Perry L. Blackshear, Jr.
Narrator

Kirk Jeffrey
Interviewer

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KJ: This is Kirk Jeffrey on August 21st, 2000. I'm at the Minnesota History Center in St. Paul, and this morning I'll be interviewing Professor Perry L. Blackshear, Jr.

Professor Blackshear, welcome to the Minnesota History Center this morning. Thanks a lot for coming down. I wonder if we could start the interview by my asking you to just—if you could fill us in on some of the main events of your career, your education, how you came to be at the University of Minnesota, some of the major research areas that you have focused on over the years.

PB: Fine. I grew up in Atlanta and went to Georgia Tech, the way a proper Atlanta engineer should, and then went to the North Africa, China, Burma, and India theaters during World War II. I came back and got a Master's degree at [Georgia] Tech, and then went to work with NACA [National Advisory Commission on Aeronautics] Lewis Lab in Cleveland.

KJ: That's the National—

PB: Advisory Committee for Aeronautics, and it morphed into NASA [National Aeronautics and Space Administration] in 1956.

Then sort of intermittently, day school, night school, I got a Ph.D. from Case [Institute of Technology]. While I was working at NACA, I had developed an instrument for measuring the surface of revolution of distorted flames, Bunsen burner flames that were distorted acoustically. I had finished the research, published the paper, and the device was in my lab leaning against the wall collecting dust when Professor Kurt Wohl, who was scheduled to come to the University of Minnesota and start a course in combustion—he was one of the German brain drains after World War II—he visited my lab and wanted to know how I attained surfaces of revolution, and I pointed to the little device.

Dr. Wohl, who was, I would guess, in his late fifties at the time, clasped his hand to his breast and said, "Oh, I've wanted all my life to have a surface of revolution integrator. How can I

obtain one?" And I picked it up and handed it to him. I'd just gotten my doctorate from Case at that time.

Two months later, I got a letter from Professor Dick Jordan at the University of Minnesota saying, "We had invited Professor Wohl to come and teach our courses in combustion. He had agreed to come. He went in for a medical checkup just last week, was told by his doctor that he would never survive a Minnesota winter. Here we are with an opening in this combustion area. We asked him if there was anyone he could suggest, and he said, 'Well, one name comes to mind.'" [Laughter] So I was at the University of Minnesota thanks to a surface of revolution integrator that I made at NACA.

KJ: That would have been in about—

PB: 1957. Then I was still interested in measurements and flames. My first graduate student, Mike Fingerson, had as his research subject the development of a temperature sensor that could work in very high-temperature environments, environments much higher than any solid could withstand. The rationale of the device was to measure the heat flux rate from the environment to a surface of known temperature, but then we would internally cool the surface of known temperature. So it could withstand very high electrically heated plasmas.

He developed the device and was giving a paper at which a member of the physiology department attended. He came up to Mike after the paper was presented and said, "That's a pretty rugged device. Do you think it could hold up in blood flow?" And we were certain that it could.

There was another student in the lab who developed a little probe that would go across an artery carrying this probe, and you could detail the velocity at different points in a dog's aorta. Mike and several other members of the lab went to the Engineers in Biology and Medicine Symposium, I think it was 1959 or 1960, to present the paper. And they came back saying, "Oh, artificial hearts are being worked on by surgeons who know absolutely nothing about engineering. Now, if you can tell us how much turbulence and how much shear stress and how much pressure oscillation the red cells can withstand, we could just wipe everybody's clock on artificial heart development." The reason they asked me is that my wife is a physician, and all medical questions were referred to her through me. So I started life as a bioengineering expert as a channel of communication between my students and my wife. [Laughter]

She, after looking into the literature, came to the wise conclusion that this is the kind of question that simply has not been asked before and only an engineer would ask it, and it was her opinion that only the engineer could answer it.

KJ: So the hunch that red blood cells could be damaged—

PB: Mechanically.

KJ: —mechanically by being put through pumps, for example, came from the engineering side?

PB: They recognized—because every device that people were making at the time would pump the blood fine, but the blood would be virtually destroyed in the process. The idea was that we had a whole new engineering science area, the handling of delicate fluids. It just seemed like something that you could sort of hunker down and have a series of students working on.

KJ: Was that a problem with the early acute pumps, like for coronary bypass surgery, too, or was that such a short-term...?

PB: Well, it was short term enough so they got away with it, and since they did get away with it, with these roller pumps, no one ever bothered to look into it further because they were getting away with pumping blood. This is a point that our first collaborator, Gene [Eugene] Bernstein, pointed out. We asked the Bush Foundation for a grant to allow us to make some basic measurements on blood, and they sent the grant to Owen Wangensteen, who then was head of surgery. Owen asked Eugene Bernstein, who was a young assistant professor in surgery and one of their upcoming stars, to come over and talk to me. And he told me that. He said that they had been using these roller pumps now for several years, and there had been no efforts to optimize its performance since it had worked adequately. They knew they were destroying some of the cells, but it was working all right, and they went ahead and used it. But he was very enthusiastic about collaborating with engineers. So from a conduit I became involved, because this was sort of up my alley, the fluid mechanics part of the thing.

So we had a whole series of students. Bernstein and I put in for and got a training grant to train surgeons in bioengineering and engineering in bioengineering. It was a different emphasis at that time than is now in bioengineering where people are trying to define someone as a bioengineer. We thought the ideal way to work would be to have a surgeon who was conversant with engineering and an engineer conversant with biological and medical terms, but still wear the hat of the engineer or the surgeon without any sort of tilt.

KJ: You came at bioengineering, if we can call it that, really as a mechanical engineer, correct?

PB: Yes.

KJ: Were there other people interested in bioengineering or medical engineering who were electrical engineers?

PB: Oh, yes, that was the dominant representation at the time. There were more electrically oriented bioengineers than there were mechanically oriented engineers. I think they claimed the field, and I guess they still do.

KJ: Yes, because of devices like pacemakers.

PB: Yes.

KJ: So by the early sixties, you were a mechanical engineer and became increasingly involved with biological or medical applications for your field of fluid mechanics.

PB: Yes. I think we did most of the early work on the mechanical properties of the red cell, and it was some of our early work on tethered red cells, cells anchored at a site, to prosthetic walls, that led to the mechanical properties of the red cells that Evan Evans and Bob [Hockmuth] in that school at Duke, and I forget the name of the engineer at Columbia, recently deceased. The bunch of them developed mechanical properties of the red cell membrane as representative of the membrane, and then they've gone on to look at other cells as well.

But we found that the red cell is a lot tougher than anyone thought, as long as you could keep the blood lipids low, but if you had post-alimentary lipid particles circulating in the blood, you could tear the cell up quite easily. Some of our dog experiments were really baffling until it was my wife who pointed out to us that it's customary in physiological experiments to fast the animal at least twenty-four hours before you do anything to them. When we started doing that, our pumps worked much better than they had before.

KJ: Did she collaborate on any of your papers? I notice more than one other Blackshear.

PB: Joseph is a cardiologist at the Mayo Clinic, and Jackson, he's another son. Gertrude, my wife, and Fernando Vargas and a bunch of physiologists did collaborate with us. But she was very much a part of the discussion. I ought to mention that. That was the most wonderful learning experience of my life. We had Ken Keller, from chemical engineering, and Eugene Bernstein from surgery, and his trainees included a wonderful physician who's still very actively locally, Mike Schwartz, who actually is the only one of the surgeons we ever got to get a degree in bioengineering. I think since then that there's been one other surgeon who's managed to get a Ph.D. in bioengineering.

But we would design experiments. Gertrude represented basic physiology, and I thought I represented the fluid mechanics. Keller was the chemical engineering aspects of fluid mechanics, which is a lot of the interfacial properties. We had a practical engineer, Frank Dorman, and the surgeons who considered themselves practical biological scientists. We would design an experiment and then examine the results and interpret the results from these different perspectives, and it was just a mind-blowing experience to see how one set of experiences could be interpreted in so many different ways, and all the things you never thought of that could be happening and explaining what was happening. That was an exciting time.

We ended up with a little blood pump about that big, and our hope and our dream, the dream of our group was that this would be an implanted artificial heart, driven magnetically across the

skin. By the way, on the artificial heart proposal, the grant proposal, Earl Bakken, who was still working out of his garage, was one of our consultants.

KJ: Back in the very early stages.

PB: Right.

KJ: I did read a paper of yours describing a little pump, I guess, or a rapidly revolving set of blades that was driven magnetically through the skin from an external sound source, kind of a circulatory assist.

PB: Bernstein's hypothesis, as the surgeon's hypothesis then, was that the heart in a patient, still alive but not healthy because of heart failure, if that heart could be supported a little bit, the patient ought to do better and the heart do better, if you could just take off part of the burden. So that was our goal. We were going to spear the apex of the left ventricle with a probe, take blood out, run it through the pump and down into the descending aorta, and simply supplement the blood being pumped by the balance of the pumping capacity of the heart.

KJ: And not just bypass the left ventricle, but give it a boost and part of the blood gets through.

PB: Right. The bypass people who are now using such a system, not our system, but such a system to keep patients alive in the so-called bridge to transplant, find that when they have been pumping patients and augmenting the work of the heart for a few months, the patients' vital signs improved to the point that they would not qualify for a heart transplant were they in that shape when they came in. I think his idea has been vindicated.

Medtronic—when Gene left to go to San Diego, we decided we ought to have some sort of a completion of our efforts, and we went to Earl Bakken. Earl had just returned from a meeting with the National Artificial Heart Program that at that time was being administered by a person that Earl considered somewhat overbearing and who had asserted to this group of bioengineering manufacturers that this was a sufficiently complex program that only something like the space program could accomplish it, that "You private enterprise people don't have a chance."

So Earl said he would show them, and so he was happy to take over the patents on our centrifugal pump and support the research for a number of years.

KJ: This would have been in the early seventies, I guess, that Professor Bernstein left for San Diego and Medtronic.

PB: I think so. Maybe mid-seventies, but I think he was still at Minnesota in 1972.

KJ: So Medtronic had some thoughts—I mean, Earl was presumably not simply doing this out of the kindness of his heart, but because he saw some possible future meaningful—

PB: Yes, but no one was buying artificial hearts at that time, but they were buying left ventricular systems, so that Medtronic then incorporated the pump design into a left ventricular assist system, the bypass support system in combination with an oxygenator. This little pump, then, with the oxygenator, did pretty much what the—what's the name of the pump that Medtronic now sells that has the many, many vanes?

KJ: I don't know. I don't know the name of it.

PB: It will come to me. But there are in Europe and around the world a number of heart bypass systems that include centrifugal pumps. I guess this was if not the first, at least one of the first.

KJ: So this is an example, then, of a technology inaugurated at the University but then passed into the corporate community.

PB: And it was a nice application of the basic study on fragile fluids that we thought pretty well established that it was the interface that made the red cells vulnerable, not the fluid mechanics, not the interface with the liquids, but the interface with the solids. So our pump represented the minimum wetted area required to pump the fluid, and we allowed the turbulence to get whatever it had to be and had quite low hemolysis.

KJ: Leaving aside the work on hemolysis and left ventricular assist or blood pumps of this sort, were there other engineering projects that you worked on that eventuated in at least experimental devices?

PB: Well, a lot of the surgeons would come to us saying "We like what Gene is getting out of you. We'd like to do something with you, too." [Laughter]

Do you remember what C. Walton Lillehei's brother's name was?

KJ: Richard Lillehei.

PB: Yes. Richard Lillehei wanted to preserve organs, and he wanted to have a chance to freeze the organs and preserve them if it were possible. So at the time it was volume change that was supposed to be destroying the cells, when the ice crystals would change volume and [unclear] the cells. We did a little review of different forms of ice, and found that if we would increase the pressure, we could get ice that would not change volume when it froze. Type IV ice, I think it is. But we proceeded to go to constant volume freezing, where you would simply put your biological stuff into such a rigid container that when you froze it, it couldn't expand. And we were able to freeze blood with no additives that would survive a hard freeze, but we never could get any nucleated cells to survive.

My son Perry, who was a senior in the biological sciences here, had gotten a job in Henry Buchwald's lab. Henry Buchwald and Richard Varco were trying to infuse at a steady rate heparin, and they wanted a depot that they could put under the skin, infuse heparin at about an M-L vein, and avoid the sinusoidal pattern of heparin variation. The principal downside of varying the heparin levels was that you get bone resorption and your patient would be exposed to bleeding episodes.

So Perry and I were riding to work together, and he described how he was putting a little impermeable capsule around a vein and was going to rely on the molecular screening of the vein tissue to monitor the flow of heparin from the depot into the vein. I said, "You know, it would be so much easier just to put a capsule containing the heparin and pressurize it and let a catheter in with the heparin. You could implant that under the skin as easily as the one you're talking about."

So he showed up in my office the same day and said, "They bought it. Do it." [Laughter]

KJ: That will teach you not to make casual comments like that, I guess.

PB: We had, that same day, a conference, and Frank Dorman, a local laboratory wizard, decided that rather than a pressurized gas it should be a pressurized phase change material or fluorocarbon. We found the fluorocarbon that would give a pressure of about a half an atmosphere at body temperature. I think it took about a day to design the capillary that would go with it that would have to be a long, skinny tube to keep the flow from exceeding one ml [milliliter] a day at that pressure.

So the design came out as a little hockey-puck-shaped can with a pressurized bellows in it [and a port that could be accessed by a needle injector]. Several years of developing and trying it out in dogs before it was commercialized, but it's still being sold as the Infusaid infuser. We tried to sell it to Medtronic.

KJ: I have a follow-up question about the infusion pump. Did it occur to you and others in the group that in addition to infusing heparin, there might be applications with insulin or chemotherapy, that it could have a much broader possible set of uses?

PB: Oh, yes, especially it occurred to Henry, and I think Perry is still working on the insulin infusion aspect of it. When he was graduated from here, he had won a Rhodes Scholarship, and he went to Oxford to three years and got a D. Phil. [degree] and then went to Harvard to finish off his medical school training. He was working at the Mass. [Massachusetts] General Hospital surgery lab, where they were installing one of these little pumps that he had helped—actually was the lead developer on, and he was assisting the surgeon that was implanting it. The surgeon was saying, "I understand this thing was developed by a kid who was still an undergraduate at the University of Minnesota. Can you imagine what he's doing now?" [Laughter] Perry said he just couldn't resist it. He said, "Assisting you." [Laughter]

KJ: Was this the origin of infusion pump technology that's so widely used today? I have a friend here in the Twin Cities who has diabetes, and he has an implanted infusion pump.

PB: Is that right? Yes, we were the first ones.

KJ: That's a remarkable achievement.

PB: We sold it to the director of research at Medtronic, whose name is in here somewhere. I'll find it. I'm embarrassed, because he was our most outstanding speaker at a freshman seminar series that we held last year.

KJ: You mean you sold the rights to him as a person?

PB: No, we sold the idea to him as having something that there were enough cardio-active drugs so that you could think of chemical pacemakers as being an augmented market for Medtronic to pursue. He was convinced, but he couldn't sell management at that time. But since Medtronic's interest has broadened, they came back, and one of their more serious tasks was getting around our patent in order so they could develop their own pump.

KJ: Who directly acquired or licensed the rights under your patent?

PB: The Metal Bellows Company in Massachusetts had been supplying us with titanium bellows and the cans to make the pumps. This was after World War II, and the space investments were tapering off at that time. They were making a lot of space-age parts. So the head of the company came to see what all these bellows and cans were being used for at the University of Minnesota, and he asked to be considered as the recipient of manufacturing rights if ever we went that route. After Medtronic turned us down, we turned to him.

He ran for the Senate against Ted Kennedy one year, and one of his principal campaign slogans at the time was to hold up the pump and say that he was instrumental in contributing to medical science.

KJ: At some point around this time, that is, the mid-1970s, the Food and Drug Administration, because of changes in federal law, began to acquire the power to review devices that would be implanted in the body and either would be life-sustaining or potentially life-threatening. Did that affect something like the implanted pump?

PB: I didn't get involved in it if it did. I understand that—well, in the ASAIO, American Society of Artificial Internal Organs, there was a lot of discussion, and it was an interesting discussion, the kind that I'm sure a historian would love to explore. On the one hand, there were those who could hold up instances in which ill-conceived or unproven medical devices had done considerable harm implanted by unwise enthusiasts who really thought they were going to be

doing some good but hadn't thought it through enough. And then there were those that could hold up these examples of treatment withheld because the FDA was not allowing a life-saving device to be used.

KJ: You can always find examples on both sides.

PB: It's a gutsy kind of discussion that you don't get into in other forms of engineering.

KJ: Another item that I notice on your bibliography, I don't know whether you regard this as an important project overall, was you did co-publish a paper about gastric treatment, a treatment for peptic ulcers, I guess, that Owen Wangensteen had pioneered independently. Is this something that we want to go into at all?

PB: I think so. In trying to characterize the peculiar quality of biological fluids, one of the things we looked at was the particulate nature of blood. And if, when you treat blood as a fluid, when should you pay attention to the particulate nature? It entered into the viscous behavior because the particles would tend to agglomerate at very low shear rates, and this would make the blood seem more gel-like, and indeed as the flow came to rest, the blood behaved like a loose gel. It could maintain a shape and transmit a force without moving. So that was one instance.

Then we found that the particulate nature of the blood, where the particles would be rotating in a velocity gradient, would promote the diffusion of solutes. The larger the molecular rate, the more important this became. But even for something as small as the dissolved oxygen molecules, there were instances where augmentation by diffusion could be a very important aspect of the mass transport of something like an oxygenator.

But then when we got to heat transfer, we found that the conductivity of the plasma was sufficiently high that with particles as small as human red cells, the stirring that you would get from rotating particles in the flow wouldn't promote heat transfer. But the student who was responsible for this, Avtar Singh Ajuba, was asked to explore particle suspensions that would be large enough to cause the stirring effect which should occur in some particle size. So he found that if he put in a 100 micron-long particles or spherical particles 100 microns in diameter, that at laminar flows of quite low shear rates you could get substantial augmentation of heat transfer.

Now, in the stomach freezing problem, you'd like to have as high a heat transfer coefficient on the inside of the stomach as you possibly can, because their problem is that around the stomach there are blood vessels and then fatty patches so that, in effect, part of your stomach is insulated from heat flux to the outside, part of it is right next to a heat source. What you're trying to do is destroy or to bring the surface of the stomach lining down to just a few degrees below freezing point so that you can destroy the superficial acid-secreting cells on the surface but not the structure. What you like to do is have a uniform temperature in spite of the fact that you need a high heat flux at one point. The higher the heat flux you can have, the lower the temperature gradient you need to drive the heat flux.

So by using particles to stir the flow, you've increased the heat transfer coefficient and therefore go to very low temperatures. But then, in addition, if we use flakes of ice as our particles, we have a thermostatting effect of ice-saltwater solution. I thought it was a very elegant engineering solution for getting a uniform temperature in a body that had heat sources and insulating patches next to each other.

KJ: Was that picked up? I guess gastric freezing did not come into widespread use or were there questions raised as to its effectiveness as a treatment.

PB: Yes, there are some pretty grisly stories that I don't think you want to put in your book, about guys saying, "Look at that. That thing is absolutely frozen solid. Oops." [Laughter]

KJ: So there's an example of a kind of engineering science problem for which there was a solution, and yet it didn't yield a medical treatment that was acceptable to the profession.

PB: I didn't follow up, but I think Owen, to his dying day, thought that he had something in this, and we certainly gave them at that time the most uniform interior temperature that you could possibly get. So if it was going to work, I think that they were presented with a chance to make it work.

KJ: By the 1970s, the medical technology industry, or companies based on medical technology were becoming pretty important here in the metropolitan area. Were you involved at all in helping to found or serving on advisory panels for any of these companies, even big ones like Medtronic or the smaller ones?

PB: We were consultants for Medtronic from the time we started collaborating on the heart. The young man that they put in charge of commercializing our little blood pump was Lou Cozentino. Lou had just gotten his doctorate and was, and still is, full of beans. And in addition to his interest in the blood pump, he was interested in dialysis. We would go in and talk about the blood pump, and then Lou would start challenging us with different aspects of the dialysis problem, one of which was the blood access problem where they wanted to have frequent access to the vasculature, but people really felt uncomfortable about getting stuck all the time with the needles.

So Dave Scott and I came up with an idea of a percutaneous button that allowed you to plug into your dialyzer, turn the button ninety degrees, and you'd have access to the blood. At that time, I guess, and still, pyrolytic graphite is the ideal material to have in contact with the blood. So we designed it so it could be fabricated by pyrolytic graphite, sent it out to Gulf Atomic to be fabricated, and those guys patented it on their own, the little knob.

With Medtronic's blessing and, I guess, support from the Shapiro brothers, Lou started what was then Renal Systems. And I guess Medtronic spun off a lot of companies like Renal Systems.

KJ: Sometimes knowingly and with their blessing, and sometimes people would just leave and start companies.

PB: I think they actually financially supported Renal Systems when it first started. At that time, Fred Shapiro and I were serving as consultants for the NIH [National Institutes of Health] kidney disease program. I was on a permanent panel, and then we'd go together to these ad hoc panels. We were coming back from an ad hoc panel on blood access and decided that the button idea probably ought to really be tried. So we designed, rather than have that ambitious pyrolitic graphite system, just visualized something like these self-sealing apertures that you have on some bottles that contain drugs that you draw out with a needle, only just have two punctures rather than one. Fred and I presented it to Lou, and Lou was enthusiastic about it. Fred assigned—oh, I think my old-timer's disease has me here for the time being.

KJ: There are a lot of names to remember.

PB: We assigned students to work on this in our lab, and together the group came up with—it was a product sold for a number of years by Renal Systems, and again I'm struggling with the name of the product. There were users of this blood access scheme who were very successful with it. There was one group in New Orleans where the physicians in charge of a big group of quite poor and quite uneducated dialysis patients were convinced that keeping that blood access point clean was their purpose in life, and they were able to have infection-free and pain-free blood access for years, whereas less dedicated patients would get infection. So the blood access point gave way to more routine uses of fistula, which requires the skin to be perforated every time you dialyze. But it made possible frequent dialysis, which, from the standpoint of health care, is ideal, but from the standpoint of intrusion into the patient's life is not ideal. People would much prefer twice-a-week dialysis, even though their well-being is not as well served as if they had daily dialysis.

KJ: With this system, would it be correct to call it a nipple or a kind of—pacemakers had these things in the early days, too.

PB: Where they come across the skin?

KJ: Yes. Partially it was a transcutaneous thing.

PB: Right.

KJ: An external access surface through which the dialysis probe, I guess, would be introduced.

PB: Right.

KJ: Thereby saving trauma to the skin.

PB: Well, we had something like that, too, on the infusion pump. We'd push a button on the infusion pump, and because you only stuck it once a month, the skin would heal over at the site. So you could put that under the skin. But our goal was to facilitate daily dialysis, so we left it through the skin.

KJ: Professor Blackshear, clearly, on a number of these projects that we've been talking about, you had students involved, graduate students who were apprenticing and working toward their Ph.D.s or whatever. Is that what you get in engineering, a Ph.D.?

PB: Yes.

KJ: Could you talk a little about your students and how many you've had and what has happened to them, how their careers have progressed since leaving the University?

PB: I've had, I think, twenty-five Ph.D.s, and I don't know how many master's, and then we supported a lot of students in the laboratory who were going to medical school. So lots of people that we hear from are old laboratory workers who are now orthopedic surgeons, things like that, engineers who've gone into medicine.

The first student is sort of memorable, Mike Fingerson, because he's actually the guy that got me involved in bioengineering. This same laboratory wizard, Frank Dorman, who played such a big role in bioengineering, I talked him into starting his own company, originally to sell this device that he developed as a graduate student. It rapidly broadened out into the particle tech area as well as the fluid sensing area and became TSI, which is, I guess, one of the world's biggest instrument companies now.

KJ: TSI, now, does that stand for something?

PB: Thermal Systems Incorporated.

KJ: Where is that located?

PB: It's just off of Rice Street in St. Paul, just south of Highway 694. It was public for many years and has just recently been acquired and taken private. It's a big, flourishing company, and they do work still in doing skin-blood flow research, in addition to all of their high-tech Army-related stuff. They make the tests for gas mask effectiveness and all kinds of particle sensors that take you right to the state of the art in this new nanotechnology area. So he had a very happy, productive career. He was the first student.

Then the series of students that we had that were doing the work on the fluid mechanics, how much do you handle synthesis material and how do you handle the fact that the blood is particulate? Dick Forstrom was the one who developed the test, that thought of a definitive test

on measuring the fragility of red blood cells. He was very ingenious and very enterprising, and succeeded in striking up an acquaintance with the people at the [Minnesota] Zoo, and was able to have Siberian tiger blood as part of the different kinds of blood he tested for fragility.

Incidentally, as you go through the different mammalian species, their cell size changes. Goats are the smallest. The smaller they are, the tougher they are, and the harder they are to tear apart in high-shear fields.

KJ: Where do human cells fall in the spectrum?

PB: Well, they are almost as big as elephant cells, but not quite. Then all of the mammal cells are smaller than the avian cells, and the world's champion red cell is the little amphiuma, a small amphibian that has a forty-micron nucleated cell. You couldn't get a unit of blood if you took all the amphiuma in the world and exsanguinated them.

Then Dick Collingham was the one that did the definitive work on the augmentation of diffusion in particle suspensions. That, by the way, has spawned a number of different Ph.D. dissertations around the country of people studying different ways that you can modify flow to augment the diffusion, because it does influence the functioning of important dialysis and oxygenation equipment. Also, when you're trying to separate cells from plasma, it's important.

KJ: Professor Blackshear, we were talking a moment ago about your former students and some of those who have gone on in industry. There is a lot of talk currently in the Twin Cities area, and this has happened periodically over the last twenty years, about the correct relationship between the University and the development of new industry in the area. There's concern that although we've done very well over the past fifty years, first with computing and then with medical devices, that we're in competition with other high-tech areas of the country, and that the role of the University hasn't been quite right, that somehow it needs to be turning out not only more students, but more ideas and innovations that can then be commercialized. I wonder what's your own perspective on those thoughts that we hear so much about nowadays.

PB: I think the people here have done better than they've done in the past, certainly, and better than a lot of universities do. I'm familiar with one laboratory, the Particle Technology Laboratory here in the Mechanical Engineering Department, that is a source of high-tech instrumentation for identifying ever-smaller particles and aerosols of various sorts, and they have just established a wonderful pipeline with TSI so that as soon as an invention comes out of the laboratory, it's in production in the marketplace.

I think the University's patent office has been a tremendous booster to a number of ideas. One that has nothing to do with bioengineering is their support for Professor Ed Anderson's personal rapid transit system. Have you ever run across that?

KJ: I've heard a little about it.

PB: But we were quite familiar, because a lot of the income that was coming from our infusion pump would go to support Professor Anderson's research. But you have to support them, because they felt that this would have such an enormous public impact if it would ever be accepted by anybody.

KJ: In the last, I guess, five or six years, there's been a lot of interest in creating a real School of Biomedical Engineering or Bioengineering at the University. What's your take on that?

PB: Well, I think we ought to give it a try, because we do have a special situation with the med school and the engineering school right across the street with the bioengineering building, which has now been finished and occupied, midway between the med school and the engineering school. The potential for collaboration, I think, is just tremendous. I know there's a willingness in engineering to collaborate, and I know in surgery they always have shown a willingness to collaborate.

When we were starting out, however, Keller, Bernstein, and I had looked at all of the then-existing bioengineering programs. All of them were electrical engineering-based. They were instrumentation programs. Then there were bioengineering departments at places like Mayo Clinic, where it was a very interesting dance that you could watch, where the surgeon would walk two feet in front of the bioengineer, who would always be a very obedient servant to the surgeon. One of our resolves was not to be "Uncle Tom bioengineers" when we started our collaboration with the surgeons, and I think the engineers have been pretty well holding their own here when it comes to these collaborative activities.

But I think that the thing that we felt was so wonderful about trying to keep your identity as, say, a fluid mechanician on the one hand and then collaborator on the other is that you don't feel like you're getting rusty in the area that you're supposed to have an expertise in. The present goal of our bioengineering educational program is to train someone who has all of those engineering tools, but in addition, all of those biological tools. It's asking an awful lot of students to try to take on that much.

KJ: I thought that was the purpose of collaboration, to bring together the tools but not to expect any one person to have all of these tools under his scalp.

PB: Well, I would certainly do it that way, and you can't really have a first-rate fluid mechanician and a first-rate molecular biologist unless you've got an awfully bright and awfully dedicated person.

KJ: You'd spend several extra years in training, I suppose.

PB: Yes, lots. But it's an interesting experiment, and they'll produce a product that will have a sort of built-in multiple perspective so that whereas it took six of us sitting around the table to

interpret an experiment before, maybe this one guy can put on his biological hat one minute and his engineering hat the next and his physiology hat the next and so on.

KJ: I would think that just keeping up with the journal literature would take up all your time.

PB: Do you try to read *Science* now?

KJ: No, I don't read *Science*, but I do keep up with a lot of the cardiology journals and they come out faster than I can manage them. Some of the leading journals come out now every two weeks, and there are very heavy articles in them.

PB: Our feeling then was that the bioengineering office should be a very visible office in the University, and it should actually be aggressive in trying to recognize potential collaborations where physicians would recognize a problem that he's trying to solve, would come to the bioengineering [office], and the bioengineering office would then identify engineering collaborators that would have the expertise and the interest to work with the physicians.

That would be one office that would be served. The other one would be if devices were to result or techniques would result or science would result, then the office has the capability of getting FDA approval or guiding the FDA approval process and guiding the licensing with the help of our patent office to interested local companies, sort of a facilitator office rather than an office in which the basic expertise was available in residence.

KJ: The implication seems to be that the existing companies want to—I mean, most of them have substantial research and development budgets. Medtronic and St. Jude and Guidant, you know, it runs 10 percent of their revenue. But the implication is that they are primarily going to be working on new applications or spinoffs, incremental changes to their existing knowledge base, and that they want the University to do basic research and perhaps radical new technology developments. Then once a particular invention has reached a certain point, then the companies will pick it up and commercialize it or carry it further. Does it really work that smoothly? I definitely get the impression that the companies do not want to be involved heavily in basic research. They might want to fund some of it, but not to do it in-house.

PB: I know at Medtronic they have programs where once a researcher has proven his mettle, he can make a research proposal and go off on his own. One of our students, Jim Keogh, now has such a program on the interaction between biological materials and prosthetic surfaces.

KJ: You mean he's an employee of Medtronic?

PB: Yes.

KJ: He's got an in-house research grant, essentially.

PB: Right. And he spends an awful lot of time over here and does extremely basic stuff.

KJ: So maybe my impression isn't totally correct.

PB: I think you have the whole spectrum. They recognize that some of these things are a lot longer shot. Anything having to do with biocompatibility of materials, you can right away say, "This is a long shot." When you see Ed Merrow, one of the best biomaterials researchers of the world, writing his every-ten-year paper saying, "Twenty years of frustration in the field of bioengineering or biomaterials research." [Laughter] But I think the emphasis now on nanoparticles and tissue engineering is taking all these companies into very basic research, whether they support it in-house or out-house. They see gold in the offing.

It would be a nice thing to have, to have the companies count on the University for the basic stuff and feed them money. I guess increasingly that must be the case, because we certainly aren't getting as much from the U.S. Government as we did before. You see that in the engineering publications a lot. You don't count on the federal government for your support anymore.

KJ: It sounds as if a kind of parallel path has developed with a university, through programs such as this emerging bioengineering area, doing some basic research. But the companies, at least the better established ones, also are doing some of their own.

Are there areas or matters that I haven't touched on in this interview thus far that you feel we should talk about?

PB: I was thinking about that, and one of the frustrations I feel is all the unfinished business. I feel my marbles slipping away, and all the great things that I've dabbled with over the years just tend to go down the drain. I thought that what would help me would be the J*ournal of Unfinished Business.* It would be a web-based journal in which old guys could, upon retirement from their research or teaching posts, could start publishing promising unfinished business. Now, when you look at *Science* or look at any attempt to popularize science, you see that the emphasis has shifted a great deal. My unfinished business, there would be very little on fissure engineering or nanotechnology.

KJ: Which are big areas right now.

PB: Yes, these are really hot. Of course, anything having to do with the genome and identifying genetic causes of diseases.

But the place where I think all these unfinished ideas could play a significant role is in the world in which we try to identify our own health problems and take matters into our own hands to cope with. This is an area that Earl Bakken is very enthusiastic about now, and I think one that I see is gaining momentum every week. A lot of the bioengineers of my era have developed little self-

diagnosing technologies like measuring the pressure of your synovial fluid in the knee, which is something you can do very simply. I am trying to assess the efficacy of a brace that was designed by our senior design group. I'm the guinea pig that is wearing the thing to see if it's comfortable, but then I also have to determine its efficacy.

KJ: Have you had knee surgery?

PB: Trying to avoid it.

KJ: I see. Yes, I think you're right, that there's a growing interest in empowering people to manage their own health care, manage their own health, more effectively. Medtronic itself is getting into this somewhat now. Then Earl [Bakken], with the hospital in Hawaii. It's going to be a growing area, and technologies that help people remain independent or manage themselves are important.

PB: Is one of the guys you're going to talk to Stanley Finkelstein?

KJ: No, at least he's not on my list.

PB: Stanley has pioneered some aspects of self-help. This is where you have someone in a rural area that can hook up instruments by telephone lines. In your field, cardiac status could be monitored.

KJ: Yes, much more than just a rhythm strip showing the basic heart rate, but a much more detailed readout.

PB: They have one of those, not the Palm Pilot, but one of the Microsoft-based portable computers that they keep records on and then transmit them periodically, and then they have the central assessment system. I think that kind of effort, which seems very prosaic in a way, but it sort of points to the way that you could have a lot better monitoring of our health, rather than this business of having to wait two weeks to get an appointment when a skin eruption demands immediate attention.

KJ: When pacemakers—this began in the early seventies—when there were telephone transmittal devices so that the physician or some kind of service could check the pacemaker's firing rate, which would indicate battery condition and whether the battery was about to fail, and they could call you in for a scheduled replacement rather than an emergency replacement, and that could become, indeed, a model in which, if enough information could be transmitted, then some service could identify problems at a very early stage. So the idea of a kind of annual checkup could be replaced by a notion of coming in to see the doctor when there's an indication that something is about to go wrong.

PB: Yes. There was a girl in the news recently whose battery had not been replaced and she died.

KJ: Yes, her mother refused to replace it because the mother was a—I'm not sure if she was a Christian Scientist.

PB: Was that right?

KJ: It was a religious-based decision that the pacemaker was wrong or objectionable or didn't work or something. There were signs that the battery was failing. I guess the battery had failed and the girl was—her heart went on, but she was at high risk of standstill, and that's what killed her.

PB: But don't you have the feeling that the Twin Cities has all the ingredients of becoming a really major bioengineering Mecca? We've got all these companies, we have a good University, we've got the Mayo Clinic nearby, an excellent engineering school, and, I think, a population of very well-educated and very hardworking citizens to draw on. And what's needed is the organization, and it may be that a new director of bioengineering might be able to do something with it.

KJ: Yes, it's interesting—

PB: If we could get [Mark] Yudof to do it, everybody in the Twin Cities seems to think Yudof can do anything.

KJ: Well, that's what he's paid for.

PB: That's what he's paid a lot for.

KJ: I don't know. I agree with you that we have a terrific base here and we have had, really, since the fifties with the big computer firms of that era, like Control Data and Honeywell, we've had a large pool of highly trained, technically skilled people who were then available to move into the medical area when that began to develop. What the future holds and how much interaction and connection among all these companies and the University we will see in the future, I don't know.

Of course, in the Silicon Valley, there was not a single manager, except maybe Fred Terman of Stanford [University], but that was at a pretty early stage in the development in the Silicon Valley. Once it was really going by the early and mid-sixties, there wasn't anybody who was the czar or guru who kept it.

PB: Do you have a feel for how much it's the excellence of the Stanford graduates that's responsible for that and how much is the climate? [Laughter]

KJ: Well, I think it's a historical accident. Anything like that is a historical accident.

PB: But there's something quite similar to that around MIT [Massachusetts Institute of Technology].

KJ: Yes. Stanford was clearly a vital ingredient, and Terman especially. But also the existence of Hewlett-Packard was a key thing, and then Shockley Electronics. Out of those, I think, and the emergence of Intel in the 1960s, all of this really flowered from those early developments. But I don't think anybody planned those, and it's perhaps just an accident that they came together there.

PB: But Medtronic is our Hewlett-Packard, more or less.

KJ: That's right. I'm not sure that everybody understands that, but that's certainly true.

Well, I will call the interview to a halt. We've been going an hour and a half and worked pretty hard. I want to thank you, Professor Blackshear, for joining me this morning. I know that we've ended here on an inconclusive note, asking each other questions about the future of biomedical technology in Minnesota and especially in the Twin Cities. Part of the reason for this interview project is that there's growing recognition of how important it all is for the future of our state. The Minnesota Historical Society and Bakken Library wanted to do what they could to help people understand the past development of this field and to think more clearly about its future. So, thanks a lot.

PB: Well, thank you very much, Professor Jeffrey.