Contents

PAGES 2–3
NANOTECHNOLOGY BREAKTHROUGH: SIMPLIFYING LIFE FOR DIABETICS
By Steve Lundeberg

PAGES 4–6
TARGETING TUMORS WITH 3D ANIMATION
By Rachel Robertson

PAGES 7–9
REVOLUTIONARY TESTING FOR FOOD-SUPPLY SAFETY AND ILLICIT DRUG USE
By Steve Frandzel

PAGES 10–11
TRACKING ANTIBIOTIC RESISTANCE IN THE CANALS OF HO CHI MINH CITY
By Keith Hautala

PAGES 12–13
BRINGING MEDICAL ISOTOPE PRODUCTION CLOSER TO HOME
By Jens Odegaard

ON THE COVER
Tala Navab, assistant professor of environmental engineering, works with bacterial plate cultures. Navab studies the persistence and regrowth of enteric pathogens that enter the environment from wastewater streams.

ABOVE
The core of the 1.1 MW Oregon State TRIGA Reactor that will be used for medical isotope production (see story on page 12).

EDITOR
Thuy T. Tran
CONTRIBUTING WRITERS
Steve Frandzel, Keith Hautala, Steve Lundeberg, Jens Odegaard, and Rachel Robertson
GRAPHIC DESIGNER
Jack Forkey
COPY EDITOR
Kathryn White
PHOTOGRAPHERS
Chris Becerra, Johanna Carson, Kelly James, Karl Maasdam, and Jens Odegaard.

COLLEGE OF ENGINEERING
Oregon State University
101 Covell Hall
Corvallis, OR 97331
541-737-3101
engineering.oregonstate.edu

MOMENTUM is published by the College of Engineering’s Marketing and Communications group. Comments and questions about this publication can be sent to the editor at editor@engr.oregonstate.edu
Engineering for life

Health care spending now accounts for nearly 18 percent of the gross domestic product in the United States — and it’s growing. People are not only living longer but seeking solutions that restore health and increase longevity. Modern medicine relies heavily on engineers to provide health professionals the tools they need to diagnose, treat, and prevent illness.

The College of Engineering is launching a new health initiative that leverages our research strengths and cross-school collaboration to better solve health-related problems and graduate the next generation of engineers ready to advance human health and well-being on the planet. Through this initiative the college will build strong internal partnerships — with the Colleges of Science, Veterinary Medicine, Pharmacy, and Public Health — and considerable external partnerships with industry, health care institutions, collaborating universities, and community stakeholders.

Currently, more than 30 engineering faculty members are working on health-related research. Projects vary from molecular-cell investigation to optimizing workplace health for employees working in hazardous environments.

In this issue, we highlight a few of these projects and the researchers who are working on solutions to keep us healthy and improve the quality of life for those who need it most:

- A nanotechnology breakthrough by Greg Herman, professor of chemical engineering, and Xiaosong Du, postdoctoral fellow, will soon make everyday life for patients with type 1 diabetes a lot easier. The researchers have devised a way to monitor glucose levels in the body, then dispense insulin and glucagon from a wearable pump to the patient as needed.

- Eugene Zhang, professor of computer science, and Yue Zhang, associate professor of structural engineering and computer science, are advancing mathematical modeling to make 3D images more lifelike and help technicians treat cancerous tumors with higher precision.

- Keeping consumers safe from domestic and imported food-borne contamination is both time consuming and expensive. Alan Wang, professor of electrical engineering and computer science, has developed a transportable biosensor device that could revolutionize testing for food contaminants. The device analyzes bio-fluids and chemicals at a higher specificity and sensitivity than commonly used methods and can similarly be used to test for illicit drug use.

- The use of antibiotics in livestock, and the misuse of antibiotics in humans, has created antibiotic-resistant bacteria evolving into a planetary health concern. Tala Navab, assistant professor of environmental engineering at Oregon State, is working with Mi Nguyen, group leader at NTT Hi-Tech Institute, Nguyen Tat Thanh University in Vietnam, to complete a first-of-its-kind study examining the prevalence of multiple-antibiotic-resistant enteric bacteria in septic systems and contaminated soils.

- Steven Reese, director of the Radiation Center, and Todd Palmer, professor of nuclear engineering at Oregon State, devised a way to manufacture an essential radioisotope that will soon be in short supply in North America. Technetium-99m is used in cardiac-stress tests to help physicians determine how best to diagnose heart disease and other internal disorders.

Engineers at Oregon State are improving human health around the world by streamlining processes that improve how people receive treatment and creating more efficient systems that keep people healthy.

Go Beavs!

Scott A. Ashford, Ph.D., P.E. (California)
Kearney Professor and Dean
Oregon State University
College of Engineering
Thanks to a nanotechnology breakthrough by a pair of researchers in the College of Engineering, the lives of diabetics may soon become less complicated.

Glucose monitoring and hormone therapy are daily challenges that never go away for the 3 million people living with type 1 diabetes in America. Also known as juvenile diabetes because it is often diagnosed in youth, type 1 is an autoimmune disorder in which the body attacks its own pancreas with antibodies. Type 1 diabetes accounts for about 5 percent of the diabetic population; roughly 30,000 new cases are diagnosed each year.

Greg Herman, professor of chemical engineering, and Xiaosong Du, postdoctoral fellow, have developed a means of printing transistor-based glucose sensors directly onto a catheter attached to a wearable pump. Diabetics can program the pump to deliver insulin and glucagon, the hormones they need to regulate blood sugar.

The idea is that the catheter’s integrated electronics will not only keep track of the patient’s blood-sugar levels but also transmit that information to a computerized pump, ensuring that diabetics get the insulin and glucagon they need, when they need it.

“Many of the type 1 diabetes patients in the U.S. are already wearing an insulin pump, so adding glucose sensing to the catheter would greatly simplify their lives,” Herman said.

Herman and Du achieved the innovation through fabricating transparent transistors and biosensors onto the tight curves of a tiny glass tube — a step toward better medical diagnostic techniques: fully transparent electronics combined with sensing and imaging technologies.

Earlier, Herman and Du fabricated amperometric glucose sensors onto a flat polymer film, which was then wrapped around a catheter tube. But when the sensors were tested in an animal model, the devices tended to delaminate — the sensors would come apart from the film, or the film would peel off the catheter.

Herman’s collaborators on earlier related research improved the ruggedness of these amperometric sensors. However, in this study, Herman and Du addressed the problem by microcontact printing an amorphous indium gallium zinc oxide, field-effect transistor (a-IGZO-FET) directly onto glass tubes with a 1-millimeter radius.

Traditional patterning technologies like photolithography and e-beam lithography proved troublesome for highly curved surfaces, Herman noted, but microcontact printing worked just as effectively as the researchers hoped.

“The process takes advantage of an elastomeric stamp’s ability to conform to curved substrates with minimal distortion of the printed pattern,” Herman said. “The adhesion of the deposited films to the glass tube is very good.”

How good? Well, plenty good enough to withstand all but the most aggressive intent to remove it.
“For the sensor to come off, you’d essentially have to take a file to it,” Herman said. “It’s much more rugged than what we had before, and the electronic performance is excellent — it’s the same as when fabricated on a flat surface using non-printing methods.”

Catheters are metallic or plastic, so unlike the sensor-equipped, glucose-sensing contact lens that Herman has also worked on, transparency isn’t necessarily required. But they used a glass tube anyway, in part to show off the device’s transparency.

“The idea is that we could start integrating optical fibers that have a-IGZO-FET sensors fabricated directly on them,” Herman said. “Some types of sensing need an optical response for detection, so if we can integrate an optical response with an electronic signal, we can expand the detection to other biomarkers. Field-effect sensing may increase the functionality and sensing range of optical sensing systems.”

In this way, transparent field-effect sensing can be melded with electrophysical and neural imaging devices and could greatly improve the sensitivity of an endoscope — a device inserted into the body to provide an internal view.

The Juvenile Diabetes Research Foundation and the National Science Foundation supported the team’s research into fabricating sensors on curved surfaces.

Herman and Du published their research findings in the September 2018 issue of Sensors and Actuators B: Chemical.

BY STEVE LUNDEBERG
Targeting tumors with 3D animation
Video games and movies often come to mind when we think of 3D animation. But the technology has other applications in science and medicine.

Two professors in the College of Engineering are advancing mathematical modeling to make 3D images more realistic. The techniques can not only improve our movie-going experience, but when applied to science, they can increase the accuracy of simulation models used to predict natural disasters like tornadoes, earthquakes, and tsunamis. Or, in this case, help medical professionals better target cancerous tumors.

Eugene Zhang, professor of computer science, and Yue Zhang, associate professor of structural engineering and computer science, are collaborating on a project with Dr. Wolfram Laub at Johns Hopkins Medicine to reduce patient exposure to radiation.

Specifically, the project aims to increase the precision of radiation therapy for prostate cancer. Because radiation is toxic, it is important to minimize exposure as much as possible so neighboring healthy tissues and organs are not affected.

If organs would stay in one place, it would be easier to target them, but — surprisingly — they don’t. Simply breathing can change the location of an organ. During radiation treatment, which can last hours, the volume of the patient’s bladder continuously changes as it fills and empties, which can affect the size and location of the prostate and cause the tumor to displace.

“What we are hoping to achieve is an adaptive treatment plan that is individualized for each patient,” Yue Zhang said.

To address the problem, they created a simulation of how the organs might move or change the location of a tumor by creating a model constructed from a series of 2D medical scans. They then use those scans to generate a 3D image and apply a graphic mesh, which becomes the mathematical framework of the 3D animation.

A graphic mesh is a collection of points, or vertices, in 3D space. The lines connecting these points are called edges, and the areas bounded by edges are called faces. Every cube, for instance, has eight corners — its vertices — and 12 edges separating the six faces.

The interior of each cube is another element of the mesh called a cell. If you join a number of cells together, you get a hexahedral mesh made mostly of cubes. It takes millions of cells to generate a realistic simulation of a tumor and surrounding organs.

But it gets even more complex than that.

“We have tools to describe material properties on these cells, so if it’s an organ that doesn’t move much — or is a little rigid — then we describe it with one material property,” Yue Zhang said. “But if it is something like the bladder, which is very flexible and stretches a lot, we need to use a different property to describe it.”

To add information about the material behavior of the organs to the mesh, the researchers first apply physics concepts...
and then use field processing, a new subfield of geometry processing. Because the mesh is a numerical representation of 3D space, they can deform the mesh using some simulated physical forces described by math equations. At this point, they have multi-dimensional values at each mesh grid point representing physics or biology concepts. These quantities are usually represented as vector or tensor fields.

The technology can be applied to 3D structures in any context. “Instead of modeling a shape, now we are modeling things that are on the shape. It’s one thing to model the shape of the Earth — the mountains and the oceans — but it’s another to model the magnetic field on the Earth. These are vector fields on the surface and can provide a lot of insight into things such as the air stability, pollution, and climate change,” Eugene Zhang said.

In general, field processing finds critical points where there is uncertainty in the model that can indicate change. When it’s applied to medical images, the doctor can use the simulation results to predict changes to the prostate throughout the treatment period.

It could also help track the effectiveness of the treatment and whether nearby organs are being damaged.

“I’m really hopeful that the techniques we are developing and the tools we are building will be useful, not only to architects or artists, but also to scientists and doctors who could actually save lives and overcome diseases, including various forms of cancer and AIDS,” Eugene Zhang said.

BY RACHEL ROBERTSON

Associate Professor Eugene Zhang (above) and Associate Professor Yue Zhang explain how 3D modeling can be used to improve cancer treatment.
Every bite of food we take is an act of faith. We trust that the crisp Willamette Valley apple and sweet Oregon Dungeness crab will satisfy, not sicken us. We’re almost always right, but it’s not a certainty, and the risk increases when food comes from countries with lax food safety regulations. About 20 percent of our food supply is imported, including a whopping 97 percent of our seafood.

Violations include histamines and antibiotics in seafood and pesticide-laden fruits and vegetables. Naturally occurring domoic acid can afflict crabs, prompting wildlife authorities to close fisheries when too much of the algae-produced neurotoxin shows up, financially hurting fisherman and disappointing consumers.

“Food adulteration is a severe issue in developing countries,” said Alan Wang, professor of electrical engineering and computer science. “But inspections are time consuming and expensive.”

Searching for contaminants is a two-stage process. Chromatography separates targeted molecules from a food sample, while spectrometry gauges their concentration.

Seafood samples are tested for histamines in Alan Wang’s lab.
One promising technology is surface-enhanced Raman-scattering spectroscopy (SERS), in which a laser is beamed at the sample. The light is scattered at different wavelengths, each one a unique signature for a specific type of molecule, that allows scientists to determine the quantity of each toxin.

“Chromatography and spectrometry usually require bulky equipment, so samples have to be analyzed in a lab,” Wang said. “It’s time-consuming, labor intensive, and expensive.”

New biosensors developed in his lab could transform how, and how often, we monitor food-borne contaminants. His twist on the technology pairs a method called thin-layer chromatography (TLC) with state-of-the-art portable Raman spectrometers, and he can pack the entire system onto a 1-inch by 4-inch glass slide. Wang calls it a lab-on-a-chip, and the key is diatomite. Diatomite is a plentiful sedimentary rock made of fossilized diatoms — a marine algae and the smallest photosynthetic plant on Earth. Its skeletons act as photonic crystals, a phenomenon that shows up throughout nature. They’re responsible for the striking colors of butterfly wings and opals, for example. They also resonate light in a way that greatly enhances Raman scattering signals, which means extreme accuracy.

To run tests, Wang spreads a thin layer of diatomite on the chip. Then he applies a food sample, which the porous medium absorbs. The toxins he’s looking for will diffuse and separate with the help of a solvent. Next, he conducts SERS to identify the molecules and measure their concentration. It all takes a few minutes.

“One of the most noteworthy features of this technology is that it can simultaneously perform on-chip chromatography of complex bio-fluidic samples and acquire the surface-enhanced Raman scattering spectra of the target chemicals with high specificity and sensitivity,” Wang said.

And the system’s portability means that SERS analysis can be completed with a hand-held Raman spectrometer on site — on a boat or a dock, for instance.

The system’s prowess is evident in a study where Wang tested chili powder and oil for Sudan I, a carcinogenic orange-red dye. Because of the diatomite’s photonic crystals, Raman signal
intensity increased 10-fold compared with current commercial TLC-SERS techniques that use silica gel. He successfully detected the illegal additive down to 1 part per million.

And with one alteration — placing the diatomite inside tiny, microfluidic channels rather than on glass plates — the tool can be used with even greater sensitivity to detect illicit drugs in urine, saliva, or blood.

In one study, he detected cocaine in human plasma down to 1 part per billion.

“That’s a thousand-fold increase over conventional TLC-SERS — even better than many lab-based analytical techniques,” he said. “That may be revolutionary.”

And it may be a boon for forensics. Humans quickly metabolize most drugs; after 24 hours, their levels fall below the detection threshold of most biosensors, according to Wang.

“But if you can trace drug use back 40 or even 48 hours, law enforcement could gather important evidence in DUI cases or when drug use is relevant to a crime,” he said.

Wang believes strongly in the technology, and so do agencies like the National Institutes of Health and the U.S. Department of Agriculture, which continue to support his work.

“I think the markets for food safety and drug detection are very large,” Wang said, “and I have high hopes that we’ll be out there soon.”

BY STEVE FRANDZEL
Antibiotic resistance poses a growing threat to human health around the world, as drugs that were once humanity’s frontline defense against common infections are proving useless against virulent new strains of superbugs.

Overuse and misuse of antibiotics in agricultural and health care settings are the root causes of this resistance. But there is an environmental dimension to the problem as well, says Tala Navab, assistant professor of environmental engineering at Oregon State University.

Navab is a contributing author to a landmark paper, published in the May 2018 issue of Environmental Engineering Science, that aims to establish parameters and priorities for the discipline as it designs its approach to antibiotic resistance.

Navab’s own research investigates the growth and persistence of enteric pathogens as they move through the environment — from wastewater systems to waterways, into soils, onto fields, into
crops and, potentially, onto our dinner plates.

“Septic systems are one of the main reservoirs of antibiotic resistance,” Navab said. “When people take antibiotic drugs, they don’t get completely metabolized. So bacteria start to develop resistance in the gut. Then these bacteria, along with the unmetabolized antibiotics, are passed from the body into wastewater systems, such as septic tanks, where prolonged exposure creates additional selective pressure making the bacteria more resistant.”

In the United States, most homes are connected to municipal sewers that carry wastewater directly to centralized treatment plants. Even in homes that rely on septic tanks (roughly one-fifth), the resulting sludge is commonly disposed of in wastewater treatment facilities, or in well-isolated landfills. However, in less industrially developed parts of the world, sanitation practices are typically not as rigorous.

“Studies have shown that in Vietnam the majority of the septic sludge never makes it to a landfill,” Navab said. “Instead, it is dumped directly into some sort of receiving environment — rivers, canals, other types of waterways, parks, fields — all of that. Sometimes it is applied directly to agricultural soil as fertilizer. These are all environmental reservoirs that people have access to. They’re swimming in them, fishing in them, playing in them, growing food in them — and they all have fecal contamination.”

One of Navab’s current projects is a first-of-its-kind study examining the prevalence of multiple-antibiotic-resistant enteric bacteria in septic systems and contaminated soils. She is collaborating with Mi Nguyen, research group leader at NTT Hi-Tech Institute, Nguyen Tat Thanh University, in Vietnam.

Vietnam is an ideal location for this type of study. The country has one of the highest rates of antibiotic resistance in the world. Antibiotics are easy to obtain, and improper use is rampant. Additionally, about 80 percent of the households rely on septic tanks for sanitation, even in developed urban areas like Ho Chi Minh City (also known as Saigon), the country’s largest metropolis, with some 12 million residents.

Genevieve Schutzius, an environmental engineering graduate student working with Navab, spent three months in Ho Chi Minh City during the winter of 2018. She collected samples of canal water and adjacent soils from 55 areas in 12 districts of the city. Bacteria from these samples were characterized, genotypically and phenotypically, on their antibiotic resistance content and compared to samples taken directly from septic tanks.

“We have data on the susceptibility of enteric bacteria collected from reservoirs containing nine different antibiotics that span four different mechanisms of action,” Schutzius said. “Our preliminary results found that the majority of our environmental samples contained bacteria that are resistant to two or more antibiotics, with some resistant to as many as eight antibiotics. The prevalence of resistance was somewhat higher in the septic sludge, which was expected, but the difference was not that significant.”

Navab says the purpose of this research is twofold.

“First, we need to get a comprehensive overview of the problem so we can clearly state what it is: Where and how are the prevailing practices creating conditions that favor antibiotic resistance?” Navab said. “Then we can start looking at solutions, like improving septic system design and incorporating better treatment methods, such as anaerobic digesters and other technologies.”

BY KEITH HAUTALA
Every day, approximately 40,000 people in the United States — nearly enough people to fill Reser Stadium to capacity — receive a nuclear medicine imaging procedure using the radioisotope technetium-99m (Tc-99m). Tc-99m is used in 80 percent of all nuclear medicine imaging procedures worldwide.

“Famously, it’s used in what is called a ‘stress test,’” said Steven Reese, director of the Oregon State Radiation Center and an instructor in the College of Engineering’s School of Nuclear Science and Engineering. “The idea is that you run on a treadmill and then get injected with Tc-99m, which is attached to a molecule that follows the flow of blood. Radiation detectors are then placed around the body so we can see how the heart moves the blood. It uncovers a lot of vital and accurate information for physicians, and that's why they like to use it.”

The brain, bones, kidneys, and lungs are also commonly imaged. Tc-99m is an ideal medical isotope because of its broad range of applications and short half-life of only six hours. In other words, there’s no radioactivity left in the body shortly after the procedure ends.

But there’s a hitch in getting the product to people who need it. The Tc-99m supply is bottlenecked, and the entire U.S. supply is being imported from overseas.
A quick history lesson: Tc-99m is a decay product of molybdenum-99 (Mo-99). Mo-99 is traditionally made in large nuclear reactors by neutron bombardment of high-enriched uranium housed in a container called a target. As the uranium fissions, one of the daughter products is Mo-99. The sole North American producer of Mo-99, Canada’s National Research Universal Reactor (NRU), stopped producing Mo-99 in 2016 and shut down completely in March 2018. Even before the plant closed, NRU suffered shutdowns in 2007 and 2009.

Enter Oregon State.

Not long after the 2007 NRU shut down, it occurred to Reese that Oregon State’s 1.1 MW TRIGA reactor could possibly be used to produce Mo-99. It was a wild idea for two reasons. One, because the reactor is much smaller than reactors traditionally used for producing commercial quantities of Mo-99, it has far fewer neutrons to fission uranium into Mo-99. Two, because efforts are well underway to stop using high-enriched uranium in civilian research reactors, low-enriched uranium would need to be used in the target. Together, these challenges meant that it would take a novel target design to make a useful amount of Mo-99.

Reese looped in Todd Palmer, professor of nuclear engineering, who specializes in modeling and simulation. “The original target design, it is just like a cylindrical can that contains a layer of uranium in it,” Palmer said. “It just seemed to beg for a little innovation, you know?”

Reese and Palmer brainstormed a new target design idea and then turned it over to Madicken Munk for simulation. At the time, she was an undergraduate student working for Palmer. “I was just so excited to be doing research and running simulations,” said Munk, now a postdoc at the National Center for Supercomputing Applications at the University of Illinois at Urbana-Champaign. “I performed parametric studies to figure out the design needed in order to make the most moly [Mo-99] in the limitations we had. It was a fun mental playground that I got to play in every day.”

After hundreds of simulations and numerous consultations with Todd Keller, Oregon State reactor administrator, to discuss the practical implications of how the target would work in reality, they arrived at the final design.

The target is a cylinder about 2 feet long and about 1 ½ inches in diameter. The low-enriched uranium is sandwiched between two layers of metal cladding. In the center is an annulus that allows water to flow through. It’s this water-circulating annulus that is the key to the whole design. Water increases the number of neutrons that hit the uranium, causing more fission and thus producing more Mo-99.

“This target design seemed to suggest that you could make commercial quantities of moly in a reactor as small as 1 megawatt, like we have here at Oregon State University,” Reese said. “And the reason why that’s fairly profound in the moly production community is that you go from maybe five facilities on the planet to upward of probably 30 to 40 reactors around the world.”

Because of the huge commercial potential for producing Mo-99 in research reactors in the United States, patents were filed and a company, Northwest Medical Isotopes (NWMI), was formed to bring this technology to market. Today, NWMI is moving forward with plans to construct a processing and production facility in Missouri (an ideal central location for shipping Mo-99 to medical facilities around the country).

“This facility will actually make the targets and ship the targets to the reactors. The reactors will irradiate the targets, and then they’ll be shipped back to this facility. The facility will process the moly out of the targets, clean the material up, and then make the targets again. The cycle is then repeated,” Reese said.

If all goes well, production should start up sometime around 2020, breaking the bottleneck and impacting thousands of people in the United States every day. “At this point the handoff has happened, and we’re just hoping to see it come to fruition,” Palmer said.

BY JENS ODEGAARD