Southern California: A Hotbed of Biomedical Engineering

By Jessica P. Johnson

Nine Bioengineers Describe Their Research and Why Southern California Has the Biotech Market Cornered

Theodore Berger
Ellis Meng
Steven George
Michael Khoo
Vasilis Marmarelis
Andrew McCulloch
Gert Cauwenberghs
Lucila Ohno-Machado
Jerome Schultz

This August, the IEEE Engineering in Medicine and Biology Society will hold its 34th Annual International Conference in San Diego, California, with the theme "engineering innovation in global health." Just north of the city is La Jolla—home to one of the nation's top-ranked bioengineering programs. And if you don't mind the traffic, you can venture to Los Angeles, where the west coast's very first bioengineering program began in 1974. Biotech is California's second largest employer in the high-tech industry, next only to information technology. The explosion of biomedical engineering (BME) activity in the last four decades makes this locale an appropriate setting for a meeting of one of the biomedical oldest engineering societies of the United States. As a sampling of what

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to expect at the conference, researchers from the region describe what is getting them excited about their work these days, the future of BME research, and why biotech settled by the beach.


USC

Theodore Berger *is a professor of engineering and biomedical engineering and neurobiology at the University of Southern California's (USC's) Viterbi School of Engineering. He directs the Center for Neural Engineering where multidisciplinary collaborations are forged among USC faculty. The IEEE named him as a distinguished lecturer during 2004–2005 and elected him a Senior Member in 2005.*

Q: What problems are you tackling in your research right now?
Berger: We're working on projects to understand the signal processing capabilities of brain cells, particularly in the hippocampus. There are four, maybe five layers of neurons in the hippocampus. When signals go from layer to layer, they change. So by the end, what started out as one kind of spatiotemporal pattern of pulses, ends up a very different pattern of pulses. If the hippocampus does the transformation that it's supposed to do, we end up with long-term memories. If we interfere with it or if it's malfunctioning, then we don't.

Biotech is California's second largest employer in the high-tech industry, next only to information technology.

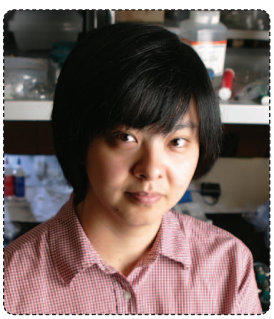
We're able to look at the short-term memory pattern of nerve pulses and form mathematical models to predict what's supposed to become the long-term memory pattern. What this helps us do is create a neural prosthesis for a malfunctioning hippocampus, for example, if someone has Alzheimer's, epilepsy, a stroke, or even blunt head trauma. In rat preparations, we put electrodes into parts of the brain where short-term memories are still normal, make the correct prediction for what the long-term memory code for that item might be, and then use another set of electrodes to electrically stimulate the output neurons of the hippocampus to generate the correct output. We can make this part of a prosthesis that will support long-term memory for animals that can't support it themselves.

We also have to learn how to model at one level in the brain and then show how it influences higher levels. People are very good at modeling at molecular, synaptic, single neuron, and neural circuit levels. But it's very difficult to have one model feed into another. We've done that to the level of single neurons and are about to go on to circuits. It allows us to take a novel drug or modify a given molecular feature of a channel of a receptor and show how synaptic and neural function changes and, as a result, cognitive function.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?
Berger: There are several forms of neural prostheses. For example, the work that's being done on artificial arms. If somebody loses an arm, the nerves for the hand and fingers are still in the arm. The information that's necessary to pick up a glass is still going there, but it stops because the nerves are cut off. If we can get the nerves to grow into a device or a kind of nonneural surface that can then interface with small motors that can move the arm, then we can go back to just thinking about picking up a glass and our arm will do it. That work is already in clinical settings, but we're going to start seeing it more.

Q: What new BME research avenues might you predict for the future?
Berger: We think that we can create neural prosthetic devices that will reproduce thought and cognitive functions: planning, memory, execution of fine motor behaviors, and emotion. Thought processes are very complicated, but that doesn't mean that we can't reduce a specific thought to a series of spatiotemporal patterns. If we can do that, and if we can manipulate them, then we should be able to change or predict a cognitive function. The future is learning the language of the brain.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?
Berger: It's very multidisciplinary here. But I think what's unique in Southern California is that neuroscience is very strong. USC has a terrific neural-engineering program. We started out being very mathematically oriented with mathematicians and engineers who had strength in modeling. What's changed over the years is that we've added and developed skills in experimental activities and medical practice besides just mathematical modeling. That's part of the reason that cross-disciplinary work has become so strong. And of course that gets embedded in the educational programs.


DIANE AINSWORTH

Ellis Meng *is an associate professor of biomedical and electrical engineering in the Viterbi School of Engineering at USC, where she directs the Biomedical Microsystems Laboratory. Her research focuses on using microtechnologies to build biomedical microdevices including implantable sensors and infusion pumps.*

Q: What problems are you tackling in your research right now?
Meng: One area of research is using microtechnologies to enable site-specific drug delivery. The purpose is to overcome adverse side effects that result when you expose a drug throughout the entire body when you take an oral pill or inject it into the circulatory system. We're trying to come up with better ways to deliver drugs with the development of an implantable infusion pump. This is not something you'd use for your everyday run-of-the-mill condition, but more for particular diseases that require chronic care, are incurable, and affect

very specific sites within the body. Currently, we're pushing toward clinical use in pediatric patients who have a specific type of cancer.

A second area of research is neural and retinal prosthetic implants that directly stimulate the brain or the retina. In humans, this is an emerging technology—the most well-known example of neural prosthetics currently is the cochlear implant. People are working on implants to treat memory loss, dementia, and to record and decode motor intent to drive robotic limbs. I'm trying to make reliable electrodes that sit in the brain and record for long periods of time that don't fail, don't induce any sort of inflammatory response, and provide this rich set of information.

We've decorated these implantable devices with an array of sensors for the goal of building next-generation prostheses that are rationally designed based on mechanical properties and the mechanical interactions of the device that occur in the brain. We've developed a whole suite of sensor technologies and we've been able to pick up, for the first time, these mechanical interactions.

One of the directions we're headed is powering implantable devices in a format that makes them practical for everyday use outside of clinical settings. If we can take all of the different technologies that are being placed in or on the body and have them all wirelessly powered and operated, patients can move around freely and begin to lead normal lives in their own homes.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?
Meng: My area of expertise is the application of microtechnologies to build new devices for clinical applications. I think it's pretty exciting that we're starting to see some of these devices—implantable pressure sensors for monitoring cardiovascular disease and drug delivery devices—produce clinical trial results. We're getting closer to seeing these technologies in the hands of patients and doctors.

Q: What new BME research avenues might you predict for the future?
Meng: What I look forward to is for us to really integrate implantable devices with the body in a truly seamless fashion so that they're biologically, electrically, and mechanically seamless. So essentially, we can produce replacement parts for the body without there being any sort of adverse reaction.

What I look forward to is for us to really integrate implantable devices with the body in a truly seamless fashion so that they're biologically, electrically, and mechanically seamless.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?
Meng: One of our greatest assets is that this community has a really rich set of supporting industries in medical devices and biotechnology. So, from an academic standpoint, this is a great place to attract students who want to make a difference and then stay in this area to work for some of these companies to produce new innovations for health care. In Southern California, we have two of the oldest BME programs in the country—at USC and UCSD. We really have a long, rich history that has been able to help the medical device industry here thrive.


UCI

Steven George *is the Edwards Lifesciences professor and director of The Edwards Lifesciences Center for Advanced Cardiovascular Technology in The Henry Samueli School of Engineering at the University of California, Irvine (UCI). He served as chair of the university's Department of Biomedical Engineering from 2002 to 2009. His research interests include tissue engineering with a focus on vascularizing tissues for in vivo and in vitro applications.*

Q: What problems are you tackling in your research right now?
George: I'm interested in engineering artificial tissues. Some are meant to be implanted to repair failing tissues and some are created to mimic a human tissue, but on a much smaller scale and for a specific type of function so we can study it to understand the function better. If you want to get complex tissues, you have to figure out a way to get them a blood supply—this is called vascularizing engineered tissues. We take human progenitor cells that can differentiate to become a variety of different cell types in the cardiovascular system. Under the right culture conditions, you can create a whole network of human capillaries, and we can get flow moving through them in vitro. We've taken that structure and put it inside an immune-compromised mouse where you can watch the mouse's vessels connect up with these human vessels. We can get blood inside the implanted tissue in about 24 hours after implant. If you do not prevascularize your tissue, it takes probably seven to ten days. The problem is that the vessels that we grow are not the type of normal network that you'd find in a healthy tissue. So we're looking for ways to make the network even more physiologic so that they behave functionally better.

For many years, I've also worked on trying to find better ways of detecting asthma and predicting when a person might be at risk for acute asthma. We just published a paper looking at ways of assessing the small airways in the lung called impulse oscillometry—pulses of sound waves that create pressure waves in the airways. The pressure pulse can penetrate the airways to different depths depending on the frequency. So using that information, you can back out information about the tissue compliance in the small airways. It looks like the smaller airways—not just because of caliber, but because of their tissue properties—are predictive of whether a person is susceptible to asthma.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?

George: Cardiovascular disease continues to be such a huge health burden in our country. The ability to figure out novel ways of treating it is a high priority. For decades, the best models of cardiomyocytes—the heart muscle cell that's damaged in a heart attack—were neonatal rat heart cells. They're different from an adult human heart cell, so how they respond to drug therapies or different interventions could be different. Now, along come human stem cells and the ability to turn them into cardiomyocytes. One of the struggles that the field is having is that when you create these heart cells from stem cells, they look more like neonatal cells. So, my lab is interested in trying to figure out how to mature them so they take on more of an adult phenotype.

Q: What new BME research avenues might you predict for the future?
George: In the next decade, induced pluripotent stem cells will revolutionize our ability to treat damaged or diseased tissue because you avoid the whole problem with immune system rejection. In principle, you can take your cells, say, from a skin biopsy and create a new tissue. The idea that we might be able to replace an organ, which is metabolic in nature rather than mechanical, that's pretty exciting.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?
George: Southern California has a wonderful community of both academic and private industry to make an impact in BME. UCSD helped us get our program started. The UC BME programs in Los Angeles, Berkeley, Davis, and ours all started around 2000, so we've all grown at about the same rate. We have a consortium of all of the programs called the Bioengineering Institute of California, and each year we have a UC systemwide bioengineering symposium.


BRIAN MORRI

Michael Khoo *is a professor of biomedical engineering and pediatrics at USC, where he served as chair of the BME department from 2003 to 2010. He specializes in cardiorespiratory system modeling, autonomic control, and noninvasive physiological monitoring and is a recipient of the Research Career Development Award from the National Institutes of Health and the Career Investigator Award from the American Lung Association.*

Q: What problems are you tackling in your research right now?
Khoo: My current projects deal with a broad spectrum of sleep-related breathing disorders (SRBDs) that ranges from classic obstructive sleep apnea (OSA) to cases where subjects just tend to not breathe sufficiently—hypoventilation. When you're experiencing OSA, you're exposed to episodes of hypoxia because your upper airway is obstructed. The individual awakens very briefly because that's the only way the upper airways can open up during sleep, and, when that happens, it triggers a fight or flight reflex. When you're subjected to these chronic spells of hypoxia and sympathetic nervous system surges, it can trigger causes of cardiovascular disease as well as disturbances in the metabolic control systems. We're developing a large-scale computational model to see how disease progresses in people who have OSA and how it can develop into hypertension or diabetes. These are the diseases of this century—obesity, metabolic diseases, and diabetes—that are attacking people right now.

SRBD is a big problem in people who are obese. So one of the things we're doing is looking at the dynamic magnetic resonance imaging (MRI) of subjects during sleep, and we try to image the upper airway as they change from wake to sleep to classify which kinds of SRBD phenotypes they belong to so that we can give the clinicians better information about what kinds of therapeutic routes they can take. We're also trying to see what the connection is between the severity of SRBD and how susceptible subjects are to impaired glucose tolerance. What we find is that SRBD is a risk factor itself for developing these glucose tolerance problems—it's not just obesity.

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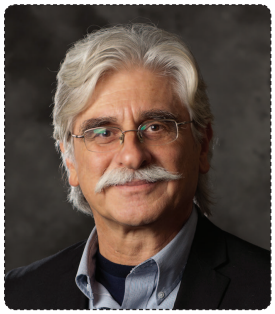
Q: What recent advances in BME research are you excited to see put to use in a clinical setting?
Khoo: In our work with the connection between obesity and SRBD, we're using noninvasive measurements such as heart rate and pulse that are sensitive to glucose in the bloodstream to predict a person's glucose intolerance. We're thinking that this can be used as a simple screening tool.

Q: What new BME research avenues might you predict for the future?
Khoo: Already, we're seeing lots of advances in the stem cell area. One of the difficulties right now is controlling how the stem cells behave. Once we understand them better, we can engineer better methods for differentiating stem cells so that they can become whatever we want them to be: cardiac cells, muscle cells. This is a major thing that will be happening in the next 20 or 30 years.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?
Khoo: Here at USC, a lot of us study systems from an electrical engineering perspective. We study control systems that get people interested in developing medical devices and imaging techniques.

Fred Grodins, who founded our program here, didn't really have any formal engineering training, but he was one of the first people to use a computer to set up models of the cardiovascular system. He developed a research program at USC for people to apply engineering techniques to study physiology. Many of us still have that ingrained into our culture, that we're more systems physiologists at heart. We're looking at problems as electrical

engineers, looking at how these systems work from a signals and systems point of view.


USC VITERBI SCHOOL OF ENGINEERING

Vasilis Marmarelis *is an IEEE Fellow and a professor of BME at the USC Viterbi School of Engineering. He founded and codirects USC's Biomedical Simulations Resource research center, which develops biomedical modeling techniques and helps to transfer those techniques to use in clinical settings.*

Q: What problems are you tackling in your research right now?
Marmarelis: We're trying to answer how information is encoded by certain parts of the brain. We believe that information is encoded as binary strings of data over time. The question is how that information is being transformed from one brain region to another. We collect data in the hippocampus—the part of the brain involved in memory formation—and the prefrontal cortex—the center for decision making and motor action, and then try to develop mathematical models that describe the transformation. The end objective is to understand information processing by neural systems, and to hopefully design an effective neural prosthesis that can help us with problems such as restoration of memory functions that are lost either through injury or aging.

California has a culture of attempting the impossible. That culture will be very conducive to the success of BME.

We're also trying to improve Alzheimer's diagnosis at the early stages when therapeutic intervention is most effective. We analyze hemodynamic data—arterial blood pressure, cerebral blood flow, and CO_2 concentration in the blood and develop computational models of the relationship among them. Alzheimer's and pre-Alzheimer's patients show a very clear impairment in CO_2-vasomotor reactivity—the process by which our brain and our cardiovascular system responds to changes in the CO_2 in our blood by increasing blood flow when the CO_2 goes up and decreasing blood flow when the CO_2 goes down. Any impairment causes severe problems in the brain. We believe that one set of such problems are neurodegenerative diseases like Alzheimer's. For the first time, we've been able to measure that impairment quantitatively with computational modeling, and our models agree with qualitative neurological measures.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?
Marmarelis: One is improvements to deep-brain stimulation procedures. This is a technique where they use depth electrodes to stimulate parts of the brain in individuals who have debilitating neurological diseases such as tremor, Parkinson's, and sometimes severe depression. Instead of stimulating with electric current, I would like to stimulate with focused ultrasound—a modality that would be noninvasive. We know that neurons are responsive to ultrasound. I view that as being a very exciting direction.

Q: What new BME research avenues might you predict for the future?
Marmarelis: I am envisioning an era of new medicine where we can analyze data and get far better diagnostic methods from computational and mathematical models of the underlying physiology of each disease. More emphasis should be given to diagnostic engineering—using engineering, computers, mathematics, and biology to improve clinical diagnosis.

Another area that has a bright future is systems biology. We've accumulated quite a bit of knowledge in molecular biology, genetic engineering, and "omics" in general. What is missing is systems biology: the integration of all these pieces of knowledge in a coherent whole that can have an impact on the diagnosis or treatment of disease.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?
Marmarelis: California has an overall culture that goes beyond any individual institution—a culture of attempting the impossible. That culture will be very conducive to the success of BME because BME, by its nature, is a cutting-edge field.

USC was the first university on the west coast to introduce BME as a formal academic department. Back in the 1970s, bioengineering was not fashionable. We were viewed with suspicion by many who were questioning our value. They could not even fathom what the field was offering. I'm gratified to see this has changed totally and drastically. BME is offering the multidisciplinary integration of different fields. Educational departments have to develop curricula that integrate the individual disciplines in the right way. This is not an easy matter.


JEREMY MCCULLOCH

Andrew McCulloch *is a professor of bioengineering and an adjunct professor of medicine at UCSD, where he was chair of the Department of Bioengineering from 2005 to 2008. He codirects the university's Cardiac Biomedical Science and Engineering Center, which investigates the molecular causes of heart failure and cardiac arrhythmia. He also cofounded Insilicomed, a company that develops predictive modeling tools to speed up the development of new medical technologies.*

Q: What problems are you tackling in your research right now?
McCulloch: We recently published an article in *Journal of Clinical Investigation* that showed how a targeted gene mutation causing dephosphorylation of a protein that's part of the molecular motor driving muscle contraction gives rise to specific early defects in heart contraction, which in turn could lead to heart failure. Using a combination of a multiscale computational model

and a knock-in mouse, we, with colleagues in the Department of Medicine, were able to predict some of the early functional changes that could be a marker for early heart failure. With the growing number of protein structures that are available, we'd like to be able to use molecular models of key proteins of interest in these multiscale models of whole heart physiology to predict how specific alterations in protein structure affect the function of the cell and the organ.

We are also testing the ability of multiscale models to predict outcomes in clinical therapies. About 10–15 years ago, cardiologists discovered that—using pacemaker technology—it was possible to improve cardiac mechanical performance in patients who have heart failure complicated by an electrical conduction delay. The problem is, it's not only a very expensive procedure, it also only works about two thirds of the time. So, we are creating patient-specific computational models of cardiac electromechanics to predict whether this procedure—known as cardiac resynchronization therapy—is likely to result in an improvement. There's some preliminary evidence that the models could be useful. We'd like to be able to apply these kinds of patient-specific models to other heart diseases such as atrial fibrillation.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?

McCulloch: Our studies to determine if multiscale models might be able to better determine which patients are going to benefit from therapy and which ones won't. Not only could it help avoid doing these risky procedures in patients who aren't going to benefit, but it may also help to identify other patients who could benefit.

Q: What new BME research avenues might you predict for the future?

McCulloch: Many people are hopeful that one of the outcomes of the new developments in stem cells will be the ability to study the patient's heart in a dish and eventually come up with better therapies. Another opportunity is that we're starting to reach a point where predictive computational models will start to find clinical utility. We'll be able to integrate a large amount of information from patients based on genomics, medical images, and other clinical measurements to develop detailed computational models of diseased organs and then use those models to better diagnose disease, predict therapeutic outcomes, and optimize therapy.

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Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?

McCulloch: One thing that distinguishes the La Jolla, California, academic community is how very interdisciplinary and collaborative it is. There are some exceptional examples on the UCSD campus and neighboring institutes—the new Sanford Consortium for Regenerative Medicine and the new Clinical and Translational Research Institute. The barriers to collaboration are much lower than in most other places because this is a young campus and a young environment. It was founded by people who had forethought and vision to realize that traditional models weren't always the most optimal for paving new frontiers in science. Early on, Shu Chien of UCSD formed the UC Systemwide Bioengineering Institute in California that was an early effort to bring together bioengineers from other academic institutions, and it helped other universities establish BME programs. We also have a large cluster of biotech companies. I think that combination of interdisciplinary science and entrepreneurs, particularly in biotechnology, is very conducive.

DANIEL KANE/UCSD JACOBS SCHOOL OF ENGINEERING

Gert Cauwenberghs *is a professor of bioengineering at the Jacobs School of Engineering at the University of California, San Diego (UCSD), where he codirects the Institute for Neural Computation. He is editor-in-chief of* IEEE Transactions on Biomedical Circuits and Systems *and program cochair of IEEE EMBC 2012 in San Diego. His research focus is on the engineering of integrated circuits and systems that interface with the human body and brain as well as computational and systems neuroscience.*

Q: What problems are you tackling in your research right now?

Cauwenberghs: My area is the interface between silicon systems and neurobiology with a recent focus on technologies for health and monitoring. The general theme is that we're developing technologies for less-invasive, more-comprehensive health monitoring and neuroscience. My research has been focusing on alternative technologies in the wireless noncontact domain. We have some extremely low-powered, low-energy wireless technologies for communicating data at much lower radiation levels. We have also recently developed biopotential sensors/electrodes that operate without gel and have demonstrated the ability to record quality, high-resolution electrocardiogram and electroencephalogram (EEG) signals through hair and through clothing. That's a major advance.

On the neuroscience side of things, we're developing silicon circuits that emulate large-scale models of cortical and other neural function at the level of the synapses and neurons, allowing us to do real-time modeling of neural function with a precision that was previously impossible even with the most advanced supercomputing technology. This is a tool for neuroscience as well as for neuroengineers—they can use these models to reduce the experimentation needed to model brain function and neurodegenerative diseases.

An example of how we're trying to couple less-invasive technologies with modeling in silicon is using inspiration from neurobiology to build silicon systems that emulate neurobiology and eventually have the systems directly interact with the brain. We're embarking on a project where we use modeling of basal ganglia and thalamocortical loops in the brain to study Parkinson's disease using EEG data, electromyogram data, motion capture, and mobile brain-imaging technologies. We're using force neurofeedback and the plasticity of the brain to work around some of the disabilities that occur in Parkinson's and other neurodegenerative diseases. This is against the prevailing paradigm of medication and deep-brain stimulation that are very intrusive.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?
Cauwenberghs: Here in Southern California, we have a very strong base of biotech and clinical neuroscience. We have a new generation of retinal prostheses that are driven by nanotechnology, and wireless arrays for recording electrical activity inside the skull for epilepsy detection. A former student, Yu Mike Chi, has now developed noncontact biopotential sensors for clinical use. There are now several companies working on wireless, noninvasive brain interface technologies to make them practical for clinical use such as epilepsy and autism research and other neurological diseases.

Q: What new BME research avenues might you predict for the future?
Cauwenberghs: I'm a firm believer that there are no true boundaries between disciplines, so a bioengineer of the future has to have a strong foundation in electrical engineering, mechanical engineering, computer science, cognitive science, neuroscience, and neurobiology. Electrical engineering is central in the design of experimentation and of systems for disease remediation. The interface between electrical and bioengineering cannot be overemphasized.

Electrical engineering is central in the design of experimentation and of systems for disease remediation.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?
Cauwenberghs: At UCSD, there is a strong basis in systems bioengineering in proximity with a very strong biology program, which gives an infusion of the natural sciences. The multiple interfaces are what allow students to benefit from the synergy between different disciplines. A strong training aspect for students is the opportunity for internships in industry as well as in labs of investigators at UCSD, the Salk Institute, the Scripps Research Institute, and others.

We have not only strong biotech in Southern California, but also a very strong wireless industry. At this interface, there is increasing interest in wireless health technology. From my perspective, besides using wireless technology for health science, it's also important to understand the impact of wireless technology on health.


JOHN HANACEK

Lucila Ohno-Machado *is the founding chief of the Division of Biomedical Informatics at the UCSD's School of Medicine. She is also an associate dean for informatics and technology, director of the Biomedical Research Informatics for Global Health Program, and editor-in-chief of the* Journal of the American Medical Informatics Association.

Q: What problems are you tackling in your research right now?
Ohno-Machado: One thing we're working on is a data-sharing infrastructure to make medical data accessible—in a way that preserves patient privacy—so that machine-learning researchers, statisticians, and other quantitative researchers can apply and test their algorithms on real data. This is part of a national center for biomedical computing called Integrating Data for Analysis, Anonymization, and Sharing (iDASH). We are also building a means to build predictive models using data in distributed research networks to assist with personalized medicine.

Current legislation requires the removal of 18 patient identifiers from medical records. That sometimes makes it problematic to extract patterns from this data. For example, if people are over a certain age, you can't disclose the exact age because there are so few of them and the risk of identification is bigger. So it is good to have some protection of privacy, but in many cases it disturbs the kind of study that you're trying to do. The idea is that a person could select the level of risk of reidentification that they're comfortable with.

We need to do a demonstration of this system first and clearly resolve the policy and patient participation issues before we can extend this elsewhere. But the technology exists, and the intent of patients to make their data contributions to society is there. What is not there is a framework to put the minds together to develop a coherent, sensible, and legal way of doing this.

Another research focus is when you give a risk estimate or a prognostication to a patient, how to determine that that number is correct. We're working toward having better methods for evaluating the calibration of predictive models since they are being increasingly used in practice. That's where you need the big data so that you can actually shorten the confidence interval.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?
Ohno-Machado: The understanding of the genome—coding and noncoding portions of the DNA—and how biological regulatory networks work are very exciting in terms of the potential to be used in clinical practice.

Q: What new BME research avenues might you predict for the future?

Ohno-Machado: Ten years from now, we won't believe that we couldn't access certain data for research because of proprietary issues or technical impediments. The amount and the quality of data will be so much better because we will be able to compare notes and recheck things. I can see a future where a patient logs into a device and can have his or her record be seen by others anywhere in the world, translated into whatever emergency department they end up in, and be treated just as if they were in their hometown. Then the product of that encounter adds to the amount of data and knowledge that we can derive so that we accelerate the pattern recognition.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?

Ohno-Machado: The amount of collaboration across research groups here is much higher than what I've seen before, and crossing boundaries between engineering, medicine, and biology is much easier too. The biomedical informatics division was long overdue. Once it did open and we reached out to the computer science, engineering, and biology departments, they received us very well.

The innovation in training programs—the ability to get away from strict curricula and adapt to individual, academic, and industry needs—is high too. BME is evolving so fast that, unless you keep up with what the trends are, you are teaching people things that are no longer relevant.

UNIVERSITY OF CALIFORNIA ARCHIVES

Jerome Schultz *is a distinguished professor of bioengineering in the Bourns College of Engineering at the University of California, Riverside, where he helped found the Department of Bioengineering in 2004 and is director of the university's Center for Bioengineering Research. In 2008, he was recognized by the American Institute of Chemical Engineers as one of the top 100 chemical engineers of the modern era.*

Q: What problems are you tackling in your research right now?

Schultz: I'm working with a physicist, Kanetada Nagamine, to develop a method for noninvasive imaging using a particle called a muon. We have some evidence that we can use this particle to detect the degree of oxygenation of blood and different tissues. This detection method would be an alternative to functional MRI, which also attempts to determine oxygenation of different tissues but by an indirect measurement. The muon technique is noninvasive and, since the radiation is very weak, it is very safe. The method could be used in a tomographic manner to acquire three-dimensional imaging of oxygenation levels in tissues and could lead to treatments of patients after a stroke. It possibly might assist in the treatment of cancer by radiation, the effectiveness of which appears to be related to tissue oxygen levels.

I've also been developing a method of measuring glucose in tissues by an optical technique. It would work by placing a tiny capsule under the skin that contains chemicals that fluoresce when illuminated. The dyes are selected so that the extent of their fluorescence is related to the blood glucose level. One could envision a watchlike device that could give readings of the glucose level continuously so that diabetics could manage their blood glucose without pricking their fingers.

In Southern California, there are hundreds of companies engaged in biomedical device research and intense entrepreneurial activity.

Q: What recent advances in BME research are you excited to see put to use in a clinical setting?

Schultz: The most exciting research is the use of stem cells for regenerative medicine—being able to take stem cells and reprogram them to have desired functions. The engineering challenge is how to retrieve the cells from the body, how to store them, and how to promote their growth in a way that's reproducible so that they can be used in medical settings for different purposes. Instead of treating people with drugs, you'd be treating them with preprogrammed cells. It's possible to take stem cells from another person and reprogram them so that they wouldn't be rejected by the immune system of the recipient. Another research goal is the development of a banking method for stem cells, similar to blood banks.

Q: What new BME research avenues might you predict for the future?

Schultz: In addition to regenerative medicine, there's hope that DNA sequencing may enable the creation of genetic profiles of individuals that might determine their susceptibility to certain diseases, to develop individualized treatments, and to try to prevent those diseases from taking place.

Q: What distinguishes the Southern California BME research community and educational programs from those in other regions?

Schultz: California accounts for maybe 25% of the total pharmaceutical and biomedical device research effort in the United States, and much of it is centered in Southern California. In Southern California, there are hundreds of companies engaged in biomedical device research and intense entrepreneurial activity. There's a culture of business people connecting with universities and entrepreneurs. It's not surprising that every major university in this region has a BME program, including some of highest ranked programs in the country.

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