Medical Engineering: A Moral Obligation

They come from diverse backgrounds, have followed unique paths, and do their work in a host of engineering and applied science disciplines, but a common denominator among the faculty of the newly formed Caltech Medical Engineering Department emerged with stunning clarity in *ENGenious*'s interviews with them: These are people with a strong moral compass who are passionate about making a positive impact on society.

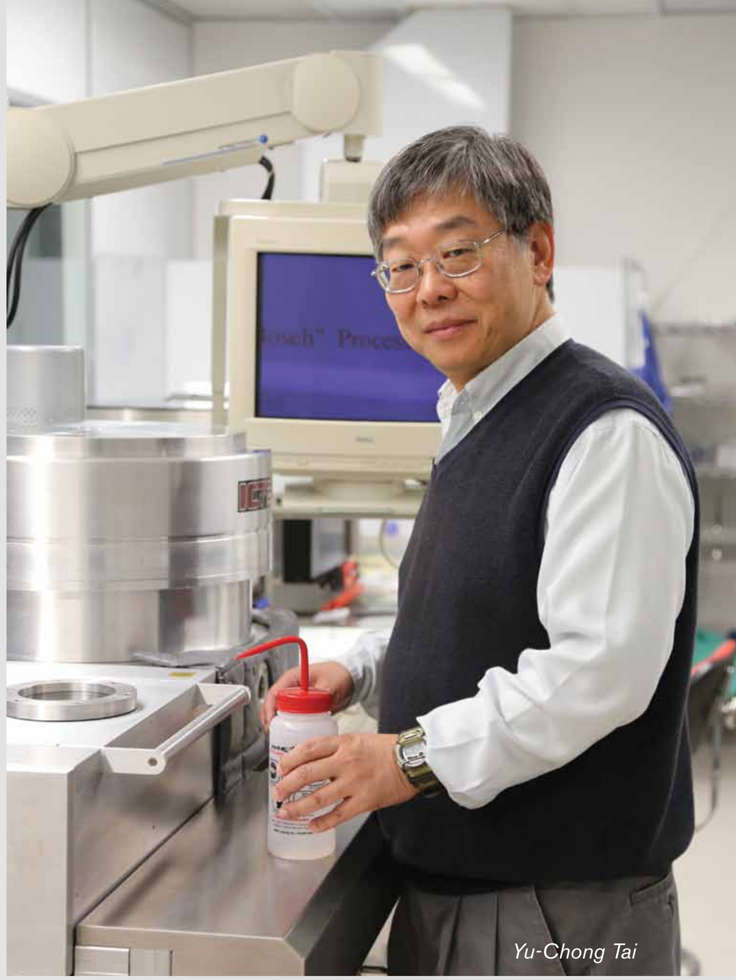
They have been working at the frontiers of translational medical engineering for years, drawing on their expertise in a wide range of fields, including electrical, aerospace, civil, mechanical, and chemical engineering as well as applied physics, materials science, and chemistry. Starting with the fundamentals of basic science and engineering and by potentiating the faculty's individual efforts, the new department aims to more efficiently leverage the research at Caltech to lower the technological barriers to diagnostics and treatment, as well as their cost. The faculty's conversation with *ENGenious* took many directions as the researchers discussed their work and its applications, including reducing patient stress, simplifying devices, and volunteering in a hospital.

ENGenious started the conversation with the Executive Officer of the new department, Yu-Chong Tai, Anna L. Rosen Professor of Electrical Engineering and Mechanical Engineering. "There are more than 60 accredited biomedical engineering programs in the United States, and there are about 100 biomedical programs in various universities and institutes," he notes. "However, from my experience, I think Caltech really has an opportunity. At other institutions they try to cover the entire biology side and take care of the engineering side, but this means the programs are often shallow on both sides. This is an issue because a lot of the work we want to do has to rely on deep engineering. That's our strength at Caltech. Our intention is to build the Caltech Medical Engineering Department in a way that is rooted in really first-class engineering and move toward medical applications."

Several of the faculty interviewed had strong views on how medical engineering at Caltech will be different from similar programs in biology. Many emphasized that the two disciplines are complementary but serve different purposes.

"Medical engineering is top-down," says Morteza Gharib, Vice Provost and Hans W. Liepmann Professor of Aeronautics and Bioinspired Engineering. "We look at the problems that are currently challenging to the field and try to come up with devices and techniques to help clinicians do their job better or make breakthroughs. Biological engineering is bottom-up; it tries to understand how biology works and then builds upon that to get to the point where it can contribute to the field. Basically we're looking at the same wall from two different sides."

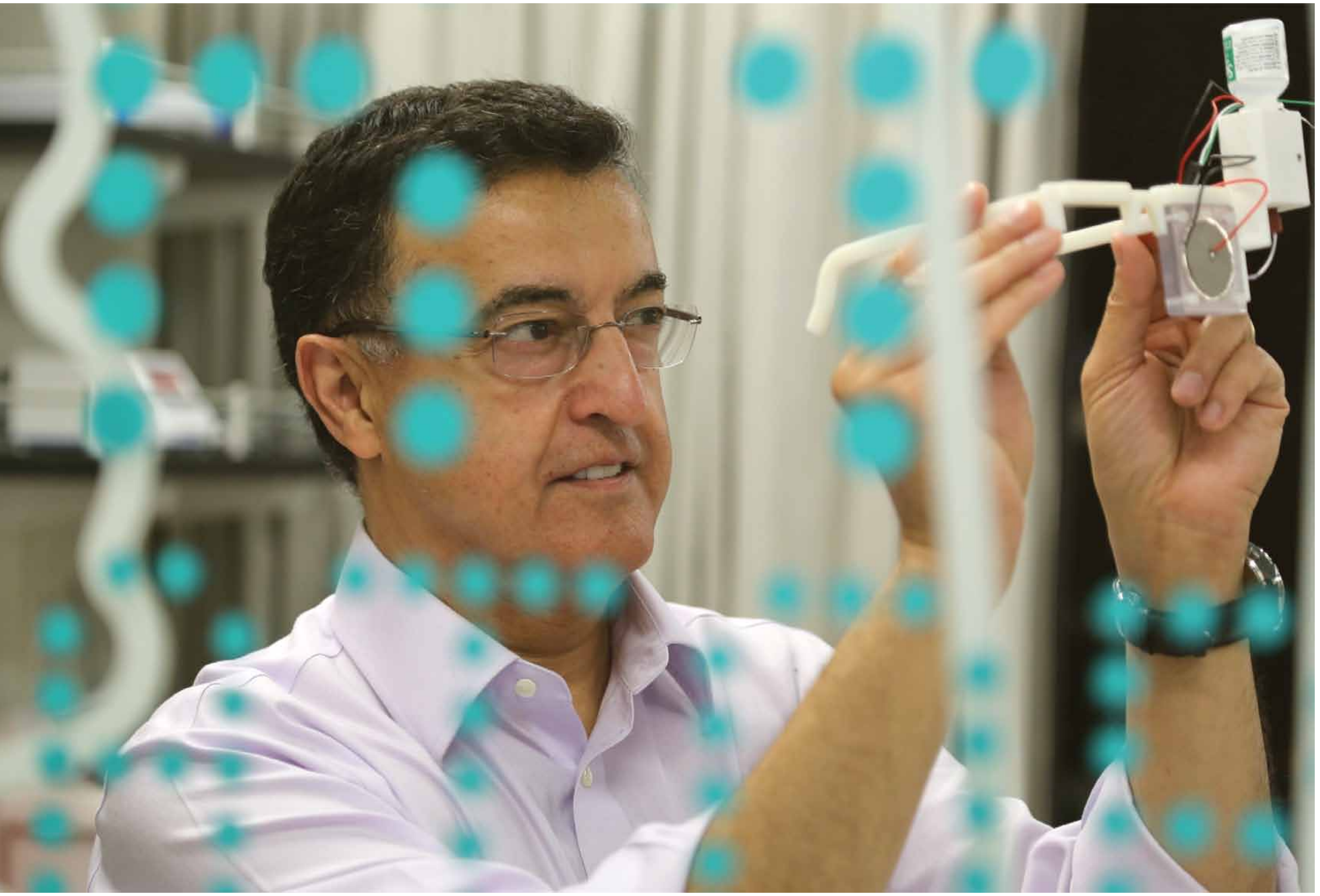
Consolidating the efforts on Caltech's side of the wall creates an



Yu-Chong Tai

> *"We have a cell phone that can do anything, but implantable technology is still in the Stone Age."*

Yu-Chong Tai, *Anna L. Rosen Professor of Electrical Engineering and Mechanical Engineering; Executive Officer for Medical Engineering*



Morteza Gharib

We're trying to learn the tricks of nature to come up with new physiological machines that are built out of your own cells, so they're not foreign to you.

Morteza Gharib, *Hans W. Liepmann Professor of Aeronautics and Bioinspired Engineering; Vice Provost*

opportunity "to combine the technology development that we do in Engineering and Applied Science (EAS), in particular, with a more focused approach on applications than you typically have," says John Dabiri, Professor of Aeronautics and Bioengineering. "This is a chance to apply what we do well to the tools used for treatment in 'the real world.' In many respects, we're going to be providing an outsider's perspective. That can be helpful. For many diseases we just need fresh ideas, and Caltech is well poised to provide them because we haven't been staring at the same problem for 20 years."

Nobel laureate and the Victor and Elizabeth Atkins Professor of Chemistry and Chemical Engineering Robert H. Grubbs also points out the advantages that Caltech engineers could bring to the field of medicine. "Biology today is very attuned to medical problems, which happened naturally," he says. "What hasn't happened naturally is getting engineers and basic scientists involved in medical problems. I see the new Medical Engineering Department at Caltech defining these kinds of medical problems. And there are an amazing number of them. On a somewhat regular basis I recruit seven or eight Caltech faculty and we fly up to San Francisco to spend a Saturday with a group of clinicians who are heads of departments. Every time, it amazes me that these very busy professionals take the time to sit with us and define different medical problems that we can collaborate on."

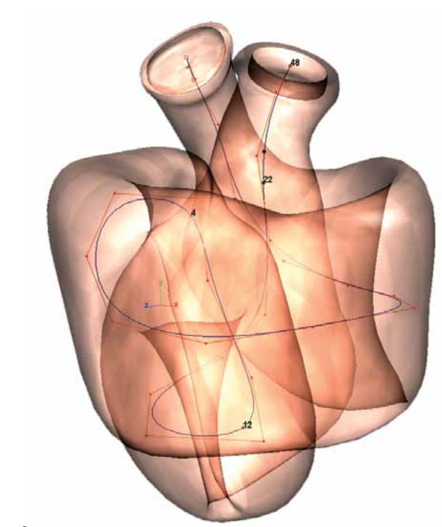
Professor Ali Hajimiri coined the phrase medical engineering at Caltech. "Bioengineering is rooted in biology and chemistry," says the Thomas G. Myers Professor of Electrical Engineering. "The medical engineering side of things is rooted in engineering; it starts from an application and tries to solve the problem using the tools that we have at our disposal. We want to solve medical problems by leveraging our engineering expertise."

For example, "How can we make batteries that can be implanted into the body and power a heart valve?" asks Julia R. Greer, Professor of Materials Science and Mechanics. "To do that, multiple systems have to synergistically work together: the materials have to be biocompatible, the power output has to be just right, there has to be no biofouling, the data acquisition and analysis has to be handled, etc. That's how all of these disciplines work together."

"The difference is whether your endpoint is to understand biology better, or to contribute to medicine," says Professor Tai. "For example, when I work on micro implants, I want to build an electrical device that can stimulate local nerves, and neuroscience is very focused on electrical stimulation. But when we make the device, we need to figure out how it should be shaped and how flexible it should be and how high the voltage should be and how much carbon there needs to be and what's the current distribution? All these are heavy on engineering. Even our colleagues from the biomedical engineering department cannot deal with the depth of these issues like we do."

Professor Tai's work on developing a zebra fish electrocardiography (ECG) device exemplifies both the depth of which he speaks and the urgency he attaches to human applications.

"Our angle is human," he says. "That's why we wanted to study the



Virtual mechanical heart developed in Professor Gharib's research group

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John O. Dabiri, *Professor of Aeronautics and Bioengineering*

John O. Dabiri

zebra fish heart. If you cut off or damage 20% of the zebra fish heart, it recovers 100%. With a human heart, if you have even minor damage, you may die. How does a fish do that? One thing we have to do to understand that is monitor the health of the heart 24/7, so we can see how fast and in which way it recovers. When we first wrote the proposal, nobody had ever measured the ECG of a zebra fish, so we had to figure out how to do it. We had to make really small microelectrodes, place them as close to the heart as possible to get the biggest signal, and do very deep analysis on the metal and the tissue interface, which involves electrical impedance. My students eventually developed a wireless ECG device that we can attach to the fish and it still swims and does its normal activities while we get an ECG."

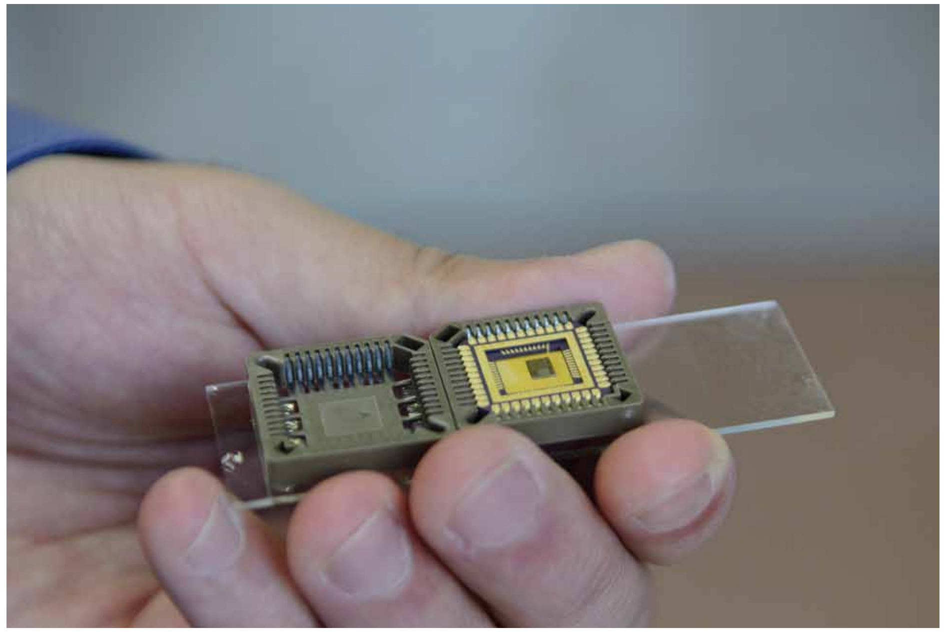
The significance for humans, says Professor Tai, is that "cardiovascular doctors want a 24/7 distributed ECG device, because cardiovascular problems evolve and move from point to point. It doesn't matter if it's wearable outside or implantable inside; the key word is 'distributed,' so they can detect gradual change in the heart. All my colleagues believe that a small, simple ECG that can be implanted is totally doable. We have a cell phone that can do anything, but implantable technology is still in the Stone Age. If our only focus is to understand the problem, and not to provide devices for a larger population, that to me is a shame. Medical engineering is not about building the first 90 yards and forgetting the final 10. We want to go the full 100 yards in reaching people. It's not okay to say that all I want is to study a problem right out of a paper. That's not biomedical engineering for us."

Professor Gharib shares both Professor Tai's perspective and his interest in solving medical problems related to the heart. "My group and I contributed in a very fundamental way to the design of heart valves that are available on the market today," he says, "but at some point I also realized we need to go back and see how nature builds heart valves, so that's how I got into this area of engineering. The heart for me is a special place because my training is in fluid mechanics and life is aquatic. It depends on the transfer of the material from nutrients to oxygen to taking the waste away. Of course, every vessel has flow, but the heart is the most fascinating dynamic entity in that respect. It's still one of the biggest challenges in medicine to have a pump that acts like a heart and that is natural to the human body. That is far from reality, but it's basically a moral obligation for engineers and scientists to look at all these problems and see how they can use current knowledge to contribute to improvements. What we're trying to establish here is a new direction for medical engineering. That's a big challenge, but Caltech has a clear advantage because of the years of research that we have already done. We are trying now to consolidate our gains and train a new generation of students who are going to be better than us. We're trying to learn the tricks of nature to come up with new physiological machines that are built out of your own cells, so they're not foreign to you. We are concentrating on how to create a micro environment like the one that nature provides when the heart grows in embryonic stages."

Imagine when you can buy a reader and then, for about a buck, you can buy a cartridge with the sensor in it that tests for lung cancer, tuberculosis, or hepatitis C. You put it in, it runs the test, and then you throw it away. They would be like apps for your smart phone.

Ali Hajimiri, *Thomas G. Myers Professor of Electrical Engineering*

Ali Hajimiri



Hajimiri's handheld medical diagnostic test cartridges

When working with him as a graduate student, John Dabiri was fascinated by Professor Gharib's application of aerodynamic concepts to the human body. He welcomed the chance to collaborate on what he describes as "probably my first foray into the application of engineering concepts to the human body" after they became colleagues. "When I was just starting on the faculty, he and I published a paper on how you can study blood currents to diagnose heart failure," says Professor Dabiri. "The challenge in many forms of heart failure is to diagnose it at earlier stages than we do now, and to develop techniques that will allow us to make that diagnosis in a way that's less expensive and not invasive. When you have heart failure, the blood flow is one of the first things to start changing, and it's a signature that potentially you can measure from outside the body. Studying the blood flow might tell us earlier than some of the methods that are used today that someone's on the path to heart failure."

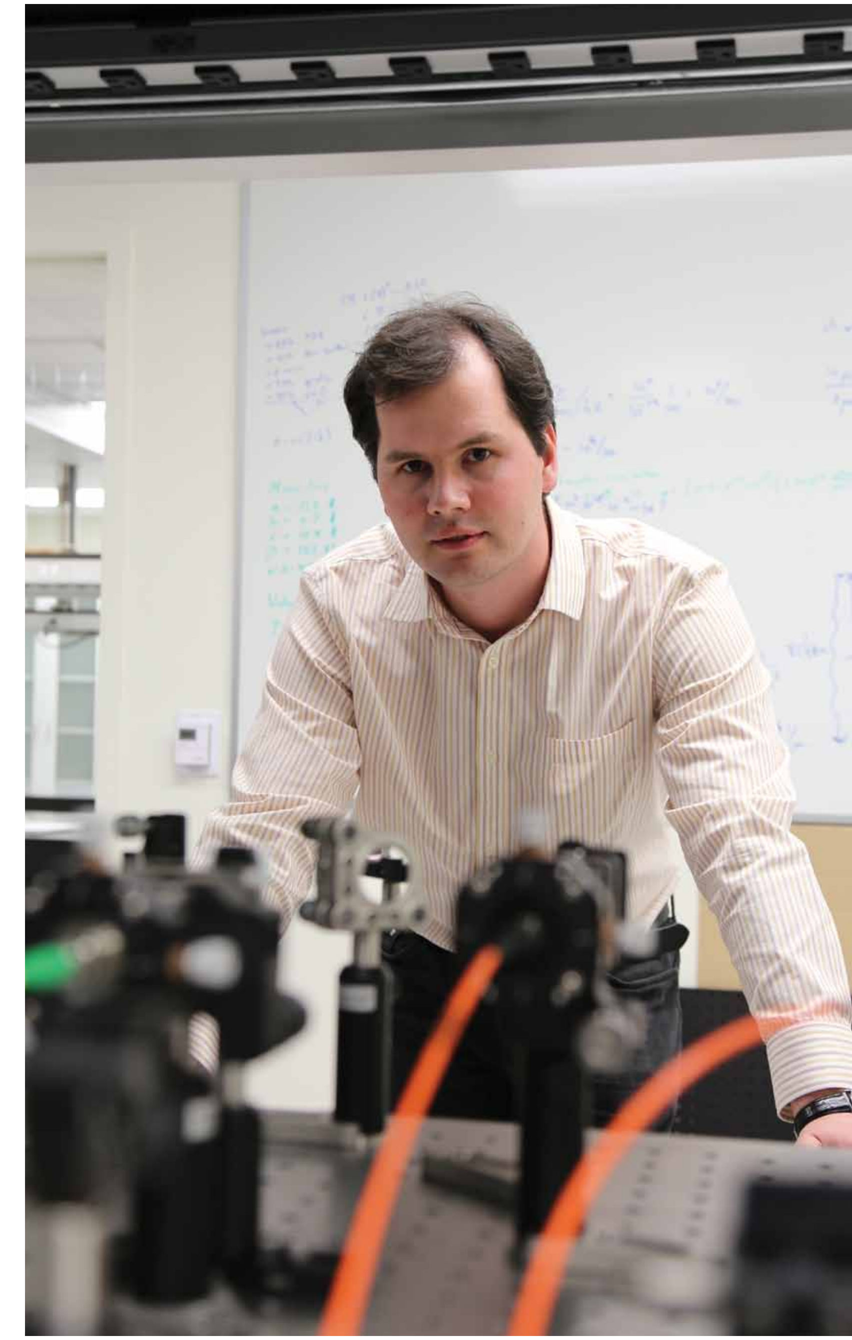
Professor Dabiri paints a vivid picture of the key process. "You have a jet of blood that comes from the left atrium into the left ventricle, two chambers of your heart, on each heart beat," he says. "It creates a vortex like a swirling doughnut of blood, and the shape and size of that vortex is correlated with disease, so you can study that to determine how well the heart is functioning. What is it about a certain shape and size of that blood vortex that leads to healthy function? The immediate goal is simply to be able to tell people that they're sick, because many people don't realize it until it's too late, but a long-term goal is to find a corrective measure that could restore that function. The uniqueness of Caltech is that we have expertise in both fluid dynamics and the types of technologies that will be required to image and measure that blood flow, and we can combine them for the benefit of our clinical partners."

Professor Dabiri finds today's students as excited about the possibilities as he was, and is. "We have students who are really passionate about fluid mechanics, for example, but some of them want to know that the work they're doing has an impact on people's quality of life," he says. "Medical engineering is going to be one of the places where the research we do in EAS affects all of our alumni and friends because, if we're successful, it's going to mean a better quality of life for all of them."

Professor Hajimiri also sees the diversity of disciplines in medical engineering and their potential applications as a lure for "students who have strong physics, math, and engineering backgrounds that they would like to apply to a medical problem. This is really a discipline that's designed for them, in the sense that they can take their strengths, combine them with the knowledge of the medical side, and apply them to a medical problem."

His own experience is a model of intellectual diversification. "A few years ago, I got really interested in biology and started going to Caltech undergraduate classes and taking labs with the students," he says. "Then I took some grad-level labs and did several projects, and based on that experience, I made everything in our wet lab. That's really helped us with the biosensors that we develop. Now that we understand both the electrical and biological sides of it, we have a much larger possibility to do research. If we have a problem with the electrical system, modifying the biological side could help. Likewise, if you have something that's very difficult in biology, we can come up with a solution by modifying the electronics. When you do both sides, you come up with things that are much more globally optimum."

Professor Hajimiri describes four medical engineering areas in which he works—biosensors, drug delivery, bioinspired engineering, and terahertz imagers—as "very hot right now." Biosensors can be used "to make a very low cost handheld device for diagnosing a lot of different diseases," he says. "We have actually made the reader, using CMOS (complementary metal oxide semiconductor) transistors, a standard technology, to make it very low cost. We also developed all the biochemistry for making electronic chips into biosensing chips.



Andrei Faraon

> *We are developing tools to deliver light into living brain tissues and to monitor the activity using quantum photonic devices for ultra-sensitive detection of magnetic fields.*
>
> Andrei Faraon, *Assistant Professor of Applied Physics and Materials Science*

Julia R. Greer

How can we make batteries that can be implanted into the body and power a heart valve?

Julia R. Greer, *Professor of Materials Science and Mechanics*

Imagine when you can buy a reader and then, for about a buck, you can buy a cartridge with the sensor in it that tests for lung cancer, tuberculosis, or hepatitis C. You put it in, it runs the test, and then you throw it away. They would be like apps for your smart phone. A lot of these tests now have to be done in a lab. Think about the demand there could be for these readers around the world. The key is that we are leveraging electrical engineering and biochemistry to create this device that has medical applications."

In therapeutics, Professor Hajimiri is using magnetic particles for drug delivery in the brain. "We have developed a sophisticated dynamic magnetic manipulation setup that allows us to 'navigate' magnetic particles any way we want. We are in the process of using this in collaboration with some researchers from City of Hope to deliver drugs to the targeted cancer sites under a National Institutes of Health (NIH) grant. This will significantly improve the efficacy of the drugs and minimize their side effects."

In the field of bioinspired engineering, Professor Hajimiri explains, "we've created systems that are really self-healing. They respond to variations in the system as well as destructive events with no external human interference. We hit them with high-powered lasers that destroy parts of the chip, and the chip finds a way of recovering and still functioning. A chip that's not designed for this purpose would fail if it loses one transistor out of half a billion."

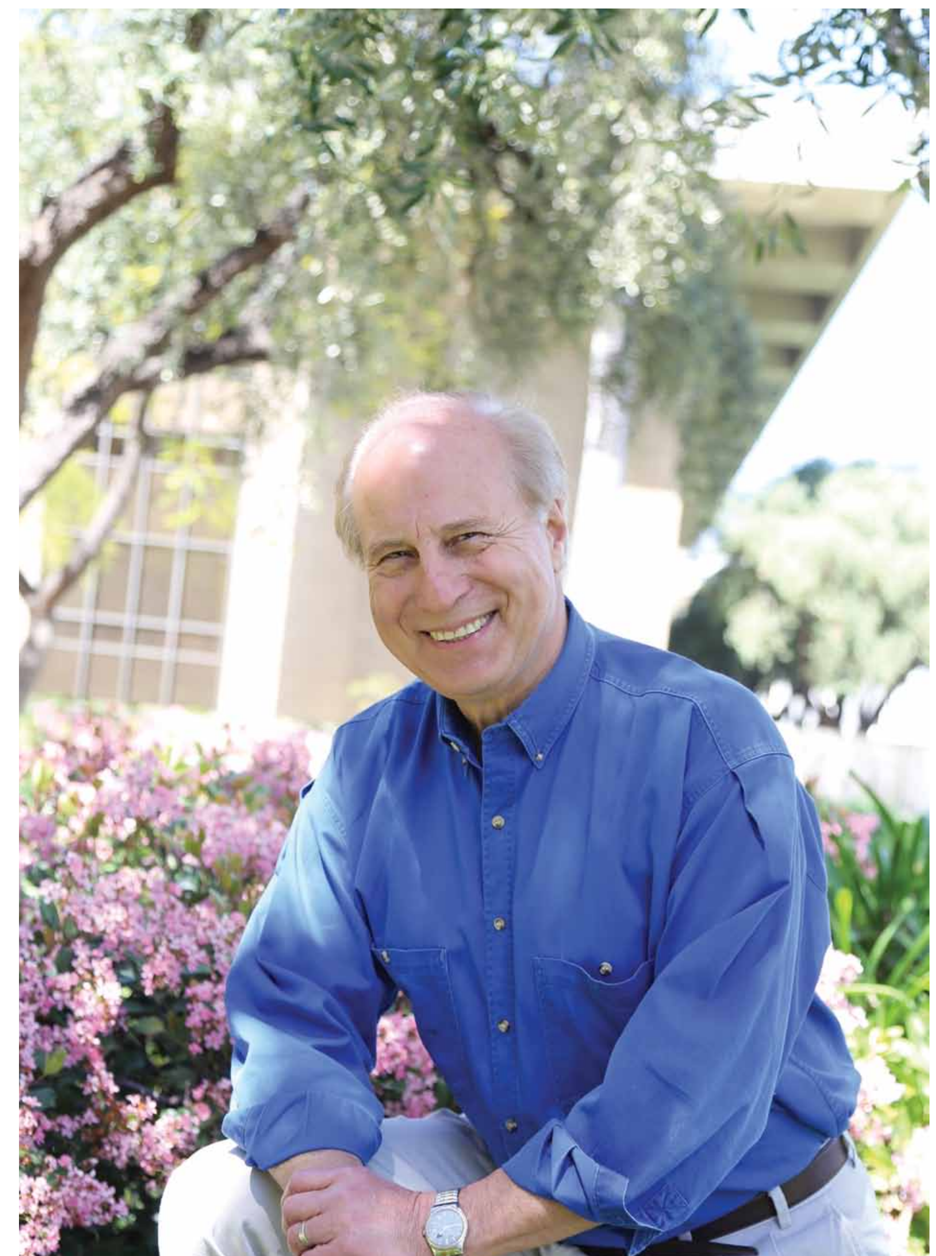
CMOS technology was also used in the Hajimiri group's terahertz imager to keep its cost low. "The behavior of certain kinds of skin cancer is different from regular skin, so you can use this as an early-detection and screening device," he says. "You can scan it across your skin and see if there are any points that need to be checked by doctors. We've also looked at that for other kinds of microscopy and imaging systems. Unlike X-rays, terahertz radiations are non-ionizing, which means that they do not induce chemical change because the photon energy is low. It's a much less damaging kind of radiation for imaging."

Andrei Faraon, Assistant Professor of Applied Physics and Materials Science, is interested in photonics, specifically biophotonics, which he describes as "using photonic devices to learn more about biological systems for diagnostics and to control biological functions." He is collaborating with Michael Roukes (Robert M. Abbey Professor of Physics, Applied Physics, and Bioengineering) in developing nano-scale photonic devices for sensing of biological reactions at the single-cell level.

"The neuroscience community recently started to use light to control brain function," Professor Faraon explains, "and currently there is a large nation-wide initiative to map the entire brain and understand how it works. Toward this end, we are developing tools to deliver light into living brain tissues and to monitor the activity using quantum photonic devices for ultra-sensitive detection of magnetic fields."

We're bringing together hospitals, distributors, manufacturers, and clever Caltech design to constantly improve our wheelchairs and make them cheaper. . . . To me, that's the key to great innovation.

Kenneth A. Pickar, *Visiting Professor of Mechanical and Civil Engineering*



Kenneth A. Pickar

Working at the same scale as Professor Faraon but toward a different end, Professor of Materials Science and Mechanics Julia Greer has "started interacting with several neurologists in trying to develop submicron- and nano-scale devices for cell or neuron manipulations," she says. "We are making a 3-D platform scaffold for intracellular interrogation by electrical and optical probes. We recently acquired an amazing two-photon lithography tool that allows us to print nano- and micro-structures in three dimensions. This has opened up a rich set of opportunities for biomedical applications."

Professor Greer is also interested in researching "smart materials that can be compatible with the body and help heal and monitor disease." Specifically, her team has been working on creating three-dimensional scaf-

Azita Emami

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Azita Emami, *Professor of Electrical Engineering*

folds for cell growth and migration, using magnesium, a biocompatible metal, and hydroxyapatite, a mineral that comprises up to 50% of bone by weight. "These scaffolds will help us understand the processes of bone formation," says Professor Greer. "We can then learn how and why bones break and maybe figure out a way to delay and prevent failure. Once we have studied these phenomena at the fundamental level, we will be able to create artificial bone scaffolds that the natural bone will grow through and around, and strengthen it without having to take the scaffold out."

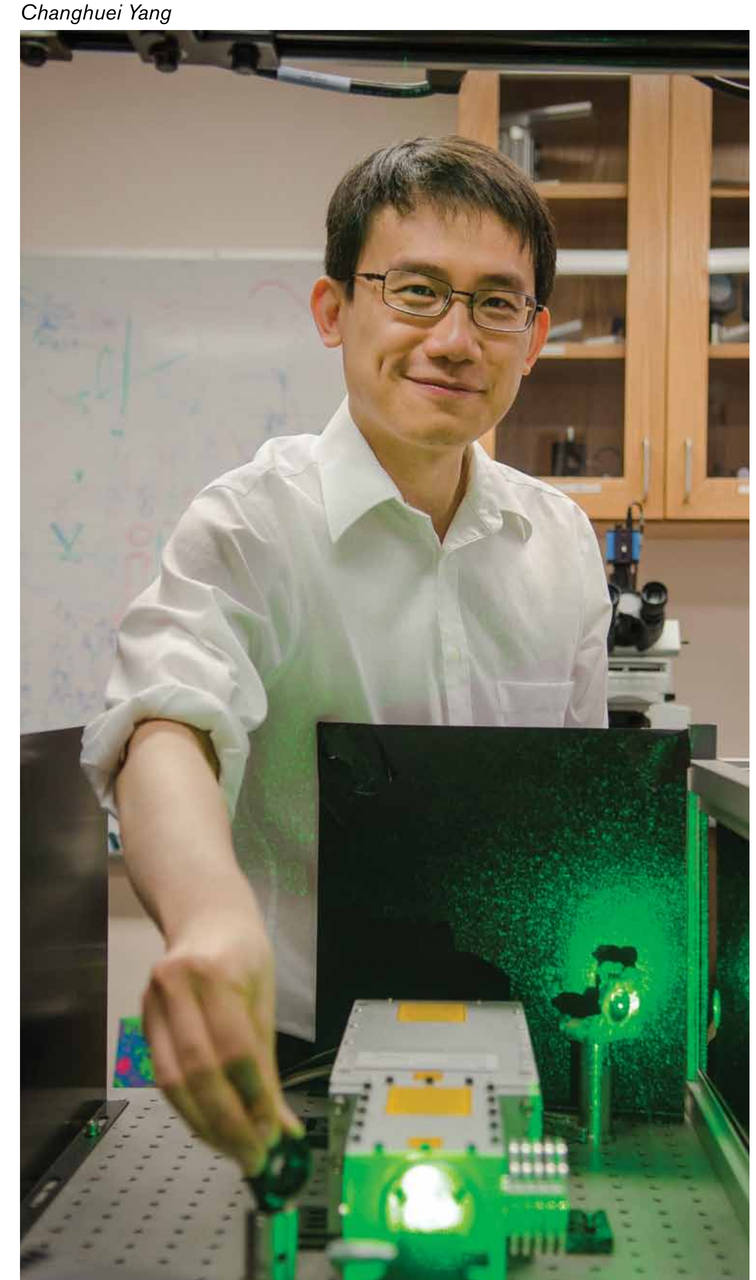
In addition to working with researchers such as Professor Greer, students in the new Medical Engineering Department would have the opportunity to take a unique Caltech course called Product Design for the Developing World taught by Kenneth A. Pickar, Visiting Professor of Mechanical and Civil Engineering. Professor Pickar's medical engineering interest is in "rehabilitative devices that either help people recover from serious injury or enable them to function to the best of their abilities."

Professor Pickar, who has many years of experience in taking students to developing countries, explains that "it was pretty obvious that there were big gaps in Guatemala and India on things that we take for granted here, which my students have attempted to fill by observing actual problems and then working backwards from that. For instance, their wheelchairs were very poorly designed for the environment, were flimsy, and were either free or way too expensive."

The problem is making affordable wheelchairs that are adapted to the environment. "We're scaling our wheelchairs so we can make them cheaply, employing bicycle parts in the critical regions," says Professor Pickar, "and we're bringing together hospitals, distributors, manufacturers, and clever Caltech design to constantly improve our wheelchairs and make them cheaper. Uniting engineering and the delivery of medical care gives us a better chance of becoming problem-centered and coming up with new technologies. To me, that's the key to great innovation."

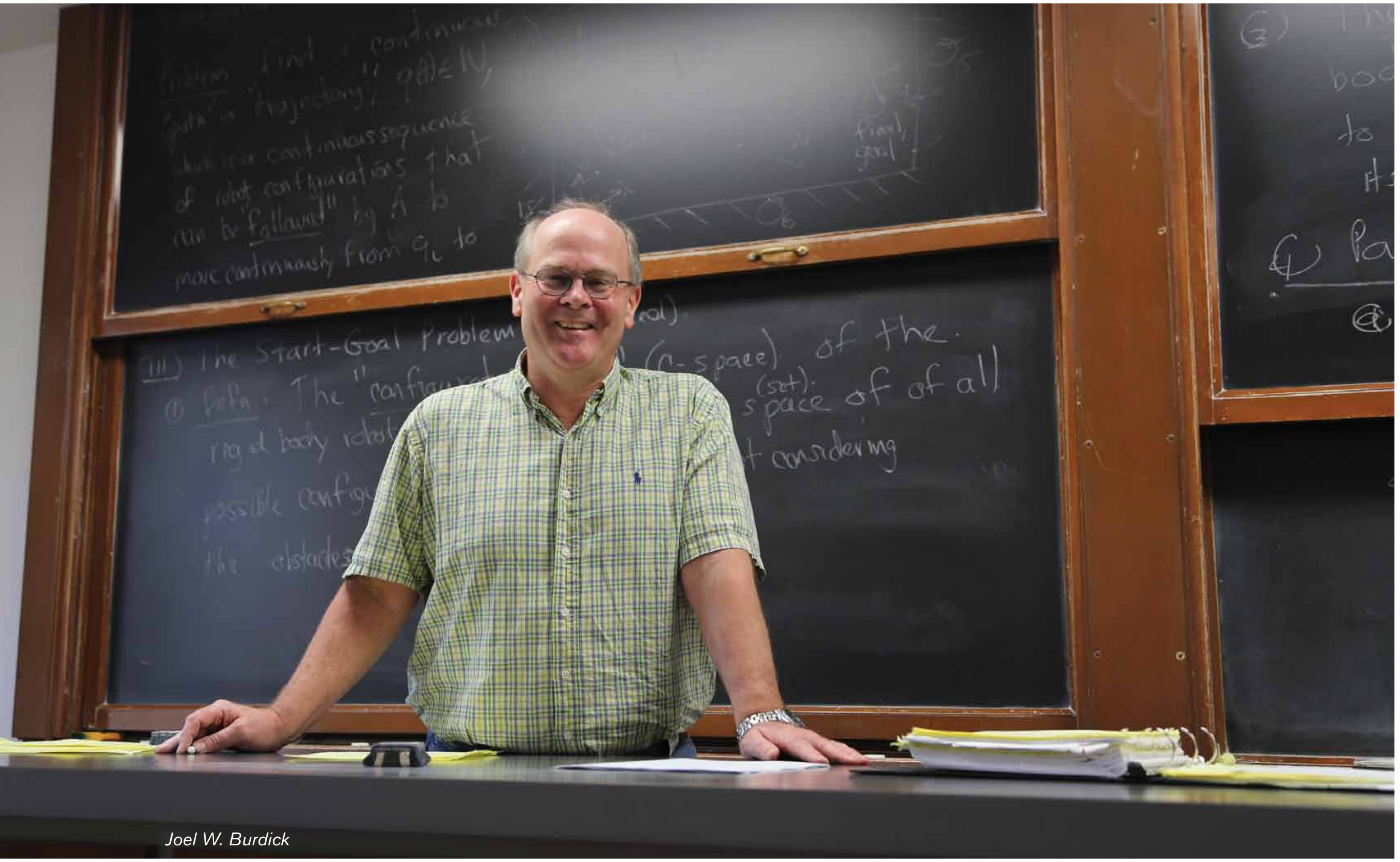
"Problem-centered" is also an apt characterization of Azita Emami's work on implants. "As electrical engineers, we can have a huge impact on medical engineering," says the Professor of Electrical Engineering, "because any system you want to build that monitors or actuates or senses needs electronics to process the information or provide the data for the system. The challenges are very similar to those in other high-performance electronic systems, in terms of trying to make your system energy-efficient, accurate, and able to transfer

Changhuei Yang



"I especially love it when I sit down with a clinician who starts complaining about a specific problem he or she has. Then, 30 minutes into the conversation, I am finally able to parse it into a sufficiently detailed engineering problem. From then on, the conversation usually becomes a series of light-bulb moments."

Changhuei Yang, *Professor of Electrical Engineering and Bioengineering*



Joel W. Burdick

> *We're interfacing with the human nervous system, which communicates and processes data based on both chemistry and electrical impulses. The big pharmacology companies have done a great job of pushing the chemical end, but there's a variety of other nervous system disorders that may benefit from more sophisticated implantable devices that modulate the electrical activity in nerves.*

Joel W. Burdick, *Richard L. and Dorothy M. Hayman Professor of Mechanical Engineering and Bioengineering*

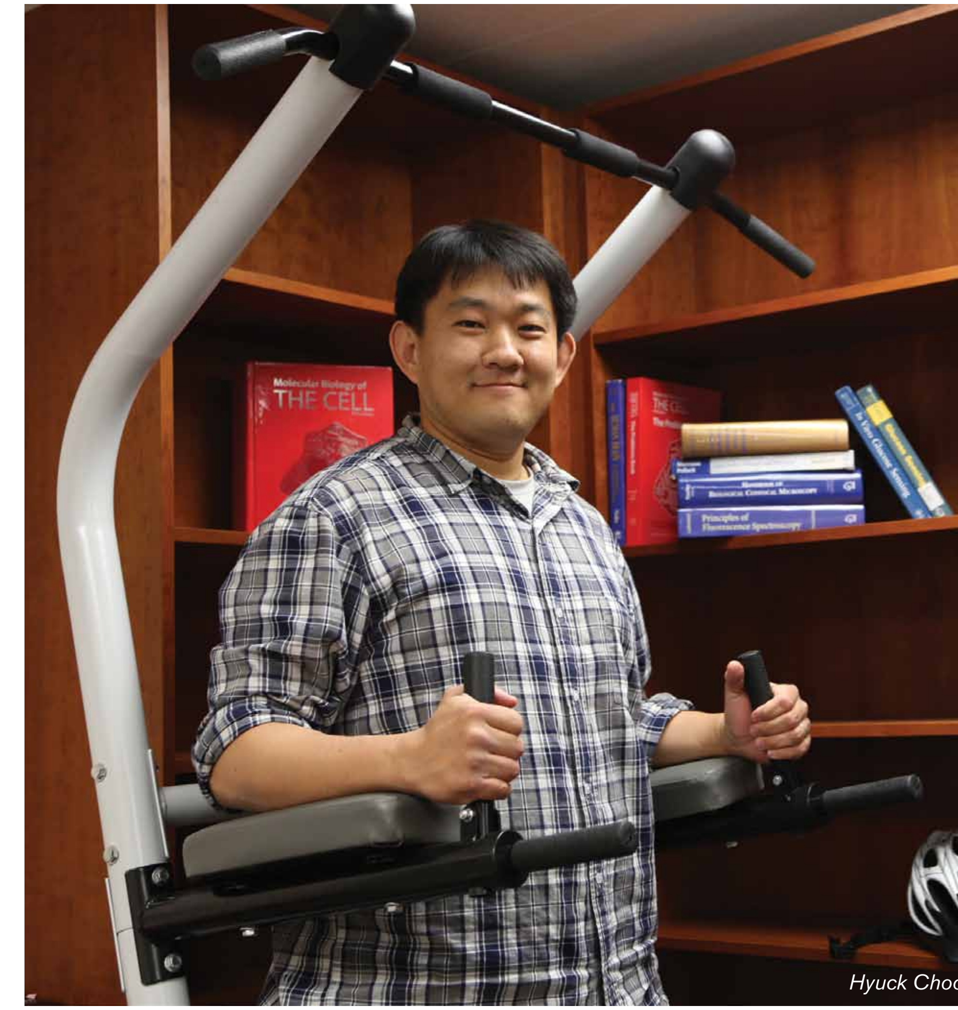
and communicate information. I started working on implants for neural stimulation and neural recording, in particular the retinal implant project, when I came to Caltech, and that motivated me to think about building minimally invasive, high-performance implants, drug delivery systems, and wearable devices that can adapt to our body both electrically and mechanically."

The products she envisions would be modular, low cost, and easy to use. "We want to come up with novel techniques to connect and integrate smaller components efficiently and use origami folding and unfolding techniques," she says. "We want to attack problems with an engineering angle that is exciting and difficult. Also ones that lead to strong PhD projects. The electronics in these modular and adaptive systems are extremely challenging, so we'll have interesting problems to solve."

Changhuei Yang is especially gratified when he aims his expertise at a medical target. As the Professor of Electrical Engineering and Bioengineering puts it, "I like to work on pretty much anything for which my group's optical and microfabrication expertise can significantly address medical needs."

He is currently pursuing two major lines of research with his group. One is a self-imaging petri dish that can stream microscopy images of cell cultures out of the incubator. "The ePetri is an exciting technology that can cut down on labor and contamination risks in diagnostic labs," says Professor Yang. By redesigning the petri dish to incorporate an inherent imaging capability, this technology opens up opportunities to perform diagnosis and experiments in ways that were previously impractical. For example, the ePetri has an inherent field of view that is orders of magnitude larger than that of standard microscopes. This makes it easy to keep highly motile cells in sight with the ePetri, while a standard microscope would have a hard time following those cells.

The other line of research in Yang's laboratory is cutting through the foggy nature of human tissues. "We appear opaque to light, not because we absorb light but because we scatter light. If we are able to switch off the scattering, we would be able to see right through the human body. That is useful because light can be used to extract biochemical information where X-ray and ultrasound fall short." Yang's group has been working on using the time-reversible nature of light to 'turn off' tissue scattering. Recently, they were able to focus light with an unprecedented sharpness and depth through tissue. Besides



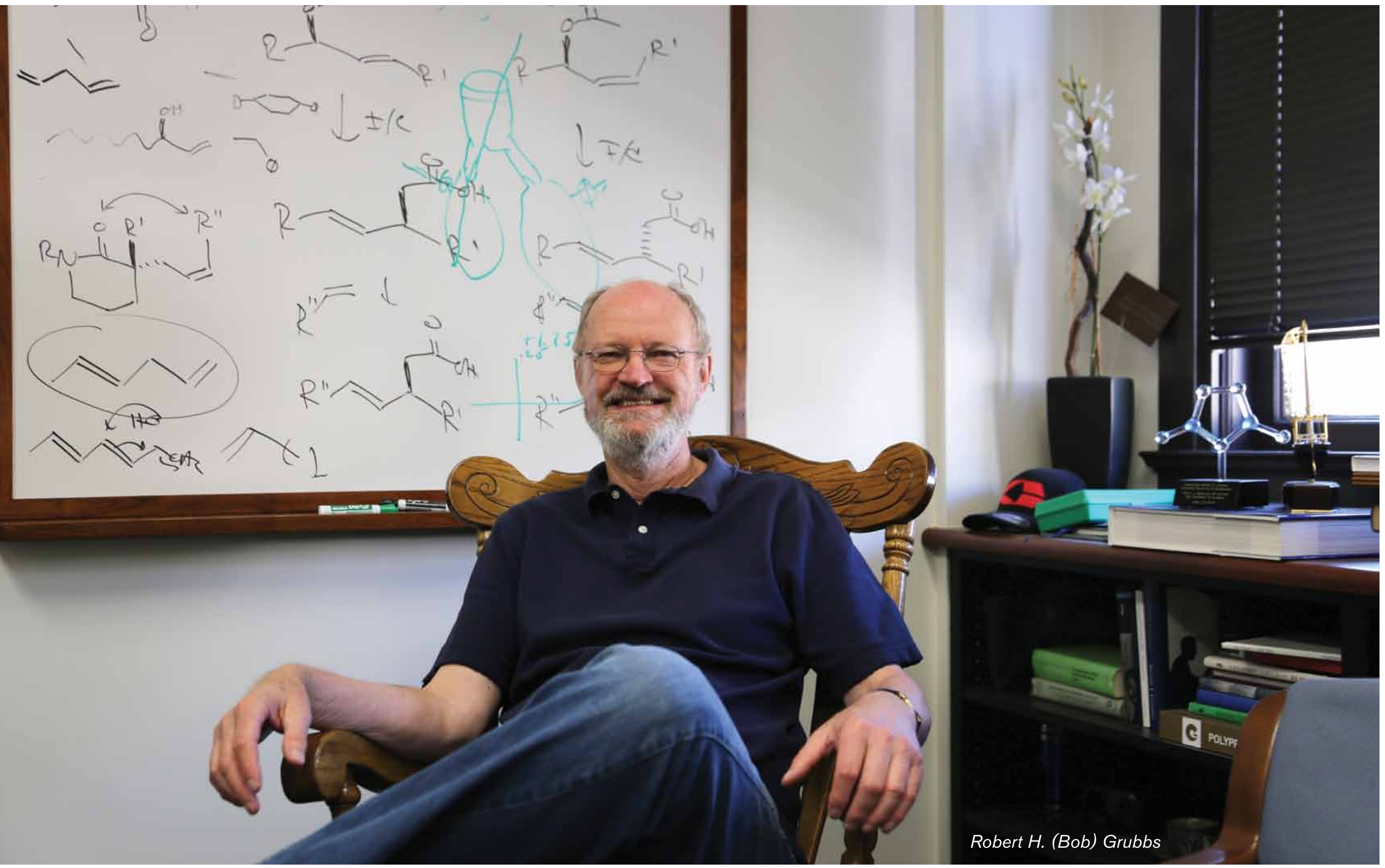
Hyuck Choo

> *People deserve to be well and free of disease and live a long life in a happy manner. . . . We're in an era where we can bring together our accumulated technology and experience, as well as our talent and creativity, to finally provide a solution to these long-lasting challenges for the human race.*

Hyuck Choo, *Assistant Professor of Electrical Engineering* extracting biochemical information, this technology "may also allow laser surgery without creating an incision, which means faster healing time and lowered infection risks."

Besides these two major research directions, Professor Yang is also engaged with clinicians and biologists on a number of other projects. Most of his projects were spawned from spontaneous discussions. He even has a favorite scenario. "I especially love it when I sit down with a clinician who starts complaining about a specific problem he or she has," he says. "Then, 30 minutes into the conversation, I am finally able to parse it into a sufficiently detailed engineering problem. From then on, the conversation usually becomes a series of light-bulb moments."

Joel W. Burdick and his team have also had many light-bulb moments while working on technology



Robert H. (Bob) Grubbs

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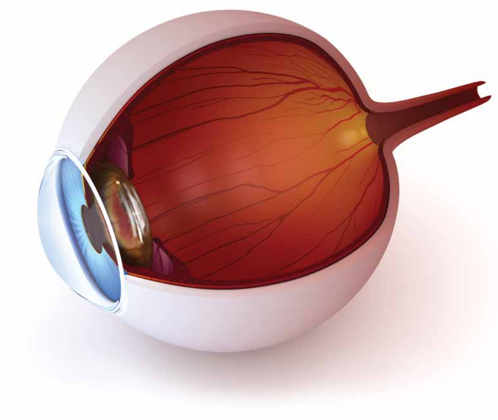
>
> Robert H. (Bob) Grubbs, *Victor and Elizabeth Atkins Professor of Chemistry*

to help patients paralyzed by spinal cord injuries. "After they're implanted with the stimulating electrodes and electronic package, they're typically in the clinic for anywhere from three to six months, recovering and getting daily training," says the Richard L. and Dorothy M. Hayman Professor of Mechanical Engineering and Bioengineering. "But after they go home, we want to provide the patients with the same kind of physical therapy that they get in the clinic. So we've been working on prototypes of what we call a home stand frame. Currently, patients are pinned into a frame that just holds them upright. But with our patients, they're able to stand independently under the influence of the electrode array, and we want them to be free to move around because it helps the recovery process. However, we also want to be able to catch them when they start to fall or at least allow them to fall in a way so they aren't harmed."

It is also desirable for the clinicians to track the patient's progress remotely. "In the clinic, there's a whole suite of sensors trained on the patient to gather data which help us improve the therapy," Professor Burdick says. "We want them to have these devices at home so we can monitor how they're doing. After every daily training session, all the data gathered by the sensors built into the frame will be transmitted to a clinic and preprocessed by algorithms, and a summary is presented to the clinicians so they can assess the patient's progress. Currently, the patients have to come back to the clinic every few weeks, but if you're able to monitor them effectively at home, you have more of what we call an event-based approach, where you call them into the clinic when they reach the next threshold."

Professor Burdick envisions a host of other medical applications for his research. In his team's spinal cord work, "we're interfacing with the human nervous system, which communicates and processes data based on both chemistry and electrical impulses," he says. "The big pharmacology companies have done a great job of pushing the chemical end, but there's a variety of other nervous system disorders that may benefit from more sophisticated implantable devices that modulate the electrical activity in nerves. There's a broad field called neural modulation, which includes back-pain devices, our spinal cord stimulators, deep brain stimulators for Parkinson's, and cardiac pacemakers. We think there are more pathologies out there that would benefit from such modulation, and that we can do a better job in the areas that we're already working on."



Professor Grubbs also sees many opportunities for medical applications relating to his research. "I have been pursuing some lines of research for 45 years, and I see the Medical Engineering Department opening up a whole set of new problems for me to work on. I think we have a real opportunity if we do it right and can make the right connections outside of Caltech to clinicians. We have to have a reality check from clinicians and surgeons saying, 'I can go into the operating room and I can do this, but I can't do that.' For example, one of my research areas relates to the inner ocular lens. This research involves making a material that can be adjusted externally. So after the lens is implanted and the patient is healed, the clinician can go back and change the refractive power. This research required us to go through human trials and has been a really interesting exercise. But it also provides a model for how we're trying to do things: a clinician or a scientist identifies a potential solution, and the next step is that the clinician has sources of funding so we can hire postdocs to improve the concept. Then, once we do a proof of concept, we form a company, that takes it the rest of the way."

After almost 40 years at Caltech, its culture might be a given for Professor Grubbs, but Hyuck Choo, Assistant Professor of Electrical Engineering since 2011, is still in awe of his fellow faculty members' "extraordinary creativity and their ability to work with and support their colleagues. I think these two things will make medical engineering at Caltech unique."

Professor Choo's path exemplifies not only those qualities but also his own determination to make a difference in the world beyond the academy. He was working on his PhD project on optical micro systems when he had an epiphany. "I started thinking about why do we do engineering," he says. "The answer is that we are

Rustem Ismagilov

> *Often the bottleneck in going from an idea to impact is actually figuring out all the engineering aspects. One competitive advantage that Caltech has is having smart people who are going to come up with new engineering principles to go from ideas and scientific discoveries to impact.*

Rustem F. Ismagilov, *Ethel Wilson Bowles and Robert Bowles Professor of Chemistry and Chemical Engineering; Director of the Jacobs Institute for Molecular Engineering for Medicine*

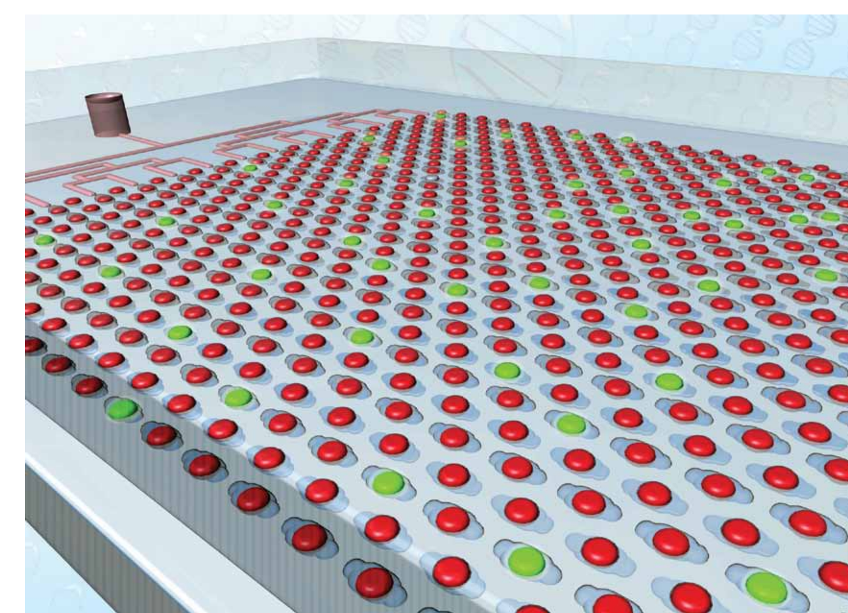
trying to improve the quality of human lives by means of technology. I figured that solving medical problems would be one of the best ways to do that."

After finishing his doctorate, he literally knocked on researchers' doors at the University of California, San Francisco, in search of one who would work with him on medical applications. "And I came across my present collaborator, Dr. David Sretavan, who specializes in glaucoma research," Professor Choo says. "I was looking for a particular case of keratoconus where the cornea develops into an abnormal shape. Dr. Sretavan said he would be interested in characterizing optical aberrations through an ocular cornea but also in measuring pressure inside the eye and monitoring pressure-regulating ocular structures at high resolution. Fast-forwarding to today, we are building an intraocular pressure sensor for glaucoma research. Glaucoma is a leading cause of blindness in the developed countries, and the increased level of intraocular pressure is the major risk factor for the disease, but medical researchers cannot say that it's a cause, because they do not have the technology that can measure the pressure inside the eye. Our ultimate goal is to optically monitor the pressure and observe the pressure-regulating system in the human eye to understand what causes glaucoma. It requires quite a feat of optical engineering to do this without damaging people's eyes."

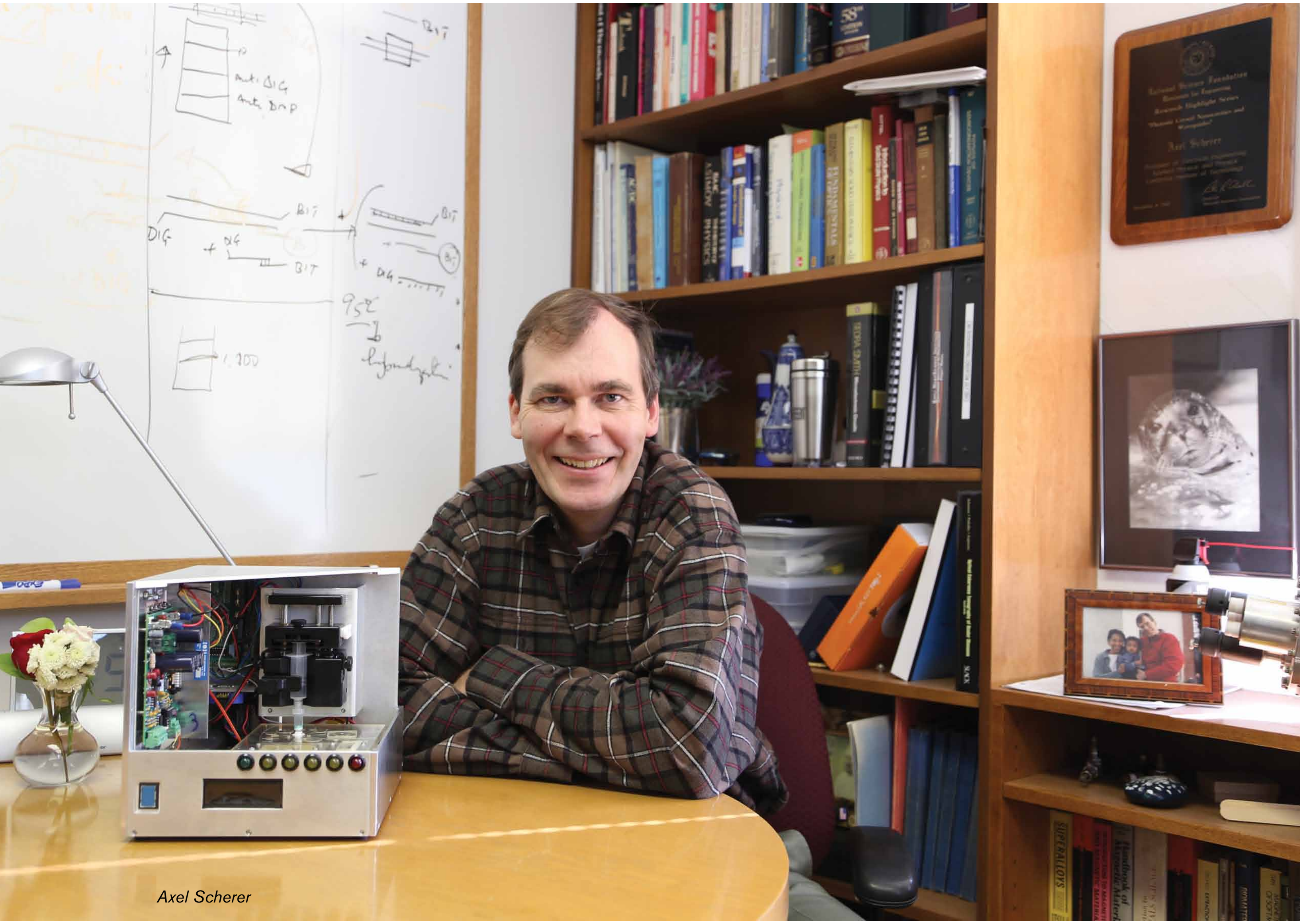
The call that Choo heeded wasn't only intellectual or compassionate; it had a spiritual dimension, one that he sees in medical engineering as a whole. Echoing Professor Gharib's belief in engineers' "moral obligation" to improve health care, he says that "people deserve to be well and free of disease and live a long life in a happy manner," citing a passage from the American Standard Version of the Christian Bible. "In Matthew 11:5, it says, 'The blind receive their sight. The lame walk and the lepers are cleansed. The deaf hear and the dead are raised up and the poor have good tidings preached to them.' I think we're in an era where we can bring together our accumulated technology and experience, as well as our talent and creativity, to finally provide a solution to these long-lasting challenges for the human race. It's already happening, too. The blind receive their sight: Professors Tai and Emami are working on retinal implants. The lepers are cleansed: if the pharmaceutical researchers bring out a better medication, we can come up with a device to deliver it. People who lost their hearing can regain it: we have the micro machining technology to design and create an artificial structure inside the auditory system that would work. And the dead are raised up: I don't know if we can do this one. But good tidings for the poor might be that we can create an economic engine from using our technology that would help people enjoy a better quality of life. It's all about helping people. That's the long-term goal of Caltech medical engineering."

Similarly, Axel Scherer is concerned with what he describes as the moral problem of how we take care of the weakest amongst us. "If we decide to just give the best medical care to the rich and forget about the poor, that sort of defines us as a culture," says the Bernard Neches Professor of Electrical Engineering, Applied Physics and Physics. "Then the question becomes, What can we do at a university? We've been supported by the Bill and Melinda Gates Foundation for the last year and a half to build instruments that are available for the developing world to do medical diagnostics. They're primarily interested in diseases that occur in tropical countries, like malaria, tuberculosis, AIDS, and sleeping sickness. These diseases require testing that usually has to be done in the field in very rugged conditions. The way it's done now, samples are taken and then transported to some central location. By the time the results come back, it may be weeks or months later, and the patient is gone. The solution is to build a set of inexpensive, automated tools that allow us to identify these diseases without any lag time. You push the button and then you do the test. These tools also have to work in very demanding environments: high humidity, high temperatures, lots of dust. In metropolitan city centers, we have many of the situations that exist in the developing world. If we can build instruments that work in these rigorous conditions, then they will also work in the Western world."

A collaborator of Professor Scherer's who is also committed to solving the problem of diagnostics in the developing world is Rustem F. Ismagilov, the Ethel Wilson Bowles and Robert Bowles Professor of Chemistry and Chemical Engineering. When asked about his medical engineering research interests, Professor Ismagilov explains, "I'm interested in three aspects. One is understanding how nature works. Another is creativity and thinking of new things that people haven't thought about before. And finally, there's making an impact. I derive the greatest satisfaction from



The single-molecule and single-cell diagnostics paradigm



Axel Scherer

"Let's focus on reducing the amount of suffering in the world and use technology to bring medical care closer and closer to the real point of care, which is the patient."

Axel Scherer, *Bernard Neches Professor of Electrical Engineering, Applied Physics and Physics*

my work if I can see how it makes an impact in the short term or I can see the path to making an impact in the long term. I think often the bottleneck in going from an idea to impact is actually figuring out all the engineering aspects. One competitive advantage that Caltech has is having smart people who are going to come up with new engineering principles to go from ideas and scientific discoveries to impact."

For instance, Professor Ismagilov explains, "We have found that using microfluidic devices and chemistry to take diagnostic measurements out of the traditional kinetic paradigm into the single-molecule counting paradigm simplifies the process. The argument we have is that in the single-molecule paradigm, the diagnostic measurement would actually be much more robust to changes in assay conditions such as temperature or imaging accuracy. Therefore, we can reduce or eliminate the need for equipment infrastructure currently used to control assay conditions or provide high-quality imaging, making the process more accessible. As an analogy, think about the spread of communication technologies. People used to have landlines for phone service. In the developing world and rural areas, you just couldn't afford that infrastructure, so you just didn't have phone service. Then cell phone technology appeared and people in these developing or rural areas leapfrogged straight to those better technologies. I argue that in these developing countries, home testing will also bypass building traditional diagnostic infrastructure and leapfrog directly to digital single-molecule measurements."

Professor Scherer explains another motivation for this research: "The most important thing is to manufacture the technological capabilities that we have available in medical applications at the lowest possible cost. That's sort of an unusual thing for a professor to say. I'm not supposed to think about cost. But hopefully we can build tools for the medical world the same way that we build consumer electronics. The DVD player has a huge amount of complexity, and I can buy one for $50. A medical instrument costs $50,000 for similar complexity. It's an engineering challenge to shrink the cost. As a society, I think it's a moral obligation to focus our efforts on making the capabilities that we are technologically able to provide available to everyone."

Some of Professor Scherer's core concepts came from his volunteer work at a hospital in Southern California. "If you work in a hospital, you realize that lots of suffering occurs needlessly because we don't have the right tools at the right place," he says. "I saw all the frustration on both the nurses' and the patients' side. I realized that technologically, there was a huge challenge that could be met by the capabilities we could develop. Let's focus on reducing the amount of suffering in the world and use technology to bring medical care closer and closer to the real point of care, which is the patient. Once we build these kinds of systems, there's a whole other kind of medical engineering that becomes possible—for example, implanting devices in the brain that allow us to control prosthetic devices, implants that detect our intention of, say, picking up a glass of water and have some robotic system do that for us. We could argue that that will replace the spinal cord with a Bluetooth connection. Let's make a difference, which is what Caltech is good at." ENG

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