own materials.

Nebeker: So in the ‘80s, your work was on polymers, block polymers, and all these things that were not immediately biomedical engineering. I’m just checking here. It was in ‘93 that you became the Bakken, after Earl E. Bakken, the founder of Medtronic, a prominent Minnesota pacemaker company professor of biomedical engineering. So, to have that title, did that mean that you had started more directly doing biomedical work at that point?

Tirrell: I’d like to mention two other things before I address the sequence of events directly. An extremely influential event in my life was going to Australia in the summer of ’82, because there was a fellow there named Jacob Israelachvili, and you’ll notice a couple of joint publications. Interestingly and not totally coincidentally, he’s here at UC Santa Barbara now. In fact, this woman who just called Pam was Jacob’s wife.

Jacob had developed a device at that time that could bring two surfaces together and measure the force as a function of separation between the two. This was a couple of years before atomic force microscopy. This is a technique that he and I both still use, and it's different from atomic force microscopy. It's not used to image surfaces. It's used to measure very well the force between two macroscopic surfaces, for example, two macroscopic surfaces covered with block co-polymers. Whether we were the first to think about block co-polymers to me is less important. We were the first to directly measure the forces. I went to Jacob's lab for the summer. He was in Australia at the time. I learned how to do this with his help and then set it up in our own lab, and we began a very fruitful period in the '80s where we used this device to measure all sorts of polymer interactions. That actually became the basis of my entrée into real biomedical stuff.

The other was that in 1987 or 1988 we were awarded an engineering research center from the National Science Foundation at the University of Minnesota. It was about a three-million-dollar-a-year grant that had several programs within it. I was the original director of the polymer program. That was very successful in the sense that we trained a lot of students and we attracted a lot of industrial support. For the first four years we had a polymer program, a coatings program, a surfactant program, and an inorganic thin films program.

As we went out to industry, we started to attract, somewhat to our surprise, a huge amount of interest from companies making biomedical devices. It shouldn't have been much of a surprise in Minneapolis, to tell you the truth. Medtronic, Saint

Jude, 3M all have a huge number of interests in this area. After a couple of years—probably '91 or '92—within the Center for Interfacial Engineering we decided to start a bio-interfaces program. That was a key moment for me. I just basically volunteered to start it and to develop the relationships with companies, and I saw that as a way of rekindling my long dormant interests in this area.

Nebeker: That area is well known as a center for medical technology and you are happening to have this center for polymer surface studies.

Tirrell: We call it the Center for Interfacial Engineering. I've probably listed it someplace as a Program Director. I don't know. Maybe I've taken it off since I've been here.

Nebeker: With the fact that a number of these biomedical companies expressed interest in that and your recognition that this was an important field, and since nobody else volunteered, you volunteered.

Tirrell: Yes. Well, before anybody else got the inkling, I volunteered before anybody else had a chance.

Nebeker: I see. So you saw this as a very good deal.

Tirrell: It was something I wanted to do, and the interest was certainly there. So we had a bio-interfaces program for the remaining duration of the lifetime of the center. These NSF centers basically have a ten year lifetime. It's not unexpected that they sunset. That is what's expected. It's a rare case when you can prolong them.

Nebeker: Can you give me some examples of the biomedical surface areas of study?

Tirrell: We were getting problems brought to us by industrial partners that related to some components of what we were already doing with polymeric materials, but they brought in some new aspects, too. Some of these things have biomedical applications. They were motivated by biomedical applications, but there was nothing intrinsically biomedical about them. They found that some certain silicon materials that they were using would have a certain surface composition measurable by surface spectroscopies when exposed to air. But if they exposed them to water, they would find that the surface composition turned over. To make a long story short, they liked the composition that they saw, which had more polar groups exposed to water.

So they came to us to seek help in ways of stabilizing that. In other words, this was a kind of a reversible change in the surface. "I put it in the air, I see this. I put it in water, I see this. I want what I see in water, even if water is not around, but it always goes back to the air surface. Is there some way we can lock in the surface." I remember that as one of the initial problems, and those were things that we could help with. They didn't actually require any clinical stuff or anything like that, so they were well suited for what we had. I personally was still working on adhesion problems, and starting to think about how to apply this to more biological and medical problems.

Nebeker: I imagine there must have been biological and medical adhesion issues frequently.

Tirrell: That's right. Then I also began to learn more about biological adhesion itself—not so much how you keep stuff stuck together in a physiological environment, but how do cells stick to one another and how they stick to surfaces, etc. This is where the kind of ideas that we're still working on, to some extent, were spawned.

I talk about them in here, by the way, in an interview with Jackie. Jackie went through my career in a different way, where I didn't talk this much.

Nebeker: I'll take a look at that.

Tirrell: That cover story is very relevant. I began to realize that there was a need in bio-materials situations to improve the interaction of synthetic material surfaces with cells, and that this could be done. This wasn't my original idea, either. This comes from a guy named Jeff Hubbell, who is now at the ETH in Zurich. At the time he was at the University of Texas. He was the one who showed that if you decorated synthetic surfaces with small pieces of proteins, called peptides, you could get an improved response of cells.

Nebeker: This is in the implant material of various sorts.

Tirrell: That's right. I started thinking about our surface forces apparatus, about our block co-polymer work, and how we could display peptides and organize a layer of peptides on the surface in a spontaneous way, and that's when we developed molecules like this. Now, this is a triad of molecules for a particular reason, but what we have done and are still doing is making synthetic molecules that we call peptide amphiphiles, where we take a small piece of protein and put a synthetic lipid tail on it. If you take a surface that's hydrophobic, like a piece of polyethylene, and dip it in a solution of these molecules, these molecules spontaneously organize on the surface with the lipid tails packing like they would in a cell membrane, and the hydrophilic head groups going out. So these are like little block co-polymers. These are the stickers and these are the things that stick out, but now they're there for the purposes of mediating the interaction that the surfaces have with their surroundings in a different way, not just to keep everything off. However, this keeping everything off comes right back into this problem, too. Lots of things could stick to that. What you also want to do is mix this with inert molecules that kind of shield the surface from cells and other things that are sticking for the wrong reason, and you can then really try to highlight the specific interaction that you get.

Nebeker: So, you're trying to do something like nature of having specific ligands there.

Tirrell: Exactly, and spaced out and interspersed in a background of protective, non-adhesive stuff. That's what we're doing now.

Nebeker: As with some of your earlier work, are you trying to do this work at a fairly general level, or is there a particular application that you have in mind?

Tirrell: Both. Most of what we do here now in Santa Barbara, as in Minnesota, is fairly general. We create lots of different surface compositions and structures and play with the peptide architecture and packing. Then we observe things about cell behavior on the surface, but we don't make implants.

Nebeker: You're not starting with a certain implant and saying, "We've got to get good adhesion with bone tissue."

Tirrell: No, although we do have some interest in that. One of the types of cells that we have worked with is endothelial cells, cells on the inside of blood vessels. Through a collaboration we are in fact looking at whether one could, in synthetic materials for small diameter vascular grafts or stints that are used to hold open blood vessels, put our coatings on to help develop a viable layer of real cells—anchor a real endothelium on a synthetic surface. It's a challenge. So far, we haven't done it. Nobody's done it very well. I think it's going to take mixtures of peptides and a couple of other things that are different from the surface treatment. Part of the problem is supplying blood and oxygen and so on to these cells. It's one thing to have a porous cellular arterial wall, and it's another thing to have an impermeable piece of plastic there. But we can go some way to keep cells healthier on totally synthetic, non-biological surfaces by decorating those surfaces with these things. These are peptide fragments that are taken from the normal extracellular matrix. So these are the things that cells are used to seeing. This comes from collagen; that's why it's a triple helix.

Nebeker: So you're able to design these and get them to position themselves as you'd like on certain surfaces.

Tirrell: That's right—to a degree.

Nebeker: It's fascinating to me. You're working out sort of the basic engineering of these kinds of surfaces, putting certain things in different places, and then at the same time trying to find particular biomedical applications.

Tirrell: I think that while we have had some collaboration to pursue particular biomedical applications, I'm really hoping that we'll have more or that somebody will just pick this up. I mean we publish it, so it's no mystery, and we give away these materials freely. I think that part of the problem, if there is a problem (and I don't actually see one), is that if we really wanted to push the implementation of these surface treatments in practical applications, we'd do something a little different from what we're doing. There are problems with these molecules in practical applications. They're very easy to put on surfaces, and they're also very easy to take off. We don't make very stable surfaces. So they're good for investigating early, short-term effects on exposure. They're not particularly good for long-term, robust attachment kinds of things. I think the question is if we really wanted to make these things more practical, we'd think more about how to make a long-term, practical, durable, robust material.

Nebeker: That could survive in a particular environment.

Tirrell: That's right. And we haven't done much of that. What we're trying to do more is to learn how to design bio-materials. For example, not with this peptide but with another, we've learned that because we can display these in such a precise orientation, we've taken the same peptide and made a linear version, or a version that's bent into a loop. Otherwise it's displayed on the same lipid tail and kind of organizes itself on the surface in a similar way, except in one case they're sticking out and in another case they're bent over. The bent over ones are a lot more active in promoting cell spreading, which is a sign of health. Cells spread on surfaces that they like.

Our chemistry might not be the best way to put cyclic looped peptides on the surface, but I think our chemistry was the best way to figure out that it was actually better and to motivate other people to think of better ways to do this. I didn't emphasize this and it may or may not be obvious, but what this methodology has is the best way of displaying the peptides in a controllable, organized, well-oriented, architecturally pure kind of way. So that may actually not be terrifically important for applications, but it's important for helping to understand whether generically this architecture is better than that one.

Nebeker: I appreciate that explanation, and again, your interest at this stage is more in understanding the surface reactions and surface preparations and so on, than in achieving a particular effect in a particular application, and also in developing the means to do precisely defined things. That, it seems to me, should come before you specialize to a particular application.

Tirrell: Well, some people are attracted to different things. I'm kind of attracted to these design ideas. That's all.

Nebeker: I did want to ask you about this Biomedical Engineering Institute at Minnesota that you directed.

Tirrell: I kind of skipped over that and sped right into what we're doing. To go back to the Center for Interfacial Engineering, we started to attract some companies and develop a program within the context of that NSF center, and it turned out that the Biomedical Engineering Institute had been started by funding from Mentronic a few years before that.

Nebeker: That had no connection with this part of the NSF?

Tirrell: No, it didn't, although it quickly got close to having such a thing because the guy who was the director of the Biomedical Engineering Institute, Fred Silver from Rutgers, served as the director before me. For a complicated series of family reasons, he later on resigned and went back to Rutgers. So we don't have to talk about that. That left the Biomedical Engineering Institute in a little bit of a quandary, and to make a long story short, I was probed to see if I would be interested in it because I had taken over this portion of the NSF center program and I said yes.

At the time, I was offered the Bakken Professorship as an incentive. As a means to do this it was understood that I would be responsible for the graduate program in biomedical engineering, as well as continuing to define a more collaborative research structure, which became the Biomedical Engineering Institute. In this capacity I reported jointly to the Dean of the Medical School and the Dean of Engineering.

Nebeker: That is a co-located institute?

Tirrell: At the time, we weren't aiming toward starting a department. After I left last year, Minnesota finally decided that they did want to start a department. Now they have a department and an Institute. There was no Institute when I started. I kind of misspoke myself. There was a Bakken professor who was responsible for the graduate program. It was sort of my idea to start an institute because I thought we needed more than a graduate program. We didn't have a department. I didn't really think we needed a department, but I felt we needed more than a graduate program. We needed some kind of focal point for the activities. So the Institute was ultimately given it's own space and it's own budget, and we attracted some funding—a Special Opportunity Grant from the Whitaker Foundation.

Nebeker: Were there other professors?

Tirrell: Yes. We basically had a three-tier structure. There was a small cohort of faculty. I'd say there were five or so, for whom a significant portion of their salary was paid by the Biomedical Engineering Institute. There was another group that was more like 20 to 25 that we called core members of the Institute. They didn't have any salary paid, but the Institute had small seed funding for research, and they participated in those programs. Then there was another group of about 80 that were faculty members that from time to time participated in advising graduate students in the graduate program, served on thesis committees, or did the occasional things. That was the kind of structure that we set up.

Nebeker: And how did you cope with the problem of the breadth of biomedical engineering?

Tirrell: We had to try, to some extent, to focus the core more narrowly on those things in which we felt we had some significant competitive advantage.

Nebeker: And the smallest group of professors, were they close to your interests?

Tirrell: No, not particularly. But they were people that were willing to take on significant responsibilities like recruiting graduate students, helping to develop our core facilities, and things like that. There was a diversity there and sometimes differences of opinion.

Nebeker: It seems to me a good sign that this institute has since turned into a department. Things have gone forward there.

Tirrell: I think so, too. It certainly is an indication that the University felt that it was a valuable and viable activity.

Nebeker: Let me just ask at this point if there are aspects of your career that have especially related to biomedical engineering that we haven't talked about.

Tirrell: I think the other thing that's worth mentioning is my current job. There's no question that I was still very interested in pursuing ideas at the interface between biology and engineering when I came here. UCSB was interested in that, too. I wouldn't say that was the reason I was hired, but it was an unavoidable major element of the whole package. That's what I talked about as an interesting thing. I think this is an important point for the future of bioengineering.

I see the interface between biology and engineering as a lot broader than medicine. There's all this material science that might eventually have something to do with medicine, but there's agriculture and the environment. It all involves having people with the analytical quantitative computational skills that one normally associates with engineers, but with a sophistication in biology that you don't normally associate with engineers. We're in the process of trying to design what I'll call bio-nonmedical engineering here at UCSB.

Nebeker: So, the emphasis on the non-medical.

Tirrell: Yes, with the emphasis on biology itself and not necessarily bio-technology, but that's another subset. I'm not talking about making chemicals or drugs exclusively, but that's another aspect that's not exclusively medical. It's rearranging pathways and metabolism to get cells to produce the products that you want. I think computer science can bring a level of sophistication to bio-informatics that biologists are unlikely to bring by themselves. It's easy to say that. Nobody gets to work in a field just by declaring themselves better skilled at it than somebody else. You actually have to work in it and do something that's better. We've hired our first computer scientist with interest in bio-informatics. I'd be happy to hire another three or four. I'm not trying to put down biomedical engineering or the Whittaker Foundation, but to me the field that's interesting is biological engineering more than biomedical engineering, per se.

Nebeker: I appreciate that clarification. It actually reminds me that a lot of what was regarded as biomedical engineering in the earliest days in the IEEE Society was really directed toward straight biology questions, with the skills that an engineer had, rather than some application. It was trying to understand physiology better with the engineering skills, and that's what you're emphasizing.

Tirrell: I would say so. We're definitely going to build up this area here in Santa Barbara. It's not an advantage not to have a medical school in this area. No matter how much I'd like to argue that we have some kind of competitive advantage, it's not an advantage not to have a medical school because the enormous breadth, capacity, and facilities for life sciences that a medical school brings is always an asset when you're pursuing anything in biology. I think this Nanosystems Institute will be a real asset, and our connection with UCLA, which we didn't emphasize here today on the biology and medicine side of things, will be a way for us to develop sub-characteristics that we might be lacking in not having a medical school. I don't mean to convey that I have any anti-medical feeling. I'm just trying to develop something here that suits our own capacity.

The other thing I would say about traditional and current electrical engineering is that if you go to companies like Medtronic or Cardiac Pacemakers, there's no dispute that these are biomedical companies. But, some of the most important technological innovations that drive those companies have nothing to do with either biology or medicine. I don't know that there would be a more important thing that could happen for Medtronic than to be able to make a tiny, powerful battery. This has nothing to do with biology or medicine, but certainly has a heck of a lot to do with pacemakers. So, it's funny. Lots of biomedical things aren't biomedical at all.

Nebeker: It's just amazing how vast the field is and how much comes into play when you start dealing with biomedical technology.

Tirrell: That's right. As always, engineers are trained to get the job done and bring what skills and assets are necessary.

Nebeker: I think the point made at the ceremony today of the interdisciplinarity being the hallmark of the work. That sounds right on, from what I've heard. Thank you for the interview.