A Scientific Dream Team

No science fiction here. Bioengineering and medicine are partnering in projects that address real life problems and offer boundless opportunities for the future.

BY DEBRA LEVY MARTINELLI

When most of us hear the term "bioengineering," visions of television's *Six Million Dollar Man* or Arnold Schwarzenegger's cyborg of *Terminator* fame come to mind. A creation of Hollywood's very fertile imagination, we think. Science fiction.

It is anything but. Bioengineering—the application of engineering principles to challenges in medicine and biology—is, quite literally, changing the way we see, hear, feel, move and think.

At the University of Oklahoma Bioengineering Center, researchers are:

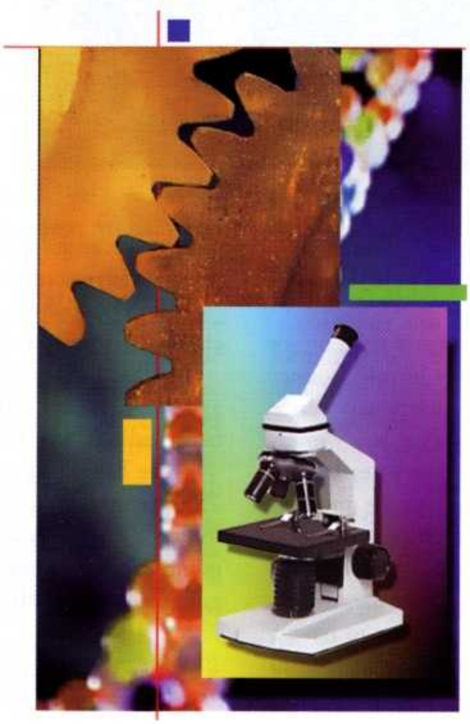
• growing bone tissue that they hope will eliminate the need for grafts and bone marrow transplants

• developing a direct brain interface that could help the disabled perform everyday tasks the able-bodied take for granted

• testing an implantable hearing device that could render hearing aids obsolete

• refining a process that improves the intravenous delivery of medications so dramatically it literally could mean the difference between life and death—and much, much more.

OUBC was established in 1998 with a $1 million Special Opportunity Award from the Whitaker Foundation, a philanthropic organization created in 1975 dedicated to helping to create and nurture bioengineering programs around the country. A partial list of other institutions that received Whitaker awards that year reads like a veritable *Who's Who* of American universities, including Cornell, Georgia Institute of Technology, Harvard, Marquette, Massachusetts Institute of Technology and the University of Pennsylvania.



"It's a group you really want to be among," says Edgar O'Rear, OUBC director and Francis W. Winn Professor of Chemical and Biomedical Engineering. "With careful planning, assistance of top biological scientists and engineers from Oklahoma and across the nation, and the support of alumni, friends and administrators, we have sought to create an interdisciplinary bioengineering program of the highest quality."

The idea behind OUBC was to create an intercampus bioengineering center through which chemical engineers, electrical/computer engineers and mechanical engineers and other interested faculty on the Norman campus could partner with physicians, scientists and other health care professionals at the Health Sciences Center in Oklahoma City to develop and test new technology. Laboratory facilities intentionally are distributed throughout the College of Engineering and therefore have no central location, but this fall the imaging and biomolecular engineering research groups of OUBC will relocate to the recently completed Peggy and Charles Stephenson Research and Technology Center.

Located at Highway 9 and Jenkins

Co-founder of HSC's Cardiac Arrhythmia Research Institute Dr. Warren "Sonny" M. Jackman, foreground, and Associate Professor of Research Dr. Hiroshi Nakagawa move magnetic-tipped catheters through the heart of a patient, who has been placed in a magnetic field, to locate the origination point of an irregular heart beat and to deliver an energy source to destroy the area. These professors assisted the manufacturer in the design, testing and upgrade of this robotics equipment.
Photo courtesy OUHSC.

Avenue, the Stephenson Center will bring together at one site biochemists, microbiologists, zoologists and bioengineers on the Norman campus to facilitate cooperation and multi-disciplinary study. The research and technology center is named for Vintage Petroleum chairman, president and CEO Charles Stephenson, a 1959 graduate of the OU College of Engineering, and his wife, Peggy, who in 2002 contributed $6 million to make the facility possible.

"One of the first programs presented to me when I came to OU in July 1998 was the emerging biomedical engineering program," says W. Arthur Porter, dean of the College of Engineering and University vice president for Technology Development. "Today, it may be the best example in our college of a truly multi-disciplinary program creating the rich learning environment among our faculty and students, as well as other University colleagues, that is the objective of the College of Engineering."

The OUBC Advisory Board is composed of some of the nation's leaders in the field:

• Y.C. Fung, founder of the bioengineering program at the University of California, San Diego, widely recognized as the father of biomechanics and the first bioengineer to receive the President's National Medal of Science, the country's highest scientific honor

• Robert Nerem, Parker H. Petit Distinguished Chair for Engineering in Medicine, director of the Parker H. Petit Institute for Bioengineering and Bioscience at the Georgia Institute of Technology and a 1959 OU aeronautical engineering graduate

• Larry McIntire, who built a leading bioengineering program at Rice University and is a distinguished researcher in engineering education and cellular and tissue engineering, and

• Yoram Rudy, professor of biomedical engineering, physiology and biophysics and professor of medicine and director of the Cardiac Bioelectricity Research and Training Center at Case Western Reserve University.

"Few, if any, programs begin with this level of input," O'Rear says.

The 21-member OUBC faculty, many of whom were recruited from such research powerhouses as Johns Hopkins and Rice, hold numerous prestigious appointments, including George Lynn Cross Research and other endowed professorships and chairs.

Not bad for a program that is marking only its sixth birthday.

Sharpening the Image

Ralph Lazzara, M.D., George Lynn Cross Professor of Medicine, a principal at the renowned Cardiac Arrhythmia Research Institute at OU's Health Sciences Center and a member of the OUBC faculty, says it is no exaggeration to describe many applications of bioengineering to medicine as revolutionary.

"There are many facets of bioengineering that relate to medicine that people just don't appreciate. Bioengineering breakthroughs that have already changed medicine include such imaging techniques as the CT scan—an engineering feat that led to a Nobel Prize—and MRI. Both have been used for medical diagnosis and treatment that previously didn't exist," he says, noting that his medical specialty, cardiology, always has been closely aligned with engineering.

"The heart makes electricity," Lazzara explains. "At the arrhythmia institute, we study that electrical function to learn why the heart may beat too fast or too slow." With Hong Liu, Charles and Jean Smith Chair in Bioengineering and professor of electrical and computer engineering, Lazzara is exploring advanced methods of medical imaging that incorporate both engineering and computer techniques.

Another OUBC researcher concentrating his efforts on MRI technology combines his passion for computer technology, physics and mathematics with a keen interest in medicine. Tamer Ibrahim's goal is to develop radio-frequency coils that, in conjunction with improvements in the other components of imaging technology, are expected to lead to significant advances in the diagnostic and treatment potential of MRI.

Ibrahim, an assistant professor of electrical engineering, predicts that the technology someday will be so precise that structures 20 times smaller than those that can be seen with currently common MRI equipment will be visible. The result, he insists, will be as impressive as opening up the human head and looking at it with only the naked eye.

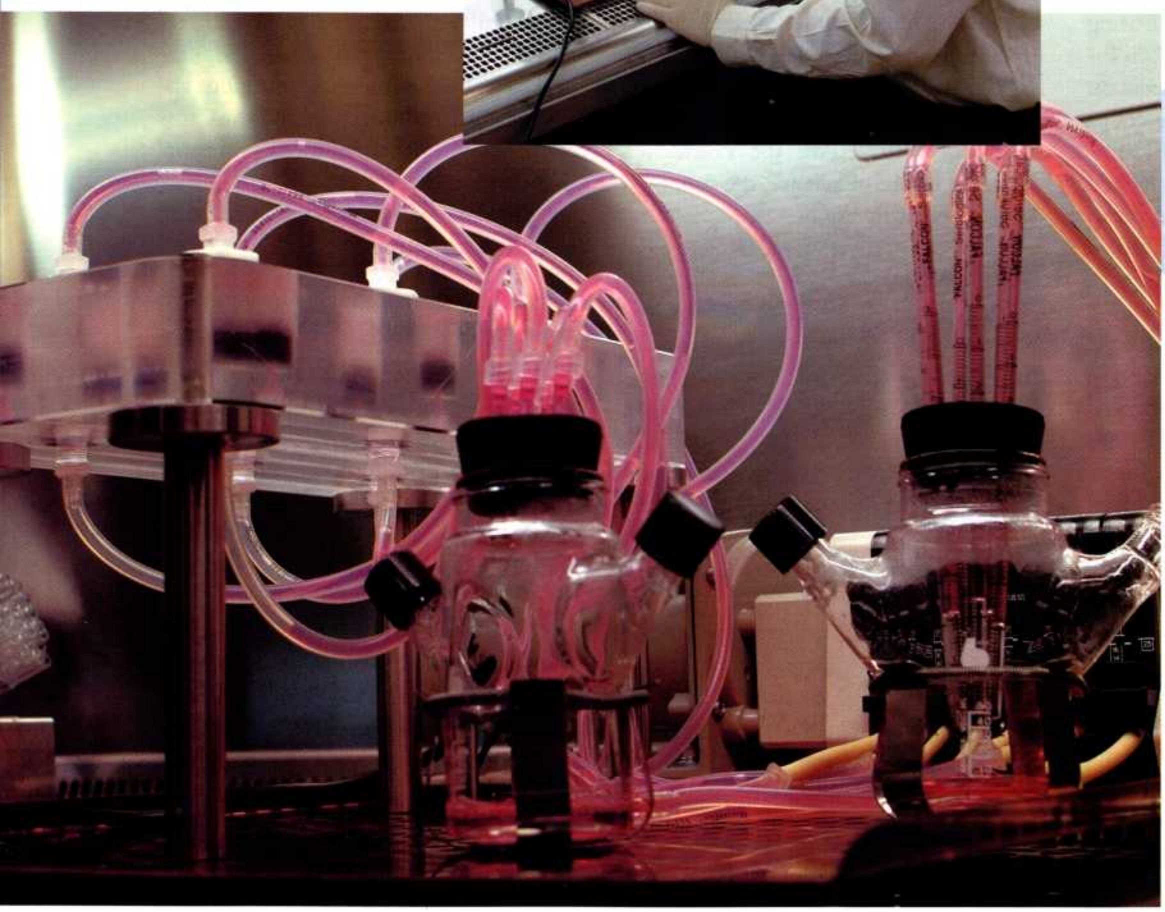
"In diagnosing multiple sclerosis and Alzheimer's, for example, a doctor today relies heavily on the patient's symptoms to make a diagnosis," he says. "With the improvement in MRI, practitioners will be able to see things that are much smaller than we can see now. Diagnosis and treatment of those diseases can be made much earlier."

Growing Bone

If the early results of bone tissue research being conducted by Vassilios Sikavitsas and his team are any indication, bone grafts—where bone is taken from another site in the body, usually the hip, and transplanted at the site of a serious fracture—soon could be a treatment of the past. The newly generated bone also could be used in patients with bone cancer, negating the need for marrow transplants.

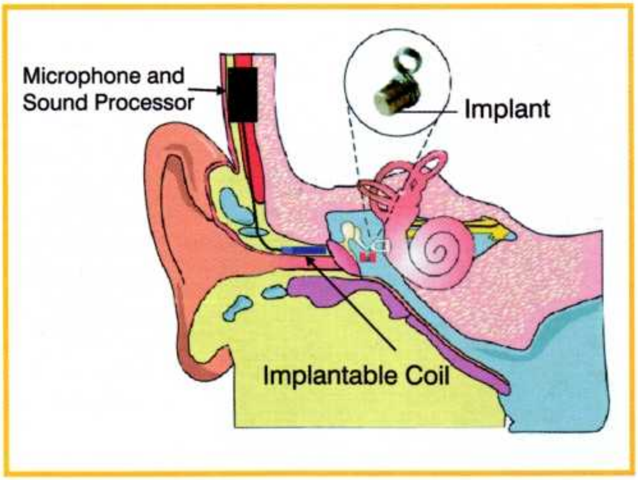
Sikavitsas, an assistant professor of

Robert Taylor



Chemical engineering assistant professor Vassilios Sikavitsas, inset, nourishes bone marrow cells in a porous scaffold that degrades as new bone tissue grows. In humans, using the patient's own marrow, the replacement bone tissue would be free from rejection, scarring and other complications.

Ron Gan's diagram illustrates her development of the totally implantable hearing system, which goes beyond the cochlear implant and conventional hearing aids to return hearing to patients whose deficit is caused by exposure to loud noise, mild ear disease or natural age-related degeneration.



chemical engineering, grows bone from cells taken from marrow and placed in a porous scaffold made of a biodegradable plastic. "The cells are continuously nourished with a glucose-based solution that flows through the scaffold. As the bone tissue grows, the scaffold degrades. When implanted at a bone site, the end result would be bone tissue generated from a person's own cells with no evidence that the scaffold was ever there," he explains.

Healthy bone growth, however, requires a constant supply of healthy blood. So Sikavitsas is collaborating with Paul DeAngelis, associate professor of biochemistry and molecular biology in the HSC College of Medicine, on a process to grow new capillaries to support the blood supply necessary to regenerate the bone. Sikavitsas says the process, known as angiogenesis, also will be the basis for future growth of hearts and other organs.

Making the Connection

Rob Rennaker is fascinated by the complexity of the human body. "It's an engineering marvel," says the assistant professor of mechanical engineering who as a child delighted in taking things apart and trying to figure out how they worked. Now he is examining how the brain interacts with other parts of the body in the hope of developing computerized prostheses that can bridge brain-body connections damaged by disease or injury.

In conjunction with other OU faculty, including Ibrahim and David Miller, Wilkonson Chair of Intelligent Systems in the School of Aerospace and Mechanical Engineering, Rennaker is developing a brain interface device. With the help of a computer, the new device would create a link between the external world and the brain in individuals with sensory or motor deficits resulting from central nervous system injury or disease.

"Everything we sense, feel and do is controlled by the neurons that make up the nervous system. Because they're electrically active cells, neurons generate voltage. We use sensitive electronics to monitor their activity. We can tell when the cells are firing and when they're not by the change in voltage," says Rennaker.

"By implanting electrodes beneath the skull and using a specially equipped hat as an interface, we could establish a connection between the brain and an external computer that would mimic the compromised connection. People with spinal cord injuries or central nervous system diseases like multiple sclerosis could perform such everyday functions as driving a car or operating a wheelchair."

Rennaker maintains that similar tools could be adapted for other parts of the body. "Little is known about the mechanisms associated with chronic pain such as angina [chest pain]. An interface with the spinal cord could be developed to diagnose or monitor neural activity from the heart or other structures and use electrical stimulation to control the pain."

Drew Sloan, a recent OU mechanical engineering graduate, now a doctoral candidate, is one of many students who have chosen to remain for their postgraduate bioengineering degrees because of the quality of OUBC's programs and faculty. Accepted at Johns Hopkins University, Case Western Reserve University, the University of Michigan and the University of Minnesota—all of which have world-class bioengineering programs—he was attracted by the opportunities available at OU.

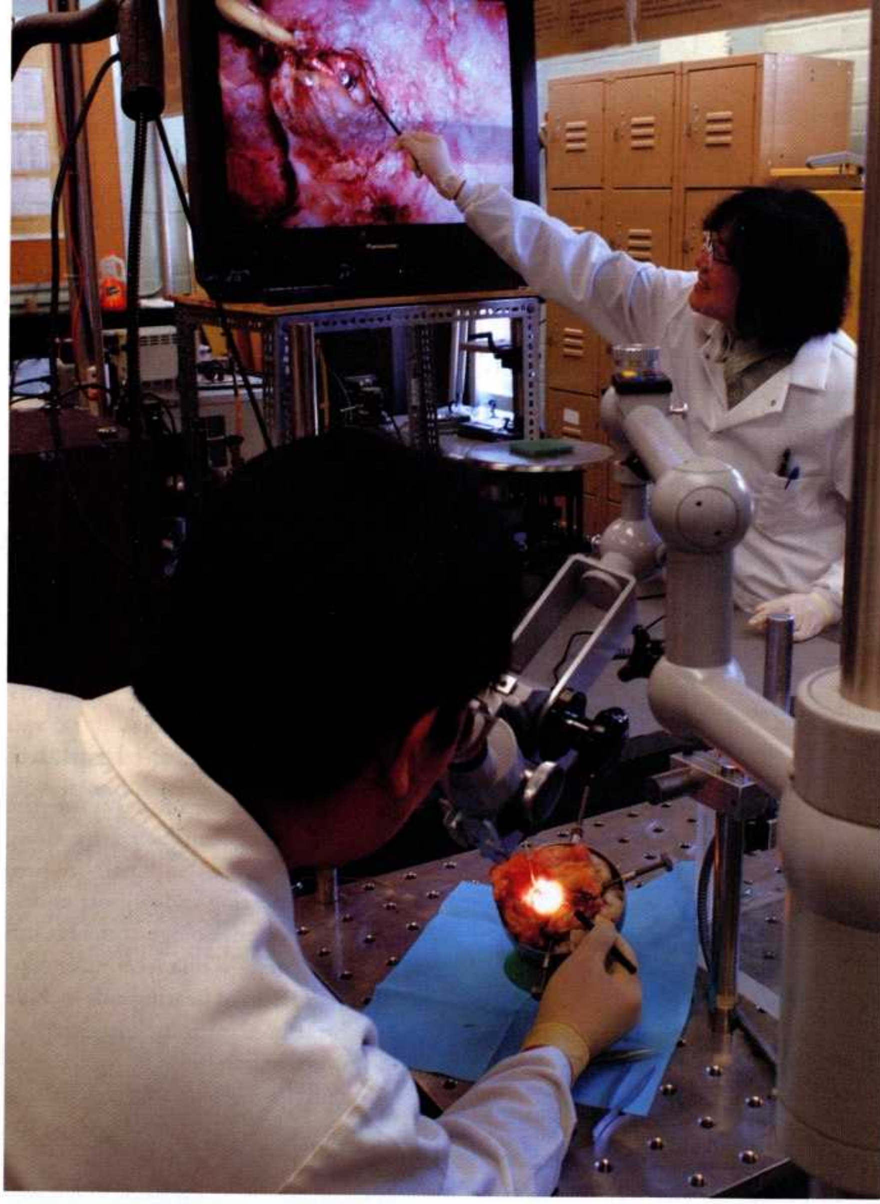
"I wanted to work with Dr. Rennaker, and I got to build my own lab," says Sloan, who in 2003 was one of 23 from a record 419 applicants awarded a Whitaker Foundation Graduate Fellowship. With Rennaker as a mentor, he is studying ways to interface directly with the brain to restore sensory functions to persons with hearing impairments.

Beyond the Cochlear Implant

The auditory system also is at the core of research being conducted by Rong Gan, Charles E. Foster Chair in Biomedical Engineering and adjunct associate professor of physiology at the Health Sciences Center. While recent developments in the field of hearing aids include the cochlear implant, which has successfully restored some level of hearing in individuals with severe hearing deficit, Gan is working on a new option: the totally implantable hearing device.

The apparatus designed by Gan and her colleagues, who include her co-investigators from the OU Health Sciences Center and the Hough Ear Institute, differs from the cochlear implant in two critical ways: It is intended specifically for individuals with mild to moderate rather than severe auditory deficits; as its name suggests, it is totally implantable in the ear with no external components. The cochlear device is partially implanted, with other parts worn externally.

"The cochlear implant was a huge contribution, but it's only for people with profound hearing impairment. The conventional hearing aid only provides amplification of sound and has a lot of feedback noise," says Gan. "Our fully implantable hearing device will re-establish the ability to hear in patients with hearing deficit caused by exposure to loud noise, mild ear disease or natural age-related degeneration." She and her



Robert Taylor

Rong Gan, at right, points to the magnification of the fully implantable hearing device, which has been placed in the cadaver ear that bioengineering doctoral student Bin Feng, foreground, is studying under the microscope. Gan's dual academic appointment is representative of the ongoing partnership between OU engineering and medicine.

team currently are testing the system in cadaver ears by measuring the device-induced sound signals transmitted to the inner ear.

Attacking Blood Clots

The training Kent Leach received at OU as a doctoral student in chemical engineering, with an emphasis in bioengineering, has been invaluable in his post-doctoral fellowship at the University of Michigan, where he is examining ways to combine gene therapy and drug delivery to promote bone formation. Leach, who earned his doctorate in 2003, worked with O'Rear on a formulation to dissolve blood clots more quickly by enabling clot-busting medication, administered intravenously, to be delivered more effectively.

"The polymer we used has unique properties that react well with blood clots," he explains. "If you were to have the misfortune of suffering a heart attack or stroke, the hospital staff currently would take a vial of drug in powder form, mix it with water and put it in an IV drip. The drug circulates in the blood and when it gets to the clot, it will stick to it and chew it up from one direction. In our work, we capitalized on this specific polymer's ability to prevent drugs such as these 'clot-busters' from getting stuck. Instead, it can get inside the clot, so that now the drug is both inside and outside, chewing up the clot in two places rather than one."

An additional benefit of the discovery is its ability to diminish bleeding complications. "This system can reduce the time for re-establishment of blood flow by as much as a factor of 10," says O'Rear.

OU was awarded a patent for the technology this past summer; the next step is to interest a pharmaceutical manufacturer to license and take it into clinical trials. "We're also getting our results published in the literature so cardiologists and scientists at drug companies will read about it and recognize the benefits," Leach says.

Science as Economic Stimulus

While these scientific advances are well known in the medical and engineering communities, the challenge for OUBC is to educate the public about their benefits. "Everyone in the state of Oklahoma needs to know the importance of bioengineering and what its applications will do for humankind," says Lazzara. "But they also need to know the importance of bioengineering as an economic stimulus for the state.

"We can already see what these kinds of advances have done for places like Duke and Case Western Reserve," he says. "Our state has to make a commitment to fund the basics. When we reach a critical mass of good people, they will generate funding, which in turn will bring in more good people and so on."

O'Rear sees an exciting time ahead for bioengineering. "We work collaboratively on important and challenging problems with the potential to help improve the quality of people's lives."

Rennaker agrees. "Over the next 20 years, I believe we'll be in the Age of Bioengineering. It'll be the equivalent of the Computer Age over the past 20 years. We'll see the development of devices as a result of bioengineering that we can only dream of today."

Debra Levy Martinelli is communications director for the OU College of Engineering.