

BME at 15

How the Department of Biomedical Engineering launched its way to excellence

A Chip That Thinks Like Us

Today's computers don't really work like brains, but they're getting closer, thanks to Rajit Manohar

Socially Assistive Robots

How kids are learning from their automated friends

2017-2018

YALE ENGINEERING

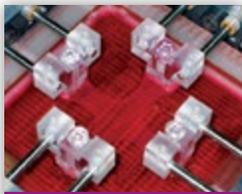


Yale

Programming for Laughs

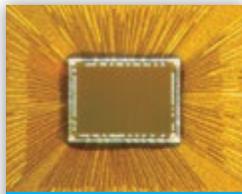
Artificial intelligence can drive cars and beat chess champs. But can it come up with a good joke?





10

BME at 15



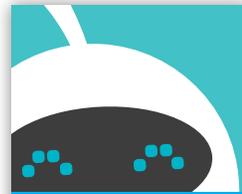
30

A Chip That Thinks Like Us



36

Programming for Laughs



52

Socially Assistive Robots

FEATURES



2

Year in Review



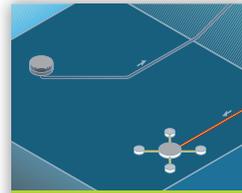
6

Making the Spooky Science of Quantum Computing Practical



18

Taking on the Hackers



24

Nanotechnology Enabled Water Treatment



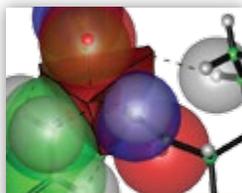
42

A Tiny Device to Improve Global Health



46

Green Engineering



56

Puzzling Proteins



60

If You Build It, They Will Come

Front & Back Covers:

Clustering of reader-submitted captions for the New Yorker caption contest, grouped by theme. The winning caption: "I don't care what planet they are from, they can pass on the left like everyone else."

EDUCATION SUSTAINABILITY INTERDISCIPLINARY MEDICAL INNOVATION TECHNOLOGY

YALE ENGINEERING 2017-2018

YALE UNIVERSITY School of Engineering & Applied Science

P.O. Box 208267 • New Haven, CT 06520

engineering@yale.edu • (203) 432-4200 seas.yale.edu

T. Kyle Vanderlick Dean

Steven Geringer Director of Communications

William Weir Director of News & Outreach

Photography Michael Marsland Humberto Jaramillo Tony Fiorini



Message From the Dean

Engineers are often described as quintessential problem solvers. That's certainly a fitting description, but I find an even more compelling description to be that of "intellectual craftsman."

When I think of a traditional craftsman, I imagine someone having expertise with various tools and techniques who uses them not only to fix things (i.e., solve problems) but also to design new creations. The craftsman is not necessarily the world's expert in any given tool, but has sufficient skill to use all the tools in their arsenal adeptly and with confidence. A good craftsman also knows what they don't know, and is quick to call upon others to bring in additional skill sets when needed for the job. Craftsmen are typically also very "people-oriented;" it is important for them to communicate well to tease out the expectations clients truly harbor about the project at hand. Last but not least, they enjoy the imaginative component of their work as virtually every job is different and requires a unique approach.

Truth be told, I don't really need to imagine the mindset of a traditional craftsman. My father owned the welding shop in our small home town and he was a phenomenal craftsman. He could fix or modify virtually anything and could even build new machines from scratch. As we like to say in the family, my dad would "vander-ize" anything and everything to make it better or to just suit his taste.

During my deanship I have always given a welcome talk when the first-year students arrive on campus, trying to convey the essence of an engineering education. As I tell the students, your tools will be the principles of science and the language of mathematics. I assure them that they don't have to be the world's expert in any given tool to be able to use it effectively. So, if physics seems especially hard, or they only get a B in multivariable calculus, they should not give up on engineering. I urge them to hang in there, to build their toolkit, and I promise they will soon reap the lifelong rewards of becoming intellectual craftsmen. In that spirit, I hope you enjoy reading this year's edition of *Yale Engineering* to learn about the problems they are solving, the new inventions they are creating, and the things they are doing just for the fun of it!

T. Kyle Vanderlick
Dean, School of Engineering & Applied Science

Year in Review

A look back at some of the news stories from the Yale School of Engineering & Applied Science over the last academic year

2016: September ▼

Surf's Up!

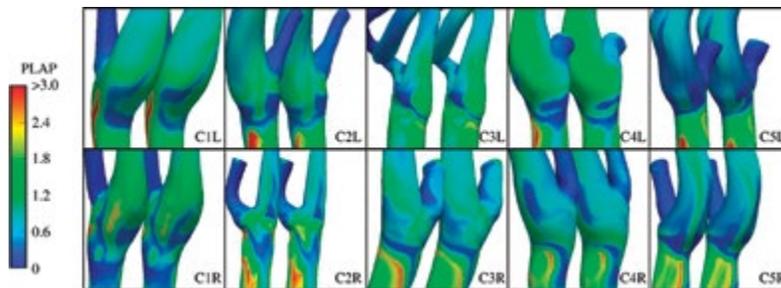
Want to surf all year round on customized waves? Katherine Berry '17 is on it. For the course Mechanical Engineering Special Projects, she built a surf park prototype to study wave formation and the economic requirements of an actual park. With instructors Jan Schroers, professor of mechanical engineering & materials science, and Larry Wilen, a Center for Engineering Innovation & Design mentor and senior research scientist, she built a small model of a park base. With a rotating arm made from PVC piping that hangs overhead, it can be adjusted to produce a variety of wave sizes and shapes.



2016: November ▶

Making Use of Microalgae

Researchers in the lab of Julie Zimmerman, professor of chemical & environmental engineering and forestry & environmental studies, developed a method to extract different compounds from microalgae, and separate those compounds by type for different uses. That could help make algae a cost-viable source for such products as biodiesel, pharmaceuti-



2016: October ▲

Tracking Clots with Supercomputers

With help from three supercomputers, including the High Performance Computing Clusters at Yale, researchers in the lab of Jay Humphrey, the John C. Malone Professor of Biomedical Engineering, are figuring out the stages of a blood clot's formation and growth in abdominal aortic aneurysms (AAAs). Although most AAAs harbor a blood clot, little is known regarding the development of the clot or its effects on the underlying aortic wall. This research could lead to a better understanding of how clots contribute to the risk of rupture of an AAA, which can be lethal.



cals and infant formula. The results of their work, led by Ph.D. student Thomas Kwan, were published in *ACS Sustainable Chemistry & Engineering*. Using a process they developed in the lab, the researchers targeted a compound known as triacylglycerides (TAGs), which have proved difficult to separate.



◀ 2016: December

Enlightening Projects

Students in the course Engineering Innovation & Design helped the Yale Center for British Art (YCBA) tell the story of three 18th-century German princesses and their influence on science and the arts. Specifically, they focused on a part of the exhibit featuring Isaac Newton's theories of light. To convey the complex ideas to a general audience, the student teams made a sculpture-like model that illustrated Newton's theories in 3D. Another student team built a device that allows patrons to manipulate prisms. The exhibit was featured at the YCBA from February to April and opened at Kensington Palace in June.

♥ 2017: January

Better Lacrosse Through Engineering

A student team in the course Engineering Innovation & Design designed and built a new practice tool for Yale's lacrosse team. The students developed a frame with six movable panels arranged in an "L" shape that can be placed in any of the goal's four corners. The device, designed to minimize injuries during practice, stands in the place of the goalie. With a remote control, coaches can specify which panels players should set their sights on.



2017: February ▶

A Virtual Space for Studying Artifacts

A collaboration between the Department of Computer Science and the Institute for the Preservation of Cultural Heritage at Yale's West Campus developed CHER-Ob, an open-source software program that allows researchers from different fields to coherently gather and study a wide-ranging body of research on a single artifact. Holly Rushmeier, a professor of computer science who led the project, said the disjointed ways that different research teams collect and archive their findings often stymie work on cultural artifacts. With CHER-Ob, research teams will have a single virtual environment for collaborative cultural heritage research, accommodating many kinds of media.

Continued →

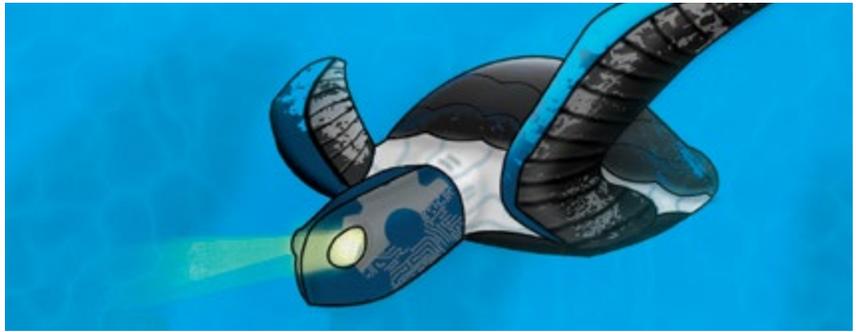
Year in Review

2017: March ▶

Turtle-Inspired Robots

Rebecca Kramer-Bottiglio, assistant professor of mechanical engineering & materials science, was awarded a Young Investigator

Research Program grant from the Office of Naval Research. With the award, Kramer-Bottiglio will create the first morphing robotic limb capable of matching its configuration and stiffness to its environment. Drawing from the differences and similarities of turtles (good in water) and tortoises (good on land), Kramer-Bottiglio's lab will develop what's known as a Biomimetic Unmanned Untethered Vehicle with a system that can change from a flipper optimized for water to a leg optimized for land.



2017: April ▼

Discovering the Science of Throwing

As cricket fielders, baseball pitchers and even office workers tossing paper in the trash have learned, there's a tradeoff between how fast you can throw and how accurate you can be. A study by Madhusudhan Venkadesan, assistant professor of mechanical engineering & materials science, has figured out why. His study, published in *Royal Society Open Science*, focuses on the origins of the speed vs. accuracy phenomenon with a series of calculations. The study also explains why certain throwing styles work best with certain tasks.



◀ 2017: May

Honoring a Computer Pioneer

Daniel Spielman, the Henry Ford II Professor of Computer Science & Mathematics, was elected to the National Academy of Sciences. Much of Spielman's work has focused on designing faster algorithms for solving systems in linear equations, and then using those algorithms to do other things faster. His contributions to computer science and mathematics have been enormous and have led to numerous applications, such as making communication faster and more reliable, broadcasting high-definition television, and improvements in medical imaging. Among other accolades in his career, Spielman is a two-time winner of the Gödel Prize and a MacArthur Fellow.

Yale

INTERDISCIPLINARY





2017: June ▶

The Many Colors of Solar Energy

While solar energy has progressed dramatically in the last few decades in efficiency and lower costs, the look of solar panels hasn't—a limitation that could hinder the technology in some commercial applications. But the lab of Andre Taylor, associate professor of chemical & environmental engineering, has

developed a solar cell that widens the choice of colors without decreasing its power conversion efficiency. His research team used a dye molecule known as ASSQ. Jaemin Kong, a postdoctoral associate who led the project, explains that the molecule acts as both a color agent and energy transfer donor.

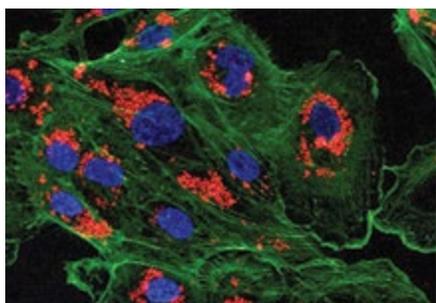
2017: July ▶

Cells in a “Tug of War”

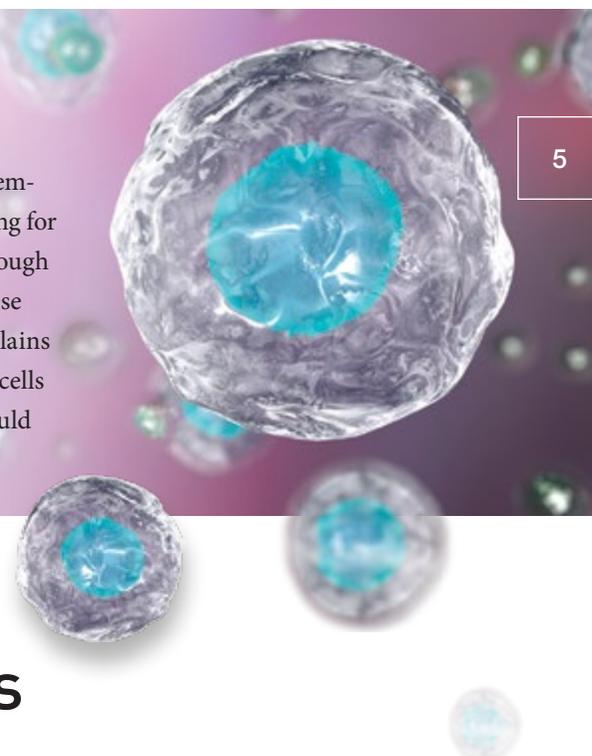
Andre Levchenko, the John C. Malone Professor of Biomedical Engineering, and members of his lab at Yale's Systems Biology Institute identified the mechanism accounting for diverse cellular migration patterns and the way that cells control their movement through a “tug-of-war” interplay between two signaling pathways. Scientists have studied these locomotion patterns but no single mechanism has been proposed until now that explains why cells employ diverse migration patterns under the same conditions, with single cells switching between them with what seems like uncanny regularity. The discovery could lead to a better understanding of how certain types of cancer spread.

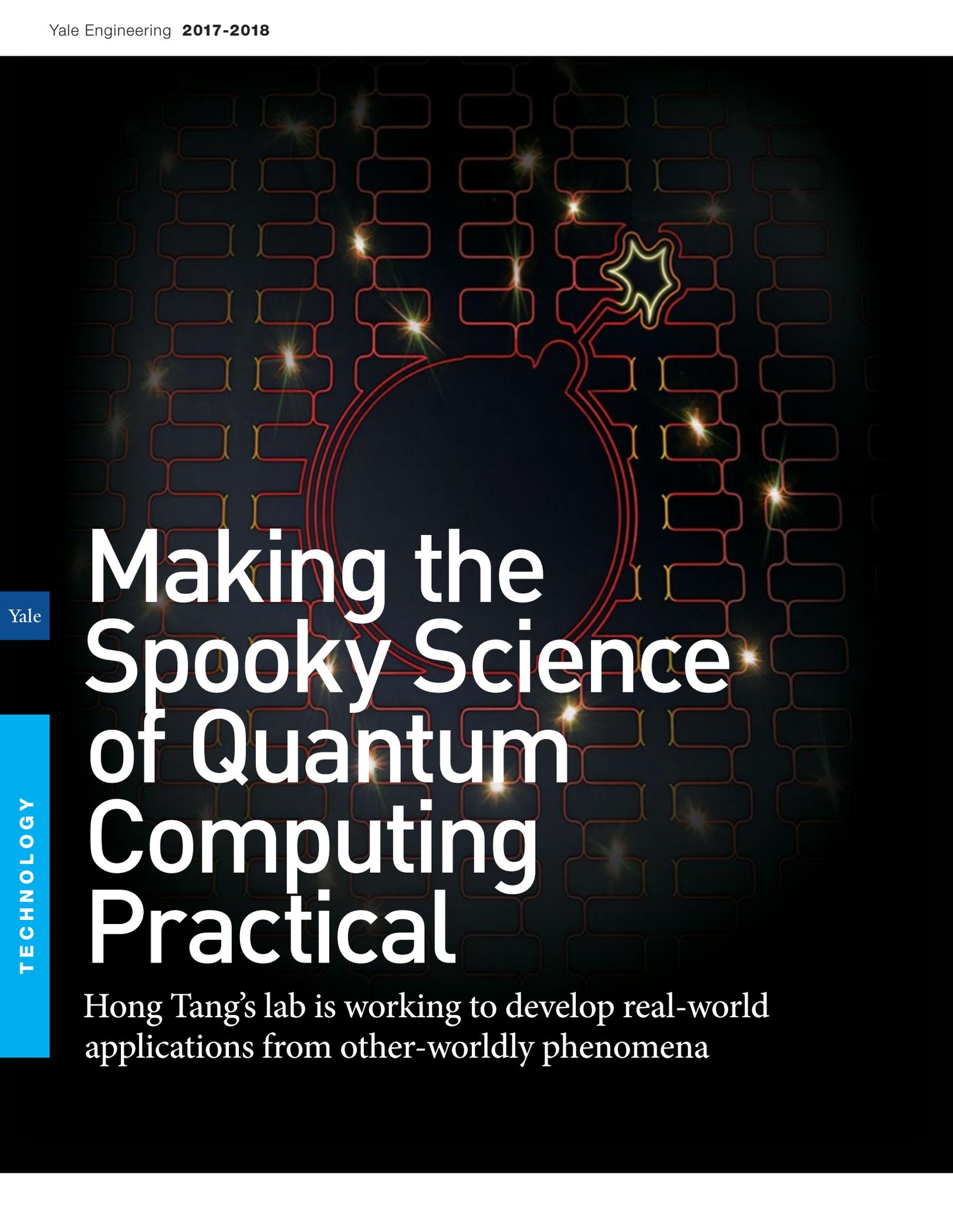
2017: August ▼

Protecting Organ Transplants with Nanoparticles



Using nanoparticles, Yale researchers developed a drug-delivery system to reduce organ transplant rejections. Led by Mark Saltzman, Goizueta Foundation Professor of Chemical and Biomedical Engineering, and Jordan Pober, Bayer Professor of Translational Medicine, the team's drug delivery system uses nanoparticles to carry small interfering RNA (siRNA) to the site of the graft. The slow release of the siRNA helps prevent the activation of white blood cells that identify and attack foreign bodies, which is one of the main culprits behind organ rejection.





Making the Spooky Science of Quantum Computing Practical

Hong Tang's lab is working to develop real-world applications from other-worldly phenomena

Yale

TECHNOLOGY

Quantum computing is based on the very strange ability of particles to exist in more than one state at a time (even veteran quantum researchers find this kind of eerie). Scientists hope to harness this phenomenon to create computers far more powerful than conventional machines in which information is stored as bits represented by the binary system of ones and zeros. Ideally, doing so would lead to technology that would be invaluable to a number of fields — the stock market, weather modeling, cryptography, and complex computer simulation, to a name a few.

It sounds like science fiction, but quantum computing currently exists — albeit with some serious caveats. For instance, a quantum computer currently operates at IBM’s Thomas J. Watson Center. However, its operating temperature needs to be kept slightly above absolute zero (making it one of the coldest places on Earth) because quantum states are so easily disrupted by heat. For all that, its computing power still doesn’t match the computer in your office, where the thermostat likely has a much more reasonable setting.

So, yes, it could be a while before quantum computing is a part of everyday life. But there was also a time when our classical computers were room-sized behemoths, and few people ever envisioned the desktop models that would grow out of those, let alone into smartphones and other tiny computers.

The lab of Hong Tang, the Llewellyn West Jones, Jr. Professor of Electrical Engineering & Physics, has taken on the mission of turning this science toward a more practical, usable route.

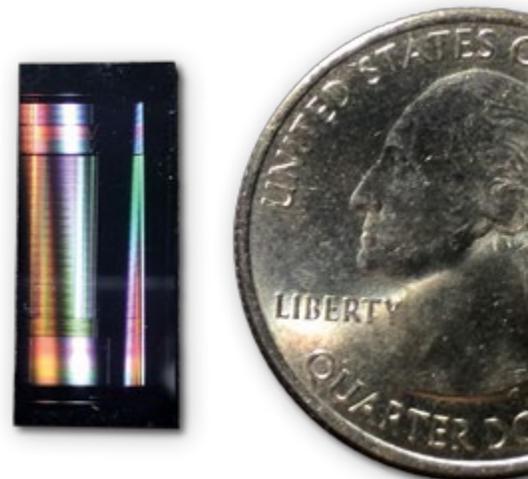
“We want to make a kind of quantum computation in a scalable fashion,” Tang said. “Meaning, you don’t just make one, but many that work together, just like the basic computers with transistors. Today’s quantum computers are nowhere close to that goal.”

Tang said they want to use optical chips as a platform to communicate between different modes. “There are pros and cons in each of the platforms, and we want to combine the benefits of each.”

A big part of that vision is getting two classes of quantum computation to work together. One involves microwave frequencies that produce superconducting qubits, and the other involves linear quantum optics operating with infrared or visible photons. Each has its drawbacks: Superconducting qubits can’t transport quantum information at room temperature, while linear quantum optics can’t process quantum information efficiently. Fuse the two, though, and the microwave and optical platforms can work together and pave the way toward a workable technology.

The challenge is getting microwave frequencies to convert to optical ones. One way to do that is with what’s known as a whispering gallery, a phenomenon in which sound waves of certain frequencies travel along curved surfaces. Go to a particular spot outside the Oyster Bar in New York’s Grand Central Terminal, and murmur very softly into the corner. Dozens of feet away, you can still be heard clearly. In Tang’s lab, though, they’re using light waves instead of acoustic ones and applying them to a device known as an optoelectronic resonator. It’s an innovation that could lead to a way of efficiently converting

Right: Tang’s device converts infrared light to visible light and back again.



Continued →

Visible and infrared modes co-exist in a microring resonator.

information from microwave photons to optical waves, which can be transmitted over optical fiber over very long distances. This would open up new possibilities in quantum communications.

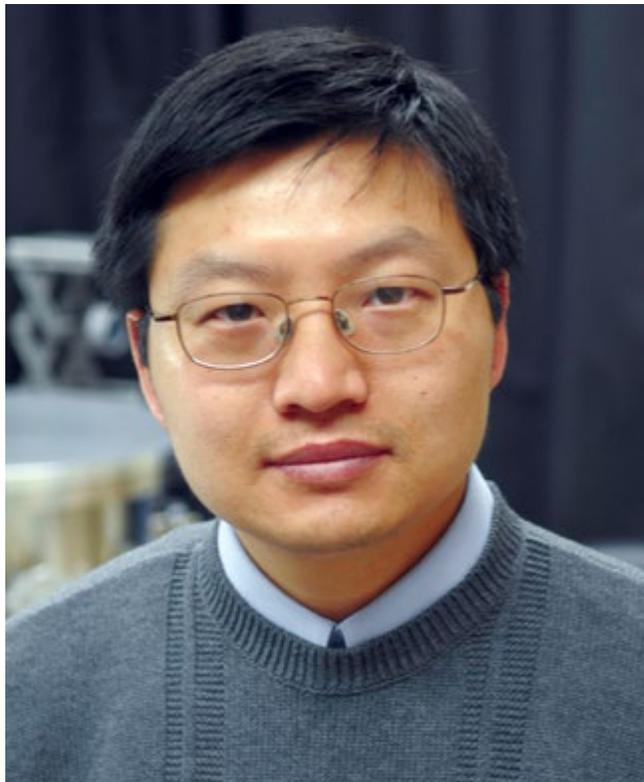
Another part of the challenge is perfecting the ability to manipulate the frequency of single photons. One approach they've taken is experimenting with different materials for the waveguide to change the frequency of the photon. By doing so, the researchers have shown that they can change a photon's frequency by up to 300 GHz without creating

any noise (loss of certain quantum properties). They do this by changing the photon's propagating medium — that is, the material in which the light travels. Silicon is typically used for the waveguide, but Tang's lab instead uses aluminum nitride as the propagating medium. That allows the researchers to stretch or compress the photon and change its frequency. But it's not easy to do, because the structure needs to change within a few trillionths of a second — and it has to happen exactly as the photon enters the waveguide.

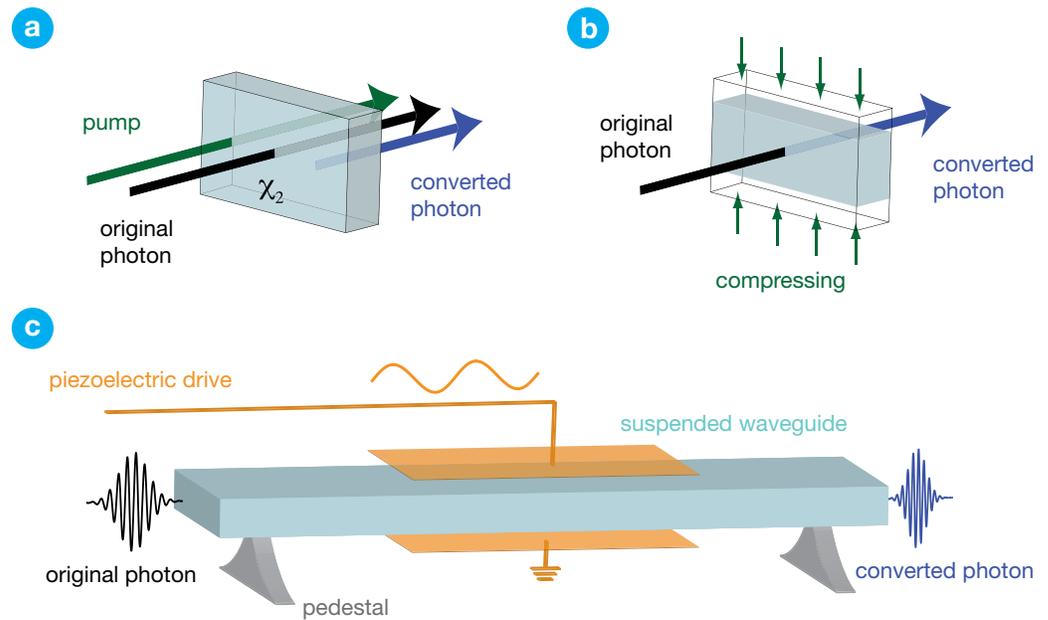
Currently, the most common technique for manipulating photon frequency is with what's known as nonlinear optical effects, in which a laser essentially acts as a pump, changing the photon frequency by providing extra photons to mix with the original one. The process requires a very strong laser, though, and that creates noise.

“It's really a community effort, and every one of us is making a contribution, but it's not something where only one person is going to make a breakthrough.”

◀ Hong Tang



Right: Principles of frequency conversion.
 a: Frequency conversion using second order (χ_2) or third order (χ_3) optical nonlinear processes.
 b: Frequency conversion induced by the mechanical deformation.
 c: Schematic of a suspended waveguide made of piezoelectric material.



Linran Fan, a Ph.D. student in Tang’s lab and one of the leaders of the project, said they avoid the need for a strong laser by converting microwave energy into mechanical stress to change the waveguide structure.

“We don’t need the optical pump, so we don’t create any noise,” Fan said.

In another project, Tang and his researchers have also developed a device that converts visible light to infrared light, a crucial step toward allowing the manipulation of qubits and the transmission of that same information over long distances. The device has the potential to be built on a scale required for quantum computers as the technology advances.

“People want to use short wavelength photons — like 700 to 800 nanometers — to do quantum computation,” said Xiang Guo, a graduate student in Tang’s lab and lead author of the study. If they want to transmit that information over a long distance through optic fibers with low loss, though, they need to convert the photons to longer wavelengths of about 1,500 nanometers. And when it reaches its destination, the photon needs to be converted back to the shorter wavelength.

In their device, lasers send two wavelengths of light into the device, and the converter generates a third frequency that acts as a kind of middle ground between the two. Once again, aluminum nitride serves as a key element.

The lab had started using the material several years ago, but found that quantum information was lost in the transmission. The team improved the material quality, which made it more transparent to light and reduced the loss of photons scattering at the boundary of the device.

Pleased with the conversion efficiency rate they achieved, the researchers continue to explore other applications of the converter. They’ve since extended the system to generate an optical frequency comb (a laser that pulses frequency lines that are equally spaced) in infrared wavelength, which immediately converts them into a visible frequency comb.

“Because the frequency conversion was very well optimized in our system, we obtained an unprecedented high-efficiency, broadband visible frequency comb, which could be quite useful to increase the bandwidth of device operations,” Guo said.

At this point, the work in Tang’s lab is all fundamental research, and Tang said no one can be sure when any of it — or that of any other lab’s — will make its way to the market.

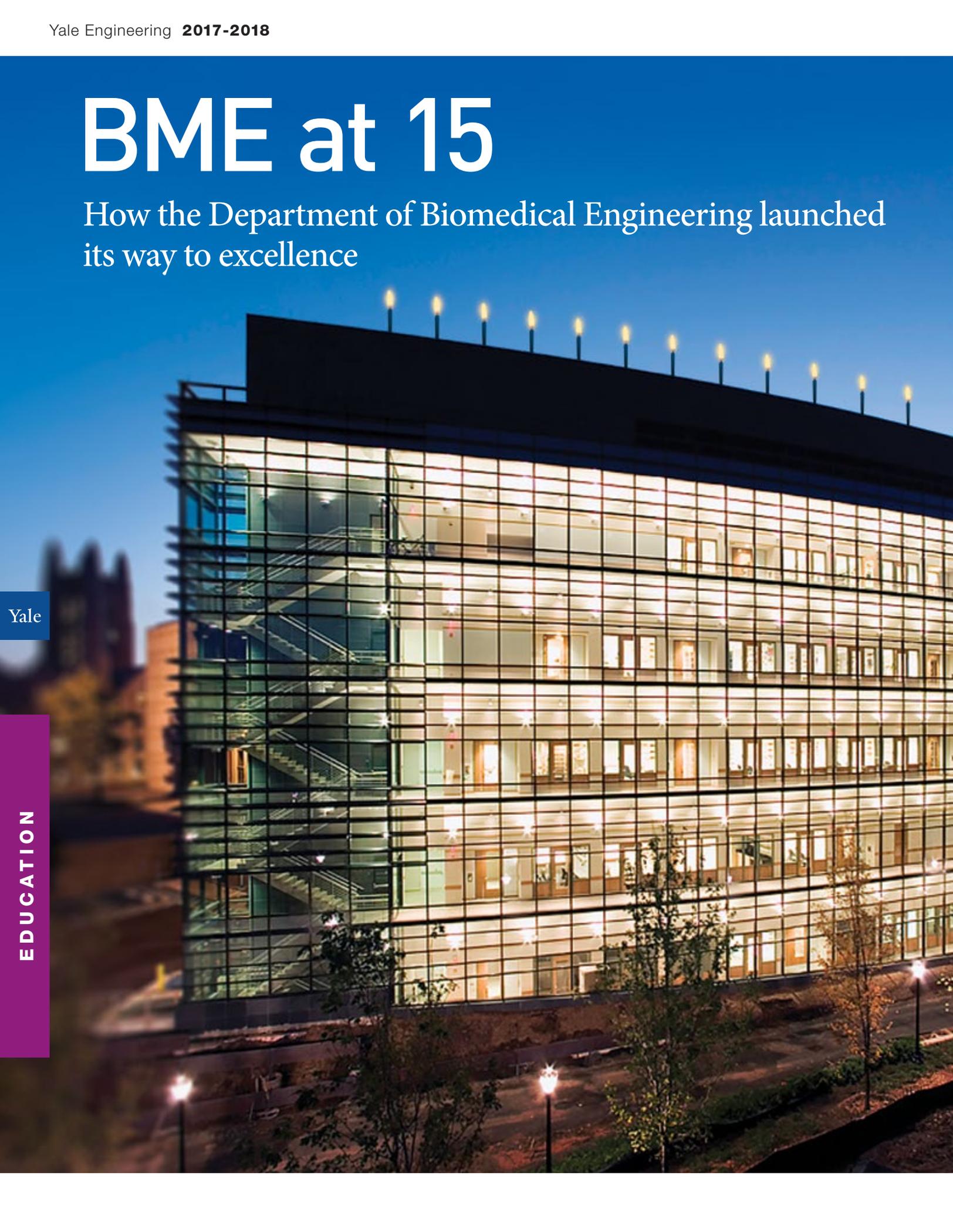
“It’s really a community effort, and every one of us is making a contribution, but it’s not something where only one person is going to make a breakthrough,” Tang said. “A lot of people are just interested in proof of principle, so we need engineers to come in and make it more robust, more scalable. That doesn’t come in a day.”

BME at 15

How the Department of Biomedical Engineering launched its way to excellence

Yale

EDUCATION





The Daniel L. Malone Engineering Center houses the Department of Biomedical Engineering faculty offices and laboratories.

Until the mid-1960s, biology and engineering didn't have much to do with each other. But then imaging technology, computers, and computational methods became more powerful. That made it easier to observe, study, and mathematically model the machinery that makes up all life - and engineers were eager to apply their skills.

In 2002, Mark Saltzman arrived at Yale as the university's first tenured biomedical engineering professor, a key hire for what was at the time a young program quickly gaining momentum. The biomedical engineering (BME) major had been established four years earlier, and the discipline — building on decades of significant Yale research in engineering, the life sciences, and medicine — was being championed by Yale administrators as a key area of investment in the university's future.

Yale's commitment convinced Saltzman — a renowned innovator in polymeric materials for drug delivery systems and tissue engineering — to join Yale not only as a member of the faculty but also to shepherd the BME program to departmental status. True to that vision, within one year of Saltzman's arrival, the Department of Biomedical Engineering was created, and Saltzman was appointed BME's founding Chair.

Over the past 15 years, the department has experienced a meteoric growth and rise in external recognition. Just seven years after becoming a department, the National Research Council ranked Yale BME the 6th best program in the U.S. Now totaling 17 primary and 16 affiliated faculty members, the BME department has grown from a collection of excellent individual laboratories to a collaborative center for research and education.

Continued →

Connections to Medicine

Over the years, Yale School of Medicine had already made considerable investments to create world-class biomedical imaging. BME leveraged this expertise by inviting many in the core imaging group to serve as founding faculty members. This included a primary appointment in BME to pair with the still-existing primary appointments in the Department of Diagnostic Radiology. Current jointly-appointed faculty members are Richard Carson (also Director of the Yale PET Center), Jim Duncan, Fahmeed Hyder, Doug Rothman, and Larry Staib. Steve Zucker, the David & Lucille Packard Professor of Biomedical Engineering and Computer Science, adds to the current strength in image analysis and computer vision.

The new department received an early boost with a \$13 million grant from the National Institute of Biomedical Imaging and Bioengineering (NIBIB) that funded a 10-year project to develop advanced imaging techniques for the treatment of neocortical epilepsy. Working with the

University of Minnesota and Albert Einstein College of Medicine, the research was led by Jim Duncan, the Ebenezer K. Hunt Professor of Biomedical Engineering, Radiology & Biomedical Imaging, and Electrical Engineering.

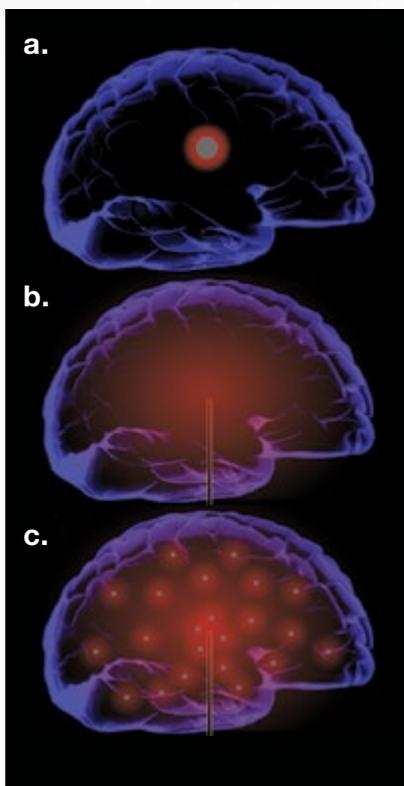
“The NIBIB grant immediately showed the legitimacy, as well as the potential accomplishments, of Yale biomedical engineers,” Duncan said. “And as a joint venture with Dennis Spencer, then Chair of the Department of Neurosurgery, and collaborators in the mathematics and biology departments, the research also provided a model for how BME could bring together diverse thinkers for a common purpose. All BME departments want that, and Yale had it.”

Jay Humphrey, the John C. Malone Professor of Biomedical Engineering and current Chair, said the department remains particularly strong because Yale’s School of Medicine is so strong. It’s a partnership, he said, very much in keeping with President Peter Salovey’s vision of “one Yale.”

BME’s personnel links to the School of Medicine are numerous: As BME Chair, Humphrey regularly attends meetings

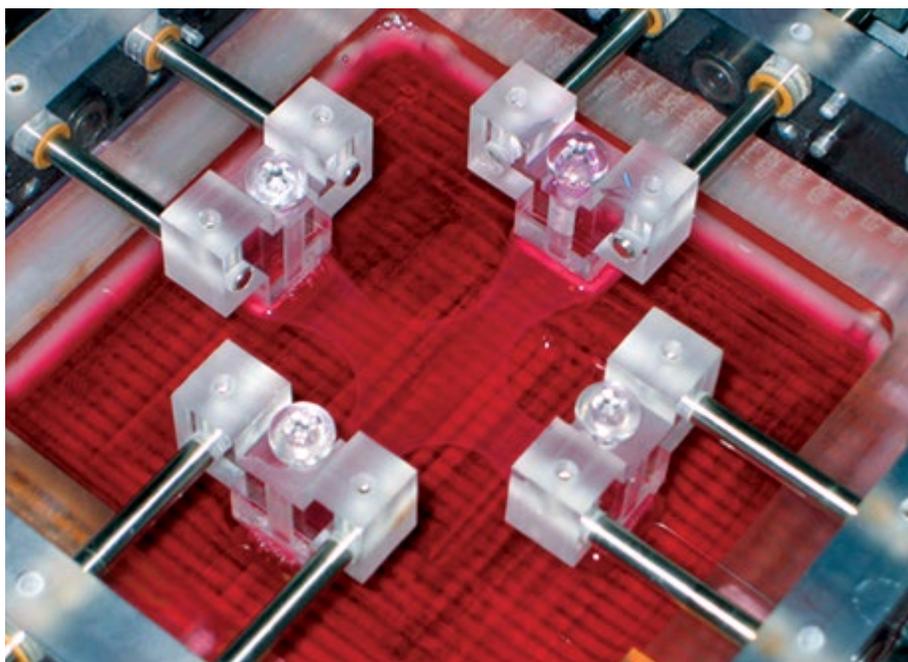
Yale

EDUCATION



Left: Convection-enhanced delivery of drug-loaded nanomaterials.

Right: Cruciform-shaped tissue equivalent (light pink) engineered to quantify the effects of biaxial loading on arterial cell responses.





Stuart Campbell



Richard Carson



Jim Duncan



Tarek Fahmy



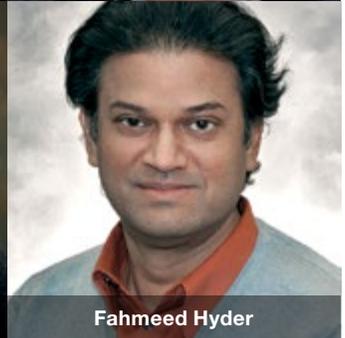
Rong Fan



Anjelica Gonzalez



Jay Humphrey



Fahmeed Hyder



Themis Kyriakides

Biomedical Engineering Faculty



Andre Levchenko



Michael Mak



Kathryn Miller-Jensen



Michael Murrell



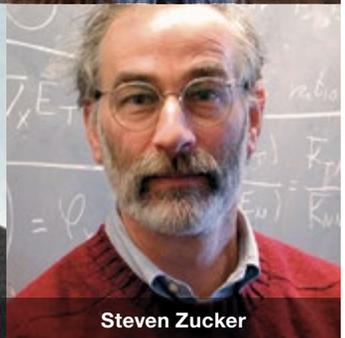
Mark Saltzman



Lawrence Staib



Douglas Rothman



Steven Zucker

Continued →

with officials at the medical school. He also serves on the steering committee of the Vascular Biology and Therapeutics Program. Meanwhile, Saltzman serves as co-founder of the Yale Center for Biomedical Innovation & Technology (CBIT). Both the Director of Undergraduate Studies and Director of Graduate Studies for BME — Jim Duncan and Richard Carson, respectively — are jointly appointed between BME and Radiology. Themis Kyriakides, associate professor of biomedical engineering and pathology, brings expertise in biomaterials and tissue-device interactions, which are driven largely by inflammation. “So the BME faculty who are engaged with our undergraduates, graduate students, and faculty are very invested in the medical school,” Humphrey said.

whose nanotechnology and immunobiology research has led to numerous breakthroughs, including methods for boosting a patient's immune system using biologically-inspired nanomaterials. With Laura Niklason joining as an affiliated faculty member in 2006 after her move from Duke to Yale, the department strengthened its focus on tissue engineering. Pioneering “off-the-shelf” tissue engineered arteries and whole lungs, Niklason’s research aims to create working organs that can be used for human implants. Her tissue engineered vascular graft is currently in clinical trials for use in kidney dialysis patients.

In 2010, Saltzman found an ideal colleague in Humphrey, previously with Texas A&M. His research explores how vascular cells respond to mechanical stimuli, with the aim of using clinical diagnostics, medical images, and patient histories to develop predictive models of disease progression. Such scientific advances — some of which he has also used to advance engineered vascular tissue for implantation — had already established Humphrey as a powerhouse leader in his field.

Key Hires

Crucial to the department’s growth was the number of smart hires made in its first few years. As examples, in 2005 the department hired a promising new researcher, now associate professor of biomedical engineering Tarek Fahmy,

Yale BME by the Numbers

Founded

2002

Primary

Faculty Members

17

Affiliated

Faculty Members

16

Graduate Student Fellowships (total)

11

- 3 › American Heart Association Fellowships
- 5 › National Science Foundation Fellowships
- 1 › National Research Service Award Fellowship
- 1 › Paul & Daisy Doros Fellowship for New Americans
- 1 › Whitaker International Fellowship

B.S. Degrees

Awarded since 2006

280

National Science Foundation

Faculty Early Development

Awards (CAREER)

6

Ph.D. Graduates

100+

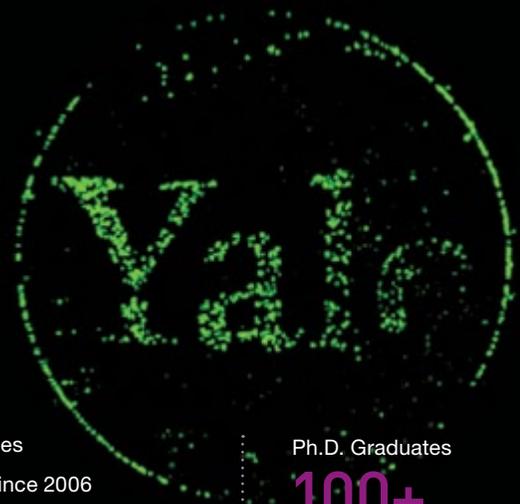
MD/Ph.D. Graduates

11

Packard Foundation

Awards

1



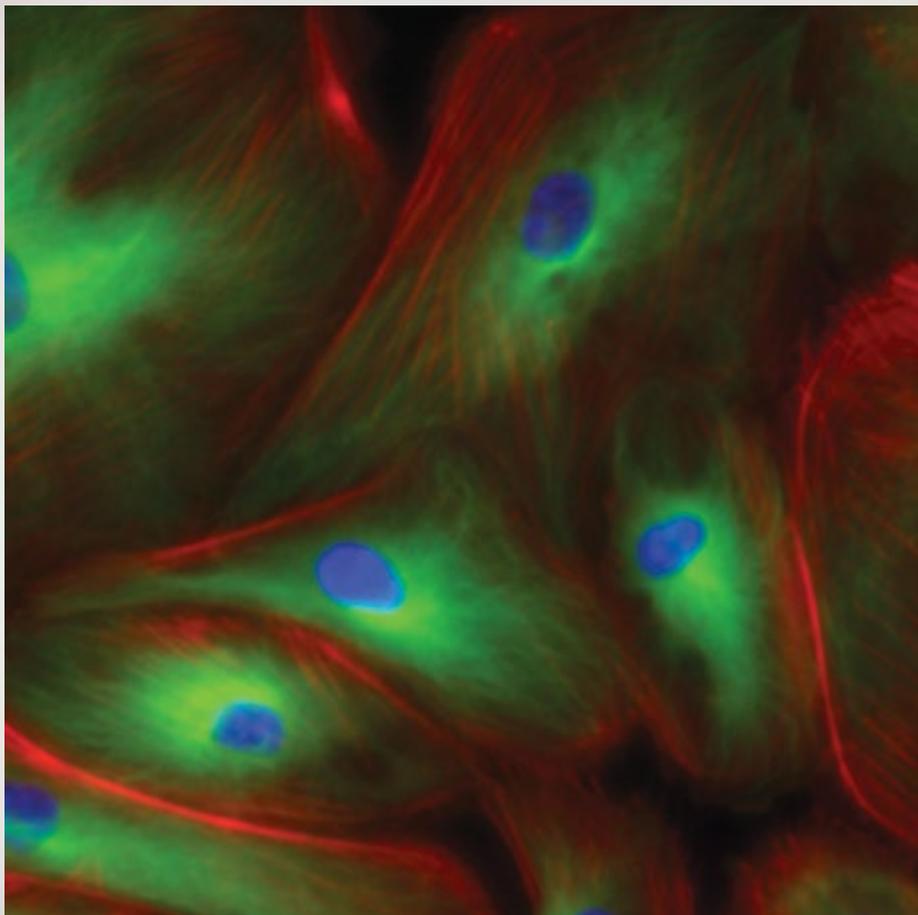
Right: *Fluorescent stained pericyte cells showing internal actin fibers and surface proteins.*

“I came to Yale because it’s a university unlike any other I know — the collaboration is instinctive, with people freely sharing equipment, supplies, and ideas, almost without question. It’s part of the very fabric of what Yale is,” Humphrey says. “I not only knew that Yale’s vascular biology and therapeutics program was the strongest in the country, I also knew how remarkably easy it would be to forge new collaborations with the engineers, scientists, and clinicians here.”

In addition to Humphrey, the department bolstered its strength in immunoengineering and biomechanics by hiring Anjelica Gonzalez, now the Donna L. Dubinsky Associate Professor of Biomedical Engineering, and Stuart Campbell, now associate professor of biomedical engineering. Gonzalez’s lab produces engineered tissues to investigate the immune system’s complex responses to inflammatory signals. Campbell uses a mix of computational techniques and engineered tissues to explore mechanisms that underlie genetic forms of heart disease.

Expanding into Systems Biology

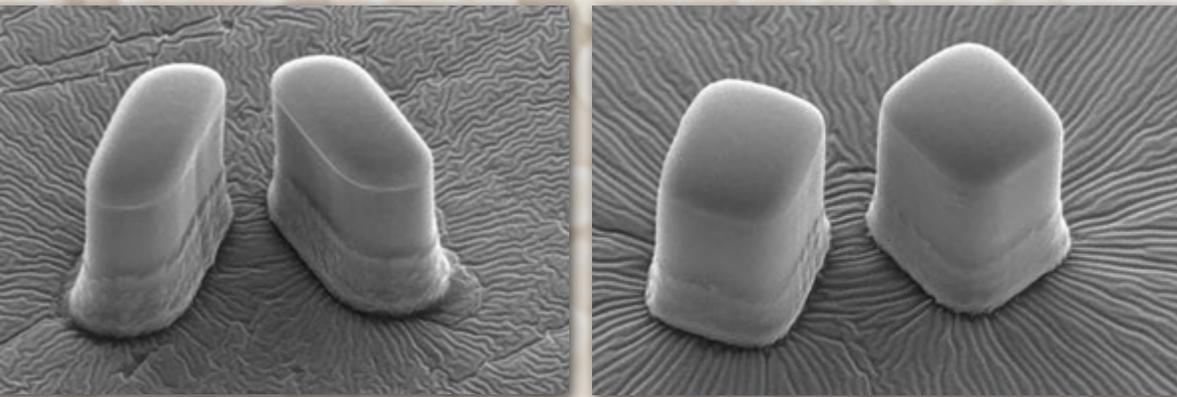
At the same time, the department was also looking to expand into the emerging field of systems biology. “Systems biology came about largely in response to a philosophical change in the way we look at problems,” Humphrey said. “Historically, biology became very reductionist. We moved from looking at an organ to looking at tissue, and then to a cell and then to a certain protein within a cell. Systems biology takes everything we learn at different scales and tries to put it back together. It’s a more integrative way of looking at things.”



Saltzman said the department was in a good position at the time to make its mark on the relatively new discipline of Systems Biology because researchers could again build upon one of the university’s strengths. “This field connects engineering to the rest of the university in a way unlike any other research interest we could have,” he said. Alongside the search that brought in Humphrey, two new junior faculty members joined BME in 2010: Rong Fan, now associate professor of biomedical engineering, and Kathryn Miller-Jensen, now associate professor of biomedical engineering and molecular, cellular, & developmental biology. Saltzman notes that, as soon as the search committee identified these two researchers as their prime candidates, enthusiasm within the department quickly rose for the field of Systems Biology as a whole. “That’s when it clicked for everyone,” he says.

That same year, Yale announced the creation of the Systems Biology Institute on the West Campus complex. Andre Levchenko, the John C. Malone Professor of Biomedical Engineering, was recruited from Johns Hopkins and named the Institute’s inaugural director. A leading researcher

Continued →



Left: Scanning electron microscope image of a trap used to isolate single cells in a microfluidic device.

in intracellular signal transduction and cell-cell communication, Levchenko combines molecular biology with cutting-edge imaging, modeling, and microfabrication to investigate cell communication during the cell cycle, locomotion, and cell death. In particular, he is interested in the role of such communication in such pathologies as cancer and AIDS. Levchenko and colleagues recently were awarded a \$9.5M grant from the NIH to use methods of systems biology to battle some of the deadliest cancers.

BME further bolstered its presence in the interdisciplinary Systems Biology Institute in 2015 by hiring Michael Murrell, assistant professor of biomedical engineering. Murrell combines experimental models of the mechanical machinery within the cell with concepts from soft matter physics. He does so to gain a fundamental understanding of the influence of mechanics on cell and tissue behavior, including fundamental processes such as cell division and cell migration.

An Entrepreneurial Spirit

Humphrey has seen in recent years a trend that students don't just want to make breakthroughs in fundamental science, they also want to find practical ways to translate these discoveries into clinical advances as well as to establish viable businesses.

"We see them seeking to be entrepreneurs rather than just engineers who may go off and become part of a big company," he said. "A lot of our students go to graduate school or medical school, but others want to start companies and really advance new ideas." It's a very positive

development, he said. "That's the kind of student we expect to be here at Yale, one who wants to get out and start their own company and raise their own venture capital and really have an impact."

Among those success stories is 3Derm Systems, founded in 2012 by biomedical engineer Liz Asai and electrical engineer/computer scientist Elliot Swart based on technology they had created as Yale undergraduates. Their inexpensive handheld imager takes 3D pictures of skin to allow dermatologists to remotely analyze and monitor patients' skin conditions. The technology helps detect skin cancer at earlier, more treatable stages.

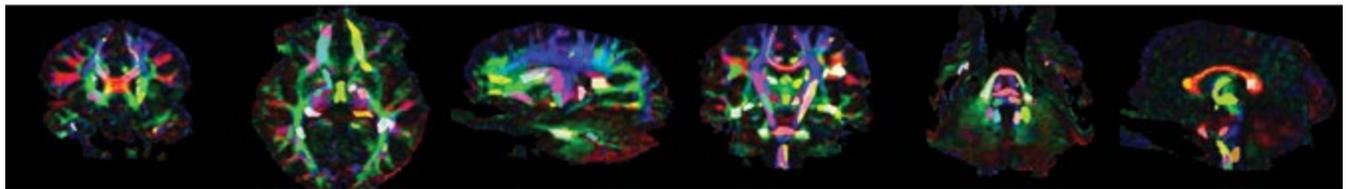
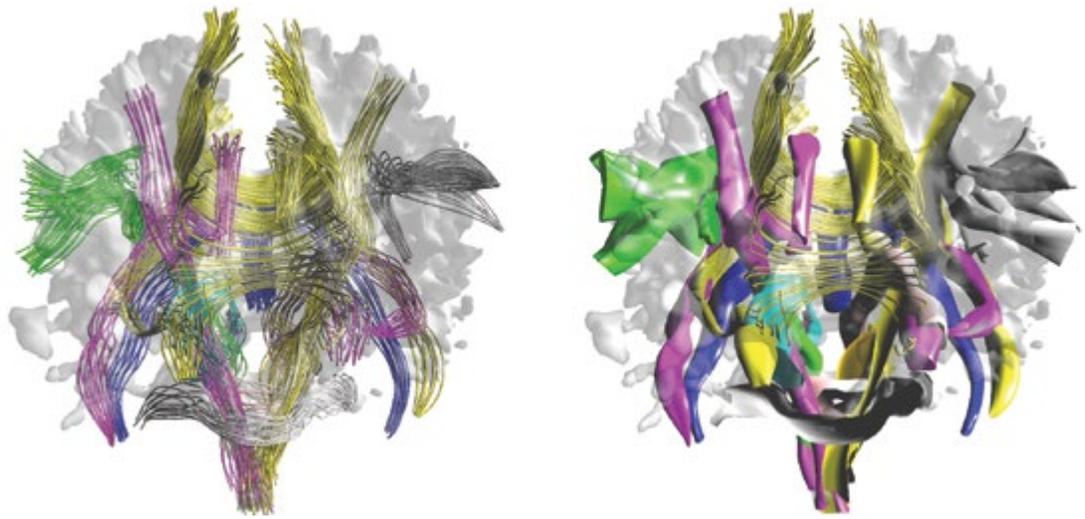
The same year, under the leadership of Anjelica Gonzalez, a team of BME students and faculty developed a new device called PremieBreathe, a low-cost infant respirator that delivers warmed, humidified, and oxygenated air to reduce airway irritation and keep premature infants breathing normally. The work is supported by USAID and VentureWell, and initial prototypes have already been tested in collaboration with hospitals in Ethiopia.

More recently, BME grad Andres Ornelas-Vargas '17 co-founded Acantha Medical, a company that developed a device to better perform a common procedure known as central venous catheterization. The company won the grand prize in June at the Infymaker Awards.

That spirit of innovation has been fostered by a number of initiatives in the last 15 years. The Center for Engineering Innovation & Design (CEID), which opened in August 2012, has centralized a large portion of the engineering landscape. Students can go there to synthesize information from multiple courses, and even launch entrepreneurial projects. It also offers a number of design-based engineering

Top: 3D visualizations of extracted anatomical tracts showing either tract surfaces or curves indicating neuronal fiber courses.

Bottom: 2D slices through the tracts overlaid on magnetic resonance diffusion images.



courses, including the biomedical engineering/mechanical engineering course “Medical Device Design & Innovation,” co-taught by CEID assistant director Joe Zinter and Alyssa Siefert, engineering director for CBIT. A laparoscopic surgical technique, a next-generation manikin for improved CPR training, and a device that drastically improves the prospects of successful intestinal transplant have all come out of the course.

“Before the medical device course existed, complex BME projects like that could only be undertaken with faculty support — meaning only projects that aligned with the faculty member’s interest got the green light,” says Saltzman.

It didn’t take long for the department to develop a culture that encouraged students to explore their interests. That’s what drew Siefert to apply as a Ph.D. student in 2009. At the time, she was interested in neuroimaging, tissue engineering and nanotechnology. Yale was strong in all three, with renowned principal investigators in each field.

“There were multiple faculty members who I could see as my advisor and I knew there would be other options if one didn’t work out,” she said. “Since most of the people in biomedical engineering are so interdisciplinary and open to opportunities that may not seem directly relevant, there’s a lot of openness and freedom for a grad student.”

Looking to the Future

The department marches forward. It continues to make new hires, the most recent being Michael Mak, whose research focuses on multiscale mechanobiology in cancer and development. Humphrey said BME will continue to expand the scope of its mission. Another frontier he wants the department to aim for is chemical biology, which can include synthesis of chemicals for therapeutic advantage. “We already have expertise in drug delivery,” he said, “hence having a focus on drug development would complement one of our strengths as well as strengths across our campus, from Chemistry to the Medical School.”

The BME department’s rapid expansion and success is evidence that the original mission set out 15 years ago is still on point. The focus on hiring investigators who are highly collaborative has been successful because everyone at Yale, from students to faculty, wants to work together to make an impact.

“Students are attracted to BME because it’s not only intellectually challenging, it is also critically important,” says Humphrey. “Yale students in particular want to make a difference in the world, and many seek to do so by improving healthcare. Yale BME will continue to contribute significantly to this pursuit.” 



Yale

TECHNOLOGY

Taking on the Hackers

SEAS researchers take on the increasing threats to cybersecurity

Every few days, the news brings us stories of massive data breaches, resulting in the theft of massive amounts of money, or the release of sensitive information. Whether you're making a routine online transaction or casting a vote in a national election, the issue of cybersecurity has everyone on watch.

As fast as technology progresses, hackers find new means to exploit it. It's a problem that requires strategies on several fronts and rethinking approaches to software, hardware and the law. At SEAS, a number of faculty members are exploring the question of how we make computing more secure and reliable.

A Hacker-Proof Operating System

Ideally, a computer's operating system would have at its core a small, trustworthy kernel that can manage all the hardware resources and also provide isolation and protection for different software components. But operating systems are complicated, and just one flaw in the code can elude detection by its makers and leave a system vulnerable to hackers. Completely eliminating those flaws, however, is extremely challenging.

"The evolution of computer systems has been heavily influenced by business considerations — people want to be the first to the market," said Zhong Shao, professor and department chair of computer science. To save time, developers often rely on legacy code, a practice that seemed fine when no one imagined that computers would play such a critical role in our lives. Now, with so many different platforms in use, the Internet of Things taking off, and self-driving cars just around the corner, we need greater assurances that our operating systems are secure and reliable.

To that end, Shao is leading a team in the construction of CertiKOS (Certified Kit Operating System). It's an operating system based on formal verification, in which the kernel's interdependent components are carefully untangled, and mathematical specifications are written for each kernel module's intended behavior. To do so, they structure the kernel using certified abstraction layers and design each component so that it can be formally verified separately and linked by the layer framework.

Continued →



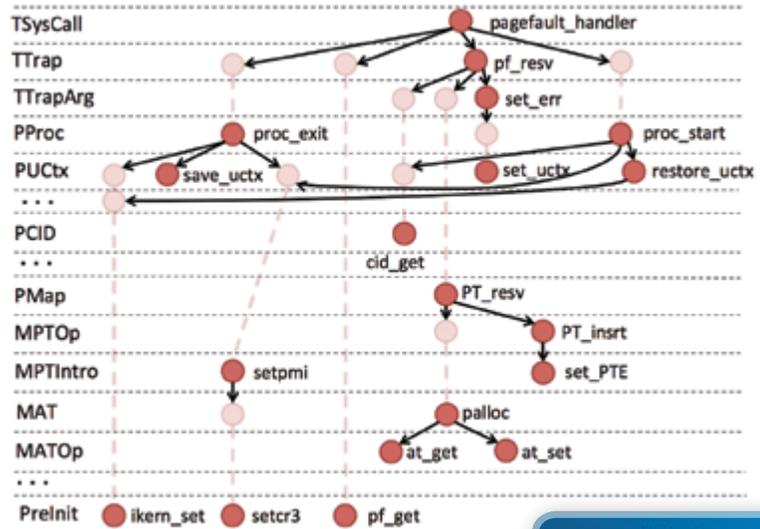
Zhong Shao

This differs from the conventional way of checking a program’s reliability, in which the software developer tests the program against numerous scenarios. One of the things that sets CertiKOS apart from other previously verified systems is that it’s a concurrent operating system, which allows it to run on computers with multiple processors. For complex software with concurrency, testing can no longer cover the program’s state space, so it cannot eliminate all the bugs in the system.

Computing has reached a point where allowing the possibility of any bugs is no longer acceptable. Shao compares an operating system to a government, which is also multi-layered and manages and facilitates processes. Its structure also means that corruption in just one layer can damage others as well.

“The CertiKOS approach is to apply formal principled techniques to decompose these very complex systems into many carefully designed abstraction layers,” Shao said. “For each complex component, you try to figure out its semantic structure. We build the operating system in a clean way, layer by layer.”

If the layers aren’t organized in a way that’s consistent, Shao said, you’ll likely create a bad foundation for any new features. If you really understand the semantic underpinnings of these different features, though, then they can serve as a foundation for a system that’s more extensible — that is, able to take on new features and be adapted for different application domains.



CertiKOS offers a clean-slate design with end-to-end guarantees on extensibility, security, and resilience.



A big challenge of the project is making sure that it’s not seen as an academic exercise, Shao said. That means growing the CertiKOS ecosystem to the point that it can be deployed in many realistic application domains. “We still need engineers to make the product more comprehensive, and apply it to more platforms,” he said. “Otherwise people won’t take it seriously.”

Shao acknowledges that the project is quite ambitious and the new CertiKOS ecosystem could disrupt and transform how the computer industry has been working for decades. But he also knows that the current way of doing things is unsustainable.

“For the future, we need to build a new operating system ecosystem that has to be super clean and provides a bug-free and hacker-proof guarantee,” he said. “Otherwise, the cyber world, self-driving cars, IoTs, blockchains, and the future of artificial intelligence could all run into serious problems.”

Securing Your Vote

Keeping up with the constantly morphing field of cyberconflict has proven tricky in many areas, including the law. To that end Joan Feigenbaum, the Grace Murray Hopper Professor of Computer Science & Economics,

has teamed up with Professors Oona Hathaway and Scott Shapiro from the Yale School of Law to work on new ways of thinking about cybersecurity.

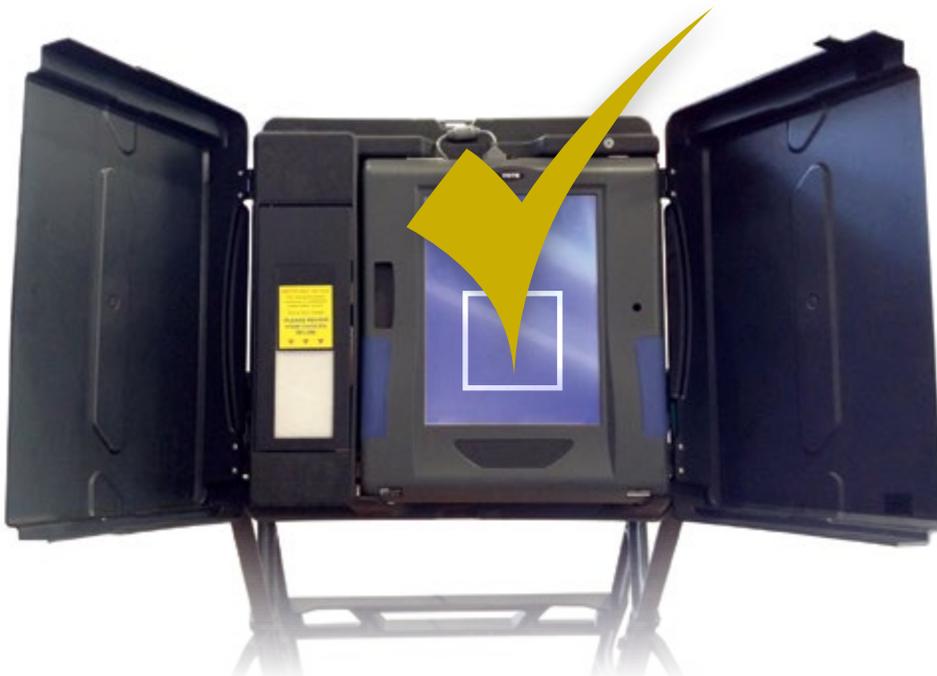
The collaboration, funded with a two-year \$406,000 grant from the William and Flora Hewlett Foundation, includes the course “The Law and Technology of Cyberconflict.” For the first semester, the students (10 law and 11 computer science) met for weekly seminars. In the second semester, students worked individually and in teams on projects that address pressing cyberconflict issues. One team of students, Sahil Gupta, Patrick Lauppe, and Shreyas Ravishankar, developed a cryptocurrency they call “FedCoin.” It’s similar to BitCoin, but would be sanctioned by the Federal Reserve, or any nation’s central bank. It would possess the security properties of modern cryptography with the legal and social properties of conventional currencies.

Another team, composed of computer science students Soham Sankaran, Sachith Gullapalli and Lincoln Swaine-Moore, took on a particularly timely project. They focused on developing a system that allows voters to verify that their votes were recorded and counted correctly, without allowing access to information on other voters’ ballots. Previously, researchers Tal Moran and Mori Naor had shown that this system could work in theory, but hadn’t built a system based on their ideas. To see how it would

fare in real life — ideally, at the scale of a national election — the three students developed their own system to demonstrate that it could work in practice.

Taking the papers that Moran and Naor published, the students implemented the cryptography and interface that made up the theoretical system of vote casting, tallying, and verification. They added a few new features as well, including a system for verifying receipts and receipt signatures. It’s a crucial addition, since Moran and Naor acknowledged that their theoretical system was vulnerable to corrupt voters who could conceivably falsify voter receipts or diminish the legitimacy of an election by “crying wolf” about fake receipts. Their system incorporates receipts that contain “commitments” to the vote — that is, short pieces of information determined by the vote. These commitments could be used by the voter (who already knows how he or she voted) for verification purposes, but would most likely be of no use to someone who didn’t know the vote cast by the actual voter.

The next step for the project is to test out the system in an election with real voters and see how intuitive the interface is for people unfamiliar with the system. They would also like to make the system open source to get community feedback and allow others to customize the system to their own specific needs.



Joan Feigenbaum

Continued →

Better Security from a Device's 'Fingerprint'

All electronic devices — even the same products by the same manufacturers — possess unique variations in their hardware. Jakub Szefer, assistant professor of electrical engineering, thinks he can use these variations to create additional security for users of these devices.

Szefer's project, for which he won a Faculty Early Career Development (CAREER) Award from the National Science Foundation this year, focuses on using a device's hardware "fingerprint" to increase security of everyday computing devices. Nearly every computing device, smart phone, or Internet of Things device depends on a data-storage system known as dynamic random-access memory (DRAM). The charge in the DRAM's cell's storage capacitors dissipates over time, so a refresh mechanism is needed to recharge the capacitors and keep the data in storage.

When a manufacturer fabricates the DRAM chip, the manufacturing process can result in different wire lengths, changes in the capacitors' thickness, and other microscopic variations. These differences are very slight, but enough to result in each DRAM having its own unique decay behavior.

"When you turn off the refresh mechanism, the data decays, but different DRAM cells decay at different rates — that's where the fingerprint comes in," Szefer said. "The decay rate of the collection of DRAM cells is unique to each model, as a result of the manufacturing variations."

The uniqueness of each device can be used to make it more secure. For instance, an iPhone user now might log in to a banking site using a password — which could be stolen. But if the security system also includes the device's hardware fingerprint, someone would need both the password and the user's iPhone itself to get into the banking site.

The ideas that come out of the research can be readily deployed, since the project centers on hardware already present in the devices. Putting the fingerprint to practical use, however, is part of the challenge of the project. To keep from completely disabling the refresh mechanism, which would render the device useless, Szefer needs to selectively disable some regions of the DRAM while preventing data in other regions from decaying. That way, they can read the fingerprint, but the rest of the DRAM would be refreshed and the device could keep running.

The project could also leverage the physical properties of the computer hardware to develop new hardware-based versions of cryptographic protocols. For instance, it could incorporate what's known as Oblivious Transfer, in which two parties can exchange certain pieces of information but keep others secret. Such protocols have been incorporated into software programs, but those are based purely on different decaying mathematical models that could theoretically be broken by a clever hacker. Szefer said that intertwining the cryptographic protocols with a device's hardware could create one more layer of security.

Another possibility Szefer is exploring is using this technology to create a system for checking whether a device is counterfeit or not — a problem that plagues smaller electronics in particular. For instance, the manufacturer could take the fingerprint of every device that's produced. A system could then be set up that would let consumers check the authenticity of their devices.

Jakub Szefer



Maintaining Privacy, and Self-Correcting Chips

When two parties share data on a large scale, it's not always easy to control what information is released and what is kept private. Aiming to change that, assistant professor of computer science Mariana Raykova is working on a program that allows multiple users to share data without running afoul of privacy concerns and legal restrictions.

Raykova, who received a Google Faculty Research Award this year for the project, noted that there are often legal agreements between parties stipulating that only a subset of data that's part of a larger body of data can be used. But knowing for sure that these agreements are honored is a complicated matter. In one scenario, two or three hospitals may need to share information about a particular medical procedure of a patient. Due to HIPAA and other privacy concerns, however, the patient's other medical data shouldn't be open to all three parties. Raykova's group is developing cryptographic techniques that allow the various parties to design a model that fits their specific needs.

Exactly how Google makes use of its data is proprietary, but Raykova said there are a number of ways that her team's project could benefit the search engine giant. Google collects a massive amount of user-related data, and then applies machine learning techniques to build models that neatly explain the behavior of those users. Often, the data comes from multiple sources. Some advertisers on Google, for instance, want a better idea of how effective their ads are: Do users go to the company's website, for example, or purchase its products? Conversely, these companies might have data that's helpful to Google about people using the search engine.

Raykova said the same technology could be applied to numerous other uses, such as for tax and judicial databases. One of the main challenges in developing these techniques is making them efficient, she said, since translating a regular computation into a secure computation can take a large amount of computing time and other resources.



Mariana Raykova

She is also working on another pressing security concern: chips with faulty or malicious integrated circuits (IC). It's a problem that happens when semiconductor designers outsource circuitry to possibly untrusted fabricators. Because of the complexity of certain chips, flaws within these outsourced circuits can go unnoticed by the developers, but could ultimately harm the product. Current solutions are limited to legal and contractual obligations, or post-fabrication IC testing — neither of these is considered adequate.

The project, titled “Verifiable Hardware: Chips that Prove their Own Correctness,” won a \$3 million National Science Foundation grant. In addition to Raykova, the project includes researchers from University of Virginia; New York University; University of California, San Diego; and CUNY City College.

The researchers are looking at the wider benefits of their project by developing new practical approaches to the problem of general verifiable computation. Verifiable hardware, they say, is critical to building future computing systems that are reliable and free from major security failures. Ultimately, they're aiming to use open-source tools to make verifiable hardware accessible for use in cryptographic hardware applications. 



Yale

SUSTAINABILITY

Nanotechnology Enabled Water Treatment

Yale researchers are delivering solutions and preparing the next generation to do the same.



Yale's environmental engineering program has a reputation as one of the top in the nation (it has twice cracked the *U.S. News & World Report's* annual graduate program rankings), so it's no surprise that a number of its faculty members would be part of an ambitious effort known as Nanotechnology Enabled Water Treatment (NEWT) to provide clean water to millions of people and make U.S. energy production more sustainable and cost-effective. Since August of 2015, Yale researchers have been working with scientists from other universities, as well as government and industry organizations, to focus on compact, mobile, off-grid water-treatment systems.

Two years into the project, Yale's participants have delivered some impressive advances in their mission — and they're getting the next generation of engineers on board with the goal of using nanotechnology to help make clean drinking water accessible to all.

Based out of Rice University in Houston, the effort is funded with an \$18.5 million grant from the National Science Foundation. Professors from the Department of Chemical & Environmental Engineering Menachem Elimelech, Jaehong Kim and Julie Zimmerman are working as part of NEWT. Small enough to fit in a tractor trailer, NEWT's modular water-treatment systems will use nanoengineered catalysts, membranes and light-activated materials to convert water from any source into drinking water. This includes pond water, seawater and floodwater. Solar energy will power the systems, even under cloudy conditions.

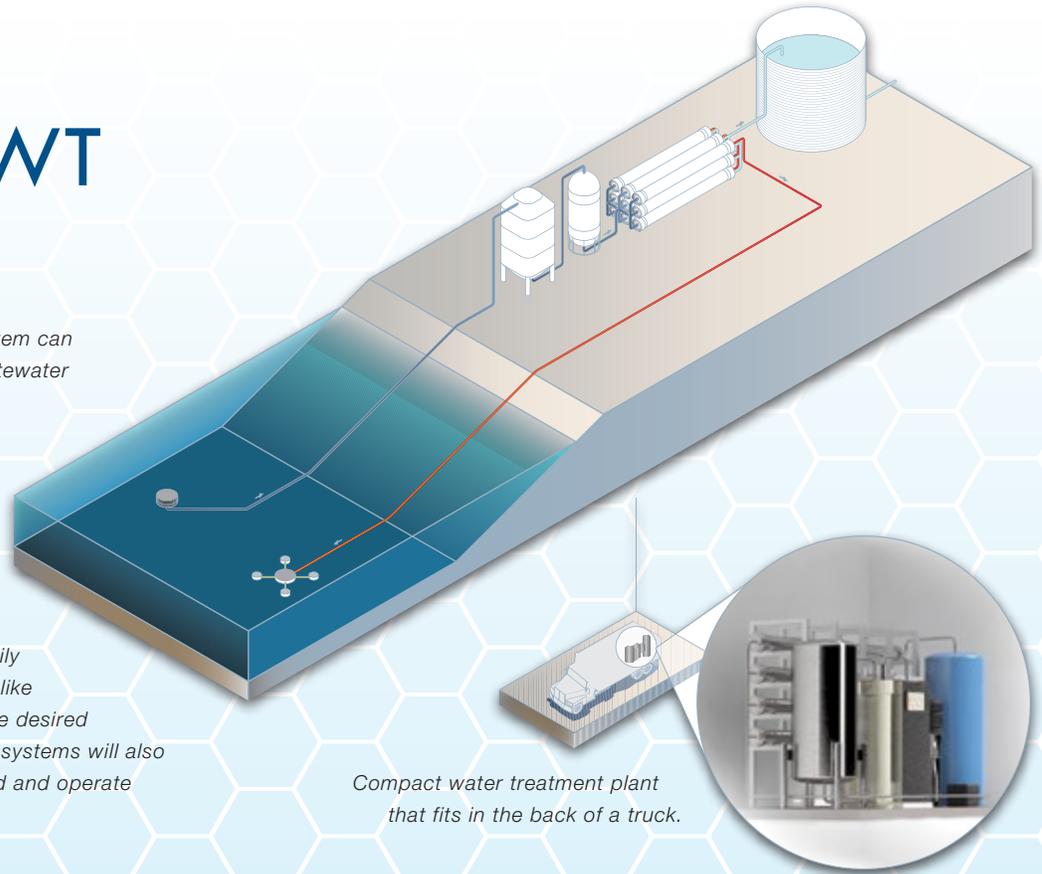
True to that vision is one of the first major projects to come out of NEWT, a system known as nanophotonics-enabled solar membrane distillation (NESMD). Yale researchers, working with collaborators from Rice University, designed this system to use solar energy and nanoparticles to make saltwater drinkable. It incorporates a porous membrane with carbon black nanoparticles. The nanoparticles use sunlight energy to heat water on one side of the membrane, which

Continued →



The NEWT industrial water system can treat a variety of industrial wastewater to different water-quality levels according to industry's need for discharge or reuse.

By using nanotechnology, small modular units can be easily configured and reconfigured — like LEGO™ blocks — to provide the desired water quality. Modular, off-grid systems will also be significantly cheaper to build and operate than a treatment plant.



Compact water treatment plant that fits in the back of a truck.

Yale

filters out salt and other non-volatile contaminants while allowing water vapor to pass through it.

The technology is still in its early stages, so the researchers are still considering a wide range of applications. Among other possibilities, the system could potentially be used in households in less developed areas, as well as to treat water produced by fracking and shale oil and gas extraction operations.

“The integration of photothermal heating capabilities within a water purification membrane for direct, solar-driven desalination opens new opportunities in water purification,” said Elimelech, co-author of the study and NEWT’s lead researcher for membrane processes.

The most common desalination process takes saline water and passes it through a membrane. It then emerges on the other side, free of salt. Known as reverse osmosis, the process is very energy-efficient, but it doesn’t work with water with very high salinity. Many other desalination systems involve thermal processes in which water is evaporated using heat and then condensed. While effective, the method is energy-inefficient due to the amount of heat required. Thermal pro-

cesses are often situated nearby power or chemical plants that provide steam as the heat source. According to Elimelech, the Roberto C. Goizueta Professor of Chemical & Environmental Engineering, conventional methods to desalinate 1,000 liters of seawater take up about as much power as 30 100-watt light bulbs being used for an hour. Applied to a larger scale, that adds up to a significant amount of energy.

There’s also membrane distillation, which uses both heat and membranes. It can desalinate high-salinity water using low-grade or waste heat. However, it still requires an external heat source, which means that it needs to be connected to some form of energy infrastructure.

The heat source for the NESMD system, however, is in the membrane itself. Embedded on one side of the membrane, the nanoparticles use sunlight to heat the water and drive the desalination process.

“Instead of heating the water before it comes into the module, you heat it on the membrane surface itself,” said Akshay Deshmukh, a Ph.D. student in Elimelech’s lab. “One of the big advantages of this is that it can be used anywhere because it’s dependent on sunlight.”

SUSTAINABILITY

Naomi Halas, professor of biomedical engineering, chemistry, physics & astronomy at Rice University and the leader of NEWT's nanophotonics research efforts, said NESMD also differs from traditional membrane distillation in that it benefits from increasing efficiency with scale.

"It requires minimal pumping energy for optimal distillate conversion, and there are a number of ways we can further optimize the technology to make it more productive and efficient," she said.

Making the Science Relevant to a New Generation

Standing at a nano-hood in the lab of Julie Zimmerman, professor of chemical & environmental engineering and forestry & environmental studies, Rosie Du is trying out

and comparing different methods for separating carbon nanotubes.

It may sound like a typical day's work in an environmental engineering lab, but Rosie isn't a typical lab worker. She's a junior at Amity High School in Woodbridge, CT, who's taking part in NEWT's summer lab program, in which four students from area high schools spend eight weeks in the labs of Zimmerman and Elimelech.

Besides satisfying one of NSF's educational requirements, the program also gives high school students the opportunity to work in a lab — something few people get to do before attending college — and participate in the kind of research that the Center is conducting. Once there, the students can set their own pace. Some are self-motivated and take on their own projects with some coaching from their mentors, while others take on a more supportive role.

Working with NEWT is Pathways to Science, a Yale program that works directly with area schools to encourage

Continued →



High school student Rosie Du and her summer lab mentor, Ph.D. student Mark Falinski.



middle and high school students to learn more about the STEM fields. The programming for Pathways to Science varies from lectures and workshops and other one-time events, to much more immersive programs.

“The model that we’ve set up allows students to be exposed to all different areas of STEM,” said Maria Parente, program manager for Pathways to Science. “If they get interested in a subject, they can delve a little deeper into that area. If they say ‘That’s not what I want,’ they can get back on the train and try something else instead.”

It was through Pathways to Science events that Rosie had heard about the summer internship program. Working in the lab sounded like a great way to spend a summer, said Rosie, who added that she’s long been interested in science.

“I think it’s really interesting that you can come up with your own procedure and think about problems that you see around you,” she said. “Then, you can try to come up with a solution or test a way to try to solve that problem.”

Her mentor, Mark Falinski, a Ph.D. student in Zimmerman’s lab, said Rosie’s work has been a benefit to their research.

“From the beginning, she did almost all her data analysis by herself — she set up all the samples, and prepared everything,” he said. “She would find the procedures that she’s going to use. My main role in helping her was to look at the procedure and we would see how it worked

and I would make suggestions on how we could do this slightly better.”

Rosie said she’s been thinking about going into either English or one of the STEM fields. After her eight weeks in the lab, she leaning more toward the latter.

This is the second year that NEWT has offered its summer lab program. They have various ways to get the word out about the program, but one of the most effective is through the NEWT Café. The event invites middle and high school students to Yale for a few hours to talk about nanotechnology and water treatment and how engineers are connecting the two. Demonstrations show how nanotechnology and water treatment can work together.

Amanda Lounsbury and Humberto Jaramillo, who have headed up the NEWT outreach efforts, say one of the goals of the NEWT Café is getting young people to see how the science is relevant to everyday life. At a recent event, for instance, they discussed the water crisis in Flint, Michigan.

“We’re showing the importance of this research — ‘You guys have to get involved, it’s something that’s happening in our communities and not just undeveloped countries,’ said Jaramillo, a Ph.D. student in Elimelech’s lab. “That way, they get the sense of how it’s their own concern, and it’s not something abstract.”

It’s also important to make sure that the events have hands-on experiments.

Yale

SUSTAINABILITY



“I don’t sit well with lectures and I find that students don’t either,” said Lounsbury, a Ph.D. student in the Zimmerman lab. “I had just finished taking a teaching course on flipping the classroom and I wanted to do something like that. I was part of the NEWT Student Leadership Council and outreach is something that’s always been very important to me because that’s what got me involved, and I think it’s important to start early.”

As a Ph.D. student with plenty already on his hands, Jaramillo was a little wary at first of Lounsbury’s suggestion that they start up the NEWT Café.

“Amanda was like ‘We’re going to make a NEWT Café!’ and I’m thinking ‘This is going to be a lot of work.’ But once I got involved it was really exciting to be doing something more.” Their enthusiasm paid off.

“NSF came to review the Center, and this program was spoken about a lot,” Jaramillo said, adding that officials were particularly impressed with how the program taught the students about both water treatment and nanotechnology — and how NEWT brings the two fields together. “I think the objective of describing the vision of the Center really came through.”

Putting on the event takes a fair amount of planning. As Lounsbury notes, it’s not just a matter of choosing the right materials.

“It’s realizing how the whole day fits together in terms of NEWT and what your students will get out of each activ-

Above: The NEWT Café aims to inspire the next generation of engineers by bringing middle and high school students to Yale to learn about nanotechnology and water treatment. Demonstrations show how technology and water treatment can work together.

ity,” she said. “Explaining a multimillion-dollar Center, all of its types of research, and how it fits into our world is a lot of thinking and planning.”

And their enthusiasm was matched by the kids who attended. Lounsbury said she expected most of the students would be there because their parents made them go as a way to boost their college applications. What they found, though, was that many of them were genuinely happy to be there, even on a weekend.

“Getting that kind of excitement from kids was amazing,” she said. “We want to maintain the excitement of those who already have it, but we also want to motivate the kids who might be thinking ‘This isn’t for me.’”

Lounsbury and Jaramillo said both the NEWT Café and the summer program were the kinds of things they wished were around when they were younger.

“I always loved science, but if you told me I’d be a Ph.D. student even 12 years ago, I would have been like ‘Yeah right,’” she said. “I was lucky to have supportive teachers and parents. I think if I had been in a different school district or had slightly less supportive parents, I probably would have ended up a make-up artist.” 

A Chip That Thinks Like Us

Today's computers don't really work like brains, but they're getting closer, thanks to Rajit Manohar

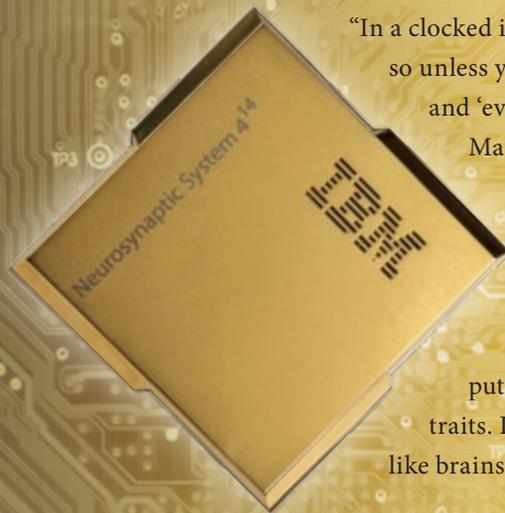
Yale

TECHNOLOGY



Imagine working in an office where, once you've finished one task, you had to wait until everyone in all the other cubicles completed the tasks they were working on before you could move on to your next assignment.

That's how most digital devices that rely on synchronous circuits work. Built-in clocks allow the same amount of time for the completion of each computational function. Based on a binary system of ones and zeros, it's reliable, but it also means that the system can run only as fast as the slowest function in the chain.



“In a clocked implementation, everything has to fit into a time budget, so unless you make everything faster, your chip doesn't run faster — and ‘everything’ includes things you don't always need,” said Rajit Manohar, the John C. Malone Professor of Electrical Engineering and Computer Science.

Even before Siri and Google Home became our household companions, we've had a tendency to anthropomorphize computers. It's long been common for people to speak of computers in terms of “thinking” and to ascribe them brain-related traits. In truth, though, conventional computers really don't function like brains at all. But computer science is getting closer.

One sign of this is TrueNorth, a 4-square-centimeter chip that possesses some 5.4 billion transistors, and 1 million “neurons” that communicate via 256 million “synapses.” Starting while he was a faculty member at Cornell, Manohar came to work on the chip with a team of IBM researchers in a years-long collaboration that resulted in TrueNorth. Funded by the Defense Advanced Research Projects Agency (DARPA) as part of its Systems of Neuromorphic Adaptive Plastic Scalable Electronics (SyNAPSE) program, TrueNorth is a pioneering example of the neuromorphic chip — a new breed of computer circuitry modeled after the brain. It's the size of a postage stamp and it could be the start of a revolution in how we make and use computers.

Above: TrueNorth, a 4-square-centimeter chip possesses 5.4 billion transistors and 1 million “neurons” that communicate via 256 million “synapses.”

Manohar, who started at Yale in January, came to the project through his work with asynchronous systems, one of his research specialties. In devices with these types of circuits, each function is allowed as little or as much time as needed to complete its task. “It's like a relay race — you hand the baton to the next person when you're there,” he said. To allow for greater complexity and use much less energy, all of these functions work asynchronously and in parallel — similar to how neuroscientists believe the brain operates.

Continued →

“There’s clearly not a single, carefully synchronized signal that goes to every single neuron in your brain, so it seems that asynchrony is a natural way to think about how computation there occurs,” Manohar said.

Although asynchronous systems are often thought of as a new branch of study within computer science, their roots go back to the earliest versions of the modern computer. Manohar notes that even the blueprint of the modern computer (the “Von Neumann” machine) from the 1940s explains that asynchronous computation is advantageous. Many early machines were built this way, but computer architecture soon grew in complexity and included a lot more wires. Ensuring that a signal was sent and received correctly within the machine got trickier. An internal timekeeper was needed to make sure that things ran properly, and synchronous circuits became the law of the land.

What the machines gained in orderliness, though, they lost in speed. Take for instance, the computer in your phone. It’s running at 1 GHz — a billion steps per second — so every step has to fit in one nanosecond. Whatever you’re calculating has to be subdivided into equal blocks of time. If one step finishes early, you have to wait. That can add up to a lot of wasted time.

“Frankly, it’s rare that you have computation where individual things all take the same amount of time,” he said. “Not all computations are equally difficult.”

If one step takes too long, an error occurs. In that case, the process has to be broken into smaller steps, or the step size has to be bigger — and that slows everything else down.

Nonetheless, this didn’t pose much concern until the 1980s, when chips started getting bigger and more complicated and the clocks used to keep up with the computing power got more and more expensive to run — taking up as much as 20 percent of a chip’s power consumption.

“So people started looking at asynchronous circuits again in the early ‘80s.”

The neurons of TrueNorth work in parallel with each other, each doing what it needs to do to complete a task. They communicate via bursts of electric current, known as spikes. One of the most remarkable things about TrueNorth is how power-efficient it is. Drawing 70 milliwatts of power — equal to that of a hearing aid — its consumption is miniscule compared to conventional computers performing similar tasks.

Dharmendra Modha, lead researcher of the Cognitive Computing group at IBM Almaden Research Center and principal investigator of the DARPA SyNAPSE project, said he recruited Manohar because he’s a “world leader” in the technology required for the project and he had developed “powerful and proven tools.”

“Neurons in the brain are event-driven and operate without any synchronizing clock,” Modha said. “To achieve the ambitious metrics of DARPA SyNAPSE, a key element was to design and implement event-driven circuits for which asynchronous circuits are natural.”

“The brain is an asynchronous system that we don’t really understand very well, and it can do certain things that we don’t know how to get computers to do today — and that’s interesting.”

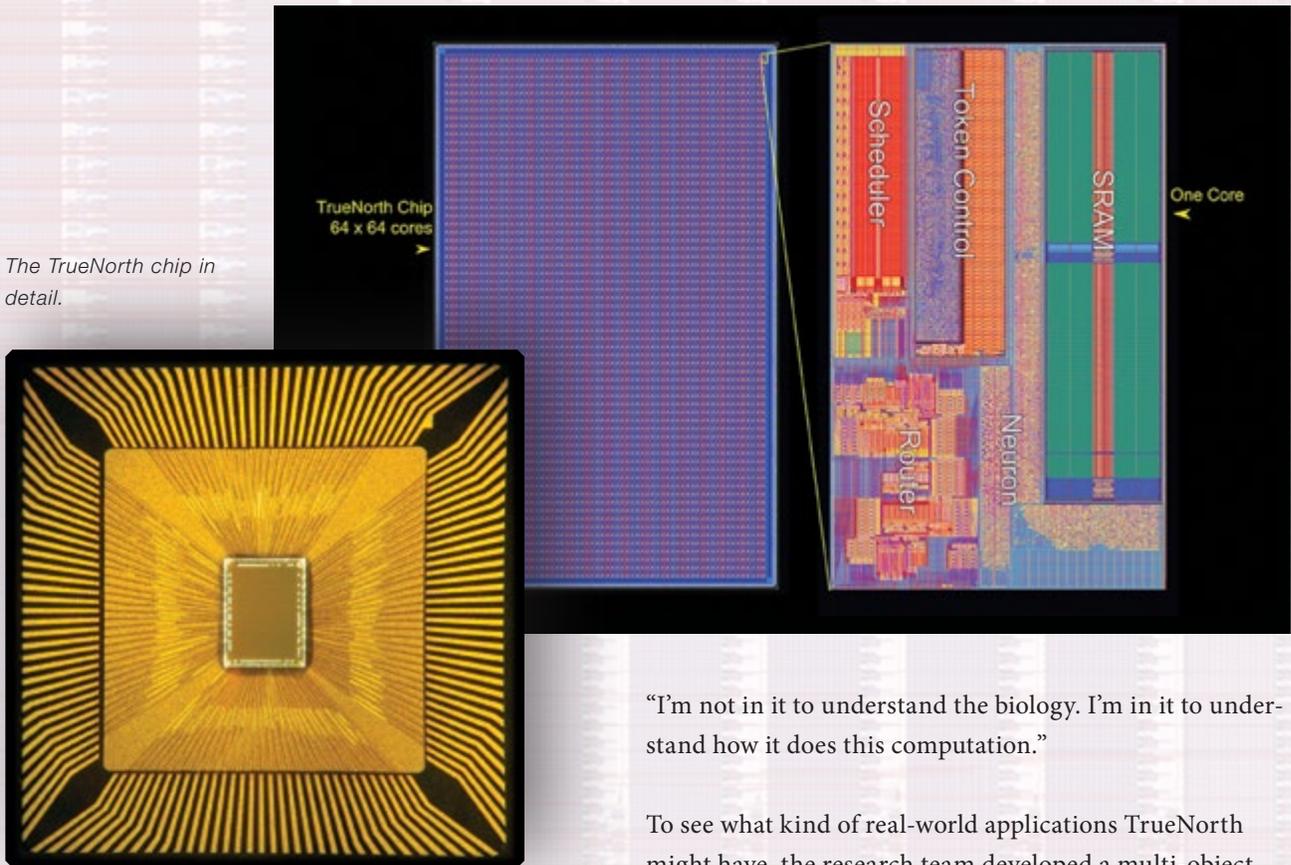
› Rajit Manohar

Yale

TECHNOLOGY



The TrueNorth chip in detail.



Neuroscience has given us a much better understanding of what's happening in the brain, and that information inspired the architecture of the TrueNorth chip. But it's a stretch to call TrueNorth a copy of the brain's functions since we still don't know exactly how the brain works. That's one of the things that fascinates Manohar about his work.

"The brain is an asynchronous system that we don't really understand very well, and it can do certain things that we don't know how to get computers to do today — and that's interesting," he said. Also, there's evidence that the brain has a "massively powerful asynchronous computational substrate" that can learn how to do a lot of different applications.

"And it can execute those applications at an efficiency that we don't know how to do on a computer. That's also interesting."

Many other efforts in neuromorphic computing start with the aim of better understanding how the brain works. The makers of TrueNorth approached their project from the other direction; how can the processes of the brain make for better computing? That also suits Manohar's interests.

"I'm not in it to understand the biology. I'm in it to understand how it does this computation."

To see what kind of real-world applications TrueNorth might have, the research team developed a multi-object detection and classification application and tested it with two challenges: one was to detect people, bicyclists, cars, trucks, and buses that appear periodically on a video; the other was to correctly identify each object. TrueNorth proved adept at both tasks.

Even if it captures just a fraction of the human brain's complexity — according to its makers, the chip has the brain power of a bumblebee — that's enough to accomplish some remarkable tasks. For instance, it allows users to change the channel without touching the TV or a remote control. Samsung, which has evaluated the TrueNorth chip, announced that it is developing a system in which TV users can control their sets simply by gesturing. Officials at the Los Alamos National Lab have also discussed using it for some supercomputing calculations.

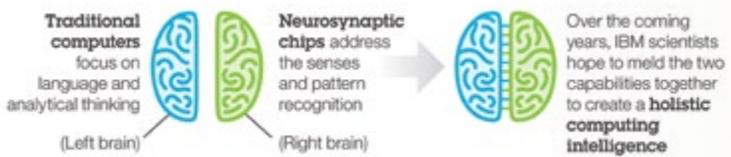
Manohar is also the founder of Achronix Semiconductor, a company that specializes in high-performance asynchronous field programmable gate arrays (FPGA) chips. *MIT Technology Review* listed him as one of "35 Innovators Under 35" for his work on low-power microprocessor design. His other specialties include low-power embedded systems, concurrent systems, and formal methods for circuit design.

Continued →

A Brain-Inspired Computer



What is cognitive computing?
Cognitive computing aims to emulate the human brain's abilities for perception, action and cognition. The neurosynaptic chip, designed to emulate the neurons and synapses in the human brain, breaks path with traditional architectures used for the last 70 years.



Manohar says he came to computer science by way of mathematics.

“At some point, I wanted to use mathematics for something more applied,” he said. “I thought computer science was interesting from an applied math perspective — a lot of the techniques and some of the foundations are very mathematical.”

The unprecedented nature of TrueNorth meant a huge amount of resources were put into it. Not only did the research team invent the chip, they needed to invent the tools used to build it, since existing current computer-assisted design (CAD) software wasn't adequate.

“One of the things that prevents people from working on asynchronous circuits are the lack of tools to design them,” he said. “There's a huge industry that spends billions of dollars each year improving these CAD tools, but they aren't tailored to the work we're doing on asynchronous design, so we have to write our own CAD tools.”

Since the unveiling of TrueNorth, the number of researchers working on asynchronous circuits has increased significantly, but it's still a small community. The CAD software that Manohar's team used was designed specifically for the team's use. But if they can modify them to be more universal, Manohar believes the field will break out, and the technology will advance even more rapidly.

Yale

TECHNOLOGY

Different from a standard chip

Traditional chips run all of the time.
This new neurosynaptic chip is event-driven and **operates only when it needs to**, resulting in a cooler operating environment and lower energy use.

The neurosynaptic chip veers from the traditional von Neumann architecture, which inherently creates a bottleneck limiting performance of the system.



Unprecedented scale

This second generation chip is the culmination of almost a decade of research and development, and is a huge leap forward from the initial single-core hardware prototype developed in 2011.

1/10th of a Watt powers the neurosynaptic chip's 256 million synapses...with the goal to simulate 1 trillion synapses using only 4 kW of energy

Infographic Courtesy of IBM



“One of the things we want to do is to have a complete set of tools that we could put in open source and let other researchers use. Often I hear from people in industry say ‘Hey I’d like to try this, but I don’t know how to start because I don’t have the tools.’”

The Benefits of Thinking Like a Brain

The architecture of today’s conventional computers still derive from the Von Neumann model of the 1940s. We don’t use the cardboard punch cards, but the basic idea is still the same. Advances have lessened how long it takes for the memory to transfer data to the processor. But the data still needs to shuttle back and forth, and that requires time and power. For decades, computers have steadily shrunk in size but grown in power. Computer scientists, though, say we’re getting close to the limit of how much we can keep souping up processors. Neuromorphic chips could break open a whole new field that will allow the trend to continue, quite possibly at an even quicker pace.

One of the radical departures from conventional systems is that the storage of data on TrueNorth and the calculation of it aren’t separated. Its neural network can work multiple tasks without the timekeeping mechanism, breaking free of the linear operation that bogs down conventional operations.

Then there’s the matter of what these chips can allow computers to do. Conventional computers are great at brute force calculations. They’re less adept at recognizing faces or picking out specific voices and tasks that involve pattern recognition. That’s why those CAPTCHA functions

that instruct you to pick out Einstein’s face or copy a short alphanumeric pattern to prove you’re human are so effective at keeping out bots.

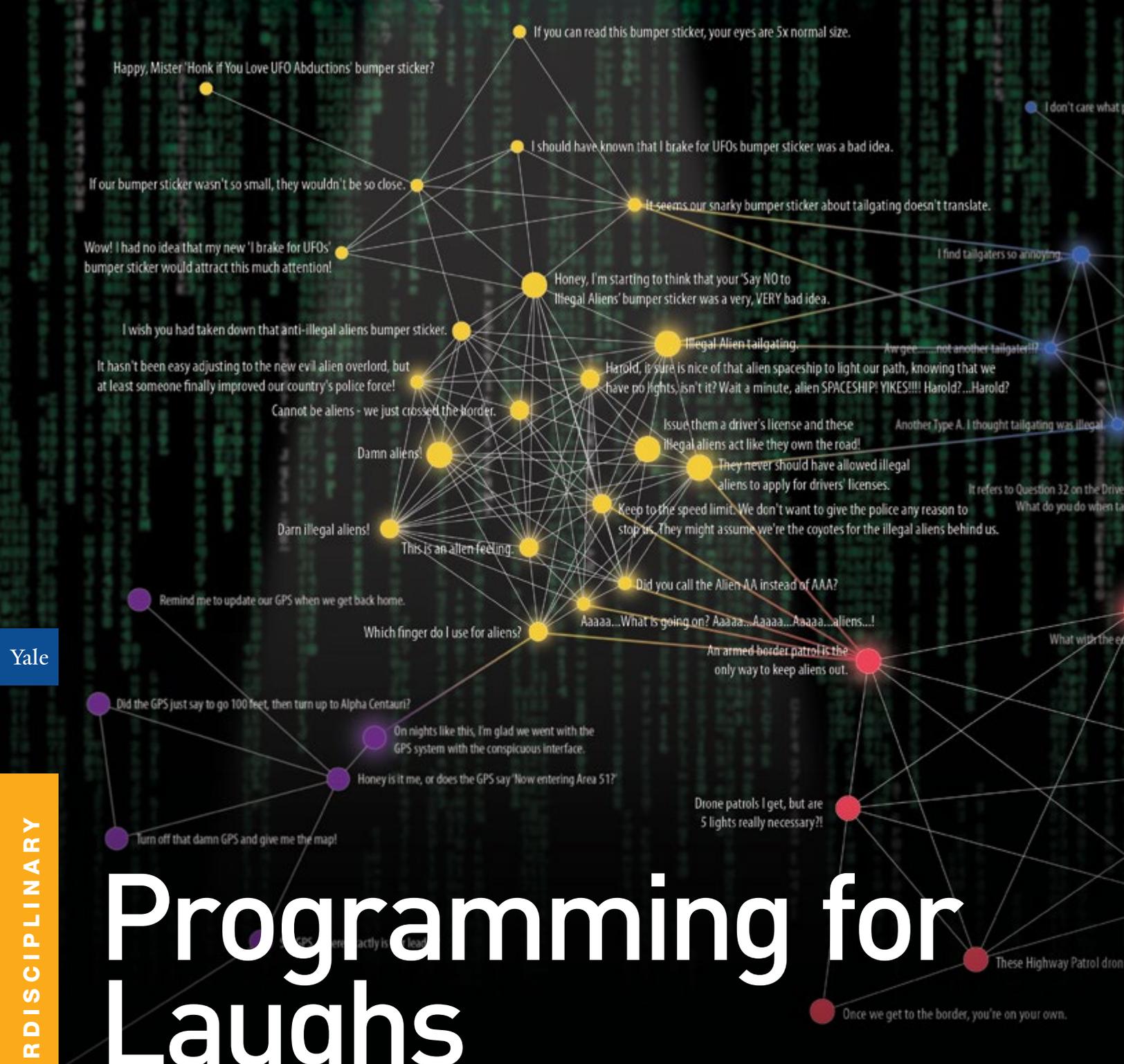
While neuromorphic computing has advanced greatly since computer scientists first began seriously discussing it in the 1980s, the field is still in the early stage, and many in the field are excited about what can be done with the chips as the technology becomes more sophisticated. As with any potentially game-changing technology, it’s impossible to imagine all possible commercial applications, but many in the field say neuromorphic chips could be key to realizing ready-for-primetime self-driving cars, more human-like robots, and devices to help people with visual impairments.

Of course, getting to that point is no small task. Manohar is currently working with a team of researchers from the University of Waterloo and Stanford University on a multichip system that Manohar says would be the next step forward in neuromorphics.

“We’d like to demonstrate significantly higher efficiency compared to all the existing platforms — that’s always the goal,” he said. “We think we know how to do that.”

He predicts it won’t be long before this kind of technology ends up in everyday devices.

“These neurocomputing algorithms currently provide state-of-the-art performance for tasks like object detection and recognizing faces — tasks that a lot of companies care about today,” he said. “Imagine having photos or videos that you search for in the same way that you search for text today; these types of chips are way more efficient at that kind of computation.”



Yale

INTERDISCIPLINARY

Programming for Laughs

Artificial intelligence can drive cars and beat chess champs. But can it come up with a good joke?

We have a long history of yelling at our machines — cars that break down, televisions broadcasting our failing teams. But now, our machines understand us. And they're talking back. They're digging out recipes for us in the kitchen, navigating our car trips, finishing our sentences on Internet search engines, and translating foreign languages.

For that we have computational linguistics, also known as natural language processing (NLP), to thank. It's one of the research focuses of Dragomir Radev, the A. Bartlett Giamatti Professor of Computer Science. It's an area of study where computer science, linguistics, and artificial intelligence intersect, and it has become increasingly prominent in our lives, from Apple's Siri to automated customer service.

In a nutshell, NLP is a means of training computers to understand human language. This is no easy thing. Human language is fluid; words change over time or with context. Take, for instance, the phrase "in a nutshell." It could either mean "in a few words," or "the edible kernel found inside the hard casing of a type of fruit." Distinguishing these two very different meanings comes easily to us, but can be confounding to a computer. Natural languages are designed for the human mind — the wording can be imprecise, and still the meaning is clear. With formal languages — computer code for instance — every character needs to be in order or everything goes out of whack. NLP bridges that gap.

Radev's work employs a number of computational techniques, including artificial neural networks, also known as deep learning. Essentially, computers learn to recognize complex patterns by being fed vast and wide-ranging amounts of data. Words, phrases, syntax, and grammar rules are assigned mathematical values. The idea isn't new, but it picked up in the last couple of decades as digital data storage and computer processing power have increased dramatically. If you've used Google Translate recently, and noticed a boost in speed and accuracy of the results, that's because the company switched to a neural network system.

Some argue that computers aren't truly learning language since they're not acquiring language the way humans do. Toddlers learn to speak not by poring over massive collections of texts but by engaging with the world around them with all five senses. The difference doesn't concern Radev.

"It doesn't affect how we do research because we're not dealing with humans," he said. "How we teach language to computers doesn't have to be the same way humans understand language. When you build an airplane, you don't say 'Birds flap their wings, let's build planes that flap their wings.' That's not how to do it, at least not in practice. We just want them to fly, whether their wings move or not."

As one indication of the level of interest in these subjects, 132 students signed up for Radev's NLP course last semester.

Continued →

If you can read this bumper sticker, your eyes are 5x normal size.

Happy, Mister 'Honk if You Love UFO Abductions' bumper sticker?

I should have known that I brain for UFO's bumper sticker was a bad idea.

Teaching Humor to Computers

Previously, he taught NLP to more than 10,000 students in a massive open online course (MOOC). This fall, he teaches a course on artificial intelligence, the study of teaching computers to perform tasks that would be considered intelligent when humans do them. The course covers logic, learning, and reasoning. It includes challenging assignments that ask the students to build systems that can play two-player games like Othello and Go, solve mazes, simulate autonomous car driving, translate texts using neural networks, and learn from interacting with the environment. This is now the largest class in the Computer Science department, with more than 200 enrolled students this semester.

Computers can figure out how the galaxies formed, sift through unimaginable amounts of data and calculate a prime number of more than 17 million digits. But can they tell a joke? Probably not for a while, Radev said, but he's still going to try.

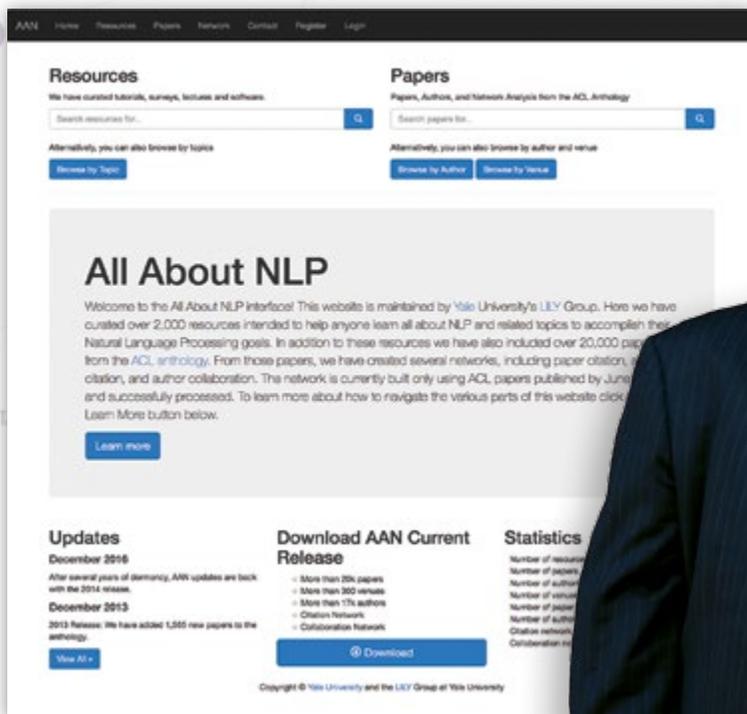
With another project, AAN (All About NLP), Radev is also helping those interested in NLP navigate their way through the increasing body of research on the subject. He and his students from the LILY lab (Language, Information, and Learning at Yale) have collected more than 25,000 papers and more than 3,000 tutorials, surveys, presentations, code libraries, and lectures on NLP and computational linguistics. The ultimate goal is to use NLP to automatically generate educational resources for those seeking it, and to steer them in the right direction. It includes single-paper summaries, multi-source descriptions of algorithms, research topic surveys, and user recommendations for teaching resources.

As part of an ongoing project, Radev has been working with Robert Mankoff, the recently retired cartoons editor for the *New Yorker*. Specifically, they've focused on the magazine's weekly caption contest in which readers submit captions to a cartoonist's illustration. The caption judged the funniest wins.

The magazine receives thousands of submissions every week from would-be cartoonists. The editors then winnow those down to three finalists, to be judged by *New Yorker* readers. It's an arduous process that perhaps could be made easier with the help of NLP. Radev explains that each contest inspires multiple submissions based on the same idea. One illustration, for instance, might inspire many submissions with a similar play on words regarding a horse standing at a bar. A bartending goose serving the horse in the same picture, meanwhile, begets a different batch of closely-related jokes.

Left: *The All About NLP Resources* home page

Right: *Dragomir Radev*



Yale

INTERDISCIPLINARY

Radev, Mankoff, and collaborators at Columbia University and Yahoo Labs have designed a program that intends to identify themes in the submitted captions.

“The purpose is so that the editors don’t have to read through 5,000 submissions every week,” Radev said. “If 100 are all the same joke, they could read just one or two. If the basic idea is funny, then they can dig in deeper and pick out specific ones. If it’s not funny, they can just skip the whole cluster.”

Branching off from that is a project in which computers would generate their own funny captions. One early stumbling block they encountered was that, while computers have gotten very good at picking out objects in photos, illustrations still give them a lot of trouble. To get around that, he and his students described the images of about 500 cartoons in a language that the program can recognize.

“Now, it might be much easier to come up with new jokes by looking at descriptions of the cartoons and at the submissions already made — because that’s a good starting point,” he said. “We could combine two captions into one, or modify an existing caption by adding a few words to make it sound funnier.”

It’s a particularly tricky challenge. So far, computers have bested humans at chess, the ancient game of Go, and even the trivia show Jeopardy. But humor is a uniquely human trait and Radev doesn’t expect that the result will put any cartoonists out of a job anytime soon (nor, for that matter, does he think automated translators will replace their human counterparts). “It may or may not work, but it will be very interesting to be able to see if a computer can understand *New Yorker* cartoons and get the jokes,” he said.

Radev is interested in what’s known as computational creativity. It’s what would allow programs such as Watson, Siri and, Alexa to not only provide correct answers, but even display a bit of personality. There are already attempts to make our devices a little chummier. Siri, for example, occasionally gives some gentle snark: Q: “Siri, what’s the meaning of life?” A: “42” (a reference to the classic book *The Hitchhiker’s Guide to the Galaxy*).

“But it doesn’t really have a sense of humor — that’s pre-programmed by the humans,” Radev said. “It would be interesting in the future to come up with systems that actually can understand and generate funny text.”

Coaching the Next Generation of Computational Linguists

Radev, who grew up in Bulgaria, is fluent in several languages. “I like how similar, yet how different languages are,” he said. “And the fact that there are rules, but the rules aren’t strict, which makes it more interesting. I don’t like pure math because things are too strict. Languages are somewhere right in the middle.”

In 2006, Radev co-founded the North American Computational Linguistics Olympiad (NACLO), an annual competition that brings together middle and high school students from across the U.S. Besides identifying students with talent in linguistics, it also introduces them to the field of computational linguistics.

NACLO has had more than 20,000 student participants. Unlike many other high school events related to computer science, almost 50% of the participants in NACLO are female. The top finalists go on to compete in the International Linguistics Olympiad. This year’s NACLO (hosted at 200 sites throughout the U.S., including Yale) sent eight participants to the international competition in Dublin in August.

NACLO participants are given a series of problems drawn from a variety of languages to solve, usually involving translation. Some call for traditional linguistics methods, and others call for computation to arrive at the solutions. Logic and reasoning are the only skills contestants need. Radev said he and the other organizers recognize that linguistics is rarely

Continued →

Happy, Mister 'Honk if You Love UFO Abductions' bumper sticker?

If you can read this bumper sticker, your eyes are 5x normal size.

taught in high schools, so the problems are set up in a way that no prior knowledge of particular languages or linguistics is required.

Wow! I had no idea that my new 'I brake for UFOs' bumper sticker would attract this much attention!

Problems are often based around relatively obscure languages. For example, one set of sentences might be written in Taa — spoken by about 2,600 people in Botswana and Namibia — each followed by an English translation. Based on the patterns they could deduce from these sentences, the students then must translate the next set of Taa sentences with no accompanying English translations.

“We use charts so it’s easier for the high school students to understand,” said Radev, who in 2015 was named a Fellow of the Association for Computing Machinery, one of the highest honors in computer science. “This is an alien feeling. ‘This is the semantic presentation of this word, this word, that word,’ and then you have to figure out how this method works and translate some additional words into those presentations.”

Tom McCoy, who graduated from Yale this year with a major in linguistics, began competing in NACLO when he was a high school student living in Pittsburgh. He knew nothing of computational linguistics at the time, but he liked puzzles and breaking codes, and his sister suggested that he give the competition a try. Radev was one of his coaches.

“He was really great,” McCoy said. “I think the best phrase to describe him is ‘a force of nature.’ He just does so many things and does them all very well. He’s the very active pro-

I should have known that I brake for UFOs bumper sticker was a bad idea.

fessor/researcher, but then he also manages to give so much time to the Olympiad.”

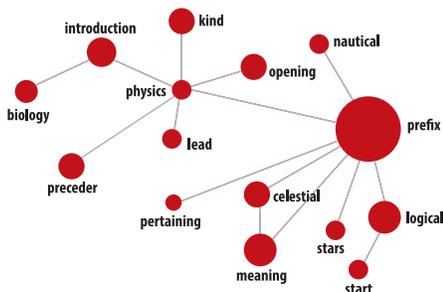
McCoy was committed to studying biology before joining NACLO, which sent him on a different course. This fall, he entered the prestigious Ph.D. program in cognitive science at Johns Hopkins with a focus on computational linguistics.

Radev recruited students for his LILY lab shortly after coming to Yale in January 2017. He quickly assembled a team of Yale students to work on a neural network system for summarizing sets of related news articles. The resulting paper, whose first author is Michihiro Yasunaga, YC’19, was accepted for presentation at the prestigious Conference on Computational Natural Language Learning in Vancouver in August. The LILY (Language, Information, and Learning lab at Yale) lab, led by Radev, now includes six PhD students and more than a dozen Yale undergraduates. The LILY team is working on a number of new papers on survey generation, medical document understanding, cross-lingual information retrieval, and dialogue systems.

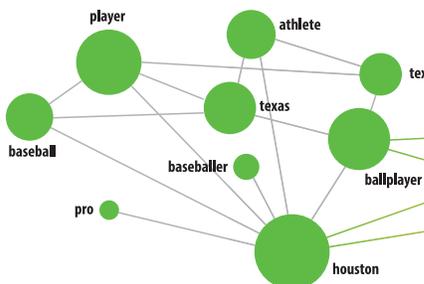
Collaborations

NLP is a field of study that lends itself well to cross-disciplinary collaborations, and Radev hasn’t wasted any time. Even before he arrived at Yale in January, Radev was in contact with several faculty members from other fields about striking up collaborations, including those from the medical school, the humanities, and the social science programs.

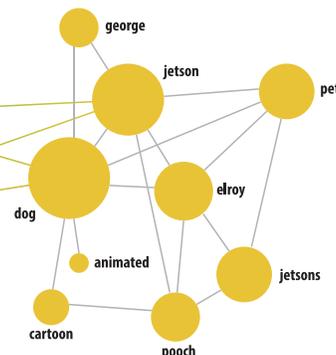
space



baseball



cartoon



Disambiguating the word “astro” as a crossword clue.

Right: Radev is working with the New Yorker to distill the thousands of submissions it receives for its weekly caption contest.

“There’s a general awareness now that natural language processing and these other tools can be helpful to those other fields,” he said. “Ten years ago, many people from other fields didn’t even know that you could do this sort of work. If we collaborate with people in political science or medicine, they get something out of it because now they can analyze data in ways they couldn’t before. And computer science people get something out of it with interesting data sets to work with for their theories.”

Political scientists could use the technology, for example, to analyze the speech and texts of elected officials. An objective analysis of strategies and rhetoric in a debate, for instance, could help discern whether a candidate appealed to nationalism or concerns about the economy. How often was name-calling used as a debating tactic? Lincoln Swaine-Moore, one of Radev’s students, analyzed last semester connections between the speech of officials and contributors to their campaigns.

“For example, if a senator gets a certain amount of funding from the pharmaceutical industry, does that mean they’ll talk more about pharm issues in their speeches?”

The fields of healthcare and medicine also stand to benefit greatly from natural language processing.

“Another possibility is to see if there is any bias in letters of recommendation to medical schools,” he said. “There are studies that show women who apply for certain jobs are treated differently. People interrupt them more frequently, or they perceive a certain trait of the person in a negative way – they might use the word ‘fiery,’ whereas a man would be described with a gentler word.”

He has also talked with Yale School of Medicine professor Harlan Krumholz about possible collaborations. Krumholz,



the Harold H. Hines Jr. Professor of Medicine, director of the Yale Open Data Access Project, and faculty co-director of the Yale Center for Research Computing, said nurses’ notes, radiology reports, and so many other documents have created a mountain of unstructured data in medicine. Radev’s expertise could help make sense of it all. As an example, he points to forms that force patients to grade their symptoms on a scale of 1 to 5.

“We give them five options, but the truth is that they have to tell me a story for me to understand how they feel,” Krumholz said. “The holy grail is figuring out how to take the largely undisciplined data that exists everywhere in medicine and turn it into something that can spark new knowledge and insights and better care.”

Doing that means getting away from a system that requires people to talk and think like computers. Instead, he said, we need computers to come up with insights from the way people naturally communicate. It’s an ambition that, not long ago, might have seemed out of reach. With the work of people like Radev, it’s starting to happen.

“That’s why I immediately thought he would be such a great addition here, and why I looked for ways to work with him,” Krumholz said. “He’s a spectacular addition to our faculty and gives us more world-class expertise. When someone like that arrives on campus, you are immediately drawn to try to see if there are opportunities for collaboration.”

Yale

MEDICAL INNOVATION

A Tiny Device to Improve Global Health

A novel method could dramatically change how tuberculosis is diagnosed and treated





Despite some advances in managing tuberculosis (TB), the disease has remained a worldwide health crisis. According to the Centers for Disease Control and Prevention, one third of the world's population is infected with TB. In 2014, there were 1.5 million TB-related deaths worldwide.

Insufficient diagnostic tools are a big part of the problem. Late detection of TB, an infectious disease that generally attacks the lungs, increases the risk that the disease will be transmitted to others and that those suffering from it will have poor health outcomes. The most common tests take days to produce results, and can only detect TB if the disease has reached a certain stage — and by that point, treatment becomes difficult.

Mark Reed and his lab are part of an effort that would dramatically change how the disease is diagnosed and treated. It's a device that uses a method pioneered by Reed and his team that quickly separates TB cells from other cells in a sample. It's sensitive enough to detect TB cells long before they become infectious, making the disease much easier to treat.

“We want something that can detect it many months before the disease actually goes full-blown, so you can do very early intervention,” Reed said.

Reed, the Harold Hodgkinson Professor of Electrical Engineering, is working in collaboration with British biotech firm QuantuMDx Group. It's an ambitious endeavor that recently received a major boost with funding from the Bill & Melinda Gates Foundation.

The device takes advantage of a phenomenon known as dielectrophoresis (DEP), in which cells can be separated by an attracting or repelling force even when no charge is present. A sample containing the cells flows through a chip on the device and is subjected to a certain voltage that pulls the cells apart. The device traps the cells by employing frequency-dependent phenomena, and can be tuned to a certain frequency that allows it to capture one type of cell over another. The TB cells are then separated from the others in the sample and trapped.

Continued →



Professor Mark Reed and Ph.D. students Zak Kobos and Shari Yosinski.

Yale

MEDICAL INNOVATION

Encouraged by the results, QuantuMDx has developed a number of prototypes currently being tested. Once it's fully operational, the handheld device will process a patient's sputum sample and be able to detect even a small number of TB cells. Reed figures that it's a few years before the device will be ready for the market.

Reed began the project several years ago with Monika Weber, then a Ph.D. student in his lab. Weber is now leading a Boston-based start-up, and Reed has continued the project with Ph.D. students Shari Yosinski and Zak Kobos. Inside the lab in Becton Center, Reed, Yosinski and Kobos have been refining the technology to reach the high level of precision needed for the device to succeed.

"When you're talking about such low limits of detection, if you miss a cell or two here and there — it will start to matter," Yosinski said.

For safety reasons, they work with a simulant containing cells that act similar to those of TB (a QuantuMDx lab, outfitted with the necessary safety precautions, later tests the same technology using actual TB samples). Testing a sample, the researchers look at the computer screen

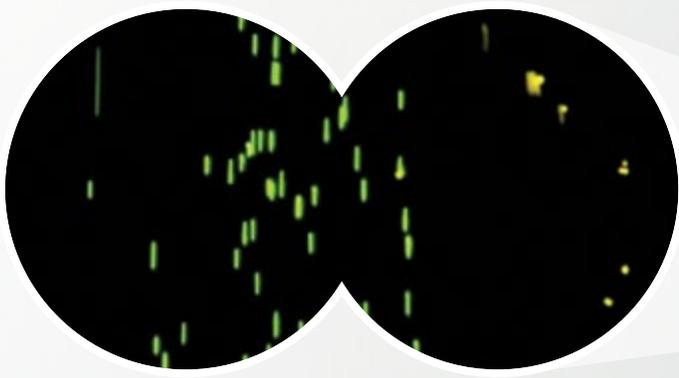
connected to a sensor. A series of spikes show up on the computer screen, telling the story of the sample's contents.

"Usually you get one spike per cell and the height of the spike is related to the width of the cell," Kobos said. "You can infer what's flowing in terms of the size, and then, because you know the bacteria population, you can infer what it actually is from the size and flow speed information."

While QuantuMDx works on turning the technology into a product ready for the market, Reed and his lab continue to hone the system to increase its accuracy and speed.

"We want to be able to capture every cell, and make sure that we're not missing any," Yosinski said. "We want to know that we can process enough volume of fluids so that the test can actually give results within a reasonable amount of time. You don't want this running for several hours before you get your test results."

Time is crucial, especially in non-clinical settings where patients often leave after a certain amount of time. Reed's goal for the device is to successfully detect and quantify the cells in 10 to 30 minutes. There are still tweaks they



Reed's device can separate cells by an attracting or repelling force even when no charge is present.



have to make, such as completing the microfluidic design to take the person's sample and have it automatically go through the system. Some materials, they've found, cause the cells to stick instead of flowing through the channel to be processed. Although the cells didn't stick when they were working on the technology in Reed's lab, there were some complications with a prototype developed by QuantuMDx, due to variations in electronics.

"These things work at high frequencies," he said, "so there's a lot of electrical engineering and electrochemistry that goes into it to get the device working and able to get a more efficient design."

The technology currently works on various pieces of lab equipment, but will eventually be miniaturized and put on a PC board. Making the device small and portable is key, since TB is a particular concern in resource-poor areas.

Reed notes that well-equipped labs can use a microscope for optical detection, but that's not much use when you're going out into more remote areas. "Here, if a person gets tuberculosis, they can be treated in a hospital pretty quickly," Reed said. That's not always an option in other areas of the world.

"If you ever want to be in the field or do this at a low cost, you can't bring your microscope around and do fluorescence imaging," he said. "This device would literally be cellphone-sized and you can put a sample in there and it would then internally do the separation and then the count. Here, we can have a portable unit that you can take to a village and be able to test everybody and catch it early on before it starts to infect a person and spread." 🏠

Green Engineering

Julie Zimmerman and Paul Anastas published a guidepost to engineering in a way that's both environmentally and economically beneficial. More than 14 years later, it still holds up.

Yale

SUSTAINABILITY



“Innovation in design engineering has resulted in feats ranging from the microchip to space travel. Now, that same innovative tradition must be used to design sustainability into products, processes, and systems in a way that is scalable.”

From the “12 Principles of Green Engineering” by Julie Zimmerman and Paul Anastas, March 1, 2003, *Environmental Science & Technology*

These days, it’s common for businesses to tout the sustainability of its products, or its environmentally friendly manufacturing processes. Of course, this wasn’t always the case.

In 2003, Julie Zimmerman and Paul Anastas published “The 12 Principles of Green Engineering” in the journal *Environmental Science & Technology*. It was intended as a guide to help engineers and corporations design and develop products, processes and services that are both benign to human health and the environment while being competitive in the marketplace.

“Green engineering,” a term that they coined, focuses on how to advance sustainability through innovative science and technology. It builds on the successful traditions of environmental engineering by integrating the conventional skillsets with a broader systems view. The challenges that engineers are being asked to meet today are far more subtle, complex and diffuse and in many cases global as well as multi-generational. Addressing these new challenges will require new knowledge, new talents, new skills, and a new awareness. As a result, Zimmerman said, the field of engineering needs to shift from being primarily focused on functional performance to being actively involved in the design and development of technology that will not contribute to adverse environmental and social impacts.

“The idea of green engineering is that there’s a lot of engineering knowledge that can be applied further upstream in the process to prevent issues from arising in the first place,” said Zimmerman, professor of chemical & environmental engineering as well as forestry & environmental studies.

Continued →



More than 14 years later, the publication of the 12 principles has proven to have had a significant impact. They've been applied in construction and aerospace, and manufacturers of such consumer goods as cars and carpets have employed the principles in their work. Numerous pharmaceutical companies have also drawn from it.

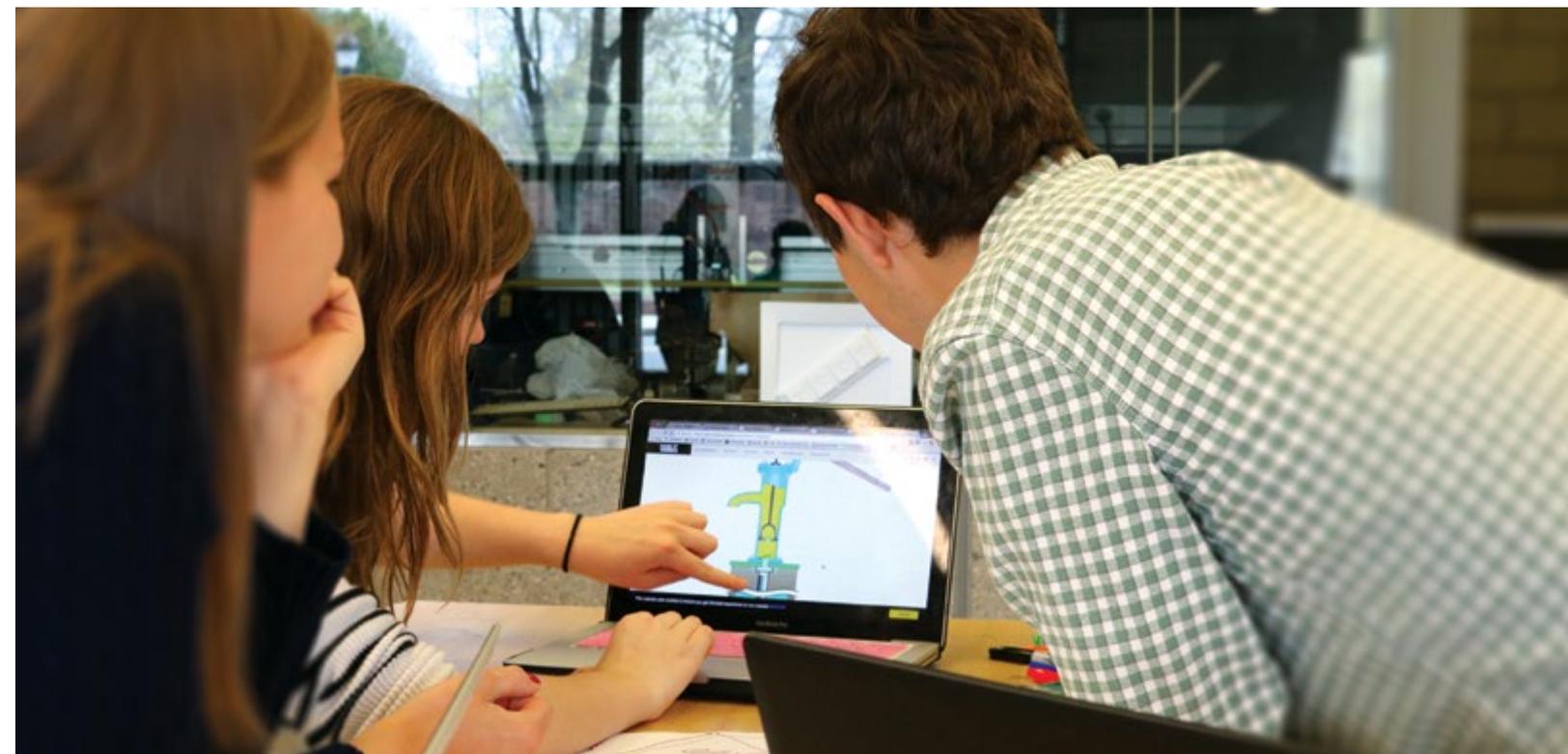
"The Principles of Green Engineering have withstood the test of time, becoming more relevant as there is a growing interest in innovation of disruptive solutions by industry and an increasing awareness of the potential unintended consequences of technology on human health and the environment," Zimmerman said.

The idea for the 12 principles grew out of any earlier publication Anastas co-authored on the principles of

green chemistry. That paper offered guidelines on how to make molecules and the synthetic pathways to make those molecules. Anastas and Zimmerman decided they should create something analogous for engineers and designers.

"It dealt with questions like 'Once you have all these great molecules and materials from green chemistry, how do you put them together into sustainable products, processes and systems?'" Zimmerman said. "The idea grew from green chemistry and the need to think broadly about tangible goods and services that you want to design for sustainability."

The response was nearly immediate. Less than a year later, they edited a special issue of *Environmental Science & Technology* that contained a series of papers by research-



ers on how they employed the principles in their work. “It was nice to put out this framework and then really quickly be able to show their relevance and utility across all of the engineering disciplines and a wide variety of industrial sectors,” she said.

Zimmerman and Anastas, the Teresa and H. John Heinz III Professor in the Practice of Chemistry for the Environment at the Yale School of Forestry & Environmental Studies, also use the principles as a basis for their course on Green Engineering, which they co-teach.

This course provides a hands-on foundation to green engineering and the design and assessment of green products. “Approaching sustainability from a design perspective requires the need for a fundamental conceptual

Above: Students in the Green Engineering course have worked with major corporations such as U.S. Foods, Petco, Hyatt, and Hasbro to provide sustainability solutions to their products.

shift — from the current paradigms of production toward a more sustainable system, based on efficient and effective use of benign materials and energy across the life cycle,” she said. “The course is centered on identifying real-world sustainability challenges and then designing, developing, prototyping and ‘pitching’ solutions to them.

The course was first offered 10 years ago. In its early stages, resources were a bit makeshift.

“Before the Center for Engineering Innovation & Design opened, we used

Continued →



A Summary of the 12 Principles of Green Engineering

1 Inherent Rather Than Circumstantial

Designers need to strive to ensure that all materials and energy inputs and outputs are as inherently nonhazardous as possible.

2 Prevention Instead of Treatment

It is better to prevent waste than to treat or clean up waste after it is formed.

3 Design for Separation

Separation and purification operations should be designed to minimize energy consumption and materials use.

4 Maximize Efficiency

Products, processes, and systems should be designed to maximize mass, energy, space, and time efficiency.

5 Output Pulled Versus Input-Pushed

Products, processes, and systems should be “output pulled” rather than “input pushed” through the use of energy and materials. For instance, allowing consumer demand to determine quantity and time of production eliminates waste associated with overproduction, waiting time, processing, inventory, and resource inputs.

6 Conserve Complexity

Embedded entropy and complexity must be viewed as an investment when making design choices on recycle, reuse, or beneficial disposition.

7 Durability Rather Than Immortality

Targeted durability, not immortality, should be a design goal.

8 Meet Need, Minimize Excess

Design for unnecessary capacity or capability (e.g., “one size fits all”) solutions should be considered a design flaw.

9 Minimize Material Diversity

Material diversity in multicomponent products should be minimized to promote disassembly and value retention.

10 Integrate Material and Energy Flows

Design of products, processes, and systems must include integration and interconnectivity with available energy and materials flows.

11 Design for a Commercial Afterlife

Products, processes, and systems should be designed for performance in a commercial “afterlife.”

12 Renewable Rather Than Depleting

Material and energy inputs should be renewable rather than depleting.

Published March 1, 2003, in
Environmental Science & Technology

to do prototyping with paper towel tubes, duct tape, and tissue boxes,” she said. Today, they have major corporations turning to students for ideas. In recent years, the course has engaged companies such as U.S. Foods, Petco, Hyatt, REI, Nike, Curtis Packaging, and Hasbro. Representatives from these companies met with the students, each presenting a specific sustainability challenge relevant to their business. By the end of the semester, student have designed, prototyped and tested their ideas.

In one challenge, for instance, students were tasked by a major hotel chain to minimize the packaging burden of individual personal care amenities including shampoo, conditioner, and body lotion. After conducting surveys, the students determined that Americans prefer not to use shared wall dispensers. The students instead created a single-serving size capsule of each product contained within a water-soluble polymer. When the capsule gets wet, the polymer dissolves, and the guest now has just the right amount of product without contributing any waste to the landfill.

For the most recent class, student teams developed a device that pulls water from the air, a self-watering lawn system, and a machine that automatically sorts recyclables.

And green engineering has taken a place in the curriculum beyond Yale. The American Institute of Chemical Engineers has incorporated keywords from green engineering and sustainability into language on accreditation. For instance, it now requires accredited engineering programs to foster in students an ability to design “within realistic constraints such as economic, environmental, social, political, ethical, health and safety, manufacturability, and sustainability.”

Outside of academia, many of the ideas outlined in the 12 principles that might have seemed idealistic at the time are now common practice. It’s no longer assumed that being mindful of the environment conflicts with a company’s profits. HP Inc. allows customers to resell their ink cartridges back to the company, which then refills and resells them. “They actually make more money on the second

one because they didn’t have to remake the cartridge,” Zimmerman said. With more than 4 billion pounds of carpet entering the United States’ waste stream each year, carpet companies have pursued green engineering to strategically address this issue. Interface, the world’s largest manufacturer of modular carpet, designed new products and a new business model by selling customers the service of a carpet instead the carpet itself. When the carpet reaches the end of its useful life, the company makes it the feedstock for the next generation of carpet and recycles it into a new floor covering to sell to the next customer.

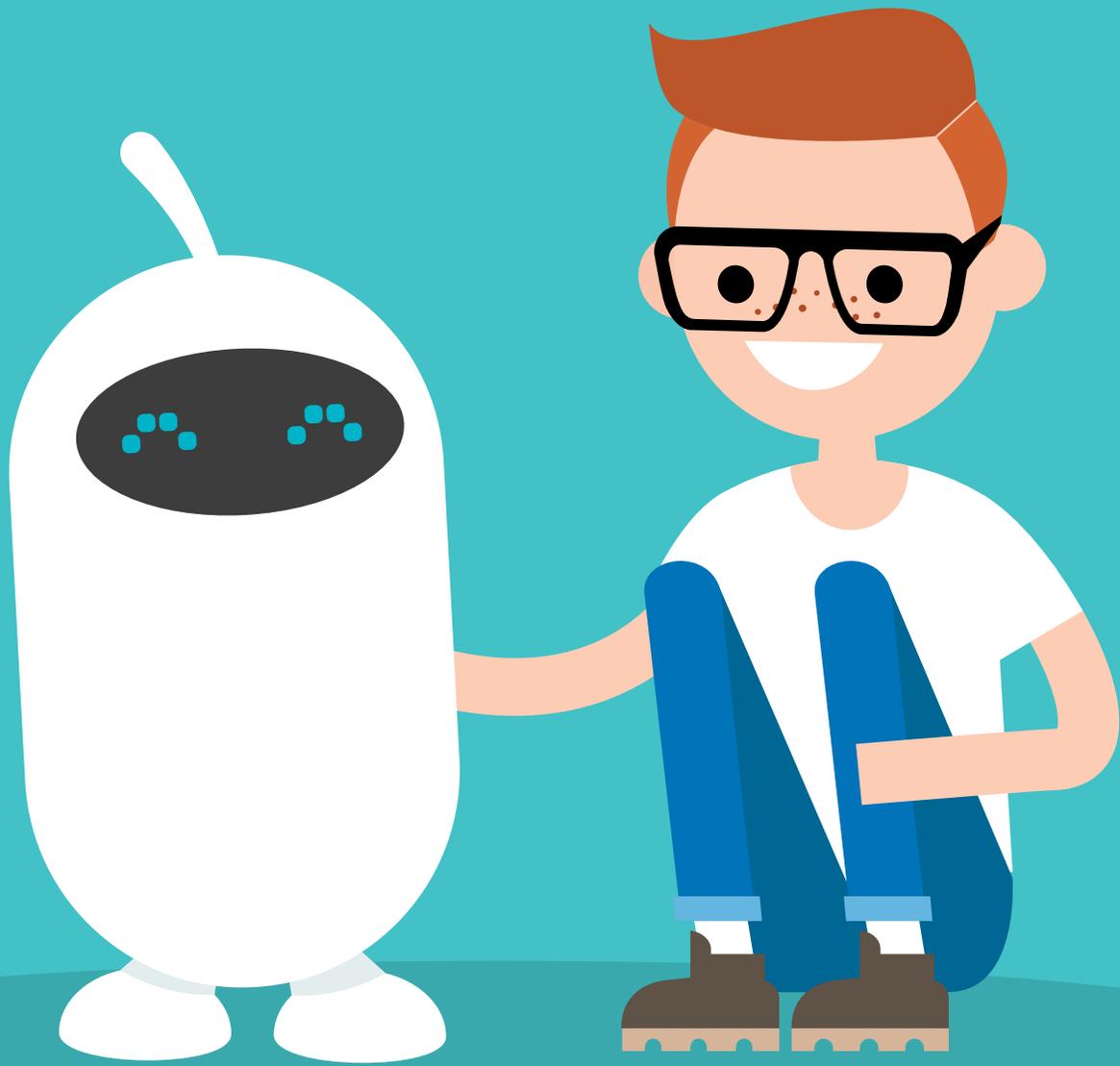
“There are so many success stories now that the myths that ‘green’ products do not work as well, or going ‘green’ costs more to the company and the customer have been disproven,” Zimmerman said.

The market has come to realize that green chemistry and engineering are actually better for business. That includes efficiency gains in terms of less waste from processing and packaging, and gains from having less inventory to manage and less liability from hazardous chemicals.

“Most importantly, because of the new innovation resulting from green chemistry and green engineering approaches, companies are realizing that this is not just about improving the bottom line, it is about top line growth,” she said. “And as more and more of these case studies come out, it becomes self-sustaining while addressing sustainability challenges.” 

Socially Assistive Robots

How kids are learning from their automated friends



Yale

TECHNOLOGY

At his desk, Ethan Crespi helps his friend count out space rocks.

“We are getting close to my departure date and I need to repair my rocket,” the friend says, adding that he would like Ethan to feed his space pets while away.

Ethan is a 7-year-old boy with autism spectrum disorder. Like other kids his age, he has lots of energy, is obsessed with Angry Birds, and loves building towers and knocking them down. Social interactions, though, give him some trouble.

“He can speak and communicate his needs,” said his mother, Jennifer Crespi. “But the exchange between two people in conversation — that seems to be more of a struggle. So is sharing what’s on his mind with the world and using his voice to express his feelings and listening to others when they’re talking.”

His friend, a robot that sits on top of a desk, is helping him with that. It’s part of an ambitious five-year project funded by the National Science Foundation for \$10 million and headed up by Brian Scassellati, professor of computer science. The research team is developing “socially assistive robots” to teach children everything from nutrition to English as a second language to how to be a better communicator.

The project was launched in 2012 and is in its final and most ambitious phase, in which the research team is deploying robots in the homes of families with autistic children. The researchers work with each family for three months. First, they conduct a baseline assessment of the child’s skills and emotional development. One month later, they drop off the robot, which takes up residence in the family’s home for 30 days. The child engages in various lessons with the robot for 30 minutes each day. One month later, the researchers assess the child a second time to see how much progress has been made, and take the robot out of the house.

A third and final assessment happens 30 days later — this time to see how well the lessons have stayed with the child over a period of time. Up to 30 families are taking part in the study.

The educational games are played between the robot, the child, and the parent. They usually focus on social skills — eye contact or turn-taking or taking someone else’s point of view. The robot leads the lessons, sometimes as a partner, other times as an opponent or mediator.

As studies go, this one is pretty involved.

“It’s a relatively big ask to say ‘I want to put something in your homes, take up four afternoons of your time and you’ve got to do this thing 30 minutes every day,’” Scassellati said. “It’s not ‘Come by my office for an hour and I’ll pay you \$20.’”

Once all the robots have been collected and the assessments completed, the researchers tackle the job of analyzing the data. All the sessions are filmed, so the video footage alone — 450 hours of it — is daunting. For this kind of study, there aren’t any shortcuts. Scassellati’s previous research has shown that short sessions with robots can have significant short-term learning results for children with autism. But they also learned that by the third or fourth day, the kids lose interest.

“It had nothing to do with the fact that they were kids with ASD. It was that they were humans and if you do the same thing over and over again, it gets boring.”

For a robot to be effective then, the researchers needed to program it with the ability to change from day-to-day and adapt to an individual child’s ways of learning. Depending on what the children do well, and what they don’t, the games in each robot change substantially. Every robot they place in a home is pretty much the same as the others on Day 1. By Day 30, each one has changed a little as it adapts

Continued →

to its host's needs. The trick is making it both fun and challenging for the child.

"We're working on the things we know they have difficulty with — we're not going in and picking the easy fruit," he said. "That means in many cases that it's going to be the hardest thing to do. But if we can show any kind of impact, then we'll feel a lot better about moving forward with it."

It helps that the kids like the robot, which is often quickly accepted as part of the home. "That makes it a lot easier on the parents," Scassellati said. "Anything we can do to decrease stress levels or increase motivation levels — that's a big win for us."

The toughest day of the project is when the family has to say goodbye to the robot. To alleviate the sting of the new friend leaving, the researchers will often distract the child while the robot gets packed up.

"On this and other studies, the most common question we get at the end is 'Can I keep the robot?' Unfortunately, the answer almost always is 'These are all prototypes, we can't sell them or give them to you.'"

To get to the point where these robots can be distributed, the researchers need to show definitive proof that they improve development outcomes. Scassellati is confident that they're close to being able to show that. It's been a long time coming. The three months of lessons and assessments make up just a small part of the project.

"Everything has been building up from conducting a single 5-minute interaction to 30 minutes of interaction for 30 days," he said. "Leading up to this, we did a lot of work with other types of curricula, other types of kids and settings, both in the lab and in schools. We also created all the technology to be able to go from something that did the same thing with every child to something that is personalized and changes as the children change. That took us five years to get all those pieces in place."

The program that controls the robot runs on code writ-

ten at four universities. It's just one of many elements of the project that's been built from the ground up. "We have custom hardware design, custom software design — everything's from scratch."

The ambitious scope of the project is reflected in the personnel required to carry it out. Five universities are participating, with 15 faculty members spanning numerous disciplines, including computer science, mechanical engineering, education, medicine and nutrition. Other Yale faculty include Aaron Dollar, associate professor of mechanical engineering, and Fred Volkmar, an autism specialist and former director of the Yale Child Study Center.

And that's just the theoretical side of things. The actual nitty-gritty of getting a robot to work properly in different environments is a whole other matter. Scassellati ran a test run of one of the robots in his own home — "maybe the most robot-friendly house in all of Connecticut." The system was immediately beleaguered by spotty wi-fi coverage and the family's rambunctious cat, which knocked over the robot.

"No one told us we had to build an anti-cat system," he said. "That never would have happened in the lab, or in the schools, but it sure happened in my house. We're learning a lot by being aggressive and putting a really high bar out there for us to get over. I think that's how we're going to learn the most."

Why use robots at all? Scassellati, who came to Yale in 2001, has spent years studying human-robot interactions. One consistent finding has been that children of certain groups — including those with hearing loss, non-native English speakers and those on the autism spectrum — respond particularly well to robots. They're still working on why that is exactly, but Scassellati said it has "something to do with the fact that the robot is social, but not too social." Many of these children are intimidated by usual social situations, and they feel safer interacting with the robots.

"These are kids who have years of experience with the idea that social interaction is challenging and something they don't understand," he said. "When they interact with the

robot, though, it triggers social responses but it doesn't trigger a lot of the other baggage they've come to associate with social interaction."

The fear of saying or doing the wrong thing is a big part of this. A study they did in 2013 found that kids learning English as a second language would often stay silent when their human teacher asked a question. It was a different story when a robot posed similar questions.

"All of a sudden, you saw the kids make mistakes in front of the robot," he said. "That was just amazing because we couldn't get them to do that in class. We could see what they knew and didn't know. Then we could start teaching and personalizing lessons based on that, and the kids showed tremendous improvement."

But it can't be just any robot. They've learned that robot-building is a delicate balance between making it lifelike, but not too lifelike. Unplugged, the researchers' robot looks pretty much like an orb on a base. Plugged-in, though, the robot becomes animated, moving its head, blinking and darting its eyes back and forth. The gestures are slight, but enough to spark a response.

"The minimalist approach has certain advantages for us," he said. "One is that the kids can project onto it what they want. It also allows us a certain amount of forgiveness. The more detailed you make something, the more exact you have to get it. Making androids that are extremely lifelike is extremely difficult to do because any little bit you get wrong ends up being shocking."

Maintaining activity is important, Scassellati said. Try talking to people while standing stock-still; they'll find it "freaky." To get it right, the researchers study puppets and cartoons. "Animators know the rules for how to make something jump up and run around and look like it's alive."

Ethan quickly welcomed the robot to his home, as did his parents. After 30 days with the robot, Crespi has seen changes in her son's behavior. Part of it, she thinks, has to do with Ethan following the eyes of his robotic friend.

"I've noticed that when Ethan's talking to me, he'll look at me more," she said. "Those initial communication bits are becoming more prevalent and happening more often."

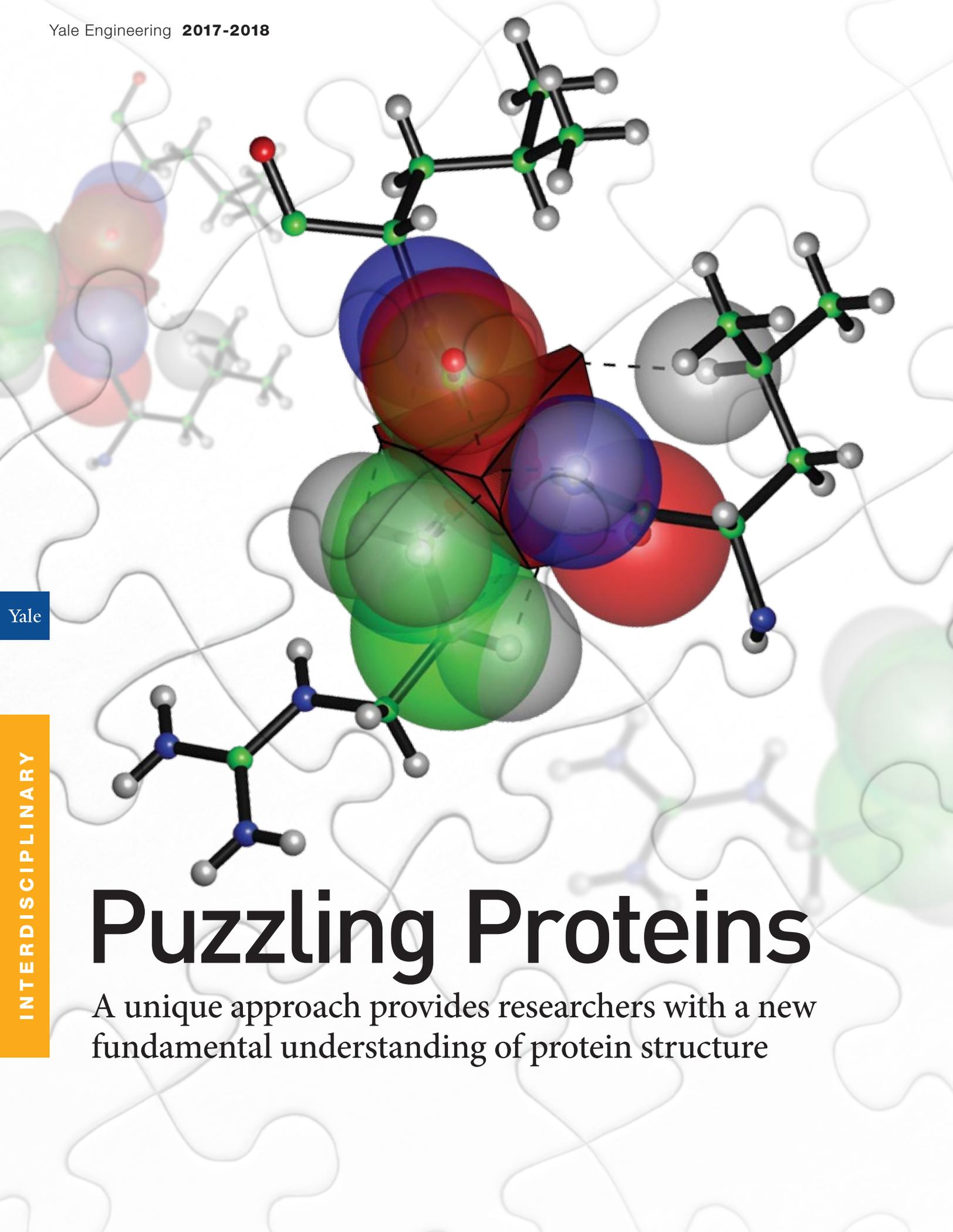
The act of conversing with the robot is also having an impact, she said. "We went to the playground one day, and there was a group of children playing in the sand. He walked up to them and said 'Hi, what are you doing?' I don't think he would have done that a month ago."

The robot would soon be leaving their home, but Crespi said she and Ethan would continue many of the lessons.

"Working with the robot has taught me to really slow down with things I take for granted that someone with autism might not understand initially," she said. "Now I'll pause and linger and use it as a moment for Ethan to focus, and I'll explain to him more explicitly than I would normally."

The Crespis got involved in the study after Ethan's parents brought him to the Yale Child Study Center for evaluation. They checked a box on a form to indicate they were open to taking part in future studies. At the time, they had no idea this meant opening their home to a robotic companion.

"I wasn't sure if Ethan would be engaged, or if we'd have to drag him into it," she said. "Then I was just watching the progress with his skills that were being worked on each day — really, it exceeded my expectations. We've gotten to know the robot and the stories about the things they notice on their trip to Earth. He's really become a good friend to Ethan." 🏠



Yale

INTERDISCIPLINARY

Puzzling Proteins

A unique approach provides researchers with a new fundamental understanding of protein structure

Since it emerged in the 1980s, the field of protein design has held promise for the development of new vaccines, energy production and storage, and other applications. To reliably develop new protein-based materials that don't exist in nature, researchers need a full understanding of the building blocks of proteins and how they interact with each other.

Many scientific problems are analogous to jigsaw puzzles. Professors Corey O'Hern and Lynne Regan have proposed to take this comparison even further with proteins, by disassembling each protein and putting it back together.

"You can't significantly improve the design of a machine, if you don't fundamentally understand the original design," said O'Hern, whose primary appointment at Yale is in mechanical engineering & materials science. "The same is true for proteins. You need to know what has worked in existing, functional proteins, and then you can take the existing structures, and improve them."

It's not enough to simply identify the individual components of proteins; one needs to know how those components interact. Proteins fold into specific three-dimensional shapes, based on the interactions between the amino acids that compose the proteins. A clearer picture of these interactions will help researchers better predict the changes in protein structures caused by mutations to the amino acids.

Getting this clearer picture, though, hasn't been easy. O'Hern has been working for a number of years with Lynne Regan, professor of molecular biophysics and biochemistry and chemistry, on developing methods for computational protein design, that promises to speed up and streamline the design process. O'Hern and Regan make an excellent team. O'Hern develops the computational models and Regan creates the physical proteins to validate and improve the models, and they interact closely throughout the entire process. Together they have published more than 15 papers together and co-mentored more than five Ph.D. students and several postdocs. They have developed what they call the "steric plus stereochemistry-based

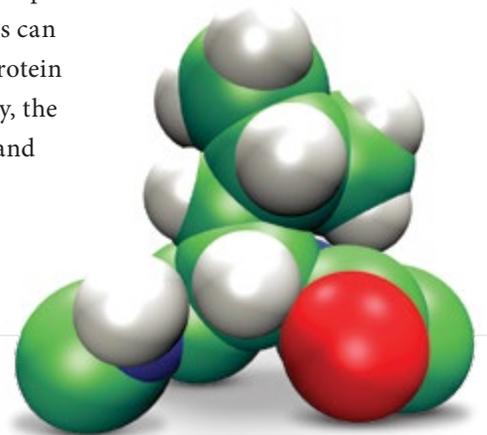
model" for protein structure which can accurately repack the cores of soluble proteins.

Proteins are made up of hundreds of amino acids, each comprising dozens of atoms bonded together. To create new proteins, researchers will delete certain amino acids or switch out one for another. Conventional methods for computational protein design have found limited success in predicting how these mutations will affect a protein's thermodynamic stability, which it needs to maintain to be functional.

Figuring out how the amino acids fit together to generate the three-dimensional structure of a functional protein is a complicated matter — and O'Hern says researchers often make it even more so. Multiple types of physical interactions are possible between the amino acids, such as electrostatics, Van der Waals', and hydrogen bonding interactions. However, these interactions are not comparable in all situations. Rosetta, the most commonly used computational software for protein design, includes all of these interactions. It's an approach that takes a great deal of computational power, sometimes prohibitively so.

O'Hern and Regan, though, have a simpler method. They model amino acids as building blocks with complex geometrical shapes. These are based on protein crystal structures that have been collected over the past 30 years in what's known as the Protein Data Bank, an online database of protein crystal structures. With their computational modeling tools, O'Hern and Regan can try all of the possible ways that amino acids can fit into the cores of protein structures. Essentially, the approach of O'Hern and

Continued →





Regan treats proteins like three-dimensional puzzles that can be taken apart and reassembled to match observed protein crystal structures with high accuracy—a process known as repacking.

From the proteins on moths' eyes (they have an anti-glare property) to their potential for new groundbreaking medicines, Regan said, the appeal of working with proteins is obvious.

“They do everything!” she said. “Hair is made of protein, nails are made of protein, the hemoglobin in your blood, everything within cells. They have an incredibly wide array of different structures and functions. So, yeah, they’re really cool.”

By starting from the ground up, and building their own computational approach, O’Hern and Regan have discovered a number of properties and functions that they otherwise wouldn’t have.

“We started off saying ‘Hey, let’s design a new protein interface,’” Regan said. “But we decided that we first needed to do all of the steps properly. During the design process, we’d keep taking a step back to say ‘Oh, we need to figure out how to do this.’ In taking those steps back, I think we discovered a new fundamental understanding about protein structure, which puts us in a much better position for designing new proteins and interfaces.”

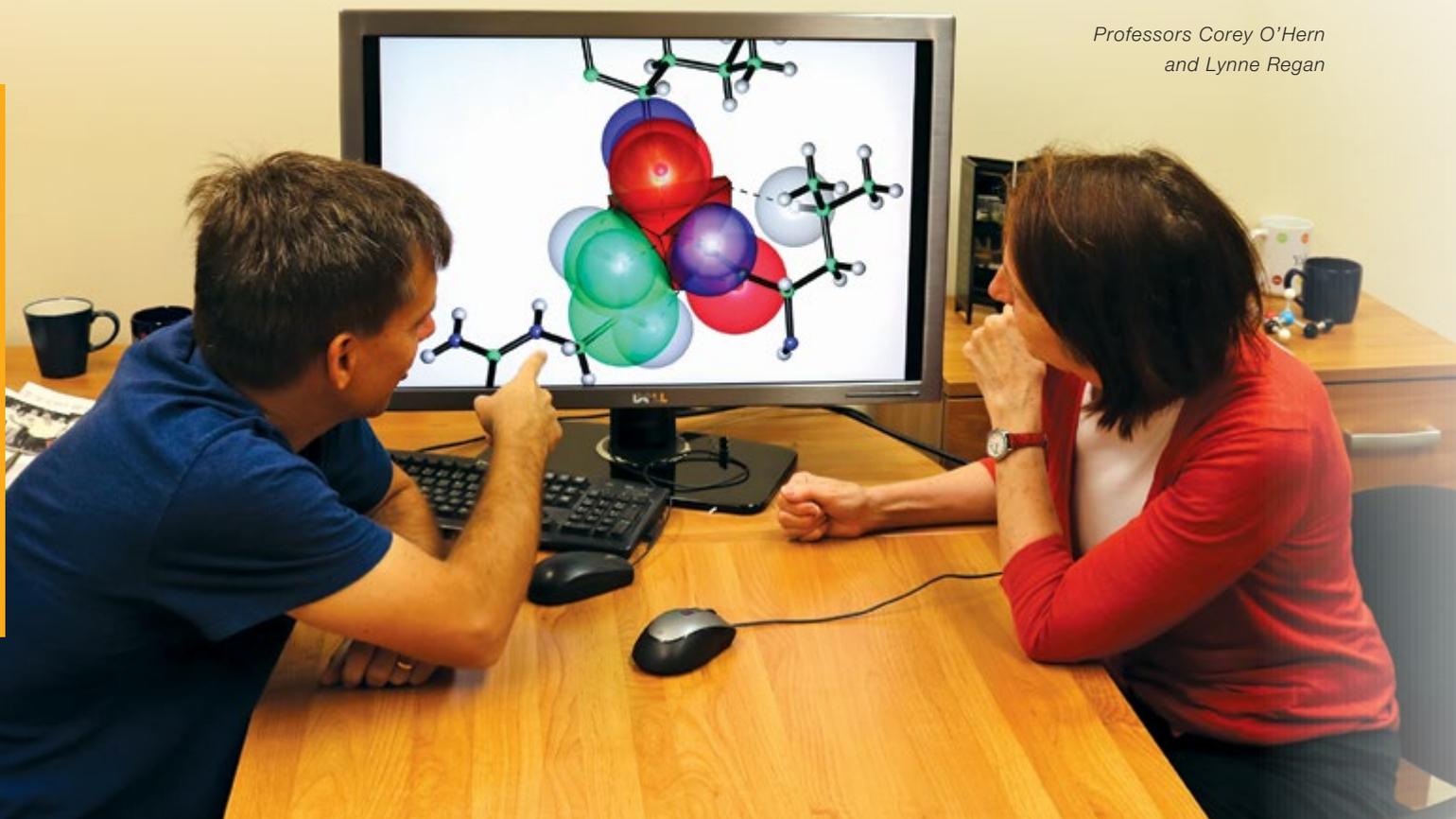
The field of protein design began to take off in the 1980s when technological advances improved methods for protein crystallography. These advances enabled the creation of the Protein Data Bank, which today contains more than 100,000 protein crystal structures, allowing researchers to investigate the atomic scale structure of proteins.

“So now, we have a detailed picture of the structure of naturally occurring proteins,” O’Hern said. “There’s not another database like it that provides such a wealth of atomic scale structural information.”

*Professors Corey O’Hern
and Lynne Regan*

Yale

INTERDISCIPLINARY



For many researchers, the database did away with the need for theoretical models or computation, and they pivoted toward what's known as knowledge-based research instead of physics-based modeling.

“These researchers said, ‘If I want to make something new, all I need to do is check the protein database, and see if something like it appears in nature.’ In this case, predictions are made based on the frequency with which amino acids appear in similar locations in the protein database.”

As useful as the database is, it's no magic bullet. For one, it's limited as a predictive tool. As O'Hern notes, it's a “little paradoxical” to try to design something new by looking at what already exists in nature.

And while the protein database provides the “what” for protein structures, it doesn't provide the “why.”

“You don't get a fundamental understanding of protein structure through a knowledge-based approach,” he said. “Instead, we would like to know which atomic interactions are dominant, which interactions are relatively weak, and under what circumstances. This will allow us to construct a physics-based model that can be used to predict protein structures for non-native amino acid sequences.”

The success of O'Hern and Regan's method, the “steric plus stereochemistry-based model,” derives from its simplicity. They focus on one interaction, known as steric repulsion — that is, repulsive interactions that prevent atoms from overlapping each other — in specifying the structure of protein cores. With their computational model, proteins become three-dimensional puzzles and each amino acid is given a geometric representation. The model can accurately predict how amino acids fit back into place after they've been removed from a protein.

“It's as if a toy company took the amino acids out of the core of the protein and left the exterior as the scaffold of a puzzle,” said O'Hern. “Then they give you the amino acids as 3D puzzle pieces, and say ‘Put the puzzle back together.’ That's what we do.”

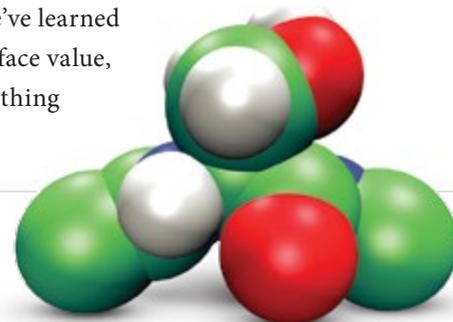
This modeling approach can provide a physical picture of the dominant interactions that determine protein structure. For example, they can sequentially add different interactions until it becomes clear which interaction is the driving force that determines the dihedral angle conformations of a given set of amino acids.

O'Hern and Regan stress that it's critical not to rush into the designing of new proteins without a detailed blueprint of existing ones. Assumptions are often made in their field, and many turn out to be wrong. They ran into those assumptions in a collaboration with Dr. Daniel DiMaio, deputy director of the Yale Cancer Center. DiMaio has discovered a novel way to trigger oncogenic activations — the mechanism that makes a cancer cell grow. He then looked into which peptides would facilitate this process, and which ones would not. That's where O'Hern and Regan come in.

“Obviously you don't want to promote cancer, but you could imagine that there are other receptors whose activity you would like to promote,” Regan said. “We're working with him because we know how things interact and I bet we could predict which peptides would work and which ones wouldn't.”

Shortly after beginning their research, they encountered some skepticism from other researchers who insisted that the types of proteins they would be working with — transmembrane proteins — are not as well-packed as others, and thus they are less likely to be accurately modeled.

“But we find no evidence that transmembrane proteins are more loosely packed,” Regan said. “In fact, they're as well packed as soluble proteins. It's really just a matter of critically examining the claims from the protein community. We've learned not to take anything at face value, and to investigate everything for ourselves.” 



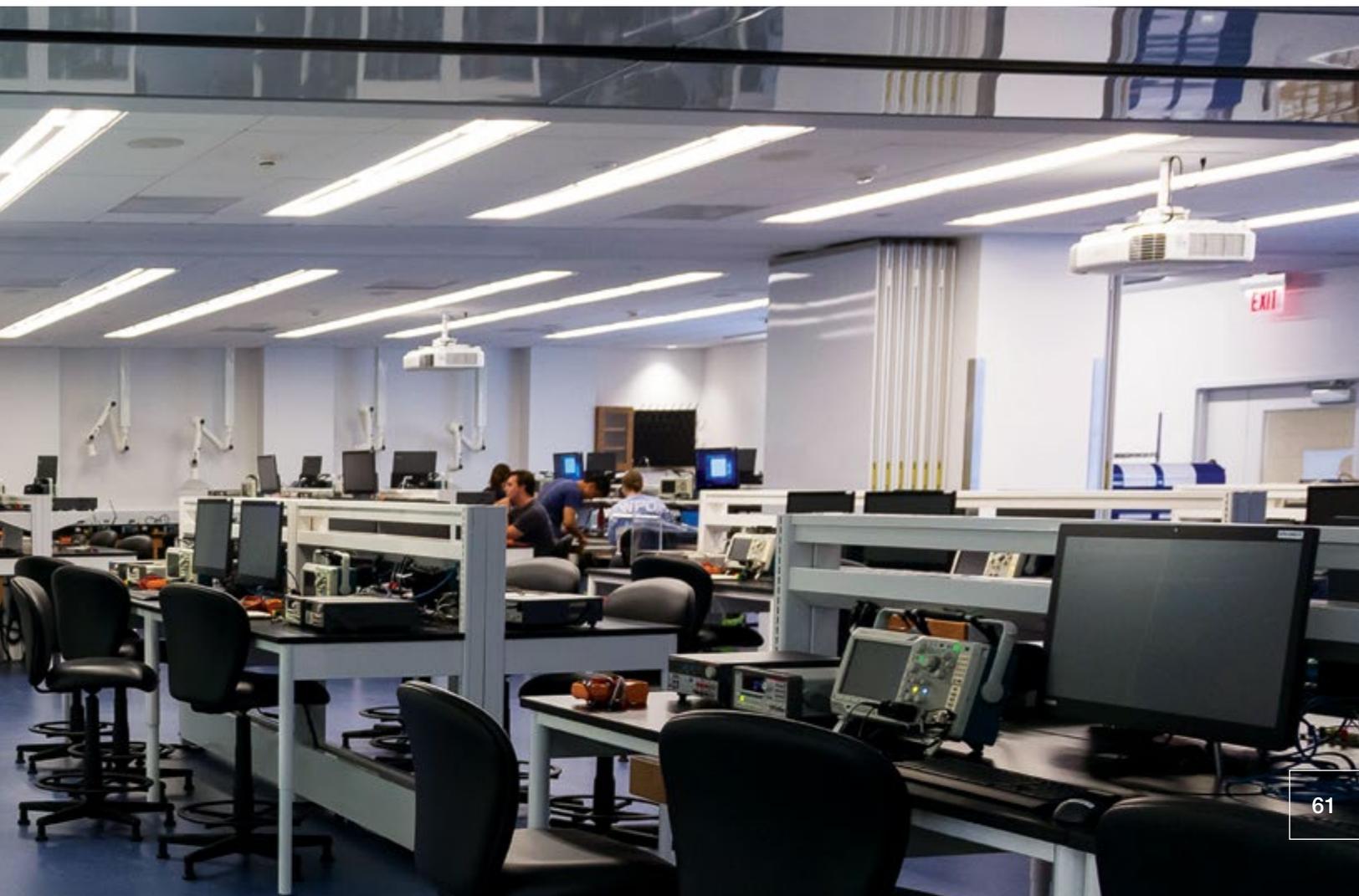


Yale

EDUCATION

If You Build It, They Will Come

The Greenberg Engineering Teaching Concourse brings students from all engineering disciplines to a collective, state-of-the-art home



As of this fall semester, those passing through Dunham Laboratory and Becton Center have a direct look at what engineering is all about. That's thanks to a large window and glass door that give a clear view into the new Linda and Glenn H. Greenberg Engineering Teaching Concourse.

Located in the center of Yale's engineering campus, across the hall from Davies Auditorium, the teaching space includes six new undergraduate teaching labs, along with two wet labs with fume hoods. The project was funded with a \$10 million donation from Glenn Greenberg '68. The opening of the concourse, which coincides with the completion of the new residential colleges, brings together labs from all disciplines in engineering — currently scattered over five buildings — into one space.

From its conception, a crucial part of the plan was that the space would serve a similar role as some of the newer labs in 17 Hillhouse, or at the Center for Engineering Innovation & Design. That is, a place where people of multiple disciplines could do their work, and end up sharing ideas with others from backgrounds they wouldn't normally meet in more conventional and insular labs. A mechanical engineering major, for instance, can get advice from a nearby electrical engineering student, or a chemical and environmental engineering study group will borrow tools normally used in biomedical engineering.

Yale President Peter Salovey has noted that the Greenberg Concourse can help create the sense of community that's key to any successful education.

Continued →

“It’s spaces like this where I know that students are going to be working at all hours and where our faculty will be teaching at all hours,” he said. “And that creates the feeling of being part of a community.”

The concourse serves as a crossroads for SEAS faculty and students, physically linking Becton Center, Dunham Laboratory, and Arthur K. Watson Hall, which is occupied by the computer science faculty. In March of last year, the university laid the groundwork to expand the Department of Computer Science and merged it into the School of Engineering.

“It was very intentional that in addition to serving as a site for all of our engineering labs, it’s also an accessible portal to Computer Science,” said SEAS Deputy Dean Vincent Wilczynski, who headed up the project. “It’s a physical connection between everything.”

One of the space’s most distinguishing features is that it can be readily adapted to different uses. SEAS Dean T. Kyle Vanderlick calls it “an entirely new way of thinking about hands-on, interdisciplinary teaching.”

“It’s flexible, adaptive, and efficient,” she said. “Students and faculty members from all disciplines will learn from each other and make the most of the full SEAS experience. This approach of co-locating our departments is more ef-



ficient, and it allows us to provide a better-quality facility than if we had built four laboratories in separate buildings.”

The space has collapsible walls that allow labs with a 24-student capacity to triple in size. Additional storage space and portable equipment will allow labs to change for different courses from one semester to the next.

“Experiments can be wheeled out and prepped for a given semester, and then wheeled back in so that a different group of students can use the facility,” Vanderlick said. “At other schools of engineering, if the chemical engineering lab was in the fall, then the place sits dormant in the spring. That



“It’s intended to put a spotlight on Engineering and to have that light spread out into the Davies hallway and light up the whole area.”

› Vincent Wilczynski, SEAS Deputy Dean

Yale

EDUCATION



Left: At the ribbon-cutting ceremony in September, President Peter Salovey cited the communal spirit of the space.

Above: (Left to Right): Dean T. Kyle Vanderlick, Glenn Greenberg '68, Linda Greenberg, Barbara Mann, J. Robert Mann, Jr., and President Peter Salovey.

Below: Dean T. Kyle Vanderlick describes the teaching concourse as "an entirely new way of thinking about hands-on, interdisciplinary teaching."

will never happen here — we'll be able to use all this space for any group at any time."

Wilczynski said plans for the new labs started a few years ago when he and Vanderlick were walking back from the Provost's Office, having just received word of SEAS' renewed accreditation.

"That's when the wheels started to turn — 'OK, now what do we do for the next cycle? Where do we need improvements?'" he said. "The labs were right at the top of the list. Before we even got back to the office, we stopped at the labs in the basement of Mason and Becton, and it was pretty apparent that we could do better."

One common theme that emerges when people talk about the concourse is how different it is from what was there before, when the space was mainly used for Electrical Engineering. When discussing the "before" half of the picture, words

like "cavernous," "dilapidated" and "isolated" come up a lot. The bright, open spaces in its current incarnation are a stark contrast.

Standing near what had once been the loading dock and is now an open space housing three labs, research support specialist Kevin Ryan points to some of the new features.

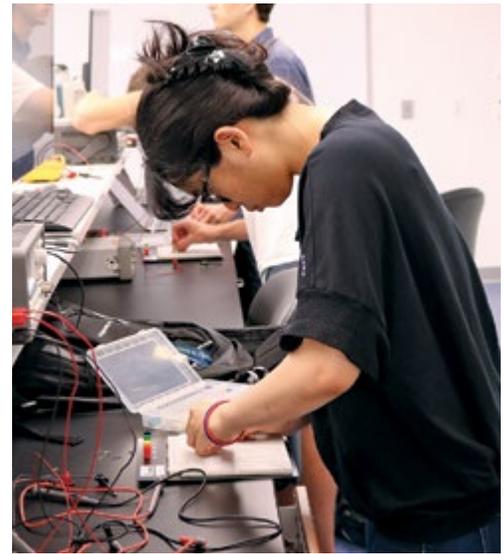
"This is a wall that comes down, which I can use to isolate this lab from the other — or I could isolate all three labs, or just these two from this one," he said. "I like to keep it open as much as possible, but depending on what's going on, the walls can minimize distraction."

Ryan said the difference between the old and new labs is so pronounced that it will take time before they know the

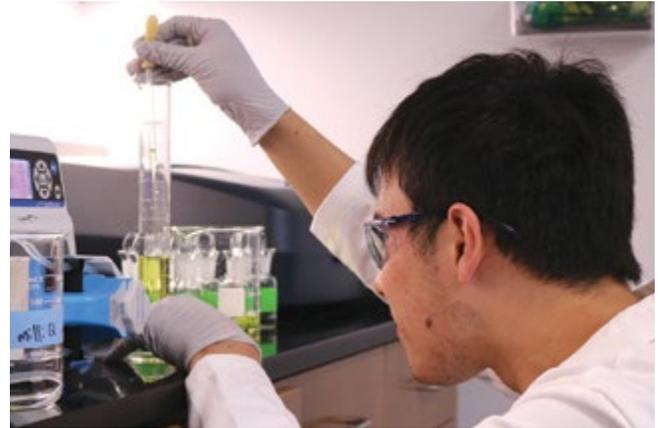




The teaching concourse brings together labs from all disciplines in engineering — currently scattered across five buildings — into one space.



full scope of the new labs' possibilities. But state-of-the-art projectors and microphones are just some of the new equipment features that are paying off just weeks after the space opened. Other welcome amenities include bigger breadboards, more powerful waveform generators, snorkels that suck up soldering smoke (the previous space made do with an old fan) and a function generator power supply that essentially acts as six instruments in one (a huge boon when it comes to saving shelf space).



Betsy Li '18, who experienced the old lab space as a freshman and now works with Ryan, said the difference is incredible.

"There's just a lot of light and it feels more open — it shows how much investment the School has been making for people who might want to become engineers," she said, adding that students now have a much greater range of

possible experiments. "The equipment is more powerful, and we can see things in better quality."

One particularly striking detail of the space is a skylight near the entrance.

"It's intended to put a spotlight on Engineering and to have that light spread out into the Davies hallway and light up the whole area," Wilczynski said. "That light acts as a beacon, and if you're walking by, it draws your eyes to the space itself."

Indeed, the visibility of the lab space means more people will see the work that goes on at SEAS. As Salovey noted, this will only help to boost interest in engineering.

"Students will come down here, and they may take a course as a sampler or they'll hear about the equipment and want to look at it," he said. "Or they'll see it and get intrigued as they wonder what's happening here. Then they get exposed to great teaching — suddenly, they're engineers." 

Yale

EDUCATION



WE'RE NOT DONE!

Visit us on the web at
seas.yale.edu

to keep up with news from Yale Engineering all year long

 facebook.com/yaleseas

 twitter.com/yaleseas



ANJELICA GONZALEZ

Donna L. Dubinsky Associate Professor of Biomedical Engineering

Anjelica Gonzalez focuses on the development of biomaterials for use as investigational tools, particularly for the investigation of immunological responses to inflammatory signals from endogenous and exogenous sources. With a multi-disciplinary approach, the Gonzalez lab combines organic chemistry, molecular biology, mathematics, computational modeling and image analysis in work with significance to diseases and disorders ranging from arthritis to cutaneous T-cell lymphoma.

NEWS

APP MERGES SNAPCHAT, CHARITY



Two recent Yale graduates have designed an app that aims to increase charitable giving among young people.

[MORE »](#)

