

EDWARD MERRILL

An Interview Conducted by

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Interview: Edward Merrill  
Interviewer: Michael Geselowitz  
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Geselowitz: I am here at MIT with Professor Merrill interviewing him for the EMBS Project. We thought we would start with him describing the field of biomedical engineering as it exists today, and then we will go back and talk about how he came to be one of the founders of the field.

Merrill: Biomedical engineering, as it exists today, calls upon the talents ranging from pure biology, pure chemistry, and pure physics to the application of all of these, and it is the intersection of many different sets. I would distinguish it from what we used to call biochemical engineering, which was back maybe in the 1950–1960 period, the fermentation processing using microbes to produce various things. As we see it now and as we saw it back in the ‘50s, biomedical engineering was quite a different thing.

Probably the best way for me to try to explain how it evolved in chemical engineering is as follows. It is a personal story. After getting my doctorate in chemical engineering at MIT, in 1947, I went to work for the Dewey & Almy Chemical Company, which became a division of W.R. Grace, but at that point it was independent.

For three years, I was a full-time employee of the Dewey & Almy Chemical Company, and in my position there as a research engineer I became involved in what is called rheology, the properties of flow of various materials, almost all of them polymeric. They’re suspensions of polyvinyl chloride powders. They were

true polymer solutions, like rubber cement and so on. I became highly interested in the properties of flow of these materials because all of them are complex; none of them are straightforward and simple. Their apparent viscosity depends upon how fast you are pushing them around, and so on.

For various reasons (which are not part of this story), I came back to MIT as an assistant professor in September 1950, but maintained warm relationships with my former colleagues at Dewey & Almy. With their help, I devised some instruments for measuring the viscosity of complex fluids. Part of my history is devoted to rheology, and I think I have four or five different instruments that I have designed to measure the viscosity of these complex systems.

I came to MIT in 1950, and for roughly the first ten years I was assigned to teach all the undergraduate classical courses in chemical engineering: stoichiometry, fluid mechanics, and so on, none of which had any direct connection with medical engineering. Then in about the time frame of 1959 or 1960, kind of by accident, two doctors at the Peter Bent Brigham Hospital in Boston by the names of Dr. Roe Wells and Dr. Robert Denton called up the Department of Chemical Engineering to find out who knew something about rheology, and they were put in touch with me. They came over and said, "Can you help us measure the viscosity of lung mucus?" It turned out to be an intractable job, a terrible job, because it's so widely variable and the mucus itself is so complex a mixture of thin and thick liquids.

As a result, they turned their interest and my interest to the flow properties of human blood. At first blush you might think that human blood is a

straightforward fluid, but it isn't. We found out it's complex and it has what we would call a "yield stress." That is to say, like yogurt or mayonnaise, as you slow down its stirring, suddenly it stops flowing so that you can get to the point where it won't flow at all, even though there is a residual pressure.

Another thing that happened about the same time, about 1960, was over at the Boston University Department of Biology, just across the river, there were two delightful professors, Herbert Berman and George Fulton. They had undertaken to do cinephotomicrography. That is to say, you put a microscope under a motion picture camera and put the microscope then on top of the cheek pouch of a living anesthetized hamster. Here is the hamster lying on the operating table, his cheek pouch has been everted, pinned down on the table, and blood is flowing through that cheek pouch, and they are taking pictures of it. These pictures show how the red cells flow through the vessels and how they go in single file through the capillaries. They show what the white cells do and that they can cluster in the conditions of disease, and they show what the platelets do, especially how the platelets will lead within seconds to clustering and blocking the flow when there is a small puncture in a vessel.

These films turned out to be extremely important to me and, indeed, to my colleagues. When I showed these pictures which Fulton and Berman had made for me to people like Edward Gilliland, the head of the department, and Tom Sherwood, one of the titans of chemical engineering, they were absolutely fascinated at what they saw: the motion of these formed elements, as they called them (the red cell, the white cell and the platelets) through these small vessels,

which is where all the complexity of exchange of oxygen and carbon monoxide and everything else takes place.

In my collaboration with Roe Wells at the Brigham, then with this input of visual information from the Fulton and Berman laboratory, we got going on a program.

Why this happened I am not quite sure, but it turned out that the source of different blood samples from Roe Wells' lab at the Peter Bent Brigham Hospital was inadequate, or at least I had difficulty getting access to it. Since the Massachusetts General Hospital is literally within sight of my building, right across the river one subway stop away, and through my connections with some of the folks over there, I got involved with their blood bank. That is to say the blood bank of the Massachusetts General Hospital, and in particular, Dr. Edwin Salzman, who was at that time a professor of surgery, and also the Associate Director of the blood bank. We got involved in an extensive program, eventually funded by the National Institutes of Health, to study in detail what controls the viscosity of blood.

There are two things that principally control the viscosity of blood, one of which was very well known, and that is the volume fraction of red cells, the so-called hematocrit, and the higher that is, the higher is the viscosity of blood. But the other one, which was not as well recognized, is the pre-clotting protein fibrinogen, which in the final stage of the intrinsic clotting system turns into a fibrin clot. But in its precursor state it does nothing, except it causes red cells to stick to each other. So at very slow flows, the more fibrinogen you have, the more the red cells tend to cluster, at least from many cases of what we would call

hyperfibrinogenemia, in which the blood was much more viscous than it should have been considering the red cell concentration of the hematocrit.

In conjunction with the Fulton-Berman film on the flow of blood through the hamster's cheek pouch and the transport properties going on, it then led me to think about what chemical engineers might be able to do in connection with medicine, since chemical engineering involves as one of its major thrusts, transport of molecules back and forth across membranes between fluids, as well as chemical reactions. We are talking about my interface travels back and forth to the Massachusetts General Hospital at its blood bank and seeing Dr. Salzman and his colleagues.

It then became of interest to think about what we would do with machines through which blood would be circulating, and there are two principle machines. One would be the so-called artificial kidney, or the hemodialyzer, in which blood is purified by being taken from a patient, run through the machine, and circulated back to the patient. This would be presumably on a chronic basis for patients who have lost kidney function. The other one, back around 1960, would have been the so-called bubble oxygenator, because at that point, blood oxygenation during open heart surgery was brought about by making a trough and simply bubbling oxygen through the blood. As we recognized at the time, this doesn't do the blood any good. It denatures proteins in the blood and breaks up red cells.

About that time, the issue of how best to oxygenate blood to take over the function of the lung during open heart surgery occurred to us. I was not the first to think of this, but we were among the first to start working on it. Of course, by

oxygenation, you have to do two things: you have to get carbon dioxide out of the blood and you have to get oxygen into the blood. It is a two-way exchange, and this brings up the issues of membranes and what kind of membranes would you use. Of course, silicon rubber membranes are ideal for two reasons. First, they cause relatively little damage to blood in terms of contact; and secondly, they are very highly permeable to oxygen and carbon dioxide.

Geselowitz: Now, this is about what year that you became interested?

Merrill: 1965. This really starts in 1960.

Geselowitz: Prior to that, devices like the artificial kidney and so forth had been held by doctors really without chemical engineers, who had not turned their attention to these problems?

Merrill: That is correct.

Geselowitz: How many chemical engineers at this time were turning their attention to these problems? How many people would you say were in your club at this time?

Merrill: I couldn't give you an accurate answer. I think we were the first department of chemical engineering to get involved seriously through doctoral research programs in these issues of the artificial kidneys and the heart/lung machines. One of my students, Dr. Nicholas Peppas, now at Purdue, constructed an "academic tree" showing my doctoral students and their doctoral students. In that tree, I can now trace, for example, who did what and when.

The earliest one to have worked in this area would be Giles Cokelet, later professor of chemical engineering at the University of Rochester, in 1963, who got his doctorate in blood viscosity, and Tony Benis the next year who worked on

blood viscosity. He became a practicing M.D. Then we have to go up to Herbert Meiselman, later professor at the University of Southern California, in '66 who worked further on blood viscosity, then we go up to Buckles in '66 who worked on the heart/lung machine and transport therein. Then Ben Lipps worked on the artificial kidney.

I received the Founders Award from the American Institute of Chemical Engineers back in November. You probably heard about the Founders Award.

Geselowitz: Right, I have heard a little piece about it.

Merrill: I was as dumbfounded as almost everybody else in my being nominated and having won it, but I won it for my alleged starting of biomedical engineering as a discipline within chemical engineering.

So, what I am talking about is how that started, and so we go back again to the decade from 1960-1970. That is an important time because in that decade, in 1963, I gave the first graduate course entitled "Chemical Engineering in Medicine" and the MIT course titled 10.56, and I offered it in 1963, 1965, 1967 and 1969. Then it was taken over by one of my doctoral students who is presently a professor here, Professor Clark Colton, who did his doctoral thesis on the artificial kidney. Colton's contribution was to completely elucidate the mass transport aspects of this so you could design the artificial kidney with the optimum membrane, the optimum flow rates of the dialyzing fluids, and of blood. This was sponsored by the National Institute of Arthritis and Metabolic Diseases, NIAMD. I'm getting ahead of my story, though. I'll come back to it.

In this chemical engineering in medicine course that I offered, we got the students

involved in calculations of gas transport rates in membrane oxygenators. We took them on visits to Boston hospitals and to The Harvard Schools of Public Health, and I think this infected a lot of students with enthusiasm for this field by being in contact with the ideas that we were presenting to them, ranging from blood rheology to membrane oxygenation to blood dialysis by the artificial kidney to clotting and thrombosis. In that era, 1960-1970, I really got things started, kind of by accident. I recall again the accidentality of this. The accidentality of this was because I was an expert in rheology. Rheology played a major role throughout.

Geselowitz: The students who took the graduate course weren't just from your group. There were other interested students or students who thought they might be interested. So, I think you're saying that many of them actually moved into or chose dissertation topics in the area.

Merrill: Yes, but not with me necessarily. For example, Charles Cooney, who is the Executive Officer of this Department and a chaired professor, was one of my students in 1963. Another one, Michael Lysaght, was a student and he became head of a biotech company in Providence and is now a full professor at Brown University in Providence. He worked with Pierre Galletti. There are several students of those days who went on to work seriously in biomedical engineering. One of my own students, Ben Lipps, did his doctoral thesis on the artificial kidney, or one aspect of it, and went on to become the President of Cordis Dow Corporation, who made artificial kidneys. Of course, as the citation I got in November points out, the greatest effect I had probably is in having inspired people who became professors to work in this field.

They would notably be people like Colton here at MIT, Nicholas Peppas at Purdue, and Michael Sefton at Toronto, and they have been enormously productive. They produce tens to hundreds of students who are working in biomedical engineering.

I would also point out that one of my very earliest doctoral students, Alan Hoffman, went on to become a professor of chemical engineering in Seattle at the University of Washington at Seattle, and is one of the most prominent in the field. But I can't say that I inspired Hoffman, because at that epoch he was working on something quite different under me, that is, radiation grafting of styrene onto cellophane, which had nothing to do with any medical problem. It was true that the concept of bringing chemical engineering principles and art into the problems of medicine and surgery got going, especially with these people—Colton and his innumerable students, Peppas and his innumerable students, and likewise Sefton. Back in the days when I got going in blood rheology, which would be starting around 1960, I had been on the faculty for ten years. I came in 1950 and in 1960 I was still an assistant professor without tenure and the then head of my department told me that my chances of being promoted to tenure were considerably less than 50/50. When I got going on this blood rheology thing, Ed Gilliland had become head of the department. He and Tom Sherwood started to change their opinion about my chances of staying on because they became excited and they thought that I had indeed gone on to a new field which would be interesting and fruitful. The head of the department who told me my chances were less than 50/50 was Walter Gordon Whitman, and it wasn't his fault. It was simply his faculty who

said, “Well, Merrill hasn’t produced anything. He hasn’t published much. He is not known for anything. He is a good teacher, but he has no research output, so we don’t think his chances are very good.”

About this time, in 1960, when I started to get into blood rheology in a big way, I finally got funding from the National Heart and Lung Institute. Gordon Brown was then the Dean of Engineering here at MIT and he was a good friend, but he said, “Ed, what you’re doing, getting into blood rheology, I think is very dangerous. I mean it’s way out of chemical engineering. It’s so far afield that none of your peers are going to be able to evaluate it. So, if it doesn’t work out and you don’t make tenure, don’t blame me.” He was very discouraging. Of course, what happened was that I squeaked through a vote of no confidence by having my senior faculty agree that I would go onto tenure. I finally got tenure as an associate professor. I think that was about 1962 or something like that.

From there on out, of course, we went on to get more and more deeply involved in medical and surgical problems, and especially my collaboration with Edwin Salzman turned into something even much larger. Salzman was at the blood bank of the Massachusetts General Hospital. He had his problems of tenure in the sense that the Massachusetts General Hospital wasn’t in a position to promote him to the level in surgery that he aspired to, but the Beth Israel Hospital in Boston did so and invited him to come on as a full professor. He changed from the Massachusetts General Hospital over to the Beth Israel, and he and I continued our collaboration.

Geselowitz: Now you had to switch to the green line. The only way to park and switch to the

green line, you had to get off at Charles.

Merrill: You got it. By this time my connection with the Peter Bent Brigham had waned. Roe Wells eventually went on to run a company. Denton went back to Philadelphia. Incidentally, if I may open a small parenthesis, the reason why Denton and then Roe Wells were so interested in lung mucus rheology was that Denton had married a woman who had two children, both of whom had cystic fibrosis. That's a miserable disease and invariably fatal and it is just a mess. There is nothing you can do about measuring lung mucus viscosity that is going to alter that. It is going to be genetic engineering. But that is what got them in it. For some reason, I think Denton's wife was a Sharpless from the Sharpless centrifuge company, and for some reason they came from Philadelphia and went back to Philadelphia. Denton was out of the act and Roe Wells left the Peter Bent Brigham. I was left working primarily with Ed Salzman at the Beth Israel. Going back to these pictures that I described, the motion pictures of the hamster's cheek pouch with Fulton and Berman, among other things we see platelet thrombosis in real time, and later on we see in some of these scenes the thrombosis followed by intrinsic clotting system. In other words, a big red clot forms. As I got going in this area of research—rheology first, then the heart/lung machine, and then the membrane oxygenator—I perceived that the universal problem was activation of blood clotting by foreign surfaces. In the context of what we were trying to do, the surfaces were primarily membranes because we tried to transport things back and forth across membranes, or they were flexible tubes, like catheters.

That brings up another part of this story that I was reflecting on. Why is it that this got going in chemical engineering and not somewhere else? Going back to 1950 and 1960, I believe what we called Course Three, which is now the Department of Material Science and Engineering (DMSE), was in fact the Department of Mining and Metallurgy, and therefore its principle interests were, as the name applies, mining and metallurgy and ceramics. So these are hard substances.

Going back to the period of 1960—1970, I am trying to reflect as to what was going on within MIT in the area of polymers and polymeric materials, and I have to say that it was entirely in this department. Chemistry had no interest in it. Polymers hadn't gotten into what is now the Department of Material Science and Engineering, and every Department of Material Science and Engineering in the country now has some polymer people working in it.

I guess it was natural that a major component of my research in biomedical engineering and various projects thereon somehow involved the issue of what kind of polymers can you use to achieve the results you want, especially that of preventing or mitigating clotting. A major part of my output over the years has been addressing that issue, which is an issue of polymer chemistry and polymer modification. I guess my major contributions have been in that area. I am credited, as you probably saw in what I sent you, by somebody who seconded my nomination for the Founders Award and said that I was one that started the perception of polyethylene oxide or polyethylene glycol, one and the same thing, as being an almost magic biomaterial in that it is remarkably inert. In 1974 or

1975, I wrote a paper for the Transactions of the America Society for Artificial Internal Organs (TASIO) and the title of it was “Polyethylene Oxide as a Biomaterial.” That turned out to be enormously important because now, as the fellow cited, all kinds of people are involved in proprietary secret research in putting polyethylene oxide and polyethylene glycol onto proteins and onto surfaces and so on.

I am coming to the end of my story. That is about it. It is a kind of serendipitous set of circumstances over these past 50 years that led to the results we got.

Geselowitz: If I am reading your story correctly, the really critical juncture seems to be between about 1960 and 1963. At the beginning of this period, you are being told that what you are doing is not tenureable by the Dean of Engineering. By the end of the period, if not being asked by the department, at least the department is not saying to you that you may not teach a course. You actually could teach a graduate course in 1963 for the first time in this topic and attract enough graduate students to make it viable.

Merrill: That’s correct.

Geselowitz: What do you see was happening in either the broader medical field or the broader engineering field that made this critical time? I’ll just throw one thing out. I’m not saying that it has anything to do with it. We all know that this was the period when federal funding through the National Institute of Health became more widely available, so that people in some of these more biomedically oriented programs could hope for some funding. Before, grants were given in very narrow, some military kind of things. This was sort of the boom of NSF and NIH

and so forth.

Merrill: Oh, indeed.

Geselowitz: So I don't know if that was a factor. But I don't want to put words in your mouth.

What do you think some the factors were?

Merrill: It is a very definite factor. In fact, it was the National Institute of Arthritis and Metabolic Diseases that came around and offered me a contract to work on the artificial kidney and they gave me an enormous sum of money to work with.

Unprecedented in its day.

Another thing that I forgot to point out, but it certainly is relevant. Although on the one hand Dean Gordon Brown thought that getting into this blood research was not in my best interest, on the other hand Jerry Wiesner (then President of MIT) and Walter Rosenblith (then Provost of MIT) were very much interested in the application of engineering to medicine and surgery. In fact, Wiesner called me into a meeting at the highest level with the head of NIH at the time, Jim Shannon, and the idea was that NIH was trying to get MIT to set up a medical school because the idea of bringing engineering into medicine was being widely promoted, and Jerry Wiesner and Walter Rosenblith were particularly interested in this.

I might also point out that by the same token my story would not be complete if I didn't mention my dear friend, John Trump of the Department of Electrical Engineering. John Trump was the one who was sitting on what we call the Rosenblith Committee and coined the phrase "Engineering and Living Systems," and that is what we worked on and what the title of it was.

John Trump, as Professor of Electrical Engineering, was also the founder of the high voltage research laboratory here. He was a co-founder of High Voltage Engineering Company along with Robert Van de Graaff, who was a professor of physics. Another part of my story has involved the use of electron irradiation to carry out polymer chemical reactions and make new and interesting polymers, thanks to the input from John Trump and from his enthusiastic collaboration with me through his laboratory. Many of my graduate students worked in the high voltage research laboratory carrying out their work. Briefly what happens, is electron beams can cross-link polymers, and they can also graft new materials onto old materials. So you can make, for example, a hydrophobic (water repelling) polyethylene sheet hydrophilic (water loving) by grafting a hydrophilic layer onto a hydrophobic support.

I should also go back to point out that about this time in 1960, when I started to get into this internal MIT community, Engineering and Living Systems, I also met colleagues like Robert Mann, Professor of Mechanical Engineering. Mechanical engineers have been involved for a very long time in things like, for example, the Cecil Drinker respirator for polio victims and Bob Mann's artificial arm for the amputee which was controlled by nervous impulses from the stump. The mechanical engineers, and I guess the electrical engineers also, had been in biomedical engineering way before chemical engineers. As to when we got going as a discipline, I guess I would have to say I probably started it, because when I did start it in 1963 there was no other department in the world of chemical engineering, as far as I know, who offered a course in chemical engineering in

medicine and biology. We were the first to start that. I think it was roughly ten years or so, after we started it, that it started to spread and propagate, and of course, no thanks to me, it is propagating itself very nicely.

Geselowitz: I read that little article you wrote about a Bostonian's account of the history, where you talked about having all these teaching hospitals. Do you also think being at MIT—the fact you mentioned earlier that perhaps the mechanical engineers and the electrical engineers had been doing engineering in Life and Living Systems earlier, and that Rosenblith and Wiesner, who were electrical engineers who got the administration into it—do you think that is one of the things that helped you foment it here?

Merrill: Absolutely. Suppose I had been at Dartmouth. They have a hospital nearby, but they don't have much engineering. I don't think it would have happened. I think it was because of the richness of the medical environment here in Boston, which is probably the richest in the nation. Can you think of a higher concentration?

Geselowitz: No, but like yourself, my education is completely Harvard and MIT, so I'm not the one to ask as impartial.

Merrill: I think this is a very important aspect of it. I don't think you need to have such a density of hospitals to carry on biomedical engineering today. Even out at Purdue, my good friend, Nick Peppas, dear man, who was the one that got me the Founders Award. Purdue University is not near any significant medical center, yet Nick manages to make the thing run. But it is not nearly as convenient as what we have over here in the Boston area.

Geselowitz: Given the disciplinary nature of chemical engineering in medicine biology, which

apparently continues to this day, and the necessity of cross-discipline cooperation, you seem to be implying-- Let me ask the correct question first. Is there a field of biomedical engineering, not biomedical engineering as a sub-discipline of chemical engineering? Could one say that there is or should or ought to be a field of biomedical engineering?

Merrill: There is. There are departments of biomedical engineering in various universities.

Geselowitz: Do those work?

Merrill: I have difficulty imagining how they could work, but I don't have the details, so I can't say they don't work. I think you have to have a fairly deep understanding of the principles of your field.

First, let me point out one other thing. In the days when I joined the chemical engineering department and the days when I was a graduate student here, it wasn't really chemical engineering. It was forms of mechanical engineering: heat transfer, for example, is primarily physics; fluid mechanics is primarily physics. There is no chemistry involved. There was some chemistry going on in terms of choosing reactors, but the importance of chemistry back in those days was far less than it is now. Now, in the last part of the century, chemistry is coming in in a much bigger way in chemical engineering departments in general. That is one of the things that sets it apart.

What I am saying is that when we talk about biomedical engineering, I don't think anyone could work on membrane transport who doesn't have some basic understanding of molecular diffusion, physical chemistry, and chemical

principles. To answer your question, when I say schools of biomedical engineering and departments of biomedical engineering, maybe it works, but I have difficulty seeing how it would work.

What I do see, of course, now is another thing. As people like Bob Langer, professor of chemical engineering at MIT, have come onto the scene and gotten into controlled drug delivery, it now turns out that biomedical engineering is far more entrepreneurial than it used to be. People are moving away from the kind of basic research that I was doing in blood viscosity, the results of which are unpatentable, to producing fruits of research that are patentable, that are products. The last one I've been involved in is the very thing sponsored by one of the foundations in Massachusetts General Hospital, which is an improved polyethylene for the artificial hip. Here is a product that is now in production and produced by Zimmer Corporation in this country and Sulzer in Switzerland. What it has accomplished is to reduce the wear rate of this polyethylene prosthesis to virtually nothing, so that instead of having to replace a prosthesis, it may be fully a lifetime implant.

I'm not saying this by way of boasting. I'm simply saying that more and more chemical engineering is coming out with products. Of course, as you doubtless know from what you've see on the outside, the big name of the thing today is tissue engineering, and chemical engineering has now gone into tissue engineering and they've become highly biological.

Geselowitz: I was going to ask you, is it safe to say now that in a way the idea of biotechnology has actually in a sense brought biomedical engineering and

biochemical engineering back together, so you're almost full circle? What we are talking about now is using biology, chemistry, and engineering to engineer living systems. That is what people are working on.

Merrill: That is correct. We had chemical engineering and we had biomedical engineering. Now we have biological engineering, and I would call tissue engineering biological engineering. What you are doing is making scaffolds in which the cells can grow. My colleague over here, Linda Griffith, is working on hepatocytes making an artificial living liver. Tissue engineering is the major thrust of biomedical engineering and chemical engineering today. Every department of any consequence in the United States—Columbia, for example—any department involved with biomedical engineering and chemical engineering is going into tissue engineering and they advertise widely that they need people in tissue engineering.

Geselowitz: But it continues, and the field is so broad and at the same time so deep that any individual practitioner needs to have come up through some core discipline that they really understand, and then they collaborate with others in other core disciplines. What did you do for readings or textbooks or problem sets when you first taught 1056?

Merrill: We used Guyton's *Textbook of Medical Physiology* as the text. It explains how blood flows from a physician's point of view. What is the rate of breathing of the normal man and what is its lung capacity? I had my students read this book written by an M.D. physiologist.

Geselowitz: He is an M.D.?

Merrill: Yes. Some of the concepts that he put forward were, in engineering terms, kind of simplistic, if not ludicrous. On the other hand, the simple facts were there. How much urine is produced per day? What is the composition of urine? What is the pH of the blood stream? What do we mean by colloid osmotic pressure? Why is the presence of protein absolutely essential in blood to keep tissue from swelling? These basic physiological principles.

Geselowitz: The first edition was 1956.

Merrill: Yes.

Geselowitz: It shows that the physicians felt a need for this kind of quantitative data, but presumably if this had come to your attention, you probably helped the M.D.s by correcting some of the engineering aspects.

Merrill: Yes. I did a review article at the invitation of *Physiological Reviews* on the viscosity of blood.

Geselowitz: This was a review article about everything that was known about the viscosity of blood among physiologists?

Merrill: Yes. They knew almost nothing about it until I taught them.

Geselowitz: This is a problem set from 10.56 (chemical engineering course)?

Merrill: This is an examination from 10.56 that was written by my student, Charles Cooney, who is now my boss. It goes into the details of how rapidly oxygen is going to be transferred to and from blood in a membrane oxygenator. To answer your question of what did I use for text, I used that as a principal text and then the rest of it was done by notes.

Geselowitz: How about today? If I walked into a major department, like at MIT or Columbia

today, I'll bet there's an advanced undergraduate course at the senior or junior level called "Introduction to Medical Applications." Do textbooks exist for such courses?

Merrill: I don't know, but let me point out that here at MIT we have two competing centers: The Center for Biomedical Engineering and the Division of Bioengineering and Environmental Health.

Geselowitz: I passed next door. There is a BMEH that I passed through on the way to your office.

Merrill: Here, for example, is one of my friends sitting at the Center for Tissue Engineering. I would say that is cohesive. You could have a Center for Tissue Engineering because, by God, you've got to bring in biology, and it is mainly biology. This is really focused. It is not biomedical engineering, it is tissue engineering.

Geselowitz: Again, it's a center, not a department. Presumably, if you'll draw faculty and students from many or several departments.

Merrill: That is correct. What I am saying is we have this bioengineering and environmental health division (I guess it is called a division), then we have the Center for Biomedical Engineering, and it's kind of a peculiar competition. In fact, it's become almost disorderly in the Boston community. I am not going to say anything more for the tape.

Geselowitz: It is just in general that the field has grown so much now that there is sort of competing angles.

Merrill: There is some competition. For example, the Massachusetts General Hospital has

a Center for Biomedical Engineering all by itself.

Geselowitz: If a hospital sets up a center for biomedical engineering, what do they mean? In other words, do they include the bio-electrical engineering, people like my father working on the artificial heart?

Merrill: I can't tell you. Another thing I can't understand is by what mechanism they can award degrees. Massachusetts General Hospital is not a university, it's a hospital. It's a teaching hospital, but it is a hospital. Do they somehow award the degrees through the Harvard Medical School?

Let me point out another thing. We have and have had for a long time a joint Harvard/MIT program in health sciences and technology. In that program, students can get a combined Ph.D./M.D. program. I have had two students in the recent past who have done exactly that. One student, Elliot Chaikof, was a practicing surgeon at the Massachusetts General Hospital already having an M.D. degree, working in the emergency ward on weekends and getting his Ph.D. with me here, working on biomaterials. Now he's a hotshot surgeon down at Emory in Georgia and an adjunct professor at Georgia Tech. He's doing fine. The other student, Ed Perez, first got his Ph.D. here working on a synthetic cornea to improve vision in the eye. He then wound up getting his M.D. at Harvard. Then he went over to San Francisco to work as a dermatologist. Here are two guys that are practicing physicians or surgeons, who went through this program.

The other thing that I observed back in the days when I was deeply involved with Boston hospitals, it turned out that in some cases some of the physicians and surgeons treated engineers as if they were light bulb changers. In other words,

there was a kind of pecking order in which the surgeon or the chief was the chief on top of everything else, and everybody else reported to him. There was a certain, how shall I say, arrogance that I think is now gone, because I think the medical profession realizes how much engineering has changed what they're doing. I would say as an innocent bystander thinking of electrical engineering, probably the most important changes have been made in the field of imaging, and that involves physics and electrical engineering. I myself as a patient have undergone CAT scans, MRIs, artheroplasty, and artheroscopy.

Geselowitz: Ultrasounds, probably?

Merrill: Yes. These diagnostic tools make all the difference in the world. They changed the whole damn thing.

Geselowitz: The M.D.s thought they knew everything and now they realize they knew nothing. Now they think they know everything, but they probably still don't.

Merrill: I was talking to my dermatologist the other day—I keep growing basal cells and he keeps taking them off. He agreed that his imaging techniques are enormously important. He said, "If I were trying to find melanoma in the lung of a patient, if I had used a stethoscope my chances would be substantially zero. With MRI, I think I can get it." I would say that it is now apparent to any responsible physician or surgeon in any hospital or other setting that medical engineering, in its broadest sense, has changed and transformed what they are doing. They can't escape it. They've got to have it.

Geselowitz: One other question I had that I think you may have already answered, is what do you think the next big thing is in chemical engineering and biology? Would you

say it's that tissue engineering that you already talked about?

Merrill: Yes.

Geselowitz: We are going to build living organisms, pretty much?

Merrill: Yes. Take the example of Genzyme Corporation.

Geselowitz: Is that the one involved with Boston University, with the patents?

Merrill: I don't think Boston University is involved in this one. What they do is in athletes who have a problem of knee cartilage damage, so that the knee is painful and doesn't move very well, they take out some of the patient's own cells, grow them in vitro outside into a patch, and then re-implant them in the patient. This is a very expensive and long process, but when they get finished, they have reconstructed the cartilage surface, so that it functions very nicely. I think that more and more we are going to see that happen.

One would say that this is the way it really should happen. We ought to see if we can put ourselves as device engineers out of business. That is to say, make Mother Nature grow back what is missing. Don't try to treat a tumor chemically or with radiation, just do something, like Judith Folkman's concept: put in a handy anti-angiogenesis factor and stop its blood supply, as Entremed Corp. is trying to do. Or, in terms of cystic fibrosis, see if you can finally find a gene therapy that would undo this.

The things that we made that were so important at the time, for example, the artificial kidney, saved thousands if not tens of thousands of lives, but it doesn't lead to a very high quality of life. It's a damn nuisance. It was through the influence of the NIH and prodded by Senator Lister Hill and his colleagues that

the government put so much money into it and turned this rare and costly procedure into a very common thing. The unit is now a commodity, five dollars, ten dollars a piece. It used to be a hundred dollars to a hundred thousand dollars.

While that has been useful, I think that the wave of the future is to go to the biology of it. We may finally get out of the act, except for the fact that it is we who are involved in the polymer structures that will make the scaffolds on which the biologists can grow the cells and then have those structures disappear.

There was a neat one, by the way, that struck me as being very, very inventive that I heard of out in the annual meeting of the American Institute of Chemical Engineers in California. A group I think at the University of Utah under Kim, has got a corporation going that now makes what is called a tri-block copolymer and it has three sections in it. The first section is polyethyleneglycol. The second section is polyglycolic acid. The third section is polyethyleneglycol, again. Polyethylene oxide is hydrophilic and it's on both ends and polyglycolic acid is in the center.

What is amazing about this is that at room temperature water solutions of it are completely soluble and fluid. You can mix all kinds of drugs and recipes, and whatever you want. If you inject it into the human body at 37.5 degrees, it jells. If you cool it down, it becomes fluid again. If you are going to deliver a shot of something locally, you inject it into the human body and it jells. There's the drug stuck in the jell, and then it diffuses into the surrounding tissue and if that tissue is tumorous it will start to do its business.

The beauty of this one is that it is also biodegradable. The central section is

polyglycolic acid. It biodegrades at a known rate. After a period of time, they could program it for two days or a week, it's falling apart.

Geselowitz: The middle part dissolves away.

Merrill: Everything dissolves and the rest of it comes out in the urine. I call that neat. It's that kind of invention that is neat. That's where I think we have a future. If there are two areas where the chemical engineers are going to be highly involved or are already, one is tissue engineering and the other one is drug delivery, for sure. For example, Bob Langer got the \$500,000 Lemelson Prize for the work he has done in drug delivery. That's primarily a problem of chemistry and delivery of chemicals. I would say these are the two major places where we can contribute.

Geselowitz: Terrific. You have answered all my questions. Do you have anything you wanted to say on the record before I turn off the tape?

Merrill: No.

Geselowitz: Okay, Professor Merrill, thank you very much.