Adv Physiol Educ 33: 144–156, 2009;
doi:10.1152/advan.90208.2008.

Standing on the shoulders of giants: Dean Franklin and his remarkable contributions to physiological measurements in animals

R. Dustan Sarazan and Karl T. R. Schweitz
Covance Laboratories Incorporated, Madison, Wisconsin

Submitted 30 October 2008; accepted in final form 28 May 2009

Sarazan RD, Schweitz KT. Standing on the shoulders of giants: Dean Franklin and his remarkable contributions to physiological measurements in animals. *Adv Physiol Educ* 33: 144–156, 2009; doi:10.1152/advan.90208.2008.—The use of electronic instrumentation to monitor physiological function in conscious research animals and humans has become routine. Beyond basic research, animal studies using these methods are required by government regulatory agencies worldwide before human testing of potential new drugs. Living, as we do, in an age of miniaturized high-tech electronic devices, we are accustomed to believing this technology is easy; however, this has not always been the case. While a broad supporting cast of engineers, physiologists, fellows, and technicians was involved, the true innovators were Dr. Robert Rushmer, Dr. Robert Van Citters, and Mr. Dean Franklin. Before Dean Franklin's death in 2007, the primary author recorded ~5 h of interviews with him at his home in Columbia, MO. An additional approximate 1.5-h interview was recorded with Dr. Van Citters via telephone. The information contained herein is based on the recollections of these men as recorded in their interviews.

Doppler flowmeter; sonomicrometer; telemetry; implantable pressure transducer

THIS ARTICLE describes some of the remarkable history of early animal instrumentation and the pioneering of technology to measure animal blood pressure, blood flow, and cardiac dimensions by telemetry. In addition to providing brief biographical sketches of Dr. Robert Rushmer, Dr. Robert Van Citters, and Mr. Dean Franklin (see the APPENDIX), the true pioneers in the field, this article discusses the history of the development of the ultrasonic differential transit time flowmeter, ultrasonic Doppler flowmeter implantable pressure transducer and the first telemetry of cardiovascular physiological signals from conscious animals. It also outlines these scientists' study of comparative physiology among a fascinating variety of animal species.

Institutional approval for all studies discussed herein was obtained according to the regulatory standards enforced at the time.

The History of the Development of Cardiac Instrumentation

Cardiac dimensions. In the early days of Dr. Robert Rushmer's laboratory at the University of Washington, in vivo physiological experiments were performed in anesthetized dogs. Rushmer initiated the development of techniques to study cardiac physiology in conscious dogs. Before Dean Franklin's arrival at the laboratory in the early 1950s, cardiac ventricular diameter was measured in conscious dogs using a variable inductance device in which the end of a steel pin was secured with a trocar to the interventricular septum, and a housing containing a coil was secured to the left ventricular free wall. The thoracotomy was then closed, and the animal recovered from anesthesia. When the heart contracted and relaxed, the pin moved in and out of the coil, and the change in inductance was proportional to the chamber diameter. While neither Franklin nor Van Citters could recall the origin of the devices, both described them as being brilliantly machined (3, 9). Two of Rushmer's fellows spent 1 day/wk in the laboratory implanting these devices, an experience they found beneficial on two levels: *1*) the size of the structures they handled helped them with small pediatric human subjects and *2*) they learned that the beating heart was far less subject to trauma than they had initially thought. In early experiments, based on general thinking at the time, the heart was allowed to rest between manipulations. After working with these dog hearts, they came to realize they could do more work on the heart than they had previously thought possible.

Another device used in Rushmer's laboratory was the mercury-in-rubber strain gauge (also known as the "Whitney" gauge). This consisted of a length of miniature latex tubing filled with mercury and stoppered on each end with a stainless steel needle, with the wires from the stoppers exiting the body. The tubing was sutured to the epicardium, and, as it elongated slightly during diastole, it provided a measure of circumferential segment length. Franklin's first responsibility upon joining the Rushmer laboratory was to fabricate Whitney gauges.

Dick Ellis, a former technician, had left the laboratory for a position with Honeywell Marine but still visited frequently and conversed with Franklin on a variety of subjects. Franklin later credited Ellis with teaching him much of what he knew about electronics. It was Ellis who suggested that Franklin consider using ultrasound to measure dimensions. Before his departure, Ellis had obtained some barium titanate piezoelectric crystal material. He left a number of 1- and 3-MHz plates in the desk that Franklin inherited from him. Upon turning the desk over to Franklin, he said, "Don't throw those away, Dean–you may find them useful someday" (3). According to Franklin, Ellis had also been considering the possibility of measuring blood flow using differential transit time (3). Ellis suggested a method whereby the output of the receiving crystal would be fed back to the transmitting signal. An oscillation would ensue, the frequency of which was proportional to the transit time between crystals. Although it was discussed in the context of a transit time flowmeter, Ellis also suggested trying this method to measure ventricular dimensions. Franklin tried this approach for 1 or 2 mo before finally determining that, although theoretically elegant, it was impractical. (Eventually, he did devise a more modern approach, which was patented by the University of Missouri in the late 1980s.)

Address for reprint requests and other correspondence: R. D. Sarazan, Covance Laboratories Inc,, 3301 Kinsman Blvd., Madison, WI 53704-2523 (e-mail: Dusty.Sarazan@covance.com).

Drawing on his military background in radar, Franklin decided to try a pulsed technique using two crystals, one on each epicardial surface. Rushmer named the resulting device a "sonocardiometer" (later changed to "sonomicrometer"), and the group soon published the results of their research (8). This represents the first breakthrough in the use of ultrasound in physiological measurement, which impacted all subsequent developments, including blood flow and echocardiography. In later years, lead zirconate titanate was substituted for barium titanate because it could withstand higher soldering temperatures without depolarizing the piezoelectric material.

A serious problem with the early sonocardiometer was that the crystals were extremely directional. The slightest tilting of a crystal could cause the signal to be lost. Franklin developed what he later described as the "stupidly simple" (3) approach of placing a drop of plastic on the face of each crystal, thus creating a lens that reduced the directionality of the system. At the time, this was a major breakthrough. After Franklin and Van Citters left the University of Washington, Rushmer, Don Baker, and others continued to develop this technology, in addition to the ultrasonic Doppler flowmeter (also invented by Franklin). This led to the development of noninvasive clinical ultrasound, including the enormously successful echocardiography. The experience that Franklin gained through the development of the sonocardiometer contributed directly to his development of the ultrasonic differential transit time flowmeter.

Blood flow. As discussed previously, the theoretical approach of using ultrasonic transit time to measure blood flow was suggested to Dean Franklin by Dick Ellis. This concept was general knowledge at the time and was being pursued by others; however, Franklin also recalled a scientist who, speaking at a national meeting in the late 1950s, argued that this was impossible to achieve (3). The trouble arose in the extremely small units of time that had to be measured; this was especially problematic given the technology available at the time.

Franklin fabricated a flow transducer and designed and built the electronics for a prototype flowmeter. Along with University of Washington fellow Kurt Wiederhielm, Franklin surgically implanted the probe on the abdominal aorta of a dog. Just a few days later, they made the first in vivo blood flow recording in a conscious animal. The flow tracing from this experiment is dated January 11, 1958. The actual flow probe from the dog is shown in Fig. 1 (4).

This flowmeter was used extensively in Rushmer's laboratory, and selected flow signals are included in the 1961 edition of his book, *Cardiovascular Dynamics*. Van Citters and Franklin used a refined version of the flowmeter at the Scripps Clinic and Research Foundation years later to measure blood flow in exercising baboons.

However, at the time, the device was marginal technology at best and constantly subject to noise and drift. The chassis for the prototype device is shown in Fig. 2 on the panel above the exercising dog. Franklin mounted the device in this fashion because its components required constant tweaking to function properly.

Others ultimately pursued the device and overcame the technical hurdles that frustrated Franklin and his colleagues in the late 1950s and early 1960s. These efforts led to a commercially successful product from Transonic. One of the improvements that Transonic made was to create a flow probe with both crystals on one side and a metal reflector on the other, which remains their standard approach. Interestingly, Franklin had previously fabricated a prototype of a probe using an identical approach (Fig. 3); however, having already moved on to developing Doppler systems, he never pursued it.

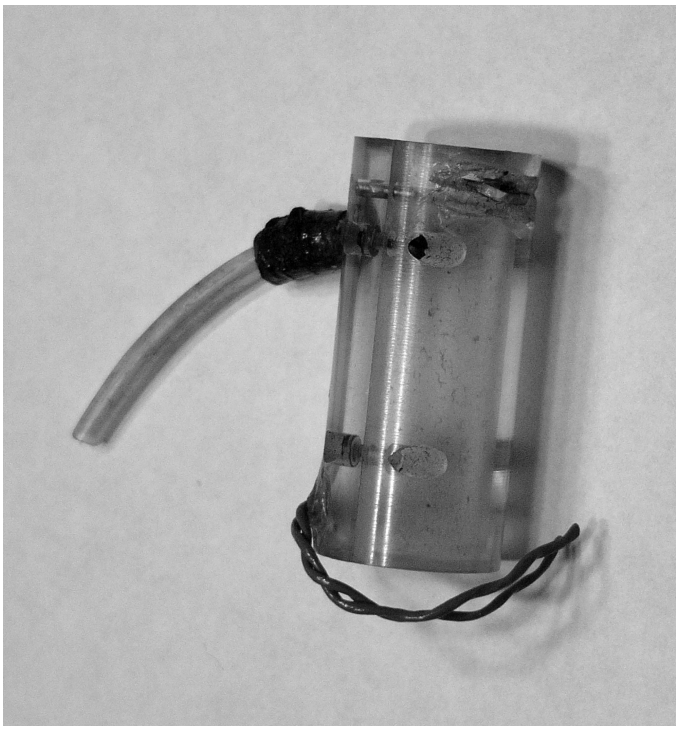

Fig. 1. The ultrasonic differential transit time flow probe that was used to collect the first in vivo blood flow signal from a conscious animal in 1958 (see Ref. 4).

Among the many inventions attributed to Dean Franklin, the one for which he remains best known is the ultrasonic Doppler flowmeter. The concept of using ultrasound and the Doppler effect to detect blood flow was developed nearly simultaneously by Franklin and Shigeo Satomura, a professor at Osaka University (Osaka, Japan). While neither knew of the other's efforts at the time, Franklin acknowledged that he had become aware of Satomura's work in 1965 when he learned of a presentation that Satomura had made to a Medical Electronics meeting in London 5 yr previously. Satomura died unexpectedly in April 1960, thus rendering him unable to pursue his discovery. During our 2006 interview (3), Dean Franklin acknowledged Satomura as the discoverer of ultrasonic Doppler blood flow detection, owing to the fact that Satomura published first.

However, Franklin is correctly given credit for having invented the first functional, quantitative Doppler flowmeter. The first actual record of Doppler flow was from an instrumented conscious dog with a flow probe placed on the abdominal aorta. The device was described by Franklin et al. in a 1961 article in *Science* (5). However, he designed and tested the first prototype device in 1958. The fascinating story of how the idea came to him the summer before he left the laboratory is best told in his own words (3):

> It was early in the morning; it's one of the few things I can remember quite vividly as to how I formulated it. It was maybe 3 o'clock in the morning in the lab, recording from the

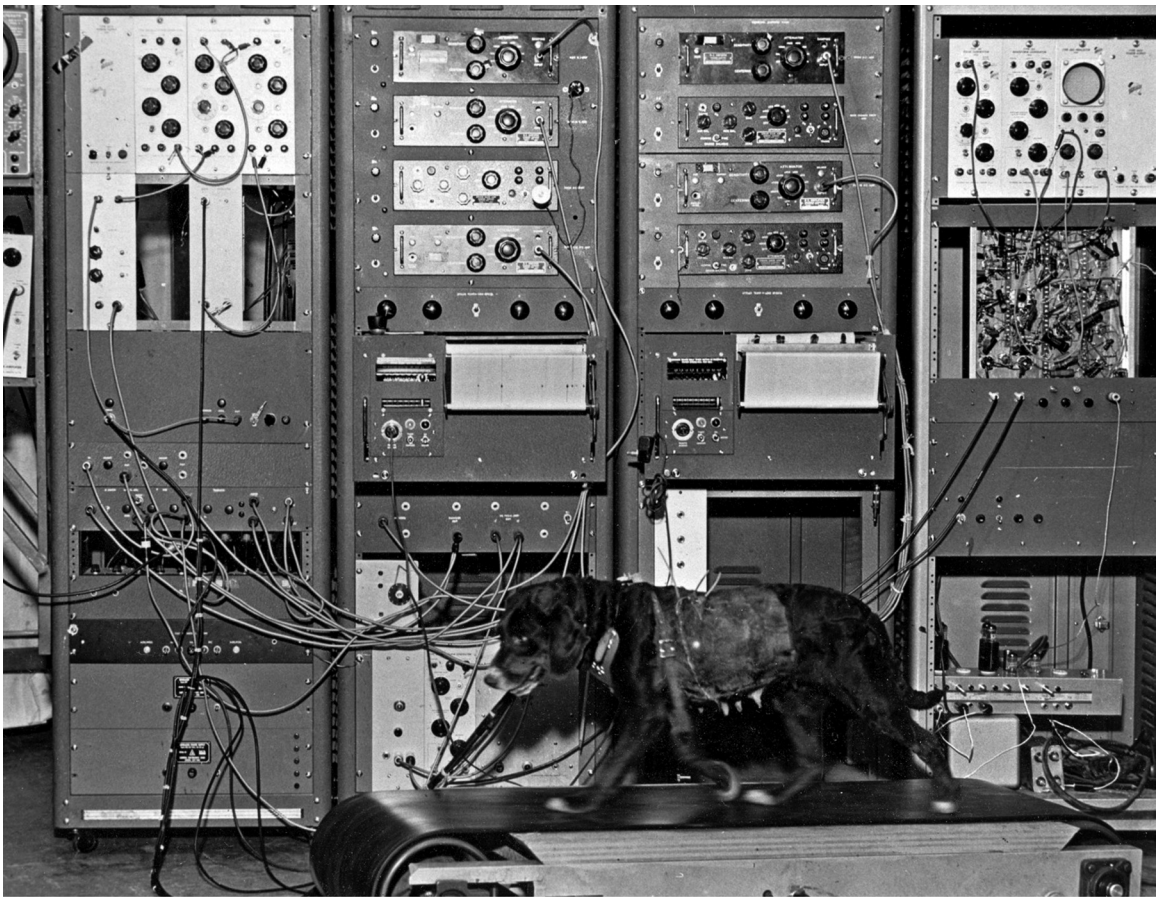

Fig. 2. A chronically instrumented dog exercising on a prototype Quinton treadmill at the University of Washington in the 1950s. The differential transit time flowmeter chassis on the right was mounted such that Dean Franklin could access the electronic components to deal with the severe drifting.

dog–interested for some reason in quiescent, sleeping dogs–and it was clear that the [transit time] flowmeter was drifting. There was no doubt about it. So I went down to the cafeteria to get a cup of coffee, came back, leaned in the doorway and thought, "Surely there must be a better way." That's when I was thinking, "Suppose I were inside the blood vessel, what would I see? Red cells going by, and that's like snowflakes in a storm. How would I measure their velocity?" And then I thought, "Well, try the sonic Doppler approach. Use the Doppler shift of ultrasound to measure the velocity of the red cells." I'd had experience with the dimension gauge, ultrasound, and the differential transit time flowmeter, so the experience there helped. The next day or the day after, I rigged up a breadboard prototype, or just a feasibility test bed is what it was. It consisted of a 6146 pentode mounted on a piece of wood, the output of which was set up as an oscillator, and I can't remember if it was 3 mHz or 1 mHz. Hook that out to what I remember was called an Airdux inductor coil–this was just a coil of wire about a foot tall. The reason for this was that I didn't know the impedance of the crystals, and I wanted to tap up and down on the coil to maximize the output of the crystal, not knowing what power I could get from it. So the oscillator, a tap on this coil, the output of this, an electrical signal, say, at 1 mHz through a capacitor. To test the power, put it in water and point it at the surface. I had heard a rule of thumb is if the jet is ~1 cm, it's about 2 Watts per cm^2. In any event, you could get an indication of the acoustic power generated in this manner, and you could adjust both the position on the tap to drive the crystal and the frequency of oscillation to make it match the resonant frequency of the piezoelectric crystal. The output of the receiver crystal was coupled to a diode detector circuit; the output of that coupled to a hi-fi amplifier audio system–a music system we had there. The results in moving tap water? A loud signal, but clearly it was from air bubbles. The

Fig. 3. An early prototype of a transit time flow probe, fabricated by Franklin, which contains two crystals on one side and a reflector on the other. This design was independently developed later by others and has become the industry standard.

signal from blood was just barely above the noise, but it could be heard, so there was a whisper in there.

After having proven the feasibility of the Doppler flowmeter, Franklin left the Rushmer laboratory in 1958 to begin attending medical school at McGill University. After 1 yr, he decided to forego medical school and return to Seattle, where he rejoined the Rushmer laboratory. In the meantime, Rushmer had hired a new technician/engineer, Bill Schlagle. Schlagle was an amateur radio hobbyist and was, therefore, knowledgeable about radiofrequency amplifiers. Working together, Franklin and Schlagle built the first operational Doppler flowmeter. As mentioned previously, the first recorded blood flow from this device was from the abdominal aorta of a dog and took place on July 1, 1960.

Meanwhile, Rushmer's laboratory was in negotiations with a large instrumentation company to develop a commercially marketable version of Franklin's transit time flowmeter. Franklin chose instead to move with Van Citters to pursue physiological research at the Scripps Clinic and Research Foundation in San Diego, CA.

Van Citters and Franklin continued to use a refined version of the ultrasonic transit time flowmeter to conduct experiments with instrumented exercising baboons. The impetus to reprise the Doppler flowmeter came during a visit by Franklin to Van Citters at the University of Washington in 1963. Van Citters wanted to telemeter hemodynamic signals from baboons. Franklin, however, expressed his belief that "telemetry is trivial; the measurement is the difficult part" (3). He then went on to describe telemetry methods for pressure and flow. Van Citters became very excited and put Franklin to the test. In response, Franklin designed and built the first Doppler flow/telemetry device. This prototype device, which still exists today (Fig. 4), was, according to Franklin, "haywired" together (3). Van Citters surgically prepared a Boxer dog with a flow probe on the abdominal aorta. Nolan Watson from the Van Citters laboratory and the dog were then flown to San Diego.

Van Citters and Franklin had established a relationship with Dr. Charles Schroeder, the legendary director of the San Diego Zoo, who is credited with leading the development of the zoo and wild animal park into the world-class institutions they are today (7). Franklin told the story as follows (3):

> Van Citters approached Schroeder when he was establishing his laboratory at Scripps and expressed interest in learning about handling baboons. Dr. Schroeder responded by saying "The zoo is yours; do as you will."

Van Citters describes a similar version of the story (9):

> I remember that I confronted Schroeder with this crazy idea of working on primates in his hospital facility. He sort of looked up at me with a scowl from his desk and said "Of course you realize the entire facilities of the zoo are at your disposal." I couldn't believe it.

The first telemetered measurements occurred at the San Diego Zoo hospital laboratory in 1963 (Fig. 5). Nolan Watson exercised the Boxer dog, outfitted with a Doppler telemetry device, outside a building at the zoo, while Franklin remained on the second floor with the receiving equipment. An anecdote from this period, as relayed by Franklin and Van Citters, is that Pete Scholander, the famous comparative physiologist at the University of California-San Diego, was visited by another renowned physiologist, Knut Schmidt-Nielson, the same day that these measurements were being taken. According to Franklin, upon stopping by during the recording of the Doppler signal, Schmidt-Nielsen remarked, "We may be seeing history made here" (3). Given that this was the first-ever telemetered physiological signal taken from a conscious animal (other than, perhaps, temperature), nothing could be truer.

Franklin demonstrated the Doppler telemetry device at several scientific meetings. He fabricated a battery-powered device with a transcutaneous transducer that he would place over the radial artery on his wrist; the audience could hear the Doppler flow signal from his pulse through an FM radio over the PA system. Franklin recalled one anecdote, which took place when he was speaking at an extravagant hotel in Bel-Air, CA. He realized that he had neglected to bring the acoustical gel necessary to couple the transducer probe to the skin. As Franklin relates, "Joe McEvoy–at the time a fellow in the laboratory from Queen's University–jumped up, took some

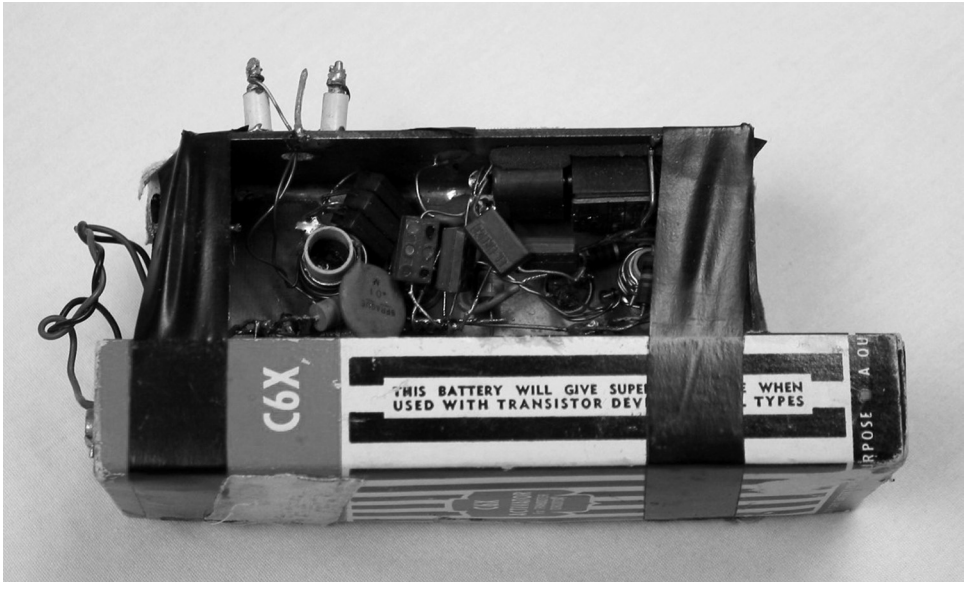

Fig. 4. The first telemetry device to transmit a hemodynamic signal from an unrestrained animal. It was used on a Boxer dog at the San Diego Zoo hospital in 1963.

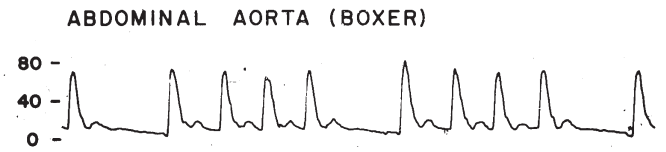

Fig. 5. Aortic blood flow velocity transmitted by a Boxer dog outside the San Diego Zoo hospital and received inside the building.

gravy from the table, and slapped it on [my arm]. It worked. Improvisation!" (3).

Given the publicity surrounding this new technology, Franklin received several requests to build individual Doppler telemetry devices. While he had no interest in doing so, others began to realize their commercial potential. Franklin had not patented the technology and had freely published it in the literature, including seminal papers in *Science* and *Nature*. Franklin approached a company in San Diego that agreed to make six devices, with his assurance that there would be buyers. Franklin purchased two, one of which is still in existence.

The method of demodulating the audio Doppler shift signal to achieve a quantitative analog flow-velocity signal began as a simple idea for Franklin but turned out to create significant controversy for others. As Franklin described it (3):

> Let's see, so what did I use? Back when, in Rushmer's laboratory, we had a hot new Tektronics oscilloscope–the kind that you could trigger on the zero crossing of the input signal–and I used this routinely in our developments. So, here we have an output of a Doppler flowmeter, and how would one look at it? Well, you trigger the horizontal sweep with a zero crossing of the signal. I won't go into it, but, in any event, that prompted me to use a zero crossing detector. There was no brilliant prediction, a theoretical prediction that it would work or not, but the observation on the oscilloscope prompted me to make a demodulator consisting of an output signal, producing an output signal proportional to the number of zero crossings per second, and which, through calibration, proved to be linearly related to flow.

Initially, this was not a problem for the company that fabricated the first six commercial Doppler flow/telemetry systems because they didn't provide the equipment to demodulate the signal. However, when they decided to scale up production and provide functional flowmeters, they made the mistake of neglecting to ask Franklin how to demodulate the output. They chose to use a saturable reactor, a type of transformer used at the time to measure the frequency of a sinusoidal alternating current (AC) (e.g., line voltage). However, it did not work well for a complex signal composed of several frequencies, like the Doppler audio signal. Several were sold, but users began to complain that the flow output varied based on the positioning of the demodulator sensitivity. Commonly known as the "Dial-A-Flow," it was a commercial failure.

Much later, scientific justification for the selection of the oscilloscope method of demodulation was provided when Franklin discovered a book that provided a mathematical treatment of the numbers of zero crossings involved in a signal with band-limited noise. The mathematical approach in the book concluded that the number was approximately halfway between the two band-limiting frequencies, which provided theoretical support for the choice in demodulating the Doppler flow signal. Franklin discussed this with Fran McLeod, with whom he had become acquainted at various scientific and engineering meetings. McLeod continued to pursue the analysis of Doppler flow signals as the subject of his subsequent PhD dissertation. McLeod would go on to devise a technique for the measurement of the direction of the Doppler shift. He shared this with Loren Parks, who incorporated it in his commercially successful Parks Obstetrical Doppler flowmeter.

Franklin and colleagues later conducted a study at the Scripps Clinic laboratory in which they demonstrated that power spectral analysis of the signal would provide an output directly proportional to volume flow using the same mathematics used for particles moving in a gas. This correlated well with the zero-crossing method of demodulation, thus providing the final theoretical support for Franklin's original approach.

Another controversy in the development of ultrasonic Doppler for measuring flow was the principle that the backscattering of the ultrasound from the piezoelectric transmitting crystal was due to an interaction with red blood cells. We now know that this is true; early on, however, many were skeptical. Recall that Franklin conceived of using ultrasonic Doppler late at night in the University of Washington by imagining himself inside an artery and wondering how to measure blood velocity. Using the analogy of standing in a snowstorm, he developed the ultrasonic Doppler idea. Upon building the first prototype on a board the next day, he was able to hear the Doppler shift signal from tap water moving past the transducer crystals. He correctly assumed this was due to ultrasonic backscatter from microscopic air bubbles in the tap water. However, as told by Franklin (3), "All the experts (physicists, physiologists, etc.) with whom I discussed the flowmeter indicated that it was certainly interesting, but most certainly the backscattered signal was not from red cells."

It was known from the Rayleigh scattering theory that the backscattered signals could not possibly be due to interaction with red blood cells, as their diameter was much smaller than the wavelength of the ultrasound signal. Franklin and colleagues measured the Doppler flow from water with progressively more of the bubbles excluded, and the signal continued to get weaker. Finally, no signal could be detected from flowing deaerated water.

The most conclusive evidence that red blood cells were the source of backscattered ultrasound came many years later, when Franklin was working with Kjell Johansson at Friday Harbor, WA. Johansson had been working with sea skates but was interested in measuring blood flow in an octopus. He and Franklin placed the Doppler flow probe on an artery, but only a faint Doppler audio signal could be heard. Upon further discussion with Johansson, Franklin learned that octopi lack formed elements in the blood to carry oxygen but, instead, carry oxygen bound to hemocyanin in plasma. The only blood cells present are a few white blood cells. Franklin took this result to be a very persuasive argument that backscattered ultrasound in mammalian blood with the Doppler flowmeter is, indeed, produced by circulating red blood cells.

The Doppler flowmeter continued to be used by Franklin and Van Citters in a variety of fascinating experiments with exotic species. Also, Rushmer's laboratory at the University of Washington developed ultrasonic Doppler and other Franklin developments into the hugely successful clinical application of transcutaneous echocardiography. This technology was transferred to ATL, which manufactured human diagnostic ultra-

sound equipment for several years before being acquired by Philips Medical Systems.

Pressure. In addition to cardiac dimensions and blood flow, pressure is the third critical parameter required to study cardiovascular physiology in animals. Attempts to monitor blood pressure in conscious animals trace back to Stephen Hales, who, in 1733, successfully cannulated an artery in a restrained horse and monitored the height of the blood column in a long, vertical glass tube. He was thus able to observe the pulsatile nature of arterial pressure (2). Other critical advances over the years included the invention of the mercury U-tube manometer by Jean L. Poiseuille in 1828 (1), the strain gauge by Herbert Tomlinson in 1876 (1), and the application of the strain gauge to fluid pressure measurement by Louis Statham in 1943 (1). E. H. Lambert and E. H. Wood, at the Mayo Clinic in 1945, were the first to use a strain gauge to measure human blood pressure (1).

However, Statham transducers were not well suited to conscious animal physiology measurements, as they rely on a long, fluid-filled catheter to conduct the pressure signal from the artery to the dome of the transducer. This made the pressure measurement subject to significant errors due to hydrostatic pressure gradients caused by the relative height of the transducer and the end of the catheter as well as damping and phase shift due to the compliance of the plastic tubing.

In the 1950s, the Rushmer laboratory was using an ingenious implantable transducer fabricated in the University of Washington Instrument Shop. In Dean Franklin's words (3),

> At the time, again, I mentioned that he had a small pressure gauge–a miniature pressure gauge. The brilliance of it was the machining of the thing. Let's call it 2 cm long by perhaps 0.5 cm in diameter, cylinder; three-quarters up the way, the cylinder was threaded, and a cap was made and threaded to screw onto that and a small opening pipe coming out of that little end. In any event, the top of the big part of the cylinder was a diaphragm of bronze, corrugated, cycled with pressure so there was a chamber between the diaphragm and the top part to the pipe. It was filled with mineral oil, and then this tube from that port through a stab wound into the left ventricle, for example. So the pressure gauge existed or rested outside the heart. The other end of the pressure gauge was vented to a flaccid balloon to prevent variation in measured pressure due to intrathoracic pressure, if that makes sense. It was just a beautifully machined thing.

This pressure device, much like the intraventricular diameter device described previously, was based on a variable inductance principle. Presumably, both were fabricated in the University Instrument Shop. Unfortunately, Franklin could not recall who originally designed the devices. While it is unknown if any of the dimension gauges are still in existence, Franklin still had three of the original pressure gauges used in the 1950s (Fig. 6).

When Franklin and Van Citters moved to the Scripps Clinic and Research Foundation in San Diego, CA, in 1962, they began conducting research on exercising baboons using Statham strain-gauge transducers and fluid-filled catheters. Animals were restrained in cages attached to treadmills; the instrumentation wires and catheters were routed through the ceiling to the instrumentation room via a specially designed helmet worn by the baboon.

It was not until Van Citters asked Franklin about the possibility of telemetry that an effort was made to solve the problem of a reliable implantable pressure transducer capable of being used with telemetry. This led to the development of what has subsequently become known as the Konigsberg pressure transducer. To quote Dean Franklin (3), "Van [Citters] has to be given credit for practically everything about the [Konigsberg] pressure gauge."

Van Citters had heard of a company in the Los Angeles area that made miniature semiconductor strain gauges to be applied to helicopter rotor blades. Van Citters and Franklin visited the company and explained what they needed for an implantable blood pressure gauge. An engineer named Ray Scherer was interested enough to travel to San Diego and observe a surgery to learn cardiovascular anatomy and see where the devices would have to be implanted. Van Citters drew what he thought would be a good prototype device. The engineer produced two prototypes, which were sent to Franklin in San Diego to evaluate. One was implanted in a dog and worked reasonably well. The other was nonfunctional.

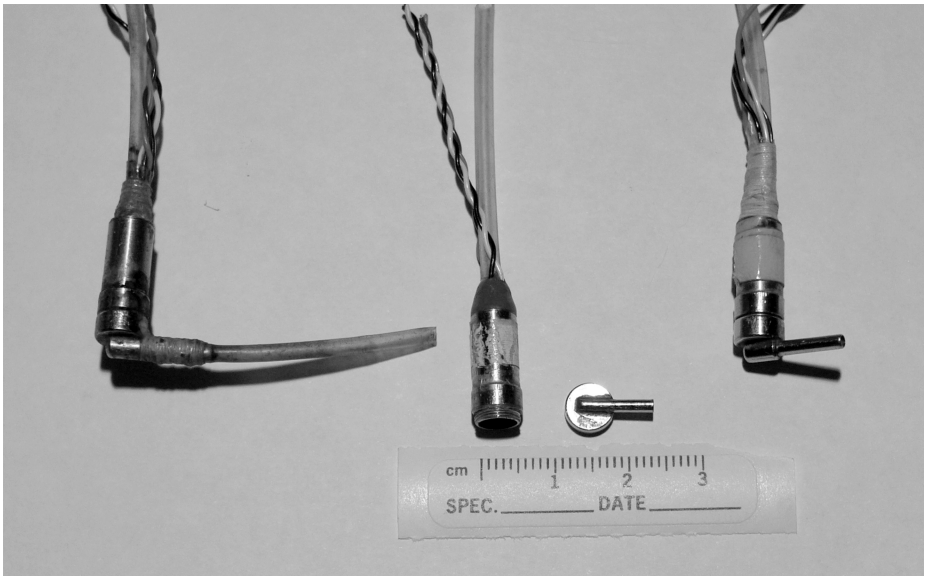

Fig. 6. Variable inductance pressure transducers that were implanted in dogs in Rushmer's laboratory in the 1950s. Each device was handmade by a machinist in the University of Washington instrument shop.

Van Citters and Franklin returned to the company and requested that they fabricate four more devices. The engineers responded that they could not produce according to the necessary standards and wanted nothing more to do with the project. Van Citters replied, "Forget that. Make me four of them–the best you can do. I want them." (9). Van Citters and Franklin took these four devices to Kenya, Africa, in 1965, where they implanted them in baboons and giraffes, leading to several legendary publications.

Eph Konigsberg, an employee with the engineering company Micro Systems, took an interest in these devices and went on to miniaturize and improve the devices over the years. These devices are still being manufactured and sold by Konigsberg Instruments. One of the original four prototypes used in the Kenya studies is shown in Fig. 7. Franklin used the Konigsberg pressure transducers in his research from 1965 until his retirement in 1991. However, that was not the end of implantable pressure transducer development.

An engineer named Brian Brockway was working toward his master's degree in the laboratory of Dr. Franz Halberg at the University of Minnesota. Halberg, the founder of the field of chronobiology, is known for coining the term "circadian rhythm." He wanted to improve the measurement of the body temperature of rats throughout the diurnal cycle by telemetry. Brockway worked with David Osgood of Butler University in Indianapolis, IN, to adapt Osgood's miniature transmitters to Halberg's research. Upon obtaining his master's degree in electrical engineering, Brockway joined Cardiac Pacemakers, where he worked for 4 yr. He then received National Institutes of Health (NIH) funding to develop new telemetry technology. He founded the company Data Sciences in 1984 and marketed the first product in 1985. This product provided telemetered electrocardiograms and body temperature from conscious rats.

Brockway and his colleagues later pursued the development of a miniature pressure sensor suitable for a self-contained, implantable telemetry device. They developed a micromachined solid-state pressure sensor based on the same Wheatstone Bridge principle that was previously used in Statham and Konigsberg transducers. In 1989, they launched their first fully implantable pressure telemetry device, which has evolved into the industry standard for physiological and pharmacological research. As of this writing, human devices using the same sensor technology are also in clinical development.

Telemetry. Although telemetry of animal body temperature had previously been achieved by Stuart MacKay (6), it was Franklin and Van Citters whose major technical advancements in the 1960s allowed remote, real-time monitoring of cardiovascular physiology end points from unrestrained animals.

As recalled by Franklin, his interest began with a conversation with Van Citters after the first publication on the functional Doppler flowmeter (5). Franklin was discussing various ways in which the Doppler flow signal might be telemetered, and Van Citters became very excited. Van Citters encouraged Franklin to develop the technology to telemeter Doppler flow (as described previously with the Boxer dog at the San Diego Zoo), which naturally led to the telemetry of pressure as well (3). The technology to telemeter pressure was developed for the first Africa trip in 1965, concurrent with the development of the implantable pressure transducer. Although telemetry of cardiovascular physiological signals would become routine, it was initially driven by the desire to remotely monitor baboons in the wild.

The ultrasonic Doppler flowmeter was ideally suited for telemetry. The output of the device before demodulation, the Doppler shift, is an audio frequency sound that can be telemetered by conventional FM radio technology. According to Van

Fig. 7. One of the first prototype implantable pressure transducers that was used in the baboons and giraffes in Africa. Improved versions of this prototype subsequently became known as Konigsberg pressure transducers, which are still in use as of this writing.

Fig. 8. Telemetry studies using a Volkswagen bus equipped with standard consumer high-fidelity audio equipment to record Doppler flow signals from instrumented dogs.

Citters (9), "We picked out commercial FM as the equipment that we could afford and use, and if you can broadcast Beethoven's Fifth, then you sure as hell can broadcast Doppler." Photos of Volkswagen buses fitted with consumer electronics for receiving and recording Doppler signals are shown in Figs. 8 and 9 (see Supplemental Videos 1 and 2).[1]

Telemetry of the analog signal from the pressure transducers was based on the use of voltage-controlled oscillators (VCOs), which used existing technology. Initially, the devices were neither temperature nor voltage controlled, so the pressure measurements would drift with battery voltage and temperature. Eventually, Franklin developed circuitry to resolve these issues. Although more stable commercial VCOs were available, these were expensive and required higher voltages than were available from the 9-V batteries used for telemetry.

Eventually, Franklin relied on telemetry for nearly all physiological measurements, even in the laboratory. As he stated in the interview (3),

> Well, one of the reasons was if you hardwire it and use power, it's very hard to get rid of the AC component of your power line. If you don't use power–if you use batteries, and that gets rid of it–why not use telemetry, you know? So, we just did. I mean, it was like a link.

In Vivo Physiology Studies in the Laboratory and in the Field

Although, as discussed previously, Robert Rushmer, Robert Van Citters, and Dean Franklin are well known for contributing to technological advancements in dimension, pressure, and flow measurements, their careers were most driven by the desire to gain an understanding of physiology. Thus, they developed technology as a means of answering complex physiological questions–questions that led to a legendary series of experiments and expeditions.

Rushmer's laboratory. A common theme among many experiments was the effect of exercise on the cardiovascular system. When Franklin first arrived in Rushmer's laboratory as an electronics technician and physics student in 1952, instrumented dogs were exercised by running up and down the hallway. As this predated telemetry, the dogs were tethered to a Sanborn chart recorder on wheels by wires attached to a fishing pole. The recorder was powered by an extension cord that was several hundred feet long. As told by Franklin (3), "Dick Ellis and I would run these experiments–one of us would be in front of the dog, encouraging him to run, and the other one behind the recorder, pushing it down the hall as fast as we could. So that constituted the exercise studies."

At the time, Wayne Quinton was the head of the University of Washington Instrument Shop and had built a prototype treadmill for Dr. Robert Bruce, a physician interested in human exercise stress testing. Quinton fabricated a second treadmill for Rushmer's laboratory to use in exercise studies in dogs (Fig. 2). Quinton subsequently led the development of the commercially successful Quinton brand treadmills and Quinton Cardiology Systems (now Cardiac Science).

As discussed previously, during the period from 1952 to 1962, Franklin invented the ultrasonic transit time flowmeter, the sonocardiometer, and the ultrasonic Doppler flowmeter. Rushmer and colleagues were concentrating on the commercialization of these technologies toward the end of this period, leading to the creation of the nearby ATL, which pioneered the development of human echocardiographic equipment. Franklin

[1] Supplemental Material for this article is available online at the *Advances in Physiology Education* website.

Fig. 9. Classic exercise physiology studies conducted near San Diego, CA. The instrumented dog (*inset*) was encouraged to chase the vehicle containing the telemetry receiving and recording equipment by the person sitting in the rear hatch (notice the legs and feet).

was more interested in studying physiology and relocated to the Scripps Clinic and Research Foundation in 1962.

Baboons. The arrival of Van Citters and Franklin in San Diego in 1962 marked the beginning of an amazing period of innovation and breakthroughs in physiology research. Although Van Citters left Scripps after about a year to return to the University of Washington, he and Franklin continued to collaborate until Van Citters was named Dean of the medical school in 1970.

Van Citters had developed an interest in nonhuman primates and had selected the baboon as an experimental model. He established an ocean-facing laboratory that consisted of two stories, with the bottom story being a baboon laboratory where each animal exercised on a treadmill built into the bottom of its cage. Franklin established the electronics and measuring laboratory on the second story. He brought with him differential transit time flowmeters and sonocardiometers from Seattle and used Statham pressure transducers to measure pressure (as the Doppler flowmeter and Konigsberg pressure transducer had not yet been developed). They had fabricated a helmet to fit on the baboon's head. The helmet was composed of two hemispheres clamped together, with a hole for the nose to stick through. The baboon could still see, and a connection at the top allowed a flexible metal cable to run through to the second floor, where measurements were made.

Van Citters learned how to handle baboons from staff at the San Diego Zoo, with the support of the zoo director, Dr. Charles Schroeder. Baboons were surgically prepared at the zoo hospital laboratory, and experiments were conducted at the La Jolla beachfront laboratory. As described by Franklin (3),

> I recall occasions in my old yellow Plymouth station wagon, bringing a baboon back from the zoo to the Scripps Laboratory, sedated with "angel dust" [phencyclidine HCl], which we were using at the time. The baboon was sitting in the back seat and Van [Citters] pointed out, "Now, it might be something when he raises up and looks out the window into a policeman's face," or something like that. We didn't have any bad experiences, but we were chancing it.

After these experiments were published, Van Citters had the idea that it would be better to study baboons within their native environment, Africa. He submitted a grant proposal to the NIH, which was approved. Many years later, Van Citters and Franklin learned from an NIH official that two of the reviewers who approved the grant discussed it at the time and said either "Should we let these guys do this or not?" (9) or "Do you realize what we've done? We've just funded the biggest boondoggle in history!" (3).

Several preparations were necessary before the 1965 African expedition could occur. One was the development of a suitable implantable pressure transducer, as described previously. The four prototype pressure transducers fabricated by Micro Systems in Pasadena, CA, were used on this trip (10). Nolan Watson, who worked with Van Citters at the University of Washington, designed backpacks to house the electronic equipment on the baboons. The backpack contained the Doppler flowmeter circuitry, VCO for blood pressure transmission, and a 100-MHz FM transmitter (Supplemental Video 3).

The proposed procedure was to capture baboons in a custom-made cage. The cage was $\sim 6 \times 3 \times 3$ ft and had a sliding door on the front that was held up by a string. The door latch was attached to a corncob suspended in the cage, which, if disturbed, would cause the door to close and trap the baboon. As related by Franklin (3),

> All of the experts in Africa laughed and said, "You might catch one, but he'll tell everybody else about it and you'll never catch another one." Well, they were pessimistic about whether we'd ever get baboons or not. The baboons hadn't heard this, apparently, because it even got to the point where, after we had

> caught and instrumented a baboon and released him, he'd come back and . . . get caught again.

One recurring problem was how to recapture instrumented baboons, as they could not always be relied on to retrap themselves in the cages. Van Citters and Nolan Watson developed an anesthetic capsule to be implanted subcutaneously and remotely fired (Figs. 10 and 11). At one end of the cylinder was a model airplane glow plug followed by a plug of nitrocellulose. A rubber gasket served as a piston and, beyond that, a quantity of phencyclidine. The wires from the glow plug were routed with the instrumentation wires to the backpack, so, stated Franklin (3), "when you wanted to recapture the baboon, you transmitted an appropriate signal, and the switch closed, fired, and a few minutes later, he'd fall out of the tree."

Battery life in the remote control receiver was another significant technical hurdle. While Van Citters was working with Micro Systems to have the implantable pressure transducers fabricated, Franklin and Nolan Watson worked on the remote control device carried by the animal. It had to be activated at all times while attached to the animal so that it could receive commands. The goal was to have a quiescent current of zero (or as near to zero as possible) to exert battery power only when transmitting information. Franklin had heard of the existence of latching relays, which switch when a pulse is applied and remain latched until the subsequent pulse. Franklin contacted the company that manufactured these devices and was told they could have some ready within 6–8 mo. Franklin visited the company and described the needs of the African expedition to the CEO. Although the latching relays were in extremely high demand–the Defense Department, space, missiles, etc.–upon hearing Franklin's story, the CEO grabbed a handful and said, "Here, take these." (3). These devices were built into the baboon backpacks and used to control the flowmeters, pressure, power, and anesthetic firing.

The surgical procedures for the implantation of Doppler flow probes and pressure transducers had been developed by Van Citters before the trip. They brought a full field laboratory, including surgery supplies, along on the trip. As no economy tours of Kenya were offered at the time, the group hired a luxury African safari outfitter to guide their expedition.

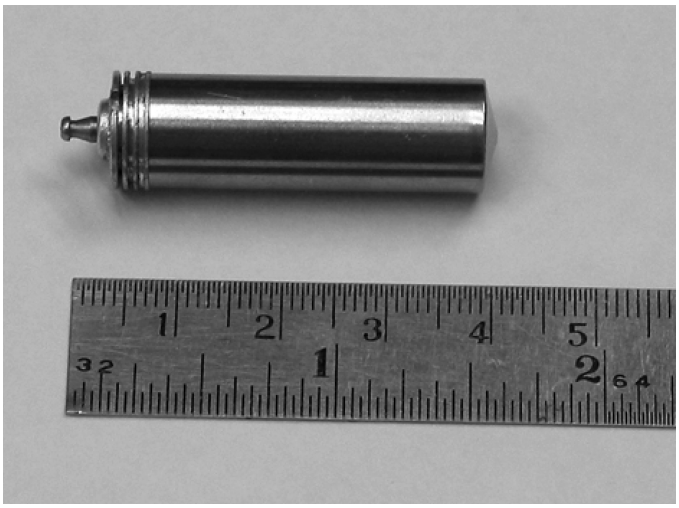

Fig. 11. Photograph of the actual anesthetic device described in Fig. 10.

The baboon expedition was highly successful (Supplemental Video 4). As told by Van Citters (9), after ~1 mo in Africa, while wrapping up their baboon work, he and Franklin decided it would be a shame to be in Africa, with giraffes all around, and not "take a crack at that."

Giraffes. According to Van Citters (9), the first giraffe study was developed over some good sherry and a fire one evening while on safari. They discussed the idea with the safari outfitters and professional hunters, who knew of people who trapped animals for zoos. The animal trappers were located living in the wild and agreed that they could, indeed, capture a giraffe. As told by Franklin (3),

> They had a large truck that we noticed was parked on top of a hill. "Why do you park it up there?" "Well, we don't have a battery." "But suppose you roll it down the hill and it doesn't

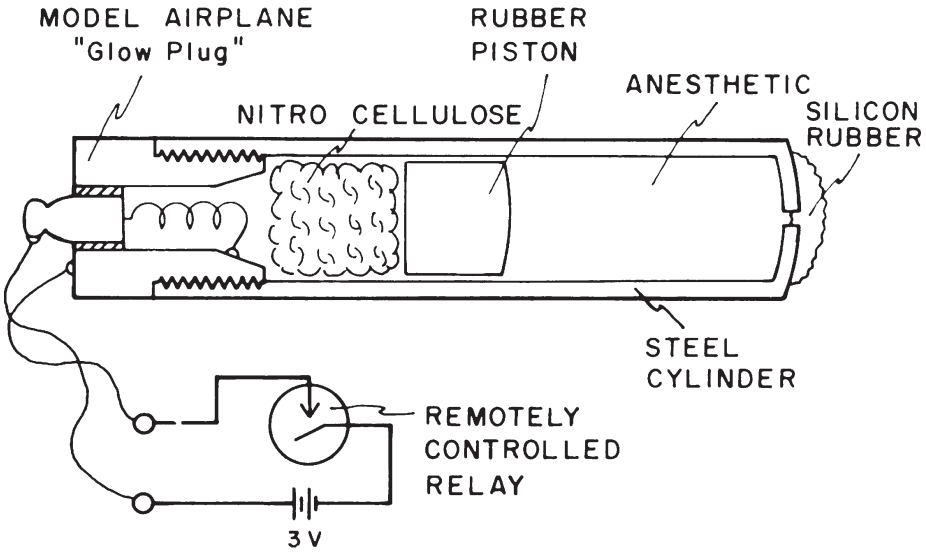

Fig. 10. Schematic of a remote-controlled anesthetic capsule designed by Van Citters and Watson to recapture instrumented baboons. The combustible nitrocellulose was ignited by the model airplane glowplug, thus releasing the anesthetic (phencyclidine) into the subcutaneous space. Moments later, the animal became unconscious and could be approached by the team.

start?" "Well, these guys can push it back up," they said, referring to the several natives that were part of their group.

As the purpose of the expedition was to study baboons, Franklin and Van Citters were not entirely prepared to instrument giraffes. Franklin worked through the night, by the light of a Coleman lantern, disassembling the baboon backpacks and assembling enough equipment to tape to a giraffe's neck. The next morning, the group caught a giraffe (Supplemental Video 5), surgically implanted a pressure transducer and Doppler flow probe in the upper carotid artery, released the giraffe, and collected data for 2 days. They caught a second giraffe and performed the same procedure. One of the giraffes stayed reasonably close to the camp while instrumented. The other went missing but was subsequently found ~8–10 miles away. After both giraffes had been recaptured, Van Citters sewed up the arteriotomies and released the animals. Both survived without complications.

Upon returning from Africa, Franklin submitted a grant proposal to the local Heart Association in San Diego, CA, for $30,000 to fund another expedition focusing exclusively on giraffes. He and Van Citters, along with some engineers and fellows, returned to Africa in 1968 to conduct additional giraffe studies. They located a more professional group that specialized in capturing animals for zoos. However, their experience with giraffes was limited to small, immature animals, which are more well suited for shipment to zoos. According to Franklin (3) (Supplemental Video 5),

> Van [Citters] said, "What can you do?" He pointed out one, and "Doc," he said, "I've never caught one that big." And of course we wanted the biggest one we could get–you know, the one with the longest neck. I've forgotten how many he captured for us– but a number.

While the giraffe trips produced fascinating stories and breakthroughs in the ability to conduct physiology experiments in the wild, their true purpose was to understand the unusual hemodynamics necessary for a giraffe to function (11). When asked what they learned about the mysteries of giraffe hemodynamics, Van Citters replied (9),

> We thought it was all very straightforward–a giraffe laying on the ground, laying flat, blood pressure nominally 250/150 [mmHg] or something of that nature. But when he stands up, he's got that long column, you know, subtract out the hydrostatic equivalent of that long column of his neck and you find out that he's perfusing at several levels at about the same as we are. And when he bends down to drink, you have to look at the whole animal and not just at his neck. And the first thing you notice [is] that his feet that were 1 or 2 feet apart while he was standing are suddenly 4 or 5 or 6 feet apart. So he's lowered his whole trunk–the whole thing has come down, and bending the head down is not a lot different than a cow bending down for a drink.

Van Citters attributed the lack of edema in their legs and feet to their extremely thick, tough skin, which he felt encased the lower extremities in such a way that edema could not occur (9).

Alaskan sled dogs. Van Citters and Franklin had also been interested in the physiology of exercise, specifically the distribution of blood flow to various organs during extreme exercise. This interest began in the early days of Rushmer's laboratory at the University of Washington, with Franklin and Dick Ellis running down the hall after an instrumented dog with a Sanborn chart recorder. Their interest was further stimulated during the African baboon studies in 1965. During a recording, a baboon was threatened by a giraffe, but renal flow did not change. Classic physiology predicted a reduction in renal flow during a fright reaction. Van Citters and Franklin had also observed that the predicted changes in renal and visceral blood flow did not occur in treadmill-exercising dogs. The primary critique of their work was that they had not exercised the dogs hard enough. Thus, they began to consider where they might find the best athletes in the world, leading them to think of the Iditarod sled dogs.

Van Citters had some connections at the Arctic Air Medical Research Laboratory at Ft. Wainwright, AL. The Air Force Colonel there had a sled dog team as a hobby. Van Citters, Dan McKown (from Franklin's laboratory at San Diego, CA), and Franklin traveled to Alaska for a weekend and instrumented several dogs. As recalled by Van Citters (9),

> I remember doing combined thoracic and abdominal surgery on those dogs all day Saturday and Sunday. I mean, I think I did something like 10 or 12 dogs, and those are long, tedious procedures. Flowmeters and pressure gauges in the thorax and then blood flow distribution, renal artery, terminal abdominal aorta, mesenteric artery, and, in some cases, coronary artery as well.

Two to three weeks later, after the dogs had recovered from surgery and been reconditioned to their previous exercise capacity, the team returned to Alaska to begin conducting experiments. All of the dogs on the team were instrumented, but only one was recorded at a time (Fig. 12 and Supplemental Video 6). The signal-conditioning circuitry was attached to the dog being monitored (the one nearest the sled) and was hardwired to the sled, which contained a high-powered VCO connected to an antenna. One member of the team would stand on the roof of a building, inside of which Franklin and Van Citters were recording. They communicated with the musher on the sled via a walkie-talkie.

The environment was extremely cold, and, at one point, a battery wire broke. Unfortunately, no one in the laboratory had a soldering iron. One team member suggested that he spit on it, which is exactly what he did. The saliva immediately froze on the cold wire and held the two ends together, allowing the experiment to continue.

The performance of the sled dogs was amazing. They were able to run 20 consecutive 4-min miles without showing any sign of exhaustion. Records indicated no evidence of blood flow redistribution away from the visceral organs, and the dogs were hemodynamically stable throughout the exercise.

After the publication of these results, reviewers criticized the work by claiming a change in these dogs would not be expected since they are athletes. They were talking about regular, unconditioned people when they said to expect blood flow redistribution.

Hibernating bears. In addition to their previously noted work, Van Citters, Franklin, and colleagues developed an interest in hibernation. As bears hibernate throughout the winter, they were curious to see what happens to the circulatory system, including renal blood flow. (Bears do not urinate during the winter, as sled dogs do.) The United States Navy had a research station at Pt. Barrow, AL. Van Citters operated on bears in the cold, outdoor weather to place Doppler flow probes on the renal arteries. During the surgeries, they used open drop ether from a gauze-covered coffee can for anesthe-

Fig. 12. Instrumented sled dog team at Ft. Wainwright, AL. The last dog in the team was wired to the transmitter equipment in the sled for the remote collection of hemodynamic data. While all dogs were instrumented, only one was studied at a time.

sia. In the event that the bears awoke, the Navy had stationed two guards with 30-caliber rifles. Franklin and Van Citters subsequently recorded hemodynamics throughout the winter hibernation period.

Other interesting studies. Van Citters, Franklin, and colleagues studied the comparative physiology of several other species over the years. They were not motivated by the desire to create new technology but, rather, to find a way to answer physiological questions that had not been answered before.

Other animals that they instrumented included elephant seals, trout, and ponies.

Coronary collateralization. Upon becoming established as Director of the Dalton Research Center at the University of Missouri-Columbia, Franklin grew interested in coronary ischemia and collateral blood flow. The origin of this work was intermittent claudication, a circulatory dysfunction in the human leg. They wondered why you could "walk through it," meaning that it slowly improved as you exercised the leg (3). Partnering with a cardiologist fellow from Japan, Franklin developed an instrumented dog model with regional measurement of myocardial function using sonomicrometer crystals (circumferential segment length and wall thickness) along with a Doppler flow probe and pneumatic occluder on the left circumflex coronary artery. They hypothesized that repeated intermittent coronary occlusions of short enough duration to avoid permanent myocardial damage would stimulate the growth of collateral circulation to the area at risk. They determined that the maximum duration of occlusion from which myocardial function could fully recover was 3 min. More importantly, they observed that the dog would awake and appear to feel the effects of the coronary ischemia at 3 min. Thus, the protocol required hourly 2-min occlusions for 8 h/day. After 140 occlusions, they were prepared to give up. However, at *occlusion 156*, myocardial function began to recover before the end of the occlusion, thus indicating that the myocardium was being perfused from an adjacent arterial source.

Having read an article in *Science Magazine* by Dr. Judah Folkman, who was attempting to prevent the neovascularization of growing tumors, Franklin wondered if the opposite–stimulating collateral vessel growth–could be achieved in the ischemic heart. Indeed, treatment of dogs with heparin did result in a significant increase in the rate of collateralization, leading to the hypothesis that myocardial ischemia patients would benefit from heparin and exercise therapy.

Conclusions

In 1991, the University of Missouri announced an early retirement "buyout" program. Franklin, having served over a decade as Director of the Dalton Research Center and remaining continuously funded by NIH since the 1960s, went home the day of the announcement and conferred with his wife, Janet. He announced his retirement the next day. Franklin maintained a laboratory at the research center for a few more years as he completed his NIH-funded research. However, his real love in retirement, which he pursued for the remaining 16 yr of his life, was playing bluegrass music on the acoustic bass guitar. He and his wife traveled the country in their camper, visiting old friends at bluegrass festivals throughout the United States. Dean Franklin was diagnosed with cancer in 2006 and succumbed to the disease in May 2007.

One question that Franklin was asked repeatedly throughout his career was why he chose not to patent any of his ideas in order that he might profit from them. His early work with ultrasound, including the invention of the ultrasonic transit time flowmeter, Doppler flowmeter, and sonocardiometer, subsequently led to the field of noninvasive clinical echocardiography. Pioneering work in this field was conducted by personnel who remained at the University of Washington laboratory after Franklin's departure to San Diego, CA. According to Van Citters (9), who lectured Franklin after the Doppler flowmeter was developed,

> I said, "Young man, this is a big one. This is your kids' college education. This is your mortgage, and this is your retirement." And he–very straightforward–said, "No, this was accomplished . . . on the USPHS grant, and it's going into the open literature. That's where it belongs."

When, during our 2006 interview (3), I asked why he didn't patent the Doppler flowmeter, Franklin's humorous response was

> Patenting wasn't in our minds at the time. Besides that, I would have become rich and developed cirrhosis at an early

age. When I could afford to buy whiskey, then I probably would have drunk it.

The primary author recalls having asked Franklin the same question in the 1980s, during his fellowship at the University of Missouri. At the time, the answer was something to the effect that he had been able to live a very good life, as it was.

Never has there been a life more well lived!

APPENDIX: BIOGRAPHICAL BACKGROUND

Dr. Robert Rushmer (1914–2001)

Dr. Robert Rushmer was the first innovator in the development of methods to monitor physiological function in conscious animal models. During World War II, Dr. Rushmer served in the United States Army Air Corps in Texas, where, using rocket sleds, he studied the effects of acceleration on chimpanzees. After the war, Dr. Rushmer moved from Texas and arrived at the University of Washington. Here, in 1958, he established one of the first cardiovascular fellowship programs. According to Dr. Van Citters, one of the first fellows, Dr. Rushmer's program was a unique program, with scientists from around the world and across several disciplines. Many program fellows went on to lead successful careers in their home countries.

The breakthroughs in physiological monitoring developed in Rushmer's laboratory in the 1950s were recounted in his book, *Cardiovascular Dynamics*, which was first published in 1961. Subsequent editions of the book chronicled the ongoing progress in biomedical instrumentation, much of which was created by alumni of Dr. Rushmer's program. Dr. Rushmer passed away in Seattle, WA, in July 2001.

Dr. Robert Van Citters (1926–present)

After serving in the military in Word War II, Dr. Robert Van Citters attended medical school at the University of Kansas, where he interned and completed a research fellowship and internal medicine residency. Dr. Van Citters successfully applied for an NIH grant to continue his research and, in 1958, joined Dr. Rushmer's training program at the University of Washington. After ~4 yr, he created a laboratory at the Scripps Clinic and Research Foundation in San Diego, CA. In collaboration with Dean Franklin, who had also relocated from Seattle to San Diego, Dr. Van Citters conducted research using chronically instrumented conscious baboons.

After a scientific exchange program in Russia in 1963, Dr. Van Citters returned to the University of Washington. After 5 yr, Dr. Van Citters was appointed to the position of Associate Dean for the research and graduate program and, shortly thereafter, appointed to fill a sudden vacancy as Dean of the University of Washington Medical School. He served as dean for ~12 yr, beginning in 1970. Now retired, Dr. Van Citters continues to reside in the Seattle area.

Dean Franklin (1929–2007)

As a 15 yr old during World War II, Dean Franklin worked as a truck driver carrying peas and other farm crops. After taking a few college courses and spending time as a butcher in Oregon, he was drafted into the Army in 1950. In the early 1950s, he was selected for electronics training in radar technology at Ft. Monmouth, NJ. He subsequently became chief instructor in the United States Army advanced radar school. In 1952, shortly after being released from military service, he was hired by Boeing in Seattle to work on the Bomark missile project.

Upon seeing a bulletin board notice in the University of Washington employment office advertising an opening for an electronics technician at the medical school, Franklin applied and was hired by Dr. Robert Rushmer. He continued to work in the Rushmer laboratory for the next 3 yr while taking classes toward his Bachelor's degree in physics.

After his time in the Rushmer laboratory, during which he invented the sonocardiometer, ultrasonic differential transit time flowmeter, and ultrasonic Doppler flowmeter, Franklin and his family relocated to Canada, where he entered medical school at McGill University. After 1 yr, however, with two new children and his wife battling a serious illness, he elected to discontinue his medical education and returned to Rushmer's laboratory.

In 1962, Franklin accepted an invitation to join Robert Van Citters at the Scripps Clinic and Research Foundation in San Diego, CA. Even upon Dr. Van Citters' subsequent move back to Seattle, the Franklin and Van Citters laboratories continued to collaborate for many years. Franklin's famous Seaweed Canyon laboratory in San Diego, which is still in operation today, was founded in 1965. From this point until his retirement, Dean Franklin's research was continuously funded through NIH grants.

In 1978, Franklin was recruited by Dr. Arnold Schwartz to the position of Vice Chairman of the Department of Pharmacology and Cell Biophysics in Cincinnati, OH. Two years later, he accepted the position of Director of the Dalton Research Center at the University of Missouri-Columbia. He retired from this position in 1991 but continued his academic work conducting NIH-funded research. In 1992, he retired completely from academic research to focus on his family; he also traveled the country playing bluegrass music on the acoustic bass guitar. Dean Franklin passed away in Columbia, MO, in May 2007.

REFERENCES

1. **Comroe JH Jr.** Retrospectroscope: hydrogen, balloons, and pressures. *Am Rev Respir Dis* 113: 73–76, 1976.
2. **Department of Medical Physics and Bioengineering, University College London.** *Blood Pressure Monitoring. The History of Blood Pressure Measurement* (online). http://www.medphys.ucl.ac.uk/teaching/undergrad/projects/2003/group_03/history.html [1 June 2009].
3. **Franklin DL.** *Personal interview by R. D. Sarazan* [19 August 2006].
4. **Franklin DL, Ellis RM, Rushmer RF.** Aortic blood flow in dogs during treadmill exercise. *J Appl Physiol* 14: 809–812, 1959.
5. **Franklin DL, Schlegel W, Rushmer RF.** Blood flow measured by doppler frequency shift of back-scattered ultrasound. *Science* 134: 564–565, 1961.
6. **Kasten K.** *Telemetry is Coming of Age* (online). http://www.raven1.net/telem1.htm [1 June 2009].
7. **Myers DG.** *Mister Zoo: the Life and Legacy of Dr. Charles Schroeder*. San Diego, CA: The Zoological Society of San Diego, 1999.
8. **Rushmer RF, Franklin DL, Ellis RM.** Left ventricular dimensions recorded by sonocardiometry. *Circ Res* 4: 684–688, 1956.
9. **Van Citters RL.** *Telephone interview by R. D. Sarazan* [8 September 2006].
10. **Van Citters RL, Franklin DL.** Telemetry of blood pressure in free-ranging animals via an intravascular gauge. *J Appl Physiol* 21: 1633–1636, 1966.
11. **Van Citters RL, Kemper WS, Franklin DF.** Blood flow and pressure in the giraffe carotid artery. *Comp Biochem Physiol* 24: 1035–1042, 1968.