COLLEGE OF ENGINEERING

Momentum!

Winter 2016

Engineering Precision Health

Oregon State UNIVERSITY

Momentum!

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FRONT COVER
Adam Higgins prepares a sample of endotoxin-spiked blood to test a microchannel device.

BACK COVER
Jessalyn Imdieke and Anthony To, undergraduate students in Elain Fu's laboratory, cut plastic laminate components using a CO_2 laser to build microfluidic devices.

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Advancing precision health at Oregon State

Advances in engineering, technology, and biomedicine are enabling rapid growth of an emerging field known as precision health — the tailoring of healthcare to individual patients instead of a one-size-fits-all approach. In his 2015 State of the Union address, President Obama announced the Precision Medicine Initiative, which promises to accelerate investments in research projects that advance the cause of precision health.

Biomedical engineering is integral to precision medicine, and Oregon State's bioengineers are at the forefront of interdisciplinary efforts to combine the power of engineering with the power of biomedical science. In this issue, we highlight the work of several researchers who are making inroads in this exciting field:

- Larry Cheng's diagnostics research is focused on detecting cancer biomarkers in the body's circulatory system to enable earlier diagnosis and targeted treatments for cancer patients. He is also developing technology to detect stress hormones in saliva, which could reduce accidents and injuries for professionals in high-stress occupations and help people with chronic illness better manage their health.
- Elain Fu's work with microfluidics promises to enable quick, accurate, simple-to-use paper-based medical tests that can be used for home healthcare management and in places in the world where healthcare facilities and personnel are not readily available. It could also help with quick, more accurate, mobile diagnosis of medical conditions like influenza and malaria.
- Stephen Ramsey's work epitomizes the power of combining engineering and medicine. As a computer scientist and a biomedical scientist, he is applying computational tools like machine learning and data mining to look for key genetic codes at the molecular level. His collaborative research project with Shay Bracha in the College of Veterinary Medicine could help medical professionals fine-tune treatments for specific cancer subtypes.
- Ravi Balasubramanian's "robo-inspired" technology, which promises to make a real difference for people with hand injuries or disabilities, earned him an Outstanding Researcher Award from the National Institutes of Health. Now, by helping us to understand how the human brain learns to perform new tasks, patients may be able to recover more quickly and easily.
- Several researchers at Oregon State are applying microchannel technology to the seemingly intractable worldwide problem of sepsis. This interdisciplinary team has made advances that could sweep endotoxin molecules from a patient's blood quickly — much more quickly than antibiotics can work — potentially saving millions of lives.

We are thrilled about these innovative projects and the promises they hold for promoting people's health. We will continue to make investments that move us closer to our goal of becoming leaders in bioengineering research, and we will continue to involve undergraduate students like Miranda Raper in research to help make their transition from school to a career seamless. Be sure to read about Miranda's exciting research — she is an Oregon State Engineer™ in the making.

Go Beavs!

Scott A. Ashford, Ph.D.
Kearney Professor and Dean
Oregon State University
College of Engineering

The evolution of bioengineering

By Krista Klinkhammer

Jim Sweeney (left) and V. John Mathews

When Jim Sweeney took a test in high school to gauge his career interests, he had to look up the profession recommended to him: biomedical engineer. The description piqued his interest enough to apply to a college that had such a program. Little did he know when he checked the "biomedical engineering" box during registration for his freshman year at Brown University that he was at the forefront of a discipline headed toward exponential growth over the next 40 years.

Biomedical engineering is a discipline within the broader field of bioengineering. At the time Sweeney entered college, only a handful of schools in the United States offered biomedical engineering or bioengineering degree programs. Technological and scientific advances contributed to establishing bioengineering as a formal discipline, and interdisciplinary collaboration fueled this growth. Given the broad nature of the field, bioengineering requires a solid foundation in engineering in addition to biological and life sciences. Successfully applying bioengineering to complex problems involves integrating these disciplines.

As Sweeney looks back from the vantage point of his position as head of the School of Chemical, Biological, and Environmental Engineering, he reflects on the significant impact bioengineering and biomedical engineering have had on medicine, healthcare, science, and engineering. Today, more than 130 accredited undergraduate programs in these disciplines exist. Even with an overall decline in private sector employment of 2.9 percent between 2001 and 2010, the United States bio-industry grew by 6.4 percent. Biomedical engineering tops Forbes' 15 Most Valuable College Majors, and is projected to have a job growth rate of 61.7 percent. According to Forbes' list of master's degrees with the highest salary potential, biomedical engineering is tied for fifth place with electrical engineering.

At Oregon State, the undergraduate bioengineering degree program formally resides in the School of Chemical, Biological, and Environmental Engineering, but the field in general touches each school in the College of Engineering. V. John Mathews, who joined Oregon State as head of the School for Electrical Engineering and Computer Science in August 2015, seeks faculty who are not only experts in their respective fields, but will contribute to bioengineering research. "I have at least three faculty members in EECS who have joint appointments in departments with a bio-emphasis, and I think every faculty member could have a part to play in potential bioengineering collaborations," he said.

Electrical engineers have long been involved in developing medical tools and technology, but when Mathews began his career, collaboration was lacking.

"When I started in academia, it was not easy for engineers and doctors to talk to each other," he said. "Later, as technology, science, and medicine progressed, we realized that we had a lot to offer each other, and we started learning each other's language. It was very clear that there was a lot we could do."

As the power of collaboration was realized, developments began to emerge.

Mathews was first exposed to applying his electrical engineering background to medical applications when a doctor approached him asking for help in analyzing ultrasound data gathered from chick embryos.

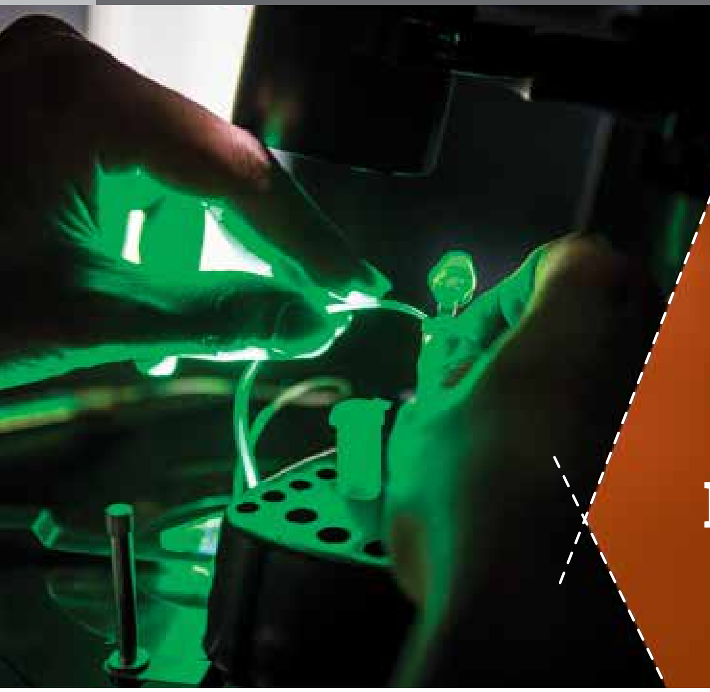
"I started looking at the data, and things became interesting," said Mathews. "We were able to find connections in the data that related to what the doctor was trying to explore."

These connections led to discussions with a doctor of maternal fetal medicine, where further research brought about the development of tools for understanding the evolution of the placental circulation system and the relationships between maternal and fetal circulation systems. These tools include a system for early detection of preeclampsia, a disease that affects between six and eight percent of all pregnant women and is one of the major causes of maternal and fetal death.

In the 1980s and 1990s, the Whitaker Foundation was a catalyst for bioengineering growth nationally. Founded by U.A. Whitaker, a prominent mechanical engineer, electrical engineer, lawyer, and entrepreneur, the organization contributed more than $700 million to various academic institutions in support of interdisciplinary medical research, with a focus on bioengineering and biomedical engineering. In 1999, Oregon State benefited from the Whitaker Foundation's generosity for the third time, when a three-year, $1 million grant allowed the creation of the undergraduate bioengineering degree program and the bioengineering education and research center.

Today, the College of Engineering strives to be a leader in bioengineering research and innovation, and to graduate engineers who will positively shape individual lives and the world. Bioengineering couples the problem-solving inherent to engineering with the humanitarian aspects of medicine and healthcare, making it an attractive option for students who want to create a better future.

"It's a very 'helping' discipline, making it attractive to a more diverse student population, including women," said Sweeney. "It's a direct way to make an impact on the world and on others." **M!**



Detecting cancer, tracking stress with micro-devices

By Gregg Kleiner

What if doctors could use a tiny microchannel device and a simple blood sample to detect cancer very early on — before a patient even shows any symptoms — and avoid invasive biopsy surgeries?

What if a similar device could be used to quickly determine the efficacy of cancer treatments like chemotherapy by revealing biomarkers in the blood and immediately adjusting the dosage?

What if soldiers, firefighters, and others could wear tiny microsensors inside their mouths that would track and transmit stress or pain levels in real-time, based on a hormone secreted in their saliva?

Larry Cheng, assistant professor of electrical and computer engineering, is focused on developing these devices. His cancer diagnostics research, which blends electrical engineering with biomedicine, seeks to detect mutant circulating tumor DNA or RNA — cancer biomarkers — in the body's circulatory system.

It's a challenging goal.

"It's hard to directly detect low amounts of the targeted mutant genes in the background among high levels of normal sequences," Cheng said. "And differentiating the minute differences in the mutated sequence is also quite challenging."

The daunting odds have not dampened Cheng's enthusiasm for the research that could potentially have a huge impact by allowing doctors to diagnose cancer earlier and fine-tune treatment regimens on the fly. Collaboration is key to making the impact Cheng envisions.

"We are engineers and not cancer biologists, so we talk to the biologists and physicians to see what they need, and then figure out a way to help them make their diagnostics more efficient using engineering," he said.

To develop these devices, researchers have to overcome two hurdles: 1) enabling high-throughput transport of blood from a sample through a sensor and 2) achieving efficient and selective capture of target DNA in the blood.

Cheng and his graduate students addressed the first hurdle by incorporating microchannel technology and a sensor into the same device on a microchip. They use microfluidics to efficiently move a lot of blood through the device in very close proximity to the sensor's surface.

To address the second hurdle, they engineered the sensor's surface area to attract and bind target DNA to a specific probe. The material glows when excited by light, and its intensity indicates how much of the molecular biomarker is present. The technique will help doctors determine the effectiveness of a current cancer therapy and make quick adjustments, instead of waiting days or weeks for test results to be returned.

In addition to his work on cancer, Cheng just received a $340,000 grant from the National Science Foundation to explore how microsensors can be used to identify certain hormones secreted in saliva when a person is under stress or experiencing symptoms like fatigue.

"The target with this project is to develop a sensor that can support real-time monitoring of salivary biomarkers," Cheng said. "We're looking at a trace-associated hormone that boosts heartbeat and is also released into the saliva. We want to detect this biomarker in order to track psychological stress."

Traditional mouth swab tests for salivary biomarkers take time for the results, but Cheng's team is working on real-time monitoring that would wirelessly transmit results every minute or two, from a device so small it could be placed inside a person's mouth.

Unlike DNA or glucose, however, this particular hormone in the saliva carries no charge and has no electrochemical reactivity, so it can't be tracked using traditional methods. And because it is mounted in the mouth, optical property analysis is not an option, either. So Cheng and his team are working to develop a polymer that will change conductance when it binds to the target hormone molecules.

"Developing this polymer is the key," Cheng said. "We can't use optical sensing, because it's too bulky for a wearable device, and we can't rely on traditional electrochemical detection the way we measure glucose, so we need to come up with a new method for detection."

The technology could be used for jet fighter pilots and military drone operators, whose stress levels can impact their response to conditions they encounter. Data from the paper-thin, flexible device could be wirelessly relayed to key personnel to help determine a pilot's psychological condition before a mission, and make adjustments to duties or workload accordingly. Others working in high-stress jobs, such as firefighters battling wildfires, might benefit from the technology in the same way. In the medical industry, the technology could be used to monitor anxiety in surgical patients and in the self-management of chronic diseases.

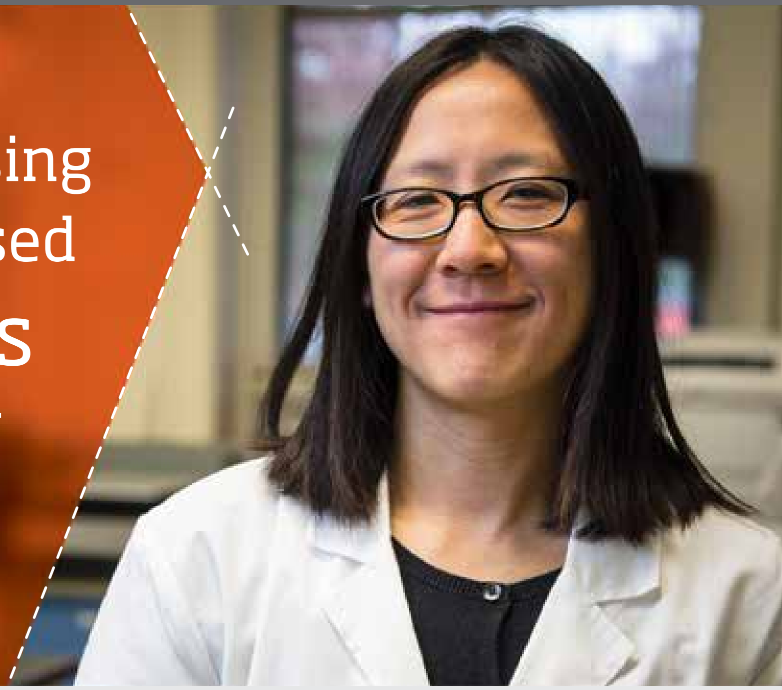
As the field of precision health continues to expand, the demand for more engineers with an understanding of both biomedicine and engineering will grow. Because most electrical engineering students have not been exposed to much biotechnology, Cheng has developed a new class called Biosensors and Medical Devices to teach students about how diagnostic tests are performed in terms of chemical, optical, and electrical responses. Students also learn how fluids flow through a microdevice, how to move molecules to a sensing surface, and the chemistry that binds molecules to that surface.

"It introduces engineering students to the concepts that are required to develop the types of biomedical devices we're working on," Cheng said. **M!**

Using a microfluidic biosensor platform, Larry Cheng examines molecular probes that can report the presence of specific bacterial DNA or viral RNA in a few drops of sample.

Using paper-based microfluidics to empower patients

By Gregg Kleiner



To help people more easily monitor their health, Elain Fu is applying the science of microfluidics to develop simple-to-administer, more accurate, paper-based medical tests that offer almost immediate results. Fu recently came to Oregon State as an assistant professor of bioengineering in the School of Chemical, Biological, and Environmental Engineering.

Paper-based microfluidics takes advantage of the capillary action of porous materials to direct fluids and reagents through test strips and display the result visually — similar to how a pregnancy test works.

Fu wants patients to be able to take out a test and use it without plugging in a device, storing chemicals in the refrigerator, or performing some elaborate procedure. Her current research focus is on a rapid-response, home-based test to help people who are born with a genetic disorder called phenylketonuria (PKU), a life-long condition caused by the lack of an enzyme that converts one essential amino acid (phenylalanine) into another (tyrosine). Without the missing enzyme, phenylalanine builds up in the blood and inhibits the transfer of other essential amino acids to the brain, resulting in permanent cognitive deficiencies.

The majority of patients with PKU treat the disorder by avoiding phenylalanine-containing foods (mainly proteins) and consuming a prescribed dose of synthetic protein formula in drinkable form. Although blood tests can be administered to determine their levels of phenylalanine, the tests take a number of days to process in a lab. This lag time is a critical barrier to improving therapy for PKU patients.

"PKU patients want to have something to help them track how diet therapy impacts their phenylalanine levels," said Fu. She is developing a simple home phenylalanine test that will give patients faster feedback on their phenylalanine levels.

A drop of blood is placed on a paper-like strip, and capillary action moves the fluid through a series of dried reagent depots in the strip. When the patient folds the top part of the test down and presses it against the lower part, a visible indicator shows the phenylalanine level in the person's blood when the sample was taken.

"Personalized medicine is all about empowering patients to take charge of their own health," Fu said. "The PKU community is very excited about having this tool to help them take charge of their own health and maintain their therapy."

Some of Fu's other research is aimed at developing more accurate, rapid-response field tests for influenza and malaria, because many such tests currently on the market perform poorly (current tests have accuracy rates of 30 to 70 percent).

"Paper microfluidic tests are uniquely suited to addressing needs in low-resource settings in the developing world, where you might not have trained technicians or even electricity," Fu said. "But they are also suited for at-home healthcare."

She hopes that her research and development of simple test kits will help not only PKU patients, but many others who would likely benefit from therapy monitoring in the home, including people with epilepsy and other neurological disorders. **M!**

How data mining and machine learning are helping fight cancer and predict heart disease

By Gregg Kleiner

As the world searches for cures to cancer and cardiovascular disease, Stephen Ramsey, assistant professor of computer science and biomedical sciences, is applying computational tools like machine learning and data mining to sift through massive datasets and tease out information buried deep within genetic codes at the molecular level. His goal is to gain insights into disease mechanisms that will lead to new therapies for prevention and treatment.

Ramsey holds an appointment in the School of Electrical Engineering and Computer Science and also in the Department of Biomedical Sciences in the College of Veterinary Medicine. For the past year, he has been attempting to more accurately quantify an individual's risk of heart disease based on genetics. He and his collaborators are looking for ways to reduce plaque buildup inside human arteries without using high doses of cholesterol-regulating statins, which produce side-effects.

The research team treated mice with a lipid-lowering drug and subsequently observed a decline in plaque buildup in the aorta. Unfortunately, the drug won't work on humans, because the mouse strain's genome is tailored to respond to the drug. The researchers hope to understand how lipid lowering, regardless of how it is achieved, leads to plaque regression and ultimately results in less inflammation in the artery wall.

"This migration of macrophage cells from the plaque is very interesting — something is causing the cells to become motile and the plaque to thin, so we want to know what the molecular trigger is that does this in mice," Ramsey said. "If we can discover that, perhaps this same molecular mechanism could be targeted in humans for therapeutic benefit."

Ramsey and his team are using machine learning to identify small regions of the genome that are important for regulating gene expression in plaque. Mapping the locations of these regulatory elements is difficult, and to accomplish their goal of globally mapping their locations across the genome, they must integrate multiple kinds of quantitative evidence. Evidence is derived from a variety of molecular measurements from cells, which requires grappling with huge, heterogeneous, biological datasets to better understand variations over the course of disease.

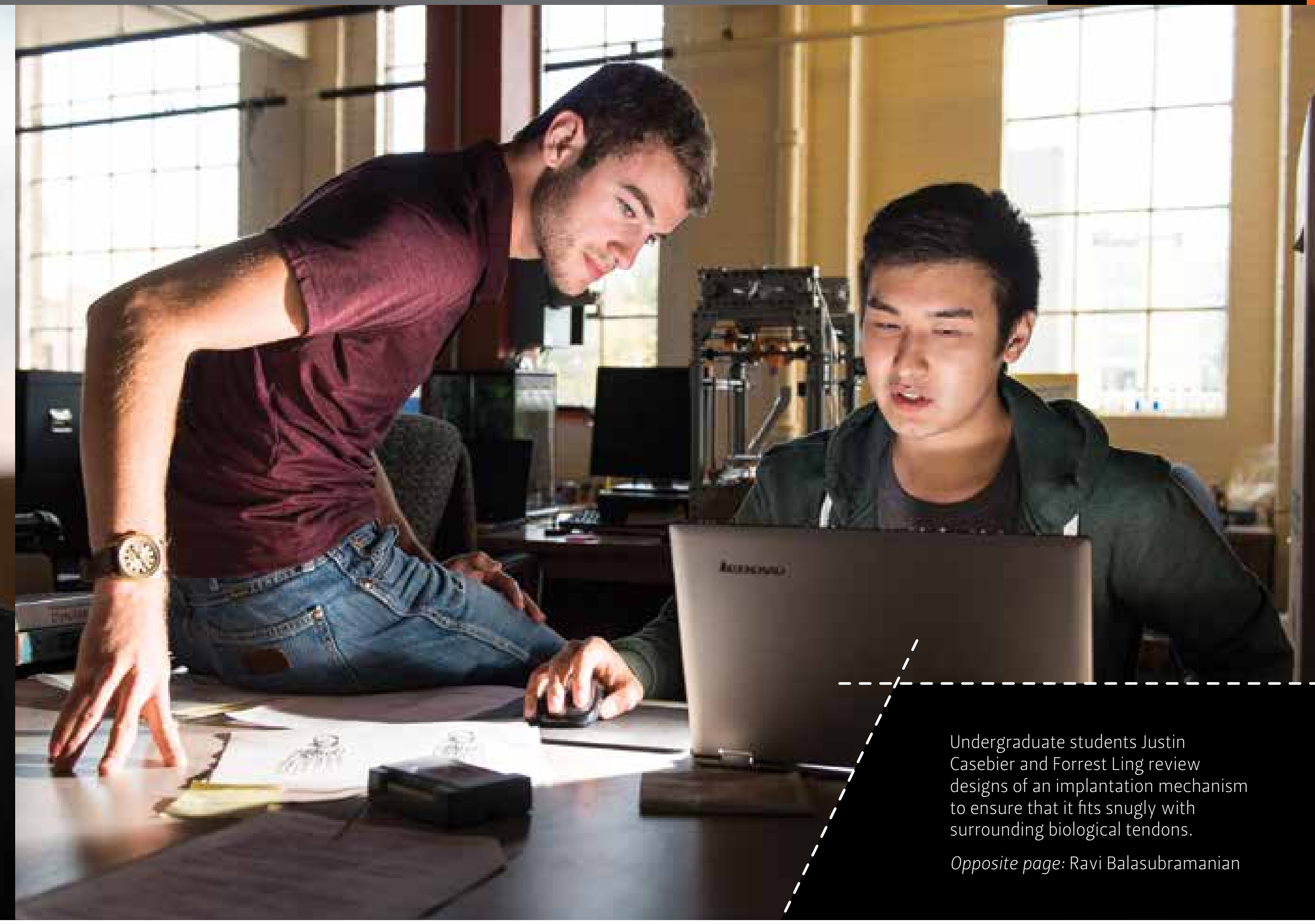
On the cancer side of his research, Ramsey is collaborating with Shay Bracha in the College of Veterinary Medicine to analyze data on gene expression and compare canine bladder cancer to human bladder cancer in hopes of fine-tuning cancer treatment for specific subtypes.

"Computer science and data science have provided a wealth of techniques that we hope will be beneficial for improving our understanding of the molecular basis of cancer," he said. "These techniques include pattern finding, data mining, data visualization, machine learning, and so on."

The costs of analysis have come down and analytical methods have improved, so it is now possible to perform genetic studies for hundreds of thousands of subjects. Tapping even more robust computational tools to mine and analyze the burgeoning amounts of this data is helping to advance precision medicine. **M!**

Biomechanical research
promises increased mobility and decreased injury

By Marie Oliver



Undergraduate students Justin Casebier and Forrest Ling review designs of an implantation mechanism to ensure that it fits snugly with surrounding biological tendons.

Opposite page: Ravi Balasubramanian

Although the human hand contains nearly 40 muscles, only three nerves control them, so the loss of just one nerve through accident, disease, or genetics can severely limit finger dexterity and weaken a person's grasp strength.

"You lose one nerve and you can't flex the fingers, which means you can't hold a cup. You can't hold a spoon. You can't hold a pen. You can't do anything, really," said Ravi Balasubramanian, assistant professor of mechanical engineering and director of the robotics and human control systems lab at Oregon State University.

In traditional orthopedic surgery, surgeons use sutures or anchors to reconnect or reroute tendons to muscles or bones. Although patients might gain mobility after this type of surgery, their fingers may be required to flex or extend together, and the distribution of force may become static. "Think of a car with only one gear; you could only go at one speed. That's basically what the suture is doing for you," said Balasubramanian.

Functionality can be affected in other body parts, too — knees, hips, feet, shoulders, elbows — anywhere tendons connect to muscle. Injuries that affect these body systems can be particularly traumatic for athletes, dancers, and others who need to rely on their bodies to perform precision movements.

Over the past 15-plus years, Balasubramanian has been trying to improve people's lives by drawing on his knowledge of mechanical engineering ('00, B.S. Mechanical Engineering, National University of Singapore) and robotics ('06, Ph.D. Robotics, Carnegie Mellon University), and blending that knowledge with a deep study of the human body. Using robotic technology as his inspiration, he developed a breakthrough technology a few years ago that provides an alternative to using sutures for attaching muscles to tendons in certain applications, such as tendon transfer surgery. His pioneering hand implant earned him an Outstanding Researcher Award from the National Center for Simulation in Rehabilitation Research at the National Institutes of Health.

His research group is now working toward animal and clinical trials of the implant. "We have already proved the concept in human and animal cadavers," said Balasubramanian. "Now we're moving toward live animal trials within the next year or so."

In recent months, supported by a National Science Foundation grant, Balasubramanian has met with more than one hundred groups, including surgeons, physiotherapists, implant companies, and insurance companies, to determine the commercialization potential for the implant. "We're learning that there are very specific conditions for which our implants will be useful," he said. It's possible that athletes may be the first to benefit from the technology, since their ability to recover from injury can mean the difference between having a career or not having a career, and even a few extra ounces of strength can make a big difference in sport performance.

Meanwhile, Balasubramanian has other research projects in the works, and they also build on his primary interest in the physics of movement.

"The goal of my research is to blend robotics and the human body, where we're drawing inspiration from the human system to improve robotics, and at the same time drawing inspiration — what I call 'robo-inspiration' — from robots to enable human function," he said. "So if my work enables an elderly person to use a robot to perform daily activities at home, that's a big plus for me. And if the robotics technology that I develop can be implanted inside a human to enable that person to lead a better quality of life, then that's a big plus for me as well."

In one project, Balasubramanian looked at how the human brain learns to perform new tasks. What his team learned could help physical therapists and other medical professionals design rehabilitation programs that will allow patients to recover more easily and without the risk of re-injuring themselves.

Many tasks in daily life involve precision positioning, and these tasks can cause excessive stress on the human body. Activities like assembling parts or operating equipment in a manufacturing environment, playing a musical instrument, or using a computer mouse, keyboard, or video-game controller involve significant use of the wrist and fingers and can cause chronic health problems like carpal tunnel syndrome or other repetitive stress injuries.

Balasubramanian's research team asked human subjects to perform various tasks, such as navigating with a computer mouse, with a commercially available robotic hand. They measured the speed and extent of the movement the subjects used, and how much force they applied in holding the hand. They observed that the force with which the subjects held the robot changed as they learned the task.

"The force they used increased and then decreased as the accuracy of the movements exponentially increased," said Balasubramanian. "The point at which the force peaked was the same time when the error reached a steady state — when accuracy stabilized."

The study team inferred two stages to the learning process. "We found that people don't care about how much effort they're using when learning a task; they care only about performing the task well enough," said Balasubramanian. "So they prioritize task performance over effort. Once a task is learned, they start reducing the effort they're using. "

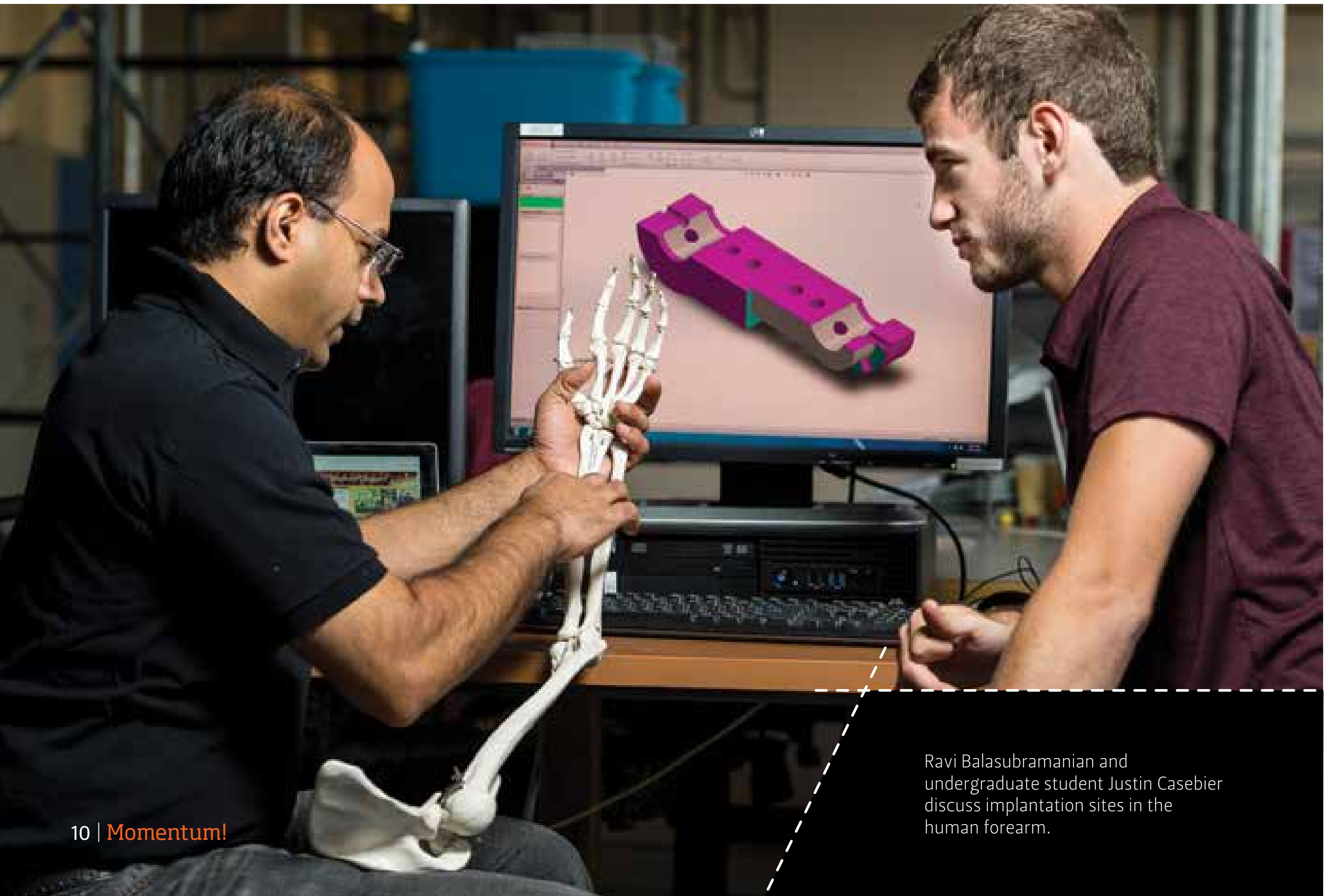
When someone is learning to perform a task and they apply too much force, they could injure themselves. "In playing tennis, for example, if you're learning a particular shot that requires you to hold the racket in certain way, our research shows that the person will hold it with a huge amount of force while learning to perform the task properly, and this can cause injury," said Balasubramanian. "So maybe we can explore new methods of learning that reduce stress early in the learning process. This understanding also could be useful in helping someone to relearn a task after surgery, a stroke, or accident."

The results also suggested that learning periods increased as the accuracy requirement increased. For example, learning to use a smaller keyboard on a smart phone takes more effort than learning accuracy on a tablet. "Coupled with the high grip force required with increased gain level, both transiently and after adaptation, this poses an increased risk of upper extremity musculoskeletal disorders, such as wrist injuries and carpal tunnel syndrome," said Balasubramanian. "This suggests that more detailed studies of hand stiffness adaptation linked with computer and device design are worth pursuing, to minimize the risk of injury."

Balasubramanian is excited to be an integral player in Oregon State's burgeoning robotics group. "It's a fantastic environment, and we create impact on an international level," he said. "All of the faculty here really enjoy working with our top-notch students."

If Balasubramanian and his colleagues continue to be robo-inspired, and to gain inspiration from the human body to design robotic technologies, they have a very good chance of succeeding in their goal of building the best robotics program in the country. **M!**

Abby P. Metzger contributed to this article.



Ravi Balasubramanian and undergraduate student Justin Casebier discuss implantation sites in the human forearm.

New hope for treating sepsis

By David Stauth

Undergraduate student Alden Moss examines a cuvette containing blood that has been treated in a microchannel device.

They used to call it "blood poisoning," and the term is still descriptive, if outdated. Like a poison, sepsis works fast and is frequently deadly. A modest infection suddenly turns into whole-body inflammation, complete with fever, flushed skin, swelling, and hyperventilation.

The risk of sepsis is surprisingly common. It can develop after an injury from an automobile accident, from a dirty wound, during an extended operation in a hospital, or opportunistically when people with a weak or compromised immune system contract an infectious disease.

In the United States, one out of every four people in a hospital emergency room is there because of sepsis. More than $20 billion was spent on this problem in 2011 — it's the single most expensive cause of hospitalization. Even with aggressive treatment, about a third of the people diagnosed with sepsis worldwide, which number in the millions, do not survive. It killed Pope John Paul II and at least two sitting U.S. presidents.

The term sepsis means "the process of decay" and was first identified by Hippocrates around 400 B.C. As a syndrome leading to multiple organ failure, it is an apt description. But unlike most forms of decay, sepsis works amazingly fast. Every hour of delay in administering an antibiotic can raise the mortality rate by another eight percent.

"Sepsis is a hidden killer, the one nobody really talks about," said Adam Higgins, associate professor of bioengineering. "It kills more people in the U.S. every year than AIDS, prostate cancer, and breast cancer combined, and you still don't hear much about it." In many cases, the death certificate may list cardiac arrest, kidney failure, or other medical condition as the cause of death, even though sepsis was the trigger for those conditions.

Fortunately, hope is on the horizon for treating this syndrome. Several researchers in the College of Engineering are working with teams of undergraduate and graduate students on a project that may soon have the whole world talking about sepsis. Finally, there may be a way to combat it with something other than antibiotics, which often don't work.

"A big part of the problem with sepsis is that it moves so rapidly," said Joe McGuire, bioengineering professor. "By the time it's apparent what the problem is, it's often too late to treat it. What we have in mind is a way to process the blood and prevent sepsis, something that could be used at any time."

The underlying cause of sepsis is endotoxins — molecules that are released from bacterial cell walls and lead to rapid, systemic inflammation. These pieces of bacteria can disrupt the immune response, causing it to overreact. Patients can quickly develop blood clots and other problems that lead to multiple organ failure. If given early enough, antibiotics and other treatments can sometimes stop the process, but they may not work as fast as the sepsis does.

"Once these bacterial fragments are in the bloodstream, antibiotics won't always work," said McGuire. "You may have successfully eradicated the living bacteria even as a patient is dying."

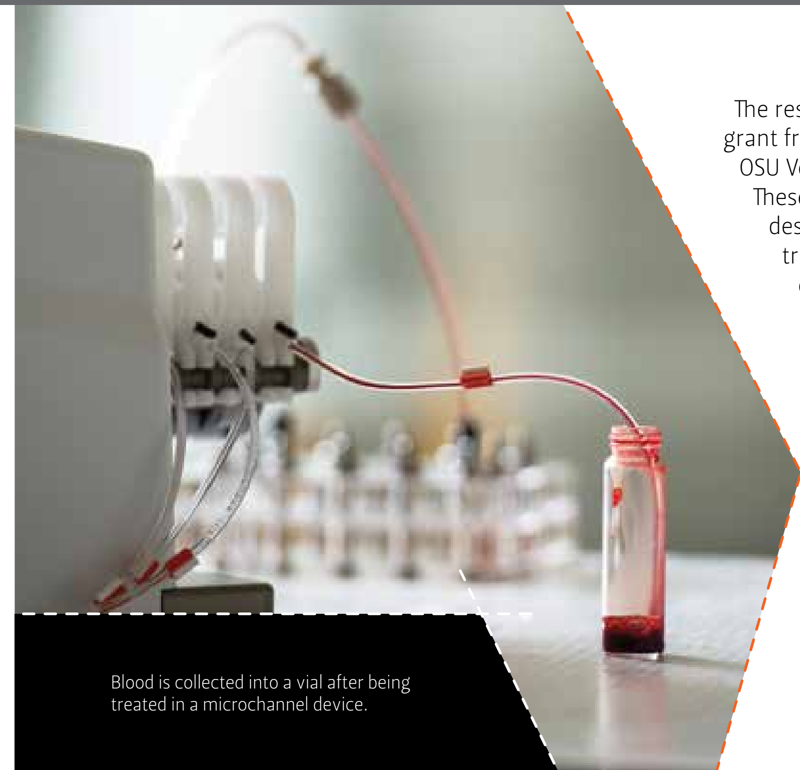
The approach in development at Oregon State is to move blood through a very small processor about the size of a coffee mug and literally grab the endotoxins and remove them. The concept is surprisingly simple, and builds on some of the university's revolutionary work with microchannel technology.

By moving fluids through tubes the width of a human hair, microchannels accelerate chemical reactions and heat transfer. They can be produced in mass quantity at low cost and stamped onto a range of metals or plastics that are then used to process large volumes of liquid in a comparatively short time. Other researchers at Oregon State are studying microchannel applications in heat exchangers, solar energy, and chemical manufacturing.

In this case, the liquid is blood, which may contain the endotoxins that cause sepsis. In Oregon State's system, blood can be pumped through thousands of microchannels coated with something researchers call "pendant polymer brushes." These are tiny strands equipped with chemicals that can grab endotoxin molecules like a fishing hook. On the business end of the strand is a peptide, a bioactive agent that binds tightly to the endotoxin and removes it from the blood, which then goes directly back to the patient. To keep blood proteins and cells from sticking or coagulating in the channels, the strands also have been designed with repeating chains of carbon and oxygen atoms anchored on the surface.

"This doesn't just kill bacteria and leave floating fragments behind; it sticks to and removes the circulating bacteria and endotoxin particles that might help trigger a sepsis reaction," said Karl Schilke, assistant professor of bioengineering.

The team hopes to use low-cost polymers to keep the technology costs low. "The device should be inexpensive enough that it can be used once and then discarded," said Schilke. "The low cost would also allow treatment even before sepsis is apparent — a prophylactic approach to prevent it, not just treat it after the fact. Anytime there's a concern about sepsis developing due to an injury, a wound, an operation, an infection, you could get ahead of the problem."



Blood is collected into a vial after being treated in a microchannel device.

The researchers recently received a $200,000 grant from the National Science Foundation and an OSU Venture Development Fund grant of $150,000. These investments will allow them to refine the design and move the technology closer to clinical trials. The emphasis is on demonstrating the efficacy of the microfluidic device architecture and surface coating, with a goal of moving the project to commercialization. The value of this medical technology could be enormous once the work is complete.

"When we first conceived of this approach to prevent sepsis, my initial reaction was, 'Wow!' " said McGuire. "Think of the number of deaths we could prevent. Think of the billions of dollars spent in intensive care that could be available for something else. Think of all the infants and young people who could have their whole lives given back to them." **M!**

Beyond the findings

Research opportunity provides confidence for female engineering student

By Krista Klinkhammer

Now entering her junior year, Miranda Raper already has three years of lab experience under her belt, and has learned a lot about how to structure and execute research. She also has developed a couple of key intangibles: the confidence to thrive as a female in the male-dominated engineering world, and a drive to help other women engineers succeed.

Raper's first exposure to research came the summer after her freshman year, when she worked in Karl Shilke's lab through the Johnson Internship Program. She quickly discovered a passion for research, and spent time on several different aspects of a project focused on a cure for sepsis, giving her a broad overview of the research (see *New Hope for Treating Sepsis*).

Becoming familiar with the analytical techniques used in the sepsis project was a key part of her learning. For example, she used optical waveguide lightmode spectroscopy to obtain *in situ* measurements of the surface immobilization of biomolecules in an aqueous environment.

"This technique measures refractive index changes from which the mass of the adsorbed species can be calculated," Raper explained. "We flowed lipopolysaccharides — which are part of the membrane in the bacteria — across a peptide-coated surface, to see if they stuck to the surface. That was an indication of whether or not there is an interaction between the two."

After her first summer, Raper continued on as an intern, and her research became more focused, turning into her honors thesis.

"I'm studying the attachment of a polymer tether to the end of the peptide and seeing if that changes how the peptide interacts or how it forms different structures," she said. "I'm trying to find out how to chemically attach the two and have it be a covalent attachment, and whether or not the peptide can adopt a helical structure."

Raper was a high school valedictorian with a professed love of math and science. She recently earned an honorable mention in the Barry Goldwater Scholarship and Excellence in Education program for her work on the sepsis project, and also won the Women in STEM award from the Honors College.

But even with this stellar résumé, studying engineering has raised some doubts in her mind from time to time. "In my first year of pro-school, classes were very difficult," she said. "It went through my mind that I'm not smart enough to be an engineer. But I know that's not true."

The challenges inherent with the discipline coupled with the uphill battle of being a minority are deal-breakers for many women.

"There are men in my field that think because you are a woman you know less, and that has been frustrating — trying to work in teams when people don't trust your judgment," she said.

Luckily for Raper, the confidence she has gained through her research has enabled her to overcome those challenges.

"I'm not afraid to speak up," she said. "I try and get everyone to work as a team, and if I have an idea I say it, regardless of whether or not it gets shut down. The fact that I now have the confidence to speak out is tremendous to me."

She is also active in the Society of Women Engineers, which provides support for her and encourages other women to stay involved in engineering.

"Women shouldn't be afraid to do what makes them happy," she said. "Keeping more women in these programs and keeping them going is important. Having that support is a real booster, so that is why I stay involved." **M!**

Miranda Raper and Karl Shilke prepare a bacterial assay to test the activity of antimicrobial polymer-peptide conjugates.

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