Embracing the Complexity of Systems

SEAS researchers are bringing an engineering approach to system biology efforts

A Department for the 21st Century

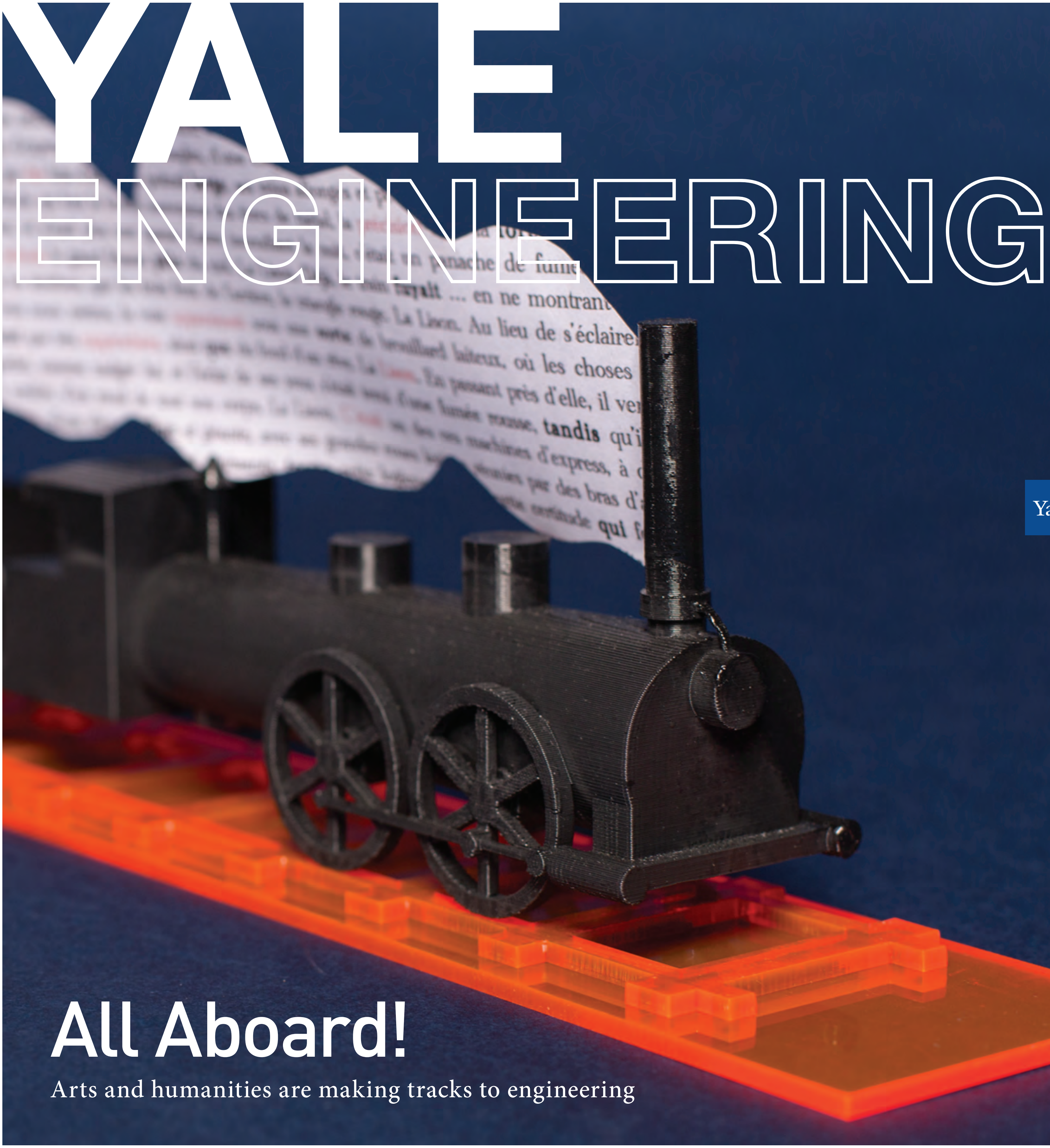
By joining forces with SEAS, Computer Science at Yale has a wider reach than ever

A Hard Look at Soft Matter

Exploring the promises of these mysterious materials

2015-2016

YALE ENGINEERING



All Aboard!

Arts and humanities are making tracks to engineering

The Publication of Yale's School of Engineering & Applied Science

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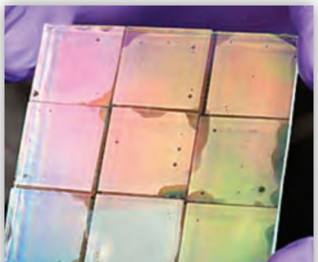

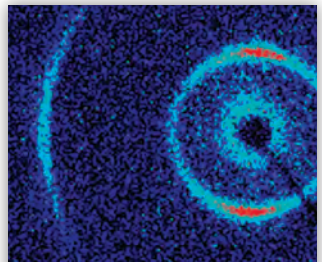

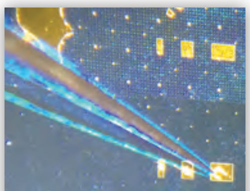

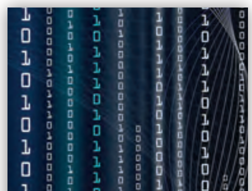

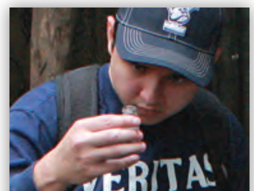

Front & Back Covers:
3D-printed train based entirely on descriptions from Emile Zola's 1890 novel "La Bête humaine" ("The Beast Within").

EDUCATION   SUSTAINABILITY   INTERDISCIPLINARY   MEDICAL INNOVATION   TECHNOLOGY

YALE ENGINEERING 2015-2016

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Message From the Dean

E L A Y ... Is this a new way to “see” YALE? Not at all! I’m pretty sure the renowned Benjamin Silliman, Jr. saw Yale in that way. And I’m definitely sure that all the engineering students in the Class of 2016 see Yale in that way. Is **E**ngineering and the **L**iberal **A**rts for **Y**ou? Then you are also seeing Yale as the perfect choice, a view shared by more than 10,000 students who have studied engineering since it was first offered as a major.

Do you see math as one of the many languages you wish you were fluent in? Are you as eager to learn the laws of physics and thermodynamics as the laws that govern ancient and modern societies? Does the art of design fascinate you as much as the design of art? Then you are seeing Yale for all that it can offer you.

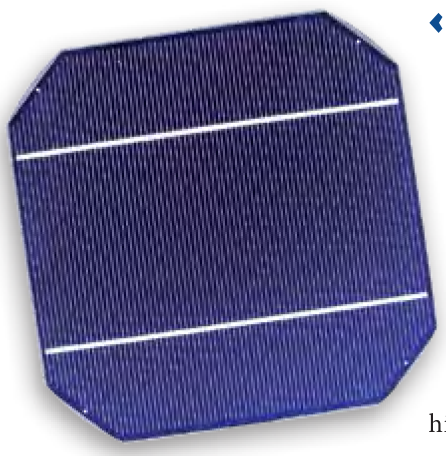
And this vision does not just apply to students. At last year's new faculty orientation, I sat at a lunch table with Professor Morgane Cadieu, a star recruit to Yale’s French Department. Before she could feast her eyes on dessert, Professor Cadieu was cooking up a new way to teach French literature in collaboration with our Center for Engineering Innovation & Design. You can learn more about her train of thought in our feature article on “Engineering Connecting to the Arts.”

There’s no doubt that all Yalies have great vision. But Yale engineers are known for seeing things in truly new ways. I hope you enjoy this year’s edition of **ELAY Engineering**!

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



2014: September

Solar Cells That Can Take The Heat

Conventional solar panels become significantly less efficient as they get hotter. But associate professor of electrical engineering Minjoo Larry Lee developed solar cells that operate efficiently at temperatures above 750 °F. Funded with a $2.5 million grant from the U.S. Department of Energy's Advanced Research Projects Agency for Energy, Lee developed photovoltaic panels that integrate with a solar thermal collector that absorbs the unused portion of the light spectrum as heat. The resulting heat energy transfers to high-temperature fluids that can power a steam turbine or be stored for later use.

Yale

INTERDISCIPLINARY

2014: October

Hacking For Health

A new instrument for noninvasive stent removal was the winning innovation of the university's first Hacking Health @ Yale. The event took place over three days at the Center for Engineering Innovation & Design, School of Medicine, and the School of Management. The event, directed by Jean Zheng, engineering director of the Yale Center for Biomedical and Interventional Technology, challenged 70 participants to find solutions to major healthcare problems. Participants formed teams and created prototypes of inventions in the CEID, using the many tools and instruments there.

2014: November

Map The Noise

Every cell reacts uniquely to the body's chemical signals, even those from the same tissue. A diverse response is called "noise." Andre Levchenko, the John C. Malone Professor of Biomedical Engineering and Director of the Yale Systems Biology Institute, led a team of scientists in developing a way to map this noise. Previous experiments in this field looked at the average behavior of up to millions of cells at a time, while the new method needed only three targets. It's a development that could be used to tailor drug delivery and even advance research in semiconductor chip design.

2014: December

The Power Of Tiny Drops

You know how a cup of water can be filled slightly above the brim without spilling? It's a phenomenon known as surface tension, and it could be the key to controlling the properties of composite materials. Eric Dufresne, associate professor of mechanical engineering and materials science, found that you can significantly modify certain materials by embedding them with liquid droplets. The sizes of the drops play a major role. For instance, tiny liquid droplets resist deformation so strongly that embedding many of them in silicone resulted in a 30 percent stiffer material.

2015: January

Lending A Hand

The Yale chapter of Engineers Without Borders (EWB) visited Rohvitangitaa, a village in Cameroon, where they began work on building a new water system. Rohvitangitaa residents approached EWB for help shortly after the same group had built a gravity-fed water distribution system in the nearby village of Kikoo. In both cases, EWB designed a new system and raised the funds to pay for the materials, and the village residents helped build it. The EWB group also has a public health team, which visits schools and goes door-to-door to teach residents about bacteria and other drinking hazards.

2015: February

Atomic Changes

Charles Ahn, the William K. Lanman, Jr. Professor of Mechanical Engineering & Materials Science, Applied Physics, and Physics, led a team of scientists in artificially altering a material's atomic properties. They did so by substantially modifying electrons' orbital properties, which are used to predict the behavior of electrons. Using this technique, the researchers demonstrated in the journal *Physical Review Letters* that they could make nickel look and behave like copper. The research has numerous potential applications. For instance, certain materials could easily be switched from magnetic to nonmagnetic and back again.

Continued

Year in Review

2015: March

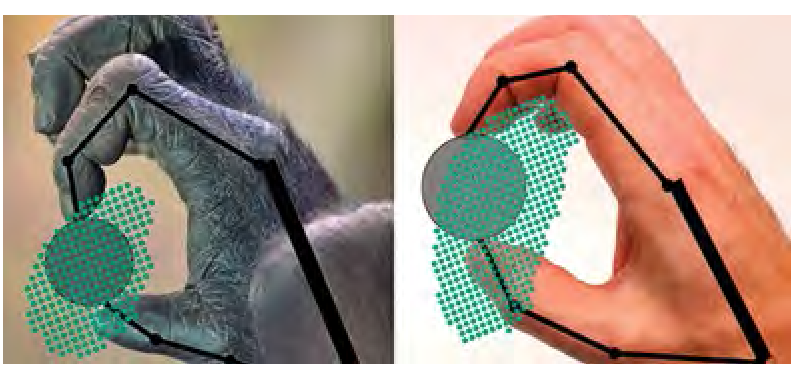
To Infinity And Beyond!

The Yale Undergraduate Aerospace Association (YUAA) hosted its third annual Aeronautica event, where it showed off its many accomplishments. The event, which was attended by President Peter Salovey, demonstrated how far the student club has progressed in its five years. The club's very first project was building and launching a weather balloon that photographed the New Haven skyline. Common projects now include rockets, radio telescopes, rovers, and aircrafts. A few weeks after the Aeronautica event, members of YUAA's Rocket Competition Team conducted three successful launches at the national Battle of the Rockets Competition.

2015: April

A Gripping Study

It turns out that even the oldest known human ancestors may have had precision grip capabilities comparable to modern humans. We know this thanks to Yale robotics engineers Thomas Feix and Aaron Dollar, the John J. Lee Associate Professor of Mechanical Engineering & Materials Science, who led a research team in creating a kinematic model of the thumb and index finger of the skeletons of living primates and the fossil remains of human ancestors. It's the first such model of digit movement during precision grasping and manipulation in a broad sample of humans, non-human primates, and fossil hominins.



2015: May

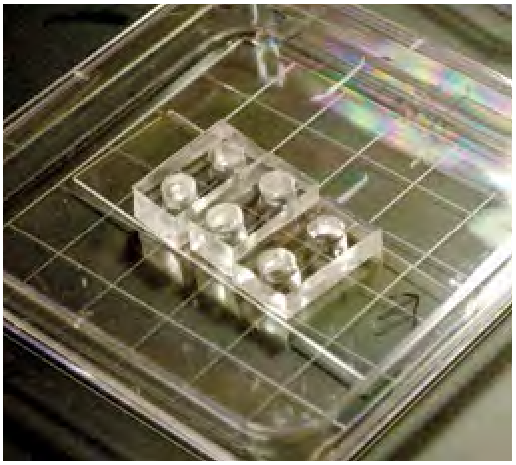
Dual Degrees

At Yale's 314th Commencement Ceremony, honorary degrees in Engineering & Technology were given to two of the world's leading innovators, Elon Musk and Dean Kamen. Yale President Peter Salovey praised Musk, CEO of SpaceX and the product architect of Tesla Motors, for "imagining the impossible, and making it happen." Of Kamen — one of America's most prominent inventors and president of the research company DEKA - Salovey said he was "developing tomorrow's science and technology leaders" through FIRST, his science education organization. Both Musk and Kamen have been featured speakers for SEAS' Victor M. Tyler Distinguished Lecturer in Engineering.

2015: June

Help Floats

Stranded disaster victims could soon be turning to luminescent balloons for help, thanks to a student invention made at the Center for Engineering Innovation & Design. Students Kamya Jagadish, Jane Smyth, and Edward Wang designed the Illumiloon for use when power and the internet are out. Stranded victims inflate a balloon and place LED bands on it, each band a different color to represent the kind of help needed — first-aid, food, and more. Floating high in the air, the device is easy for emergency workers to spot. Illumiloon won the Design for America "Inspiring Future" Award.



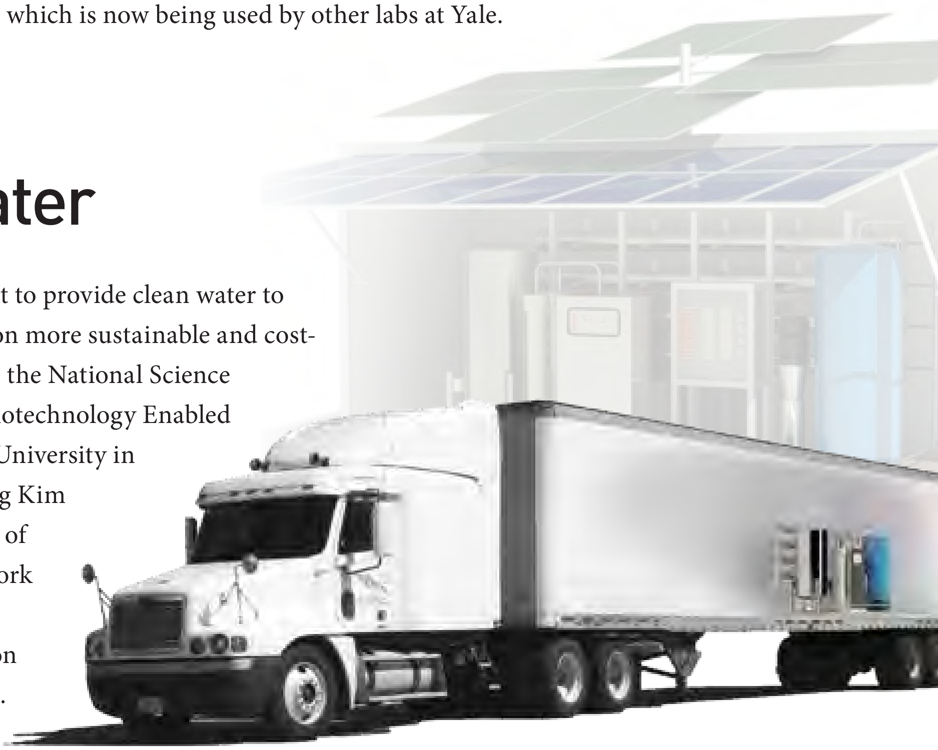
2015: July

Cell Study Made Easier

Studying cells in suspension is rarely easy, but that could change with a device created in the laboratory of Kathryn Miller-Jensen, assistant professor of biomedical engineering and molecular, cellular & developmental biology. The device conveniently tracks changes in cells floating freely in media over a period of time. Other devices serve a similar purpose, but require tubing, external pumps, and aren't particularly easy to operate. Miller-Jensen's lab has filed a provisional patent on the device, which is now being used by other labs at Yale.

2015: August

Providing Clean Water



Yale researchers became part of an ambitious effort to provide clean water to millions of people and make U.S. energy production more sustainable and cost-effective. Funded with an $18.5 million grant from the National Science Foundation, the effort will be based out of the Nanotechnology Enabled Water Treatment Systems center (NEWT) at Rice University in Houston. Professors Menachem Elimelech, Jaehong Kim and Julie Zimmerman — all from the Department of Chemical & Environmental Engineering — will work with researchers from other universities, as well as government and industry organizations, to focus on compact, mobile, off-grid water-treatment systems.

Bringing Materials Science to the Surface

Judy Cha creates novel materials for future energy applications

While completing her doctoral thesis at Cornell, Judy Cha developed expertise in a variety of analytical scanning transmission electron microscopy techniques that she used to characterize the properties and structures of innovative new materials. “But because I didn’t have control of the samples, I felt limited — I was only approached for the special measurements after somebody else had made the materials,” she says. “So when looking toward the future, I specifically sought out avenues for making my own materials.”

Now an assistant professor of mechanical engineering & materials science and residential faculty at the Energy Sciences Institute at Yale’s West Campus, Cha has quickly gained recognition for her work on the synthesis and transport measurements of two-dimensional layered nanochalcogenides. Unlike graphene, two-dimensional chalcogenides — including sulfides, selenides, tellurides, and others — are not single-atom thick but instead form layered atomic structures; molybdenum disulphide, for instance, is formed by stacking single layers of molybdenum atoms sandwiched above and below by sulfur atoms.

While bulk chalcogenides already have diverse applications as pigments, catalysts, and even lubricants, Cha uses experimental nanofabrication techniques to create novel electronic, photonic, and plasmonic properties, with an eye toward energy applications. Because these properties

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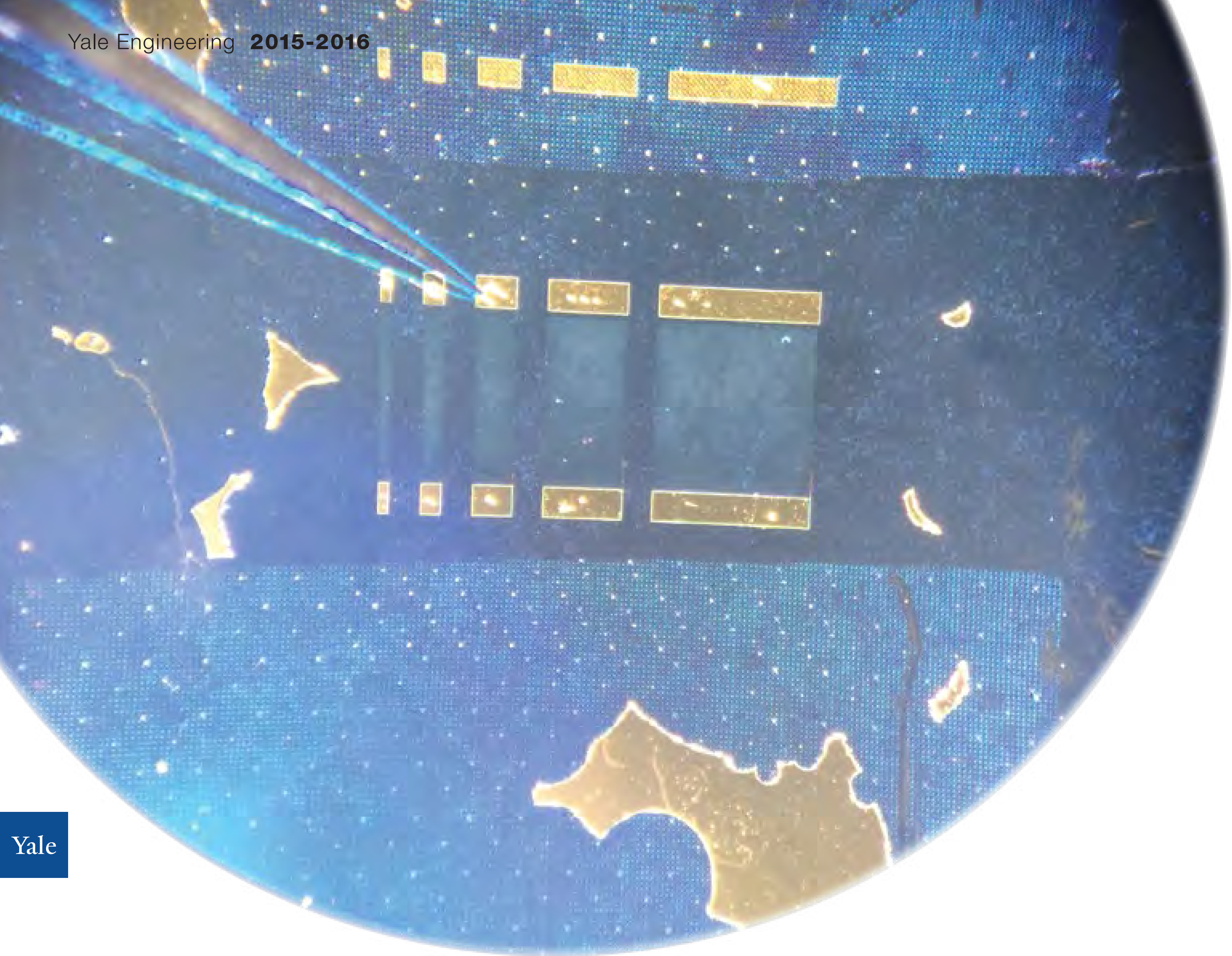


often exist only when the layers of a material are uniformly aligned, different behaviors are found in precisely layered nano configurations from what are found in bulk materials. For example, a bulk sample of molybdenum-disulfide is an indirect band gap semiconductor, while a single layer can instead be a direct band gap semiconductor, which is a critical property for opto-electronics.

While Cha's fabrication innovations are all about proper arrangement of atoms, they are also designed with an inclination toward high-yield, large-scale production. Many researchers still make two-dimensional chalcogenides "by hand," using a piece of scotch tape to peel single-layer flakes off a bulk sample. As might be expected, the process is painstakingly inefficient. In contrast, Cha uses a chemical vapor transport method, first depositing a patterned thin film of, say, molybdenum or tungsten atop a silicon substrate, then sulfurizing the materials by evaporating sulfur inside a growth furnace at a temperature between 700 and 800 °C.

"It's a more efficient production method, but it's also more flexible," says Cha. "The most basic active device is a p-type semiconductor and n-type semiconductor that have been joined together — a junction that is, in essence, a diode. With a chemical vapor transport fabrication method, I can join an n-type chalcogenide material like molybdenum disulfide and p-type chalcogenide material like tungsten disulfide in the furnace by sulfurizing a molybdenum/tungsten metal stack to create an active n-p junction. It's a one-step synthesis."

Cha's fabrication method is additionally flexible in how it aligns the surface directionality of two-dimensional chalcogenides. Although conventional chemical synthesis has focused on growing horizontally stacked two-dimensional molecular layers — a method of growth that naturally exposes the material's basal plane as the surface — Cha's method makes it equally possible for the two-dimensional materials to grow vertically from the substrate, thereby exposing the edge-sites of each layer. Each direction results in its own unique material properties. For instance, the indirect-to-direct band gap transition and large on/off ratio of horizontally grown two-dimensional molybdenum disulphide is promising for optoelectronics, while the exposed dangling bonds on the edge-sites of vertically grown two-dimensional molybdenum disulphide have an enhanced chemical reactivity useful for catalytic-reaction-based electrochemical applications. Despite these notable differences in properties, Cha has shown that their fabrication methods for both vertical and horizontal directionality are nearly identical, but for one key difference: when the metal seed layer that the materials are fabricated upon is relatively thick, the material is more likely to grow vertically; with thinner layers, the horizontal growth predominates. "With this method," says Cha, "we've demonstrated that creating the materials consistently is possible. Now we're on to optimizing the electrical properties."

Materials construction is also at the heart of Cha's work with topological insulators, a unique type of chalcogenide that became popular just as Cha graduated from graduate school. "When I first interviewed for my postdoc position at Stanford, I had a plan for exactly what I wanted to do next, which was to make semiconducting nanomaterials for memory devices. But when I began working there six months later, everyone around me was talking about topological insulators and how they would change our understanding of solid-state physics," she says. "I knew I was witnessing the birth of a new field, and I wanted to be a part of it."

Although materials are typically categorized as insulators, conductors, or semiconductors, topological insulators (TIs) intrigue scientists because their behavior bridges multiple categories: while the interior bulk of TIs behaves like an insulator, the material surface conducts electricity. Moreover, the conducting surface electrons are very robust against being scattered off their path and can therefore transmit electrical

Continued →

"Everyone around me was talking about topological insulators and how they would change our understanding of solid-state physics. I knew I was witnessing the birth of a new field, and I wanted to be a part of it."

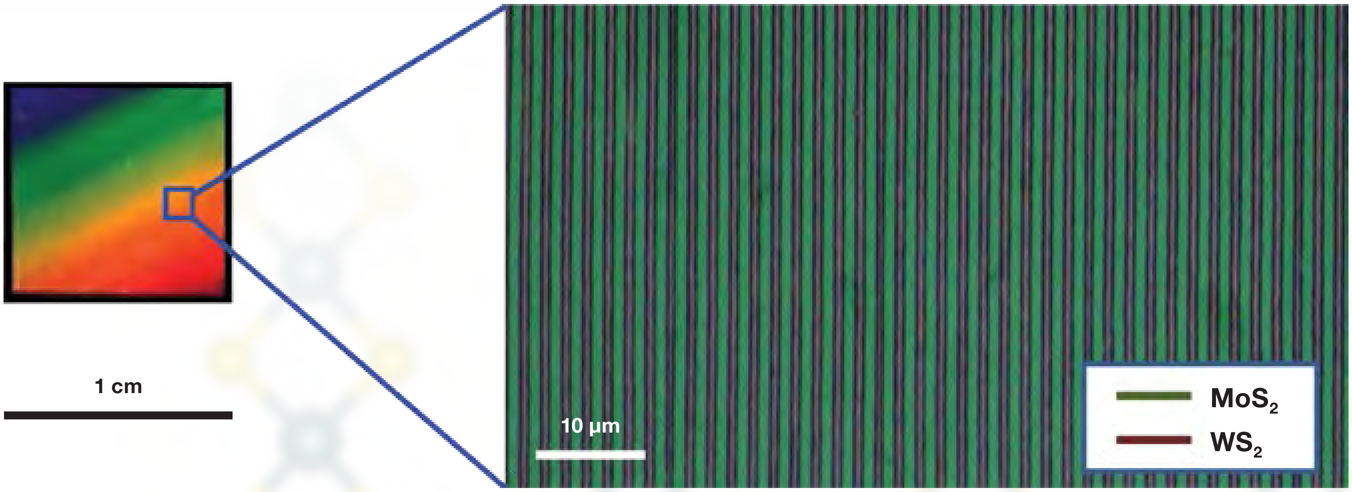
› Judy Cha

currents even in situations that would prevent transmissions in other materials. As a result, Cha notes that TIs can be used as information carriers that do not generate wasted heat. “One example application of TIs might be using them to replace all of our current copper interconnects, which would greatly reduce society’s energy consumption,” says Cha. “This could be a vital change — though it’s a goal that we’re very far from realizing.”

However, of equal interest to Cha is the way in which TIs could be used to create cutting-edge devices known as “spintronics” — devices that represent the ones and zeroes of binary code using the spin state of electrons. Because the surface electrons of TIs are “spin polarized” — meaning they all have the same spin, either up or down, when moving in the same direction — the electron spin can be combined with the more commonly utilized electron charge binary coding to simultaneously create four operation states instead of just two. In this way, TIs are ideal building blocks for the creation of a quantum computer; it was these properties that ignited Cha’s imagination when she first heard about TIs and that continues to drive her experiments with such materials today.

Cha’s recent TI research has focused on tin telluride, a topological crystalline insulator discovered even more recently than most other TIs. Like that first generation of TIs, tin telluride exhibits conducting surface electrons but the material is notable for additional unique properties. For example, because of its cubic crystalline structure, tin telluride can be doped or alloyed to exhibit a wide range of electronic properties — such as magnetism, superconductivity, and ferromagnetism — without destroying the characteristic TI properties.

But those properties only exist if the material is made right. Like her work with other chalcogenides, Cha’s TI research has centered on developing novel fabrication procedures, in this case to enhance the surface properties while minimizing undesired characteristics. Most recently she’s employed a vapor-solid growth mechanism similar to the sulfurization method described earlier. However, in addition to other concerns, multiple surface states exist on the surfaces of tin telluride, with the band structure of surface states dependent on the mirror symmetry of a particular surface. Some surface states are therefore preferable to others.



Left: *Photography image of a MoS_2/WS_2 hetero-structure film grown on a SiO_2/Si substrate.* Right: *Zoomed-in optical microscopy images of MoS_2/WS_2.*

Cha's solution is to create tin telluride samples shaped into nanoplates that span tens of micrometers across and are only a few hundred nanometers thick. "Recognizing that the most interesting aspects of TIs are in the surface effects," she says, "the goal is to cut away from the design as much as possible of what isn't the surface, leaving nanoplates that are as thin as possible and with the largest surface area possible." But according to Cha, fabrication, while challenging, is merely opening the door to the real work of getting TIs out of the lab and into public applications.

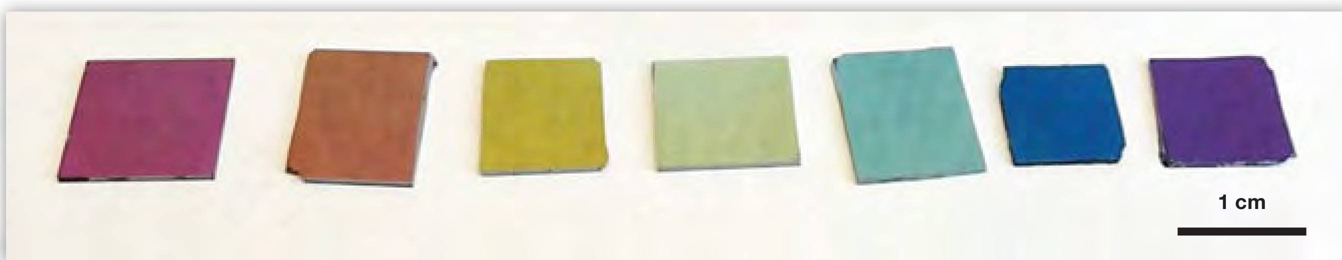
Supported by grants from the National Science Foundation and the Department of Energy, Cha's next step is to make the TI nanoplates into superconductors. In particular, this step, accomplished by doping the nanoplates with indium, could also reveal further instances of a theoretical quasiparticle known as the Majorana fermion.

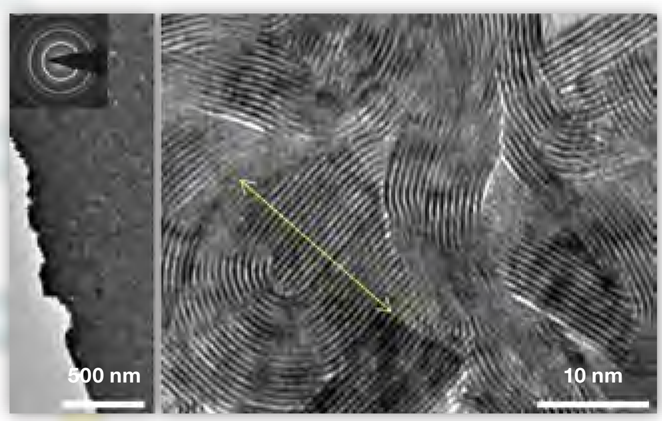
"Condensed matter physics is all about the collective dance of electrons. When the electrons are all collectively dancing about, they behave completely different from if they were all just doing their own things, behaving as what people call quasiparticles," she says. "What makes the Majorana fermion unique is that it's simultaneously its own particle and antiparticle."

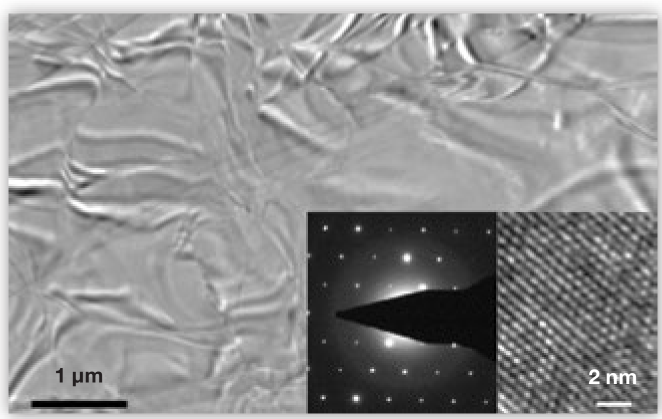
According to quantum theory, particles and antiparticles annihilate each other. The Majorana particle, however, is stable and represents, in quantum computing terms, a state that is both one and zero at the same time. Like spin polarization, this property is heralded as another potential key to building a quantum computer, and the particle's existence could also theoretically solve the Higgs-Boson mass problem.

"We're now realizing that perhaps we could look for the Majorana signature in superconducting TIs," says Cha. "More importantly, detecting these particles would also be the first step towards using and manipulating these particles as a neutral 'third charge.' It's just one more way that I see TIs at the core of the next computer revolution — and we're just at the beginning of it right now."

Top: *Photography of as-grown MoS_2 on SiO_2/Si substrates grown with Mo seed layer of 20, 15, 10, 7, 5, 2, and 0.3 nm, respectively (from left to right).* Bottom: *TEM characterizations of MoS_2 grown with 10 nm Mo (left) and 0.3 nm Mo (right).*







Embracing the Complexity of Systems

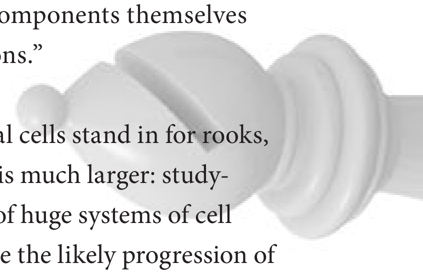
SEAS researchers are bringing an engineering approach to systems biology efforts, with major implications for the study and treatment of human disease

If you've never played chess, the rules are simple to learn. There are two players, each with six types of pieces, and each piece moves in a specific way. Learn the ways each piece can move and you can immediately sit down to play. There is no element of random chance; what happens in a game depends entirely on how the players make their pieces interact. The basic rules are among the simplest and easiest to learn of any strategy game in history.

Yet predicting how a chess game will progress is one of the most challenging modeling problems in the world. Simply by making the first move, the white player sets the game down a certain path; with the following move, the black player veers off down another. The number of possible games of chess has been estimated in excess of 10,000,000. And in all these games, not a single move is made in isolation: *every* move is a result of the input — the feedback — from the previous move, which was also a result of every move that came before.

This system of feedback loops is what makes chess so difficult to model and predict, but also makes an excellent analogy for a major area of research at Yale: systems biology.

"This is, in some sense, the essence of a systems approach," says Andre Levchenko, John C. Malone Professor of Biomedical Engineering and Director of the Systems Biology Institute at Yale's West Campus. "We are very, very interested in interactions, and put interactions at the center of the analysis — not the components themselves necessarily, but just the interactions."



In Levchenko's Institute, individual cells stand in for rooks, knights and pawns, and the game is much larger: studying (and predicting) the behavior of huge systems of cell networks, whether it's to determine the likely progression of a cancerous tumor or study the development of diabetes.

"Cells are exquisitely sensitive to a variety of different cues, chemical cues and mechanical ones," says Levchenko. "In fact that's the key to their survival, or to their proper function. If you think about what we call disease, that's the inability of cells to mount the response to cues that would be adequate. For example, instead of dying or staying put, cells may start dividing; that's in response to their own state, but also to certain cues they see in the environment. It's misinterpretation of these cues that may lead to cancer, for example."

In the past, cell studies have been limited to looking at individual pieces of the puzzle: a small group of cells at one time responding

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to one input, or even a single cell responding to a single input. In a chess game, it would be the equivalent of examining how the white player might move his rook if the black player puts it in jeopardy. This remains a common approach in drug research: cells are exposed to different doses of a drug and the exposure is held constant for a period of time. Researchers study how the cells respond to the various dosages, and hope that the results will be instructive in deciding which candidate drugs to promote for further studies and which to abandon as they are unlikely to be helpful.

But this is only looking at one piece of the system. In the chess game, the white player might not move the rook at all, but sacrifice it to save the queen that is in jeopardy from the same prior move. If you were only looking at the rook, you wouldn't predict that outcome. Similarly, in a living human, many more factors may contribute to how a given drug would affect cells, and actual results could be very different from what you would see with the narrow focus on dosage. Instead of looking at just one small piece of the larger picture, Levchenko and his Institute go several steps further.

"What we're trying to do is circumvent some of those limitations of current research," he says. "We're trying to be mindful that reality can be complex."

Here Levchenko, who comes from an engineering background, draws a parallel.

"To understand a system that someone else, or even we, have designed, that's reverse engineering," he says. "When you grow up in an engineering community, you develop appreciation for the complexity of systems, because when you try to build systems — to engineer them — you do it by design, but also by tweaks and tinkering and trying to figure out what works and doesn't work.

"Biology is very much engineering in that sense — an engineering science, because that's what we do all the time," says Levchenko.

It's no surprise, then, that among the many Yale researchers collaborating with Levchenko's Institute are several faculty members from SEAS, including Kathryn Miller-Jensen, Rong Fan, and recent hire Michael Murrell.

Fan's research will be familiar to readers of *Yale Engineering* (see "The Translator," 2013-2014 issue). The associate professor of biomedical engineering was a chemist by training, but insists he was always an engineer at heart.

"My early training was more toward technology development, and my role in systems biology research was to develop better tools," says Fan.

Among Fan's primary interests is how cells communicate. Cells can respond to their environment based on several different cues, including mechanical forces (see "The (Mechanical) Force is with Him," page 17, to read about Murrell's work in this area) and chemical signals. Given his background in chemistry, Fan has focused on cells' chemical signaling.

"Cells talk to each other, but it's unfortunate they don't understand English," laughs Fan. "They talk, but it's in a different language — they secrete proteins and bring those proteins throughout the cells and to the surface of the neighboring cells.

"The proteins secreted by one cell can mediate another cell," says Fan. "It's essentially a conversation. I think once we can measure a large protein panel, you'll be able to get an understanding of what they talk about. Then you know what they are going to do."

But the need for these kinds of large-scale measurements brings back the chess analogy: looking at just a piece of the board doesn't tell you how the game is going to progress.

"If you look at one or two proteins, that will not give you a systems-level view of a whole biological mechanism," says Fan. "In my lab, we develop a kind of microchip technology that we can use to interrogate individual cells, but also very large protein panels."

Fan has shared the device he developed for this purpose with Miller-Jensen, associate professor of biomedical engineering and molecular, cellular, and developmental biology, who studies the way that

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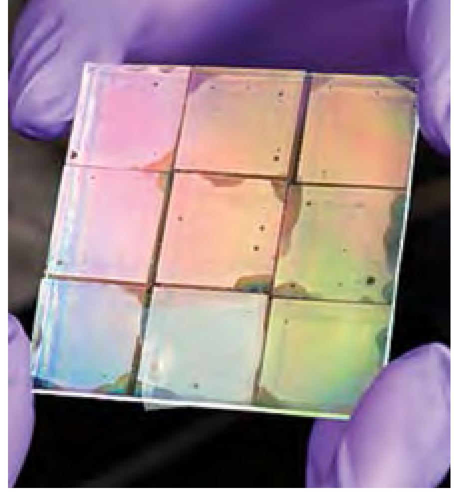
In addition to numerous SEAS faculty members, the Systems Biology Institute draws upon renowned geneticists, biologists, and physicists from across the university.



Anatomical features of highly oriented extracellular matrix in various tissues.

cells communicate to mount an immune response in the face of viral infections. Viruses can hijack cell signaling for their own benefit, allowing them to evade immune response and replicate. Among many avenues of exploration, Miller-Jensen's group uses single-cell analysis to reverse engineer the signals sent during an immune response — work for which Miller-Jensen won an NSF CAREER Award earlier this year.

Feedback from Miller-Jensen's group, in turn, is used to further develop Fan's device.

"It's a mutual scientific exchange," says Fan. "It's a way of developing a tool by testing the device on cells. Sometimes we'll see something weird and then analyze the data in depth, and realize we need to take out a protein or replace it, improving the device. So that's a mutually beneficial process, I think."

This is a critical element of modeling efforts in systems biology, as Levchenko sees it.

"The most interesting times are the times where we see that a model doesn't work, doesn't give us a correct prediction," he says. "That's an opportunity for us to learn how these systems work, because there's clearly something we don't yet understand — something we haven't taken into account. Frequently it's just the telltale sign that we can find something new and different, and that's a great thing for us."

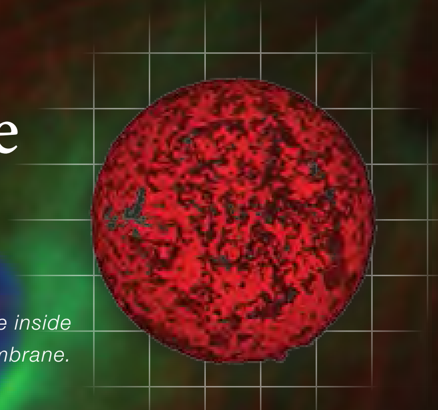
This kind of research calls for a wide range of expertise. In addition to the aforementioned SEAS researchers, key faculty at the Institute include Farren Isaacs, assistant professor of molecular, cellular, and developmental biology; Gunter Wagner, the Alison Richard Professor of Ecology and Evolutionary Biology; Murat Acar, assistant professor of molecular, cellular, and developmental biology and of physics; and Jesse Rinehart, assistant professor of cellular and molecular physiology.

Together, the researchers' efforts have wide-ranging translational applications. In diabetes, for example, multiple types of cells are involved, including pancreas and liver cells. Many studies focus solely on the pancreas, guaranteeing from the start that they will never get a full picture of the system. Similarly, cell signaling is critical in the development of cancer; when signaling is interrupted or altered, cells can begin multiplying wildly, leading to the development of tumors. This has become an important focus of the Institute, particularly for aggressive types of cancer cells, and complements the cutting-edge cancer initiatives currently led by Joseph Schlessinger at the Cancer Biology Institute at Yale's West Campus.

Given the current state of systems biology, it's natural that SEAS research would relate to work being done at the Systems Biology Institute, and Levchenko sees it as an expected evolution.

"For a very long time, biology was just cataloging parts science," says Levchenko. "Cells are very complicated; let's take this protein, categorize this protein, take another protein, categorize that protein,

The (Mechanical) Force is with Him



Structural protein actin, placed on the inside of a lipid vesicle, which mimics the membrane.

One of the newest additions to SEAS is also a member of the Yale Systems Biology Institute. Michael Murrell joined SEAS as an assistant professor of biomedical engineering this year, and his interests in the mechanical properties of cells are a natural fit with the goals of the new Institute.

"The primary focus of my work is understanding how mechanical forces are produced by cells," says Murrell. "From cell division to cell migration, cells have to produce forces, but the mechanisms for how they are generated and transmitted are not clear."

As with the Institute, Murrell's lab uses a multi-pronged approach to research. One approach involves creating a synthetic model of a cell and trying to reproduce force generation; the other attempts to study and measure the forces real cells produce.

"With the first approach, we take select protein and lipid molecules, and put them together in a way that's designed to resemble a living cell but has fewer components and is easily manipulated," Murrell explains. "The goal is to get it to resemble the physical behaviors of a living cell such as migration or division."

This is very much an engineering approach: build a system with a known set of parts, capable of being both controlled and measured — things that couldn't be accomplished as easily in a living cell.

As a complement to synthetic modeling of cell behaviors, Murrell's lab also works directly with living cells to measure the forces they produce and exert on their surroundings. With techniques in place to observe and measure cell behavior by analyzing extremely high-resolution microscopy images taken over time, they can introduce perturbations and see how the cells react. That information, in turn, shapes the approach they take with their synthetic cell models, so that the data gathered from each approach helps improve the results of the other.

"We want to understand what variables contribute to force generation in living cells, and then use that to inform our synthetic model, to try to re-create those forces from the bottom-up," explains Murrell. "With these two complementary approaches, we can gain a more complete perspective of force production and transmission in cells."

And in keeping with the goals of the Institute, Murrell's focus isn't limited to the behavior of single cells: he's also interested in larger cell systems.

"I'm interested in not only how mechanical forces are produced at the single-cell level, but actually how that translates to multi-cellular assemblies," says Murrell. "Essentially, we want to know how the ability to produce force changes when cells are in a group — when they contact and communicate with each other. "

That gets at the heart of the Systems Biology Institute: complex interactions.

"We've done a lot of work now to understand how cells can produce force, and we are still learning more, but nevertheless, the next question will always be how cells coordinate their physical behaviors in order to accomplish the tasks and needs of tissue," says Murrell. "I think that's the leading edge of the science."

and so on. That was an important, necessary step in the development of our new approaches to biology.

"Systems biology now is a step beyond that," he says. "It's thinking about how parts interact with each other — very much an engineering approach, because in engineering — yes parts are important — but how do we build something that performs as we want? How do we understand something that's been built before?"

"It's exceptionally easy for a systems biologist to talk to an engineer," says Levchenko, "because we share the appreciation for the importance of complexity for proper function. It's a synergy of philosophy; it's a synergy of techniques."

Yale

EDUCATION

A Computer Science Department for the 21st Century

By joining forces with SEAS, hiring new faculty, and expanding its curriculum, Computer Science at Yale has a wider reach than ever

Once, computer science was something of a niche subject — a line of study that didn't make much sense to pursue unless computers were going to be your line of work. Now it figures into just about every field.

"It's quite common nowadays for students to be deeply interested in technology — not for technology's sake, but in service to other things — such as media, culture, energy, politics, and commerce," said Prof. Joan Feigenbaum, the Grace Murray Hopper Professor and Chair of the Department of Computer Science. Accommodating that broader interest, she said, requires broadening the department's curriculum.

Yale made big steps toward that goal earlier this year with some major developments in computer science. Yale officials announced in March that the department would expand its faculty by more than 25 percent, growing from 20 to 26 professors. At the same time, it became part of the School of Engineering & Applied Science. Two donations, totaling $20 million, made the expansion possible.

T. Kyle Vanderlick, Dean of SEAS, said the developments were necessary in making sure that the university's computer science department is competitive and designed for the 21st century.

"A strong connection between Computer Science and Engineering is needed for both disciplines to stay vibrant," Vanderlick said. "Incorporating Computer Science into SEAS will foster our growth and progress, and it means that Yale will continue to compete for the very best students and faculty."

Enhancing computer science has been an ongoing discussion since President Peter Salovey's inauguration in 2013. In March, he said that computer science skills "are the means by which we move ideas forward in today's world." With the expansion, he said, the university was "acknowledging the vital importance of those skills."

Until this year, Computer Science was its own freestanding department. That's not uncommon, but universities are increasingly incorporating computer science into their engineering schools. Vanderlick said that makes sense. Engineering is essentially about solving problems, and the same can be said about computer science.

"At Yale especially, there's long been a close connection between computer science and SEAS," she said, adding that the Computer Science Department has six professors that were already affiliated with numerous SEAS departments.

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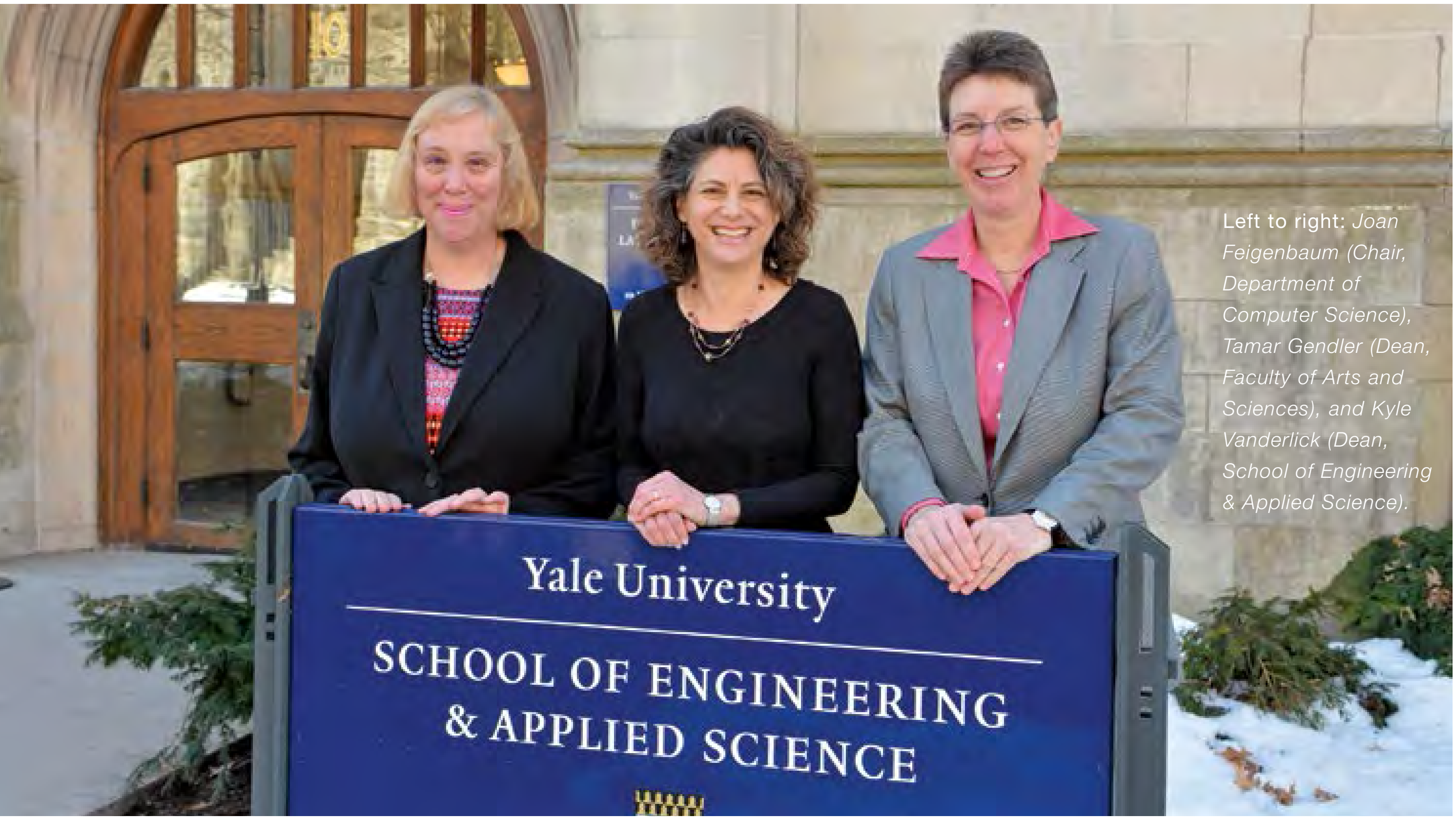

Left to right: *Joan Feigenbaum (Chair, Department of Computer Science), Tamar Gendler (Dean, Faculty of Arts and Sciences), and Kyle Vanderlick (Dean, School of Engineering & Applied Science).*

Separating engineering and computer science was common back when software and hardware were considered two separate components of computing systems. "But that's not how we think about computers anymore," Vanderlick said. As computers have become much more sophisticated, hardware and software are so integrated as to be all but inseparable. Developing software requires knowledge of the hardware, and vice versa.

Tamar Gendler said computer science became a top priority for her ever since she was appointed the University's new Dean of the Faculty of Arts and Sciences last July. She calls the expansion a "game-changing" step toward building a "world-class Department of Computer Science."

"I want to ensure that Yale has a computer science department of the caliber that a great university deserves," Gendler said.

Computer Science

Not Just for Computer Scientists

Jakub Szefer, assistant professor of electrical engineering and computer science, said he's long benefitted from the close relationship between the two entities. "The faculty members and I collaborate frequently, and I advise computer science students on senior projects," he said. "So I think the boundary has always been very fluid."

Szefer said students will benefit in a number of ways now that Computer Science is officially part of SEAS. "Rather than Engineering students being on one side and the Computer Science students doing their own thing, it will be easier for everyone to mingle at different events," he said, adding that it could open doors for them academically. "Now maybe we can attract some of them to, say, electrical engineering or robotics."

Feigenbaum agrees that the nature of computer scientists' work makes the move seamless. "When I asked (associate professor of computer science) Daniel Abadi about moving to SEAS, he said, 'Sure, I consider myself an engineer.'"

But the administrative change also brings some very tangible benefits, she said. Students will have a broader choice of courses and of advisors for research projects. The university will conduct searches for the new faculty positions in the Department of Computer Science over the next few years, bringing

Continued →

Cloud Computing and Distributed Systems:

Mahesh Balakrishnan Explains the Difference

Cloud computing has become such a part of everyday life that we often take its intricacy for granted.

"These systems tend to be very complex because these services have to scale to millions of users, and each of the users expect the services to be highly responsive — always online, not to lose their data and so on," said Mahesh Balakrishnan, one of the Computer Science Department's two new faculty hires. He began teaching courses in September.

Building a system that actually does that, he said, is something of an art form. "You need a lot of intuition and a lot of skill to get it right."

In his new role at Yale, Balakrishnan hopes to reduce the role of intuition in the field in favor of formal guidelines and protocols. "I want to make building a distributed system less of an art form and more of an engineering discipline," said Balakrishnan. He previously worked at Microsoft Research and VMware Research, where his work focused on distributed systems.

One reason this area of computing is so guided by intuition, he said, is because it's so new that there hasn't been time to figure out how to teach it. "To some extent, there are other areas of computer science where we have a better understanding of how to teach it," he said. "In systems, I don't think we're there yet. What are the right principles and abstractions?"

Daniel Abadi, associate professor of computer science, said the addition of Balakrishnan will strengthen the practical systems research at Yale. "He is renowned in particular for his work on distributed systems — for making them easier to build with elegant, performant, data-centric abstractions."

So what exactly are distributed systems, and how are they different from cloud computing?

Using what he calls an "extremely broad definition," Balakrishnan said a distributed system is any collection of computers that coordinate in some fashion to achieve a larger goal — providing more resources and greater speed. For instance, he said, it's something that includes the use of your laptop browser to access a webpage — your laptop and the remote servers constructing the webpage constitute a distributed system. The same can be said for when you check your mail on your smartphone. In that case, the phone and the email servers it contacts constitute a distributed system.

Cloud computing is a particular kind of distributed system. "If we drew circles on the whiteboard, the distributed system circle would completely enclose the cloud computing circle," Balakrishnan said. Cloud computing aims to make computation a utility, like water or electricity, in which users can harness computing power without having to operate and deploy their own infrastructure.

"You need a client that the end user interfaces with," he said. "You also need an Internet infrastructure to allow the client to talk to remote data centers, and a number of machines in those data centers that 'do work' for the end user."

So while cloud computing technically falls within the category of distributed systems, Balakrishnan tends to group it with what he calls the "Big Ideas" of computing — something that requires a lot of research progress in practically every area of computer science, including new hardware, new operating systems, network protocols, algorithms, and programming languages.

"Other Big Ideas in the past that have succeeded include the PC, the Internet, ubiquitous computing — each one of these has required heavy lifting across the board," he said.

Using Obfuscation as a Key to Computer Security

In the digital age, many of us have accumulated so much data that we often use outsourcing services to manage it all. The more we do this, the more private information we release without having a particularly good idea of how it's being used.

Mariana Raykova, who begins at Yale in January, focuses on the question of how to work with private data without losing control over it. This spring, she'll teach both introductory and higher level seminars on cryptography.

"Many of the technologies that people use today offer mostly zero protection," she said. "We're often willing to give up protection of our data as a trade-off for convenience, and we hope that companies we're working with are using best practices."

Too much of how we do business relies on trust, Raykova said. "I don't think users have available today any strong guarantees of control over their data," she said. "How is it being used? What are the implications? We are starting gradually."

Prior to joining Yale, Raykova spent a year as a postdoc in the cryptography group at the IBM Watson Research Center and two years as a computer science researcher at SRI International.

While she was at IBM, she helped develop a system known as Pinocchio, which the *MIT Technology Review* described as a "kind of lie detector that can be used to check whether a cloud service did the work it was supposed to."

She was also part of a team that made a major breakthrough in a kind of encryption known as obfuscation. Computer theorists had long toyed with the idea but it was never proven to work very well, and multiple versions proved to not work at all. But in 2014, Raykova co-authored a paper that made a splash in the cryptography world.

"Obfuscation should re-write a program so that people can run the re-written program, but cannot determine how it works or what it will do," says Daniel Spielman, Henry Ford II Professor of Computer Science and Mathematics. "There are many ways of making this notion mathematically precise. Most of the precise formulations of this had been determined to be impossible. But there was one reasonable formulation that had not yet been ruled out. This is the one that Mariana and her team showed was possible."

Specifically, they make use of something they call "multilinear jigsaw puzzles." Previous attempts at obfuscation have used indirection and other ways to essentially hide the functioning part of the code. This slows down attacks, but it won't stop someone with enough patience and computer power.

But with the jigsaw puzzle technique, each instruction in the code is encoded with some randomness, which hides that instruction. With traditional obfuscation techniques, hackers have been able to take parts of the code and execute those, or change some of the code and execute the modified program. Raykova's program, though, requires that the entire code be put together exactly as intended. Otherwise, you can't use any of it.

"Hence, the analogy with jigsaw puzzles," Raykova says. "There is only one way to arrange the encoded pieces to reveal the picture, which in the case of obfuscation, is the evaluated result."

By the researchers' calculations, reverse engineering this takes more than a little patience. With the current technology available, they say, it could take hundreds of years.

Yale

EDUCATION

“The Computer Science Department has an essential role in educating leaders — not just in computer science and technology — but in cultural production and in fields such as security policy and media.”

› Joan Feigenbaum, Computer Science Department Chair

the number of ladder faculty members from 20 to 26 — the biggest increase in faculty resources in computer science in more than 30 years. Two of the positions have already been filled, with the hiring of Mahesh Balakrishnan, who started in September, and Mariana Raykova, who starts in January *(see profiles of each on pages 21 and 22).*

Hiring more faculty members and cooperating more closely with SEAS colleagues means that the department can have multiple faculty members in key areas — that means the department will have more to offer students on both the graduate and undergraduate levels.

And working more closely with other SEAS departments, Feigenbaum said, means more hiring possibilities for Computer Science. For instance, Biomedical Engineering does a lot of work with imaging. As part of SEAS, she says, it now makes more sense for her department to look at potential hires specializing in the computational aspects of imaging. “We would not be considering that if we were not a part of SEAS,” she said.

This fall, Yale took another step toward reaching out to non-traditional computer science students by way of a new course offering, CPSC 100. In what Brian Scassellati, professor of computer science and mechanical engineering & materials science, calls a “grand experiment,” the university has joined forces with Harvard on its introductory computer science course, CS50. Since Harvard’s David J. Malan started the course in 2007, it’s been a hugely popular offering. In the Yale-Harvard incarnation, Malan and Scassellati will both give lectures, which will be live-streamed and archived online. To accommodate the hundreds of students expected to enroll, Yale made the unprecedented move of hiring undergraduates to assist with teaching, which includes leading sections and grading papers.

“CS50 really has a way of drawing in students who are not typical Computer Science majors,” said Scassellati, who also leads the Social Robotics Lab. “It’s found a way to take something that has a strong technical and math component, and make it accessible to a very diverse audience.”

This is the kind of effort, Feigenbaum said, that will allow Yale to make a mark in computing well beyond the cubicles at Google or Facebook.

“The Computer Science Department has an essential role in educating leaders — not just in computer science and technology — but in cultural production and in fields such as security policy and media,” she said. “We can teach them the power of computers and networks to improve the world — culturally, economically, and politically.”

Arthur K. Watson Building, home to the Department of Computer Science.

Engineering Connecting to the Arts

From 19th century novels to computers that make their own music, SEAS researchers enjoy the art of engineering

Yale

INTERDISCIPLINARY

"Art without engineering is dreaming.
Engineering without art is calculating."

› Robert K. Stevens, author

Consider for a moment Leonardo da Vinci, painter and prolific inventor — or Steve Jobs, whose computers shaped a generation's sense of design. Popular opinion has drawn an imaginary line between engineering and the arts, but really, the two have long enjoyed a fruitful partnership.

The connection between engineering and the arts at Yale is particularly strong. Composers, museum conservators and illustrators have all worked on recent SEAS projects, ranging from the improbable to the quirky to the futuristic. All can be described as "uniquely Yale" — innovative, ambitious and cooperative.

There's even a place for 19th century French literature. Assistant professor of French Morgane Cadieu noticed that Emile Zola filled his 1890 novel *"La Bête humaine"* ("The Beast Within") with technical minutiae of a prominently featured train — her students have even remarked that it's really a book for engineers. She wondered: What do all these details amount to, really? "Zola's novel is a landmark of realism and naturalism," she said. "Yet, when you follow the descriptions of the machine closely, you realize that they are often evasive and metaphorical."

Could an actual train be built, relying only on Zola's descriptions? To find out, she turned to Yale's Center for Engineering Innovation & Design (CEID). There, the process of translation took many forms. "We first had to translate the original French descriptions into literary English, then translate the literary words into more technical, precise terms of engineering," Cadieu said. "Finally, we translated those terms into an object, into computer code."

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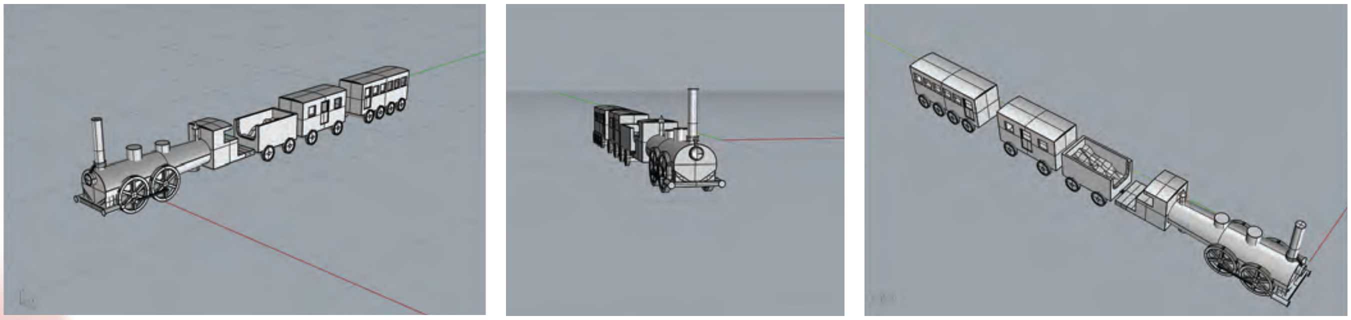


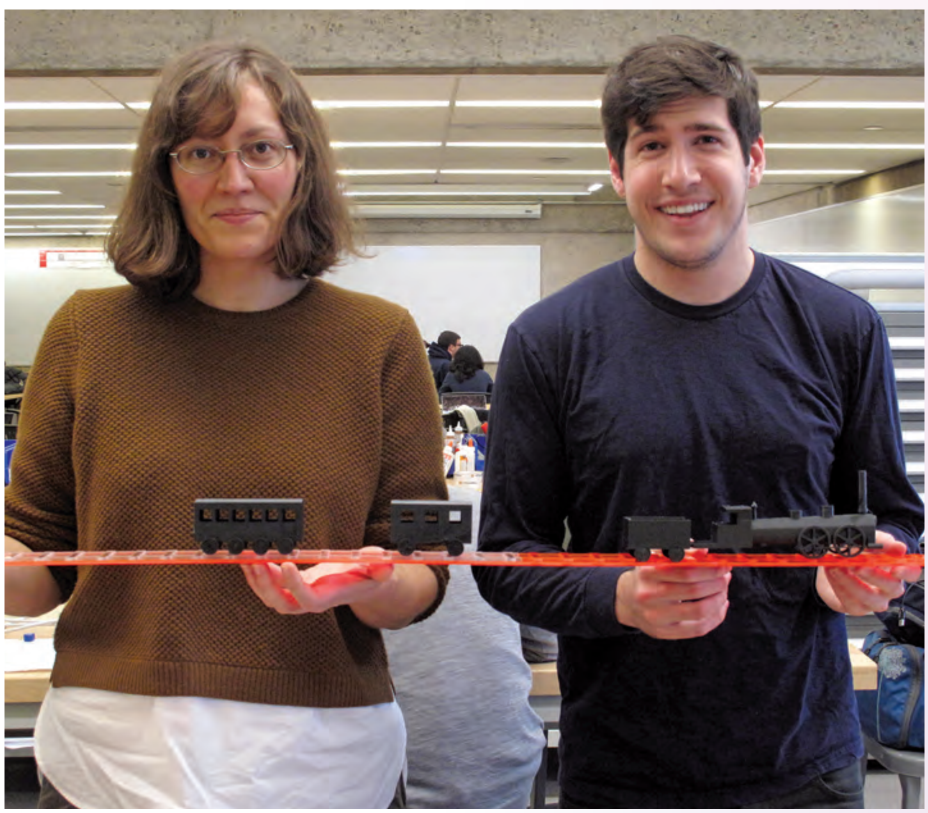
All this translation led to a computer-aided design, which then took physical form by way of one of the CEID's 3D printers. Cadieu's student research team — Sienna Jun '16, John Sununu '15, and Alexandro Gonzalez-Calvillo '16 — worked with the CEID staff, including research support specialist Glenn Weston-Murphy and CEID design fellow Ngoc Doan '14.

The project wasn't entirely literal. Some parts were built to exaggerated proportions in deference to their symbolic importance. The whistle's prominence, for instance, represented the increasing anxiety of Zola's characters. And there was the surrealist touch of a paper smoke trail hovering over the train, bearing literary descriptions.

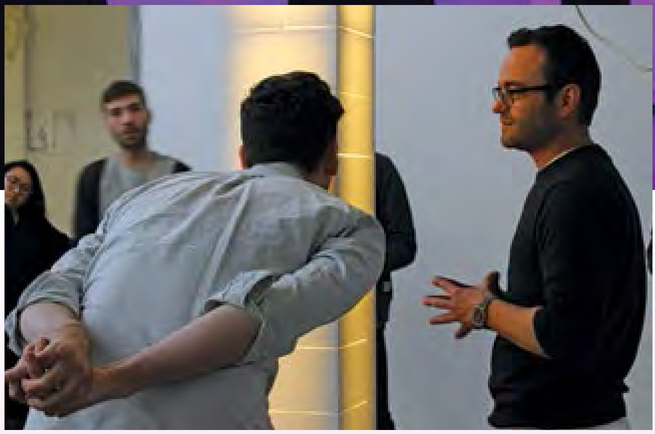
For the most part, though, the train was made as Zola described it, revealing some serious technical shortcomings. Zola proves himself a master of emotional nuance in this story of murder and betrayal. But designing a functioning train? Not so much. For one, Zola never mentions the train's back wheels. In keeping with the project's guidelines, no wheels were made, but the CEID staff kept the train upright with a nearly invisible hitch near the back of the engine.

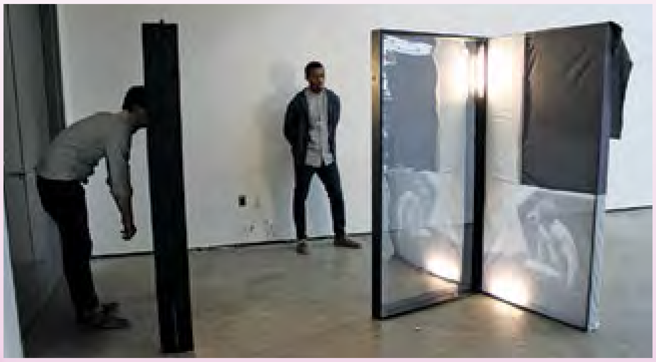
And engineering know-how also helped bring a deeper understanding to a classic text. "The project gave me a new appreciation of Zola's work and poetic interpretation of technology," Cadieu said.

Top: *CAD images of Zola's train.* Bottom: *Morgane Cadieu, assistant professor of French, and John Sununu '15 with the 3D model printed in the John Klingenstein '50 Design Lab.*



Making Art from Light





Screen Space explores how the dynamic architecture of screen and projector can be understood as a site of creative work. Students were tasked with creating a projection machine as their final project.

The mechanics of light and screen space are often taken for granted in contemporary art. Screen Space, a course taught last fall by Sarah Oppenheimer of Yale's School of Art and Joseph Zinter, associate research scientist and lecturer of mechanical engineering & materials science, served as a corrective.

The course explored the role of screens and projectors in creative works, and their evolution in the 20th century. "We were thinking about different ways of using light as an artistic medium, but in the context of mechanics and machines," said Zinter who also serves as associate director of the CEID.

For the final project, students designed and built a projection machine that explored the aesthetic language of light, color, and motion. For one project, a student set up red and blue light sources and used a neck massager to animate a mannequin head inside a black box. A set of lenses, acting as camera obscuras, lined the box sides. "So you saw the head moving 360 degrees around you," Oppenheimer said.

For Oppenheimer, whose own work blurs the boundaries between architecture and sculpture, the course explored differences in how engineers and artists approach their work.

"On one hand, in engineering, the test is whether you are able to have the project meet the criteria you set out for it," she said. "In the case of an art project, failure is often the most interesting part of the work. I think it really changed how the engineering students thought about the success of their projects and how the art students thought about their success."

Zinter said the course drew some inspiration from Thomas Wilfred, an artist who used light as his medium. Although his star has faded significantly since, Wilfred's status was once equal to those of Mark Rothko, Jackson Pollack and other contemporaries. You can see Wilfred's work next year, when the Yale University Art Gallery holds a retrospective of his work. Zinter, again bridging the worlds of engineering and art, serves as a consultant.

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Experiments in the Theater and the Lab

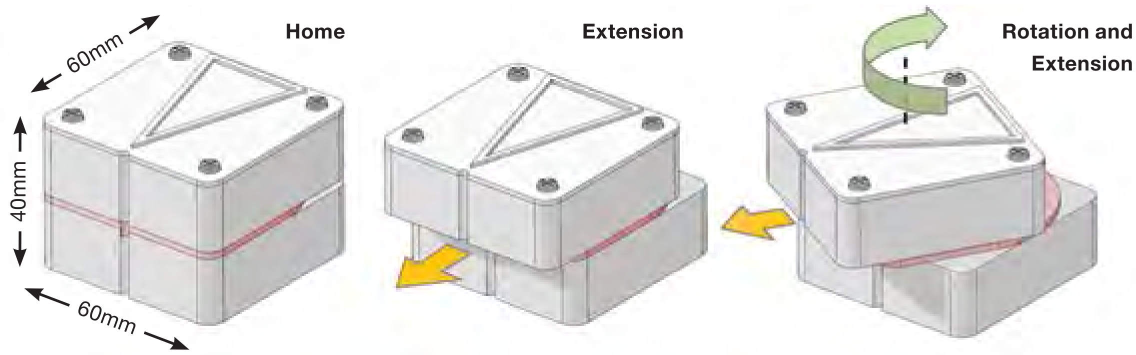
Adam Spiers

INTERDISCIPLINARY

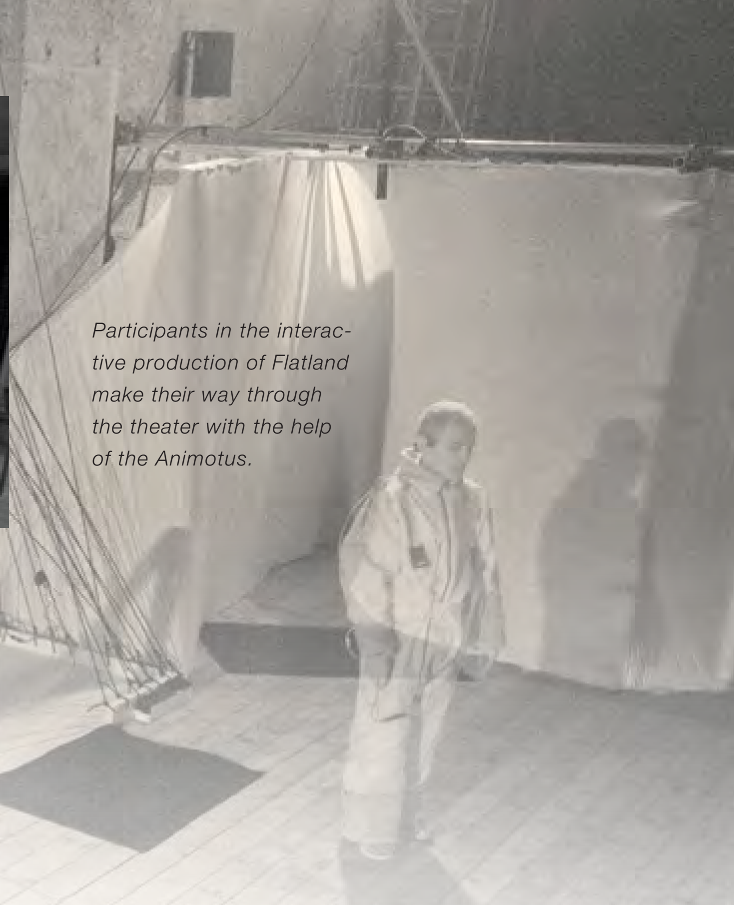
The recent and unlikely merger of mechanical engineering and avant-garde theater helped bring a classic science fiction story to life, and could help the visually impaired navigate their routes.

Adam Spiers, a postdoctoral associate in the robotics lab of Prof. Aaron Dollar, played a critical role in "Flatland," an interactive theater production of Edwin A. Abbott's 1884 story of a two-dimensional world.

Spiers, a haptics specialist, used a 3D printer to build a navigational device that guided audience members through the theater space — an old London church kept in complete darkness. The top half of the handheld, shape-shifting device — dubbed the Animotus — twists to direct the user where to turn and extends forward to indicate the distance to reach it. Spoken narrative and sound effects told the story.



The Animotus guides users by changing its shape, returning to a cube when users arrive at their destination.



Participants in the interactive production of Flatland make their way through the theater with the help of the Animotus.

Maria Oshodi, artistic director of Extant, the London-based company that produced "Flatland," said the project merged the engineering and arts worlds perfectly. "Both strands needed disciplined testing, evaluating and re-working at many stages," she said.

Spiers said work on the Animotus was "kind of a two-faced project" that produced some interesting results from both the lab and the theater. Data showed that users moved quicker than expected, indicating their confidence in the Animotus. And surveys revealed that they developed a real bond with the device. "It's about 40 minutes that they're in there with the Animotus, so they got pretty emotionally attached to it."

Building the device took some trial and error. "First, we came up with this crazy thing," he said, holding up what looks like a Whiffle Ball inside plastic flower petals. "I collaborated with an artist. He was a puppeteer and we made this cool-looking flower thing." But cool-looking doesn't always translate to functional. When Spiers got his job at Yale, Dollar told him to bring the project. That's where he developed the cube-shaped device that it is now.

"I got to use all these awesome 3D printers, laser cutters, and various engineers' knowledge," he said.

Preservation

Clearing the View

With ingenious new computer programs and the science of gecko feet (we'll explain), SEAS researchers are also helping to preserve art and increase access to it.

Micrometric and sub-micrometric contaminant particles — what most of us call "dust" — have long plagued art conservators. It robs the vitality of a painting's colors and dulls the surfaces of sculptures. The lab of SEAS Dean Kyle Vanderlick, which focuses on thin films and surface properties, recently took on the dust problem. It turns out that there's a lot in art conservation to engage researchers in her field.

"Paint cracking — that's a thin film problem," she said. "How stone falls apart, how monuments fall apart — you're talking about water in a porous environment. That's something at the nanometer level. So there's a lot of interesting thin film, surface, and interfacial physics associated with the preservation of art."

And with the recently established art conservation labs at the Institute for the Preservation of Cultural Heritage (IPCH) at Yale's West

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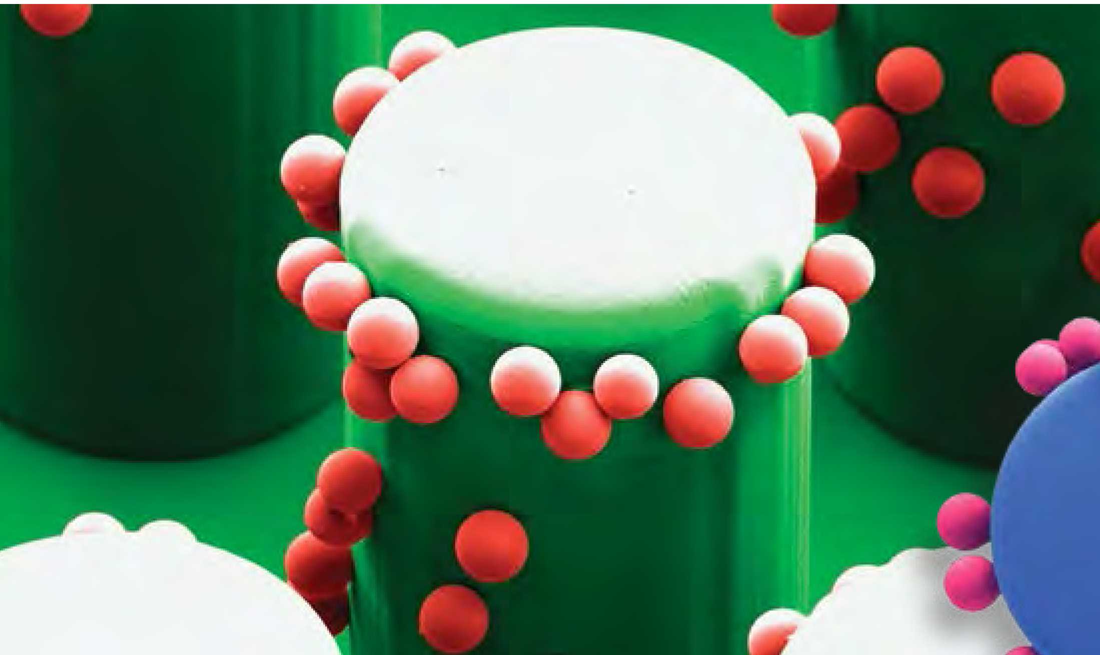
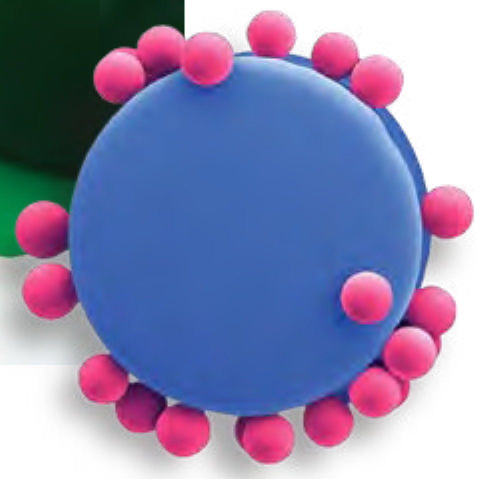



Micropillars, 2 to 50 micrometers in diameter, lift dust particles off works of art.

Campus, Vanderlick wasted no time getting involved. “This kind of laboratory and these kinds of collaborations would not exist at any other university,” she said.

Hadi Izadi, a postdoctoral associate in Vanderlick’s lab, is working with researchers at the IPCH and workers at Yale’s two art museums and the Peabody Museum of Natural History. The dust cleaning method he’s devised combines microscopic fibrils and the forces that make static cling. In the lab, he holds up what looks like an ordinary plastic sheet. It’s actually an elastic and non-sticky polymer, polydimethylsiloxane (PDMS). Under a microscope, you can see millions of tiny columns. Depending on the size of dust particles you’re removing, the pillars range from 2 to 50 micrometers in diameter — bigger particles require bigger pillars.

Izadi knows of fibrillar structures and micropillars. His previous research explored the mystery of how geckos stick to walls. A lot of it has to do with electrostatic charges and the microscopic pillars on the pads on their feet. Applying some of this science to cleaning microparticles made sense, Izadi said. “When you’re talking about dust, you’re talking about electrostatic charges.”

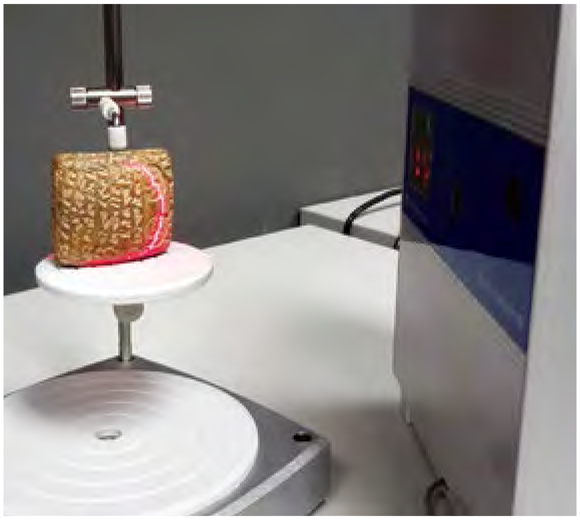
The PDMS polymer has minimal interaction with the substrate — whether it’s a painting or a sculpture — but it produces enough electrostatic charge to detach the dust particles. “When it absorbs the particles, they go around the pillars,” he said.

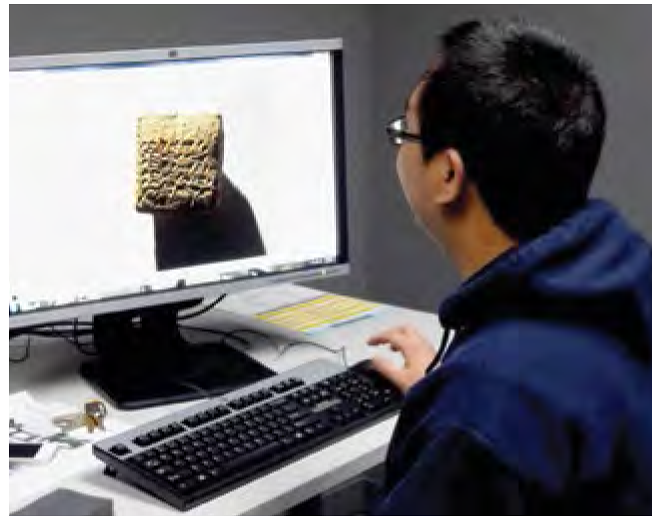
Once you match up a sheet with the appropriately sized pillars, the method of cleaning is simply a matter of tapping it to the surface. Tests on various surfaces in his lab have shown total cleaning of silica dust particles and no damage to the surface.

Thanks to a collaboration of the Computer Science Department, the IPCH and Sterling Library, researchers can now call up on their computers a cookbook tablet thousands of years old and examine it from every direction and in all kinds of light.

Starting in 2014, Holly Rushmeier, professor of computer science, helped digitize images of 14 of the Yale Babylonian Collection’s “greatest hits.” Besides the

Custom-built dome for Reflectance Transformation Imaging (RTI) features 45 lamps from different heights and angles.





Researchers can now remotely study priceless artifacts in great detail, such as these items from the Yale Babylonian Collection.

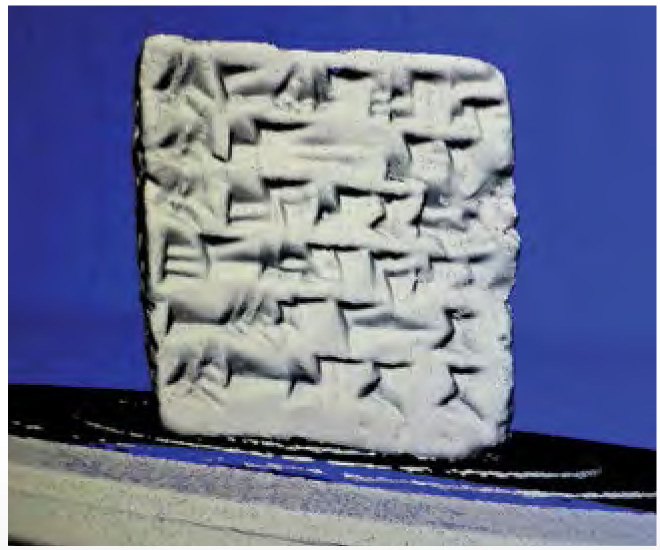
cookbook, that includes the epic of Gilgamesh, a marriage contract and the first evidence of a contract killing. Each object was placed under a custom-built dome used for reflectance transformation imaging (RTI). The dome is equipped with an overhead camera and dozens of lamps placed at different heights. The result is an image that can be examined under light from 45 different angles.

"Making out some of these characters would be difficult if you only had a static light source," said Chelsea Graham, digital imaging specialist at the IPCH, pointing to the tablet on a computer screen. "Now, you can move the light source and say 'OK, this angle helps me see that it says "one cow" instead of "one goat,"' or something like that. This was neat because we did it with a collection that had never been part of such a high-tech project before."

And to capture the surface geometry of the objects, the researchers used high-resolution 3D laser scanners to produce digital 3D images.

"It's one way to improve access to these treasures at Yale internationally and very much in accordance with the institute's aim of open access," said IPCH Director Stefan Simon. He added that the project was made possible with the assistance of Benjamin Foster, professor of assyriology and curator of the collection; and Eckart Frahm, another Yale assyriologist. Alberto Urcia, Ulla Kasten and Elizabeth Payne, from the Yale Babylonian Collection, also made valuable contributions.

One of Rushmeier's latest projects, Hyper3D, further advances the goal of better access and cultural preservation.



Funded with a grant from the Seaver Institute, the program is designed to give conservationists a better workflow when documenting artifacts, artworks and archaeological sites. The software allows multiple researchers to work on the same item and post images and notes that are easily accessible to others.

"It will provide a common base so that everyone can access the information and know the provenance of that information," Rushmeier said. "Others working on the same painting or site can share data about what's effective for preserving things."

Simon said this means that a community of researchers can share information about pigments, damages or any other data that would otherwise get tucked away into a folder.

"This could bring the field of preservation to the next level," he said.

Continued →

New Instruments, New Sounds

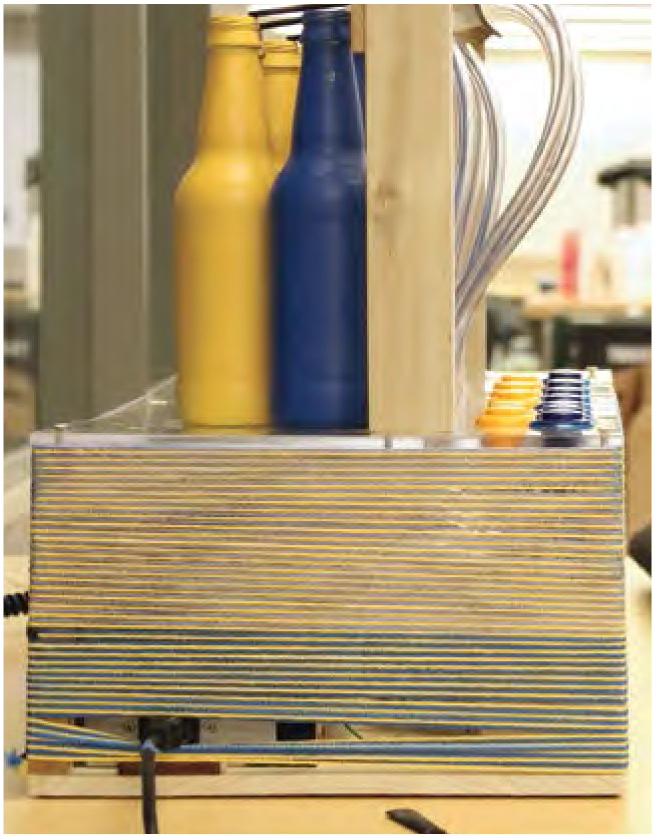
The Musical Side of Engineering

"All the composers in Hollywood are looking for new sounds that stand out," said student Jordan Plotner. "So why is there no instrument that uses the beautiful sound of blowing across glass bottles?"

Answering his own challenge, Plotner built "Helmholtz's Harmonious Homebrew," a contraption comprising 12 glass bottles, each filled with "tuned" levels of water. He took on the tuneful project last fall for "Musical Acoustics & Instrument Design," a CEID class co-taught by Konrad Kaczmarek and Larry Wilen. Instructed to let their creativity reign, the students' each invented and built an instrument.

"The CEID ecosystem is essential to this class," said Kaczmarek, a composer and lecturer in the Department of Music. "Many of the students came up with instruments that could only be built in that environment with those tools — they built instruments they couldn't build in any other context."

The class fully embraced the spirit of creativity. Student Rachel Perfecto created "Clip-B-Audio," in which the performer creates an electric circuit by drawing lines on



Top: *Taking inspiration from the Fender Rhodes piano, percussive tones are generated from tuned wooden tines struck by pencil erasers.* Bottom: *"Plotner's Harmonious Homebrew" produces sound by blowing air across the mouth of 12 tuned bottles.*

Left: *"Potenciello" combines the technology of the theremin with the performance techniques of a cello.* Right: *"Siren Song" is a polyphonic keyboard that uses light to produce sound.* Bottom: *"Lothlóritar" was designed to only be playable by two performers working together.*

paper, connecting the pencil to a metal clip on a clipboard. The distance between the lines and the clip determine the musical notes. "I'm excited to show it to my friends who are art majors, just to see what they do with it," said Perfecto. "Or maybe this is how I'll take my notes in class from now on."

With its calliope-like tone, Plotner's Harmonious Homebrew, is easy on the ears, if not easy to make. "To mimic how air escapes out of the lips when blowing across a bottle opening, I took a lot of photos of my mouth," he said. "I was able to model the shape of my lips into a mouthpiece that I could make on a 3D printer."

By semester's end, students could use laser cutters, connect circuits, solder wires, and customize software to control microprocessors. Wilen, CEID design mentor and senior research scientist at SEAS, said the hands-on project drove home the lessons better than sitting in a classroom would have. "By the end of

Continued →

the course," Wilen said, "the musicians became incredibly skilled engineers, and the engineers were amazing musicians."

....

When Donya Quick hits a key on her laptop, there's a few seconds of silence followed by a lilting melody with a vaguely 18th century sound to it.

"The program's modeled after Johann Sebastian Bach, but it never gets exactly to Bach," said Quick, a lecturer in computer science. "Right now, it would pass a music composition class. It wouldn't necessarily get the top grade in the class, but the goal isn't really to beat people at their own game."

Quick has spent the last few years developing Kulitta, a software program that makes never-before-heard music. Algorithms generate new harmonies, chord sequences and melodies. A keystroke changes styles from classical to bossa nova to jazz. Quick said it could potentially be used for music education, or reveal things about musical grammar useful to the field of natural language processing.

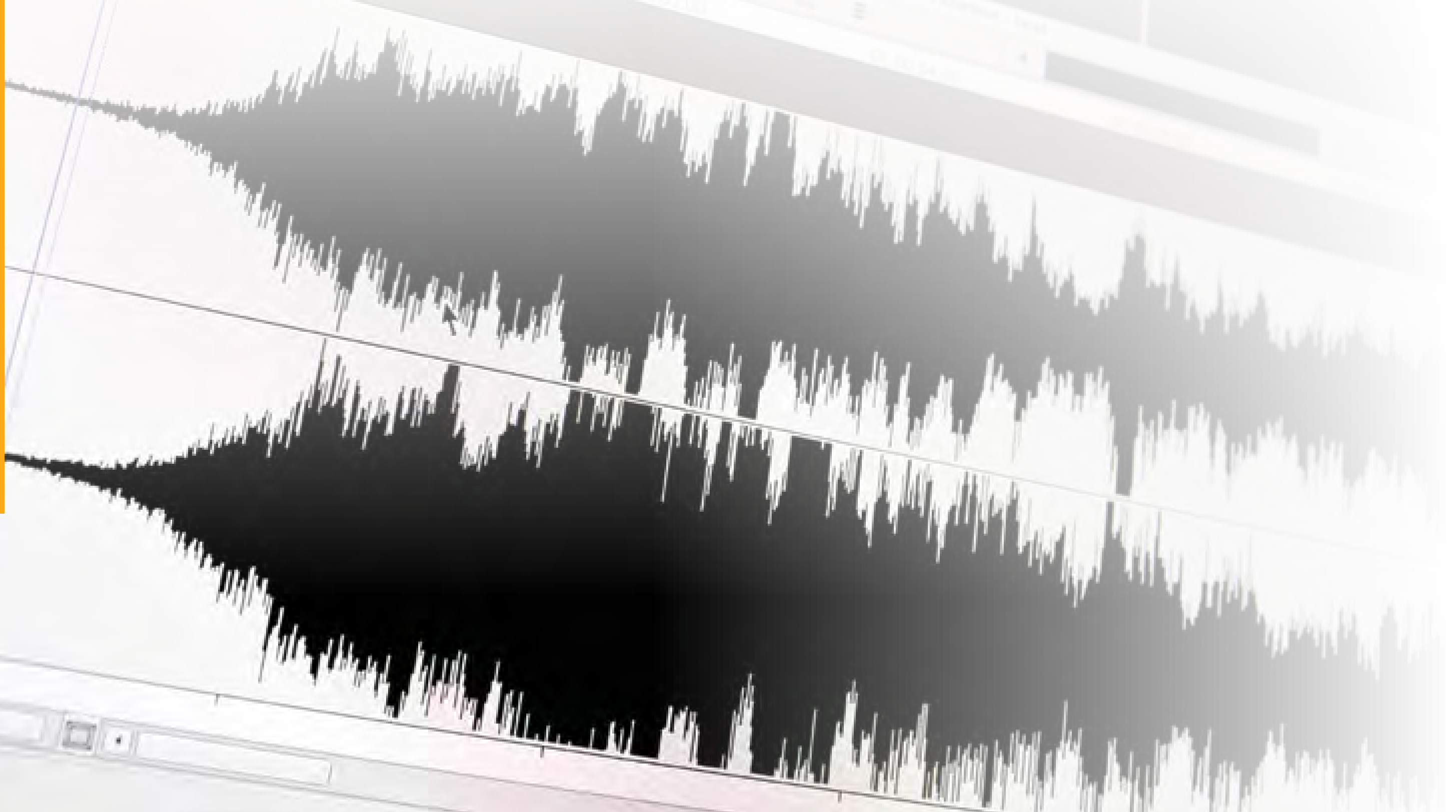
It also gives Quick some good ideas when she's composing her own music. "There have been many cases where Kulitta came up with something interesting and I thought 'That is something I never would have done with my own set of composition tricks, but I like it.'"

Most reactions to Kulitta are positive, she said, but new technology rankles some people whenever it's applied to music. "No one gets up in arms about Siri talking to you, but I guess if Siri started singing, then all of a sudden, that's offensive."

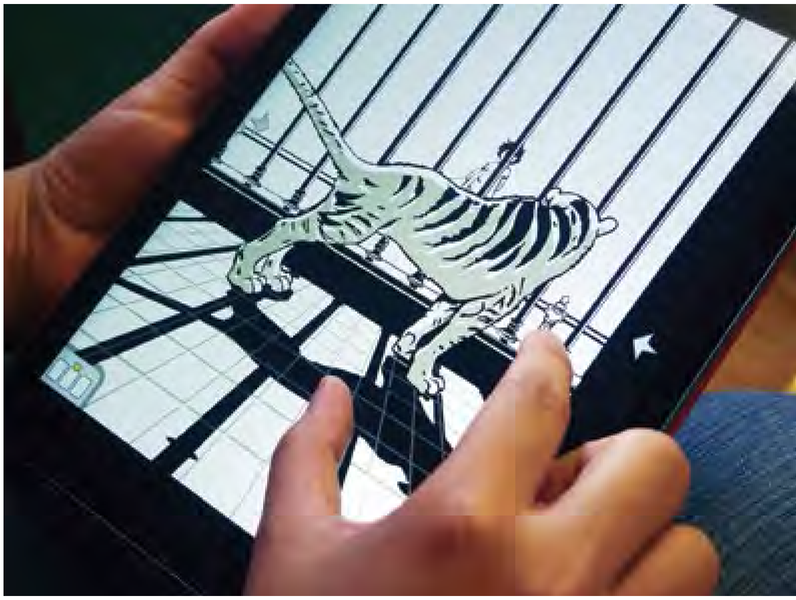
Based on student feedback, though, she's not too concerned. "Students I've talked to were especially interested in Yale, because it's fairly rare to have this kind of project involved."

This fall, she's teaching an introductory course on computer composition. "I'll take people without necessarily any computer or music background and teach them to program and teach them some things about music at the same time," she said, adding that it's for anyone who likes music and is interested in programming. "So it's a really broad audience."

Quick said computer music is a perfect vehicle for bringing together two communities often seen as being on far ends of the academic spectrum. "I think it has attracted new audiences who might have felt shut out before, both from the computing and music communities," she said.



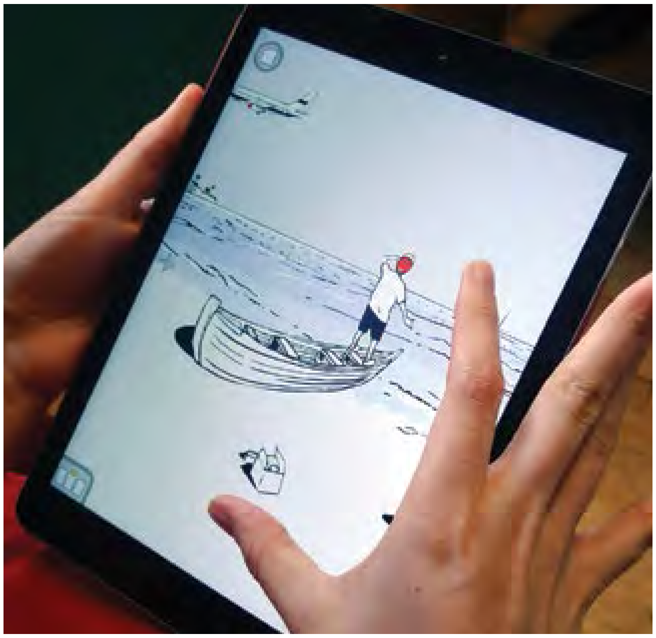
The Future of Engineering and the Arts



Julie Dorsey believes computers could transform arts education in general. At Yale, that's especially true now that the Computer Science Department recently became part of SEAS. That means more sharing of resources and know-how, said Dorsey, a professor of computer science. The department has had a Computing and the Arts program since 2008, and Dorsey expects the department's move to SEAS to bolster it significantly.

Dorsey's own work at Yale has focused on computers' contributions to the arts. Her latest project is designed to bring sketching into the digital age. As part of her software company, Mental Canvas, she developed a program that combines traditional drawing with 3D modeling.

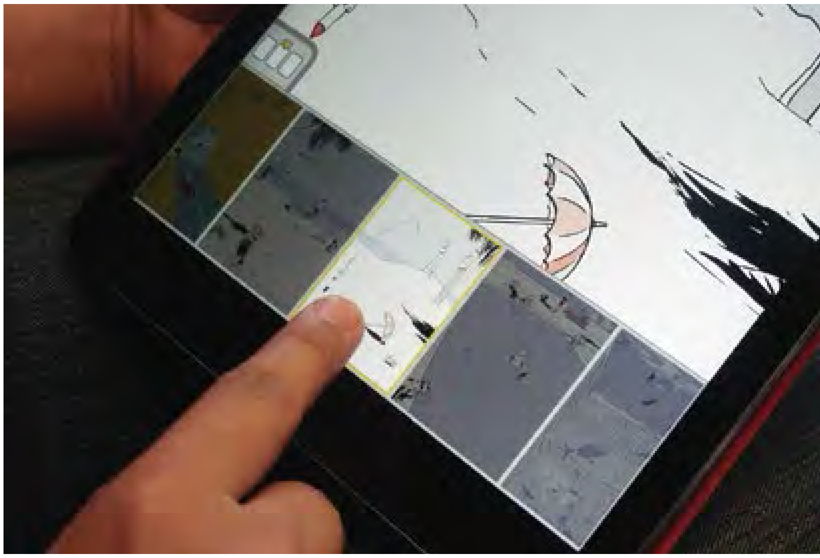
With a background in computer science and architecture, Dorsey came to Yale in 1983, drawn by the "amazing riches" of its arts programs. If there's any university where engineers and computer scientists should branch out into the arts, she said, it's Yale.



The artistic approach can help engineers, who are traditionally taught to look for the "right" solution, Dorsey said. "Over on the other side of campus, they really follow the critique model of education, where multiple points of view are entertained. I think that model of education could be brought to bear on computer science and engineering."

Dorsey said she's seeing that happen more often at SEAS. Indeed, when mechanical engineers are working on experimental theater productions and students are using laser cutters to bring new clarity to French literature, it's safe to say that the lines between engineering and the arts are pretty well blurred.

"You're bringing together groups of people who think and work in completely different ways," Dorsey said. "And that is a really interesting possibility."



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Figuring It Out in the Field

Students learn the science of safe water in far-flung locales while improving the lives of others

Student Joel Li tests the air quality in a villager's home.

Yale College senior and chemical engineering major Hannah Fornero was at the point of frustration in a remote village in the northern Nicaraguan mountains. Sitting in front of ten rudimentary ceramic pot water filters, she had been tasked with cutting the fragile filters from the base of the pots without damaging them, then attaching small sections of each filter to a plastic water bottle. Fluid containing bacteria and virus-sized microspheres would then be passed through this improvised filtration system to test the filter's effectiveness at removing harmful pathogens from the water. But after hours of trying every adhesive available to her, Fornero felt sure she needed a new strategy.

"That kind of frustration is true to the experience of being an engineer," says Jaehong Kim, professor of chemical & environmental engineering. "You plan, you fail, you get frustrated, you hope again, you fail again, feeling that it's impossible — until some alternative plan finally does succeed. By the time we're in the field, the students know that I'm OK if some things don't work right — I even hope they expect it — but one of the core challenges of this course is to react to those problems without giving up."

Kim's course, Environmental Technology in the Developing World, is one of the newest to be offered in Yale's Center for Engineering Innovation & Design (CEID). Like many CEID courses, Environmental Technology in the Developing World tasks students with improving a real world problem over the course of the semester under the mentorship of an actual "client" who works in the field.

But two things set Kim's course apart from other CEID courses. First, every student in Kim's course collaborates on the same project, for the same non-governmental organizations (NGOs), to better the lives of the same villagers. To accomplish this collaboration, each student is tasked with developing a proficiency in a specific scientific experiment that could be used to analyze the harmful pathogens, chemicals, and particulates in water and air.

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Students work to analyze and test ceramic pot filters of the Jinotega residents in an effort to reduce drinking water pathogens.

In the early weeks of the course, each student masters the technology and techniques needed to complete his or her task, then leads the rest of the team in performing the experiment. In this way, while only one student in the course becomes an expert in detecting chemicals in water with a colorimeter or analyzing the fine particulate air pollution from simple stoves, for example, every student becomes familiar with these tools for scientific investigation.

But for most students, the most unique and memorable aspect of the course is its focus on international travel to developing communities, including this year's trip to two rural villages in Nicaragua. "This course," says Kim, "is an opportunity for the next generation of researchers to not only learn about preventable water- and sanitation-related diseases, but also to actually make a difference. To me, that means organizing the class based on what a particular community or organization needs, and then going to that community to perform scientific research that can help that organization."

Taking place over spring break, this year's eight-day field trip to Nicaragua was the central turning point for the course, a simultaneous culmination of the weeks spent developing scientific expertise and also the launching point for the semester's later weeks spent analyzing the experiment results and preparing a report on their findings. During their trip, the students worked in collaboration with two NGOs: Amigos for Christ, which operates in Chinandega, and Comunidad Connect, which operates in Jinotega. "I've worked with these NGOs from the beginning, listening for what problems might become projects worth doing," says Kim. "And then I have buy-in, so not only are the NGO staff working with us while on location, but they're also the people with an investment in the outcome — they're waiting for the results, which the students produce as a formal report that they deliver to these NGOs. Then the students work hard not because they want a good grade but because they're passionate about improving lives. This is a class with a humanitarian emphasis, and while in Nicaragua, they learn about the realities of engineering outside of the lab."

The driving purpose for Kim's research, and in turn for this course, can be encapsulated in statistics: 1.5 million children die each year of preventable water- and sanitation-related diseases; in Latin America, 77 million people lack access to safe water and 100 million people lack access to sanitation. "Attempting to affect such a large-scale problem requires developing tools that might sound outrageous," says Kim, "and that encouragement of big thinking is something my course has in common with other courses in the CEID. But during the field research, the identification of problems, and subsequently the research results, inevitably gets narrowed into specifics about the communities you hope to help."

One way that this happens for Kim's students is that they must conduct their research in a place where they can't expect perfect lab conditions — a sometimes unpredictable challenge. In fact, that was the source of frustration for Hannah Fornero, the senior chemical engineering major. Fornero's role this past spring was to analyze the ceramic pot filters that Comunidad Connect gives the residents of Jinotega to reduce drinking water pathogens. Her goal at the beginning of her trip to Nicaragua was to complete all filter tests on site, then analyze the data back at Yale.

Testing the filters in the field, however, turned out to be much more difficult than expected. For one thing, the filters would need to be irreparably separated from their ceramic jars during testing, so Fornero had to purchase new filter units to trade to Jinotega residents for the units they were currently using. Moreover, this trade had to be made with no advance notice. Otherwise, a well-meaning filter owner might perform an unusually deep clean on the filter and remove the buildup that reflects the filter's everyday state. Even more challenging was the process of setting up the experiment, which necessitated using only a small section of the actual filter in each test due to limited quantity of fluorescence-emitting microspheres that she used. But the filters, made of clay and sawdust, are somewhat fragile, and even when Fornero removed the filters from the pots undamaged, none of the adhesives she found locally made a water-tight bond between the filter piece and the plastic bottle that would gather the water. After many hours of painstaking work, she determined that the tests could not be completed without additional resources, and she instead had to ship the filter materials back to Yale for testing in the CEID.

Students test the chlorine levels in the residents' water for evidence of bacteria and viruses.

Despite such frustration, chemical engineering major Rahul Kini feels that the challenges of outside-the-lab research are the central appeal of the course. "In the lab everything is given to you: if you break a beaker, you buy another one; if something catches on fire, you replace it immediately," he says. "But in the field, you have a finite amount of equipment, a finite amount of resources, not to mention time, and things always go wrong. That's frustrating, but then it feels so good when you figure out how to work around it. I can tell what quality of engineer I've become over the past three-and-a-half years by how I react to things going wrong."

In addition to facing these technical difficulties, human nature was also a crucial component of the engineering problems the students faced during this course. For example, when junior environmental engineering major Maddy Landon tested the additive chlorine levels at the first house she visited in Chinandega, the levels were perfect. But at later houses, especially as her testing carried into the afternoon, the samples had ineffectively low levels of chlorine that would make it possible for bacteria and viruses to multiply in the water.

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"It was clear that the chlorination system is working how it should," says Landon. "But Chinandega was founded long before the village had a reliable water source. What's happening now is that the villagers still believe they might run out of water any minute, so they collect the properly chlorinated water in plastic containers and cement tubs, perhaps with or without lids." In fact, one woman Landon met had roughly 500 gallons of water stored in her backyard. Although the water came from the village's treated system, the chlorine had evaporated from the water in the time between when the woman had drawn it and when Landon tested it. As a result, animals, flies, and dirt can recontaminate the water, even though the system is working as expected.

Landon further found that the individuals who choose to store that much water, in addition to making themselves vulnerable, also end up preventing others in the community from drawing water at all. "The water distribution system in Chinandega was thought out carefully by a civil engineer, and in theory, it should work perfectly," she says. "But it's gravity fed. Because villagers at the bottom of the hill are currently the higher-volume water collectors, villagers at the top of the hill can't create enough pressure to draw any water at all from their own spouts. It shows that even when it's easy to engineer systems, it's almost impossible to engineer people."

Yet at the same time as the students face these additional challenges, they also share experiences with these villagers that inform and ignite their drive to make a difference. For example, senior economics major Joel Li was in charge of testing the air quality within the villagers' houses looking for "fine" particulate matter air pollution, that can measure as small as 2.5 microns in diameter. These particulates, which are most often generated by the incineration of organic materials such as wood, can penetrate your lungs, affecting lung function and increasing the risk of lung cancer and heart disease. Li also tested the air for the presence of carbon monoxide — formed by the incomplete combustion of materials that contain carbon — and which can be fatal in high doses.

Through such measurements, Li aimed to compare the health risk of two different types of stoves, both of which are in current use in Chinandega. Such an evaluation

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is crucial for women who often spend long hours in the kitchen cooking meals for their families. The fires that heat the stoves are rarely put out, so even when not kindled to a flame, the embers can release fine particulates into the air all day. Unless the air is properly exchanged with outside air, people in other rooms of the house could be affected.

To perform his measurements, Li was invited into the villagers' homes, where he had a close-up view of how they live. "While taking these measurements, I really felt how much there is to be done for these people, especially because of how little they have," he says. "There was this one house owned by one of the friendliest people I've ever met in my life. The house was very rural, very dusty, and with intermittent water access. But as she explained how she went about her business every day cooking for her family, she started cooking for us. It was just this incredibly heartwarming moment, and yet it was also soured for me knowing that she wasn't aware of the byproducts, the carcinogens, the particulates — all this very bad stuff that she's exposed to on a daily basis because of her cooking. It was eye-opening, and I'll remember it for a long while."

Kim regards such experiences with the same importance as the science itself. In his own research, he's developing futuristic materials to solve the same low-tech problems that his students are addressing: a water bottle that when placed in the sun, uses solar rays to disinfect the water inside it; a nanoscale "band-aid" that can repair the tears in membrane-based water filters. But the problems are too big, he says, to think that he could resolve them himself. He therefore considers it an important part of his career to inspire the next generation of researchers, to show them how valuable this work is and how valuable each human life is.

For this reason, Kim sees his course as a potential conduit for so many positive changes: providing evidence that can strengthen the collaborative efforts between the Nicaraguan villagers and NGOs to improve health in rural villages; offering scientific documentation and analysis that NGOs can use to secure grants that might expand their reach; and creating opportunities for Yale students to have life-changing experience that might shape them as engineers and as people. In this way, Kim's work ripples out into communities that he might otherwise have never affected by himself.

"The course epitomized what I want to do with my environmental engineering degree," says Landon. "It was a real-world application like I've never seen before in a class, and it made me feel like I could do something important."

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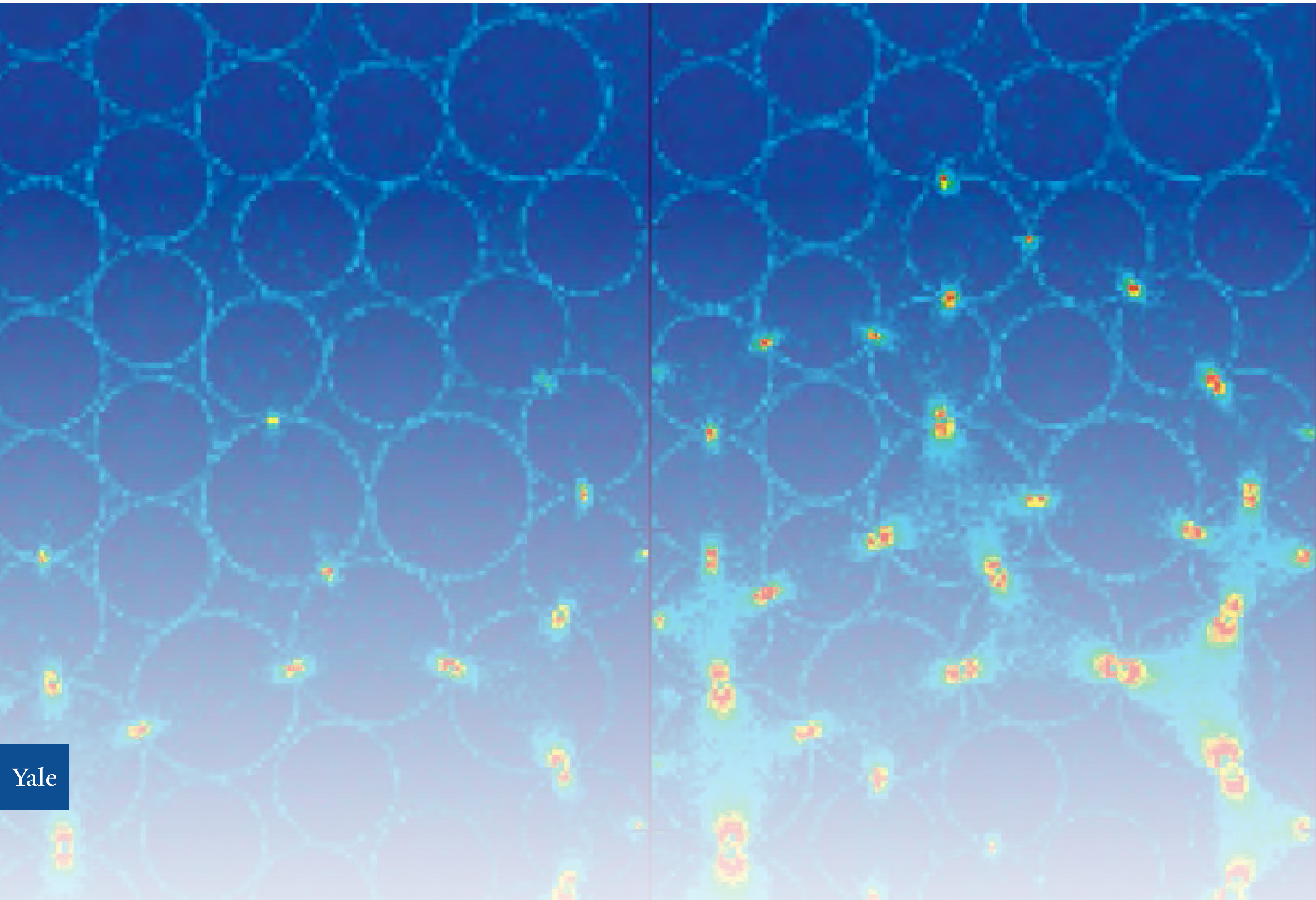
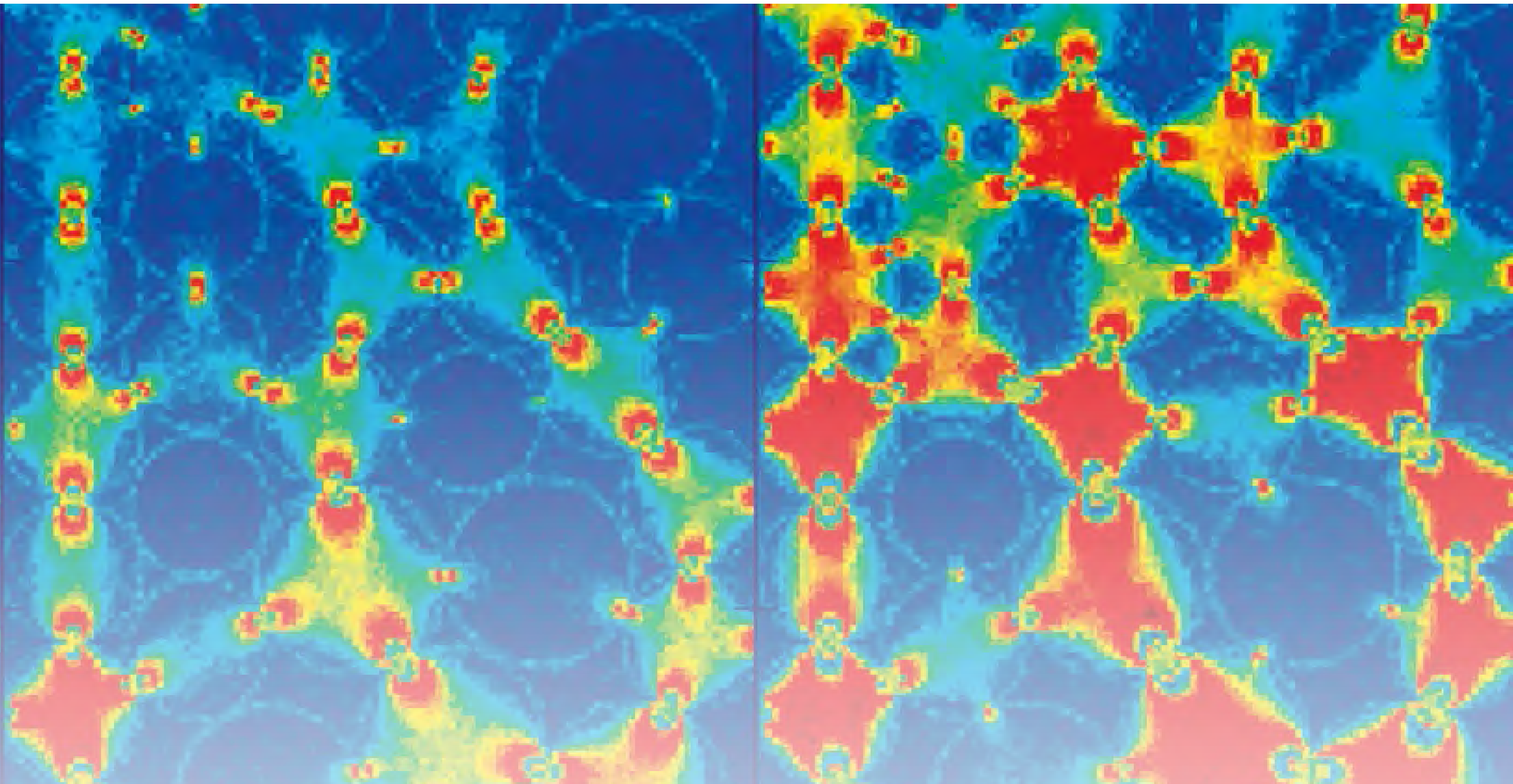


A Hard Look at Soft Matter

Exploring the promises of these mysterious materials

Background: *Experimental images of sound propagation through packings of photoelastic beads.*



How can synthetic materials better work with living tissue? Why do pill bottles jam up, and what does that tell us about earthquakes? Can butterflies bring us cleaner energy?

It's a disparate set of questions, and one that falls under the wide umbrella of soft matter and complex fluids research. The field is relatively new — physicist and Nobel laureate Pierre-Gilles de Gennes coined the term about 30 years ago — and much is still unknown about how soft materials work. But researchers are fascinated by these materials and their potentially valuable applications, and have made soft matter one the fastest growing fields in science.

It's also one of the most interdisciplinary, drawing from engineering, physics, chemistry and biology. At Yale, faculty in the Departments of Mechanical Engineering & Materials Science, Chemical & Environmental Engineering, and Biomedical Engineering are all researching — often in collaboration — how soft materials can contribute to drug delivery systems, solar energy, protective gear, and other applications.

The kinds of materials they study — cell membranes, polymers, colloids, liquid crystals, foams, gels and glasses — don't fit neatly into the conventional states of matter of liquid, solid or gas. The field even includes materials that aren't soft, like grains of sand or rocks (when they're in the state of flow, as in an avalanche, they take on the properties of soft matter).

It's a wide-ranging field, but there are common threads throughout. Owing to the molecular attractions caused by such forces as hydrophobic effects and electrostatic charges, many soft materials can organize themselves into unique molecular formations. This self-assembly capability makes for structures that behave very differently — and much less predictably — than traditional solids and liquids.

Their states can change dramatically due to fluctuations in temperature, exposure to magnetic fields, light, or various stresses. This makes them an inviting resource for researchers looking to engineer new materials and ultimately new applications for these materials.

For all their mysterious properties, soft materials make up the stuff of everyday life, such as your digital watch (liquid crystals) or shampoo (colloids). These materials, though, stand to make an even greater impact. SEAS faculty are asking the questions that could benefit the environment, lead to better healthcare, and produce cleaner energy. Here's a look at a few of their efforts in this field.

Continued →

Nanoparticles' Life-Saving Cargos

The problem with most commercial sunscreens is that they go beneath the skin and into the bloodstream. This could have hormonal side effects and even promote the skin cancers sunscreens are designed to prevent.

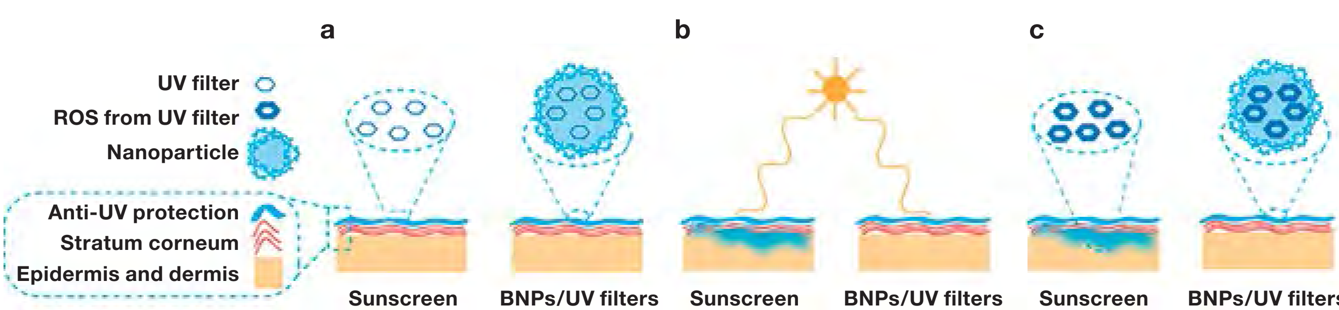
Mark Saltzman's lab, working with Michael Girardi, a professor of dermatology at the Yale School of Medicine, has found a solution to this with a new sunscreen. The key is bioadhesive nanoparticles that carry the active ingredient.

"We found that if we apply them to the skin, they don't come off, and more importantly, they don't penetrate any further into the skin," said Saltzman, Goizueta Foundation Professor of Biomedical Engineering, Chemical & Environmental Engineering and Cellular & Molecular Physiology.

Commercial sunscreens and the one from Saltzman's lab proved equally well at protecting against sunburn — the direct effect of ultraviolet rays. It's the indirect — and much less studied — effects of UV where the biggest differences are between Saltzman's sunblock and commercial brands. When the active ingredients of sunscreen absorb UV light, a chemical change triggers the generation of oxygen-carrying molecules known as reactive oxygen species (ROS). If a sunscreen's agents penetrate the skin, this chemical change could cause cellular damage, and subsequently, skin cancer.

Studies on users of commercial sunscreens have also found traces of the products' chemicals in breast milk and urine. There's evidence that these chemicals are causing disruptions with the endocrine system, including blocking sex hormone receptors.

Comparison of bioadhesive nanoparticles-based sunscreen (BNP) and commercial sunscreen. After application, commercial sunscreen penetrates into the skin whereas BNP formulation remains on stratum corneum. After sunlight exposure, UV filters produce deleterious ROS that can damage adjacent tissue; however, BNPs do not penetrate into the skin, preventing toxicity.



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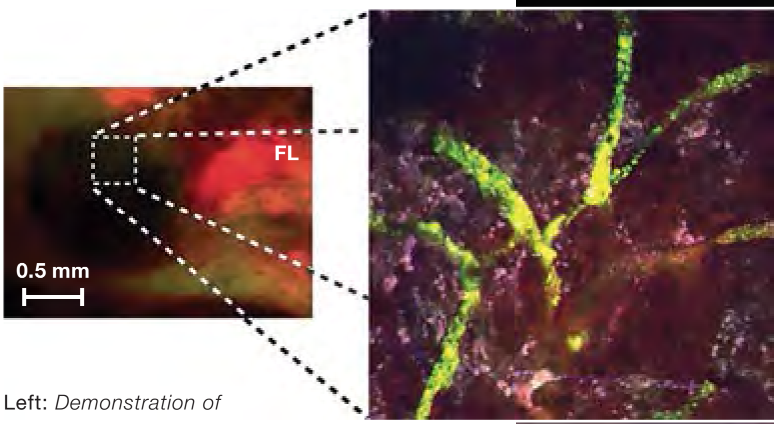
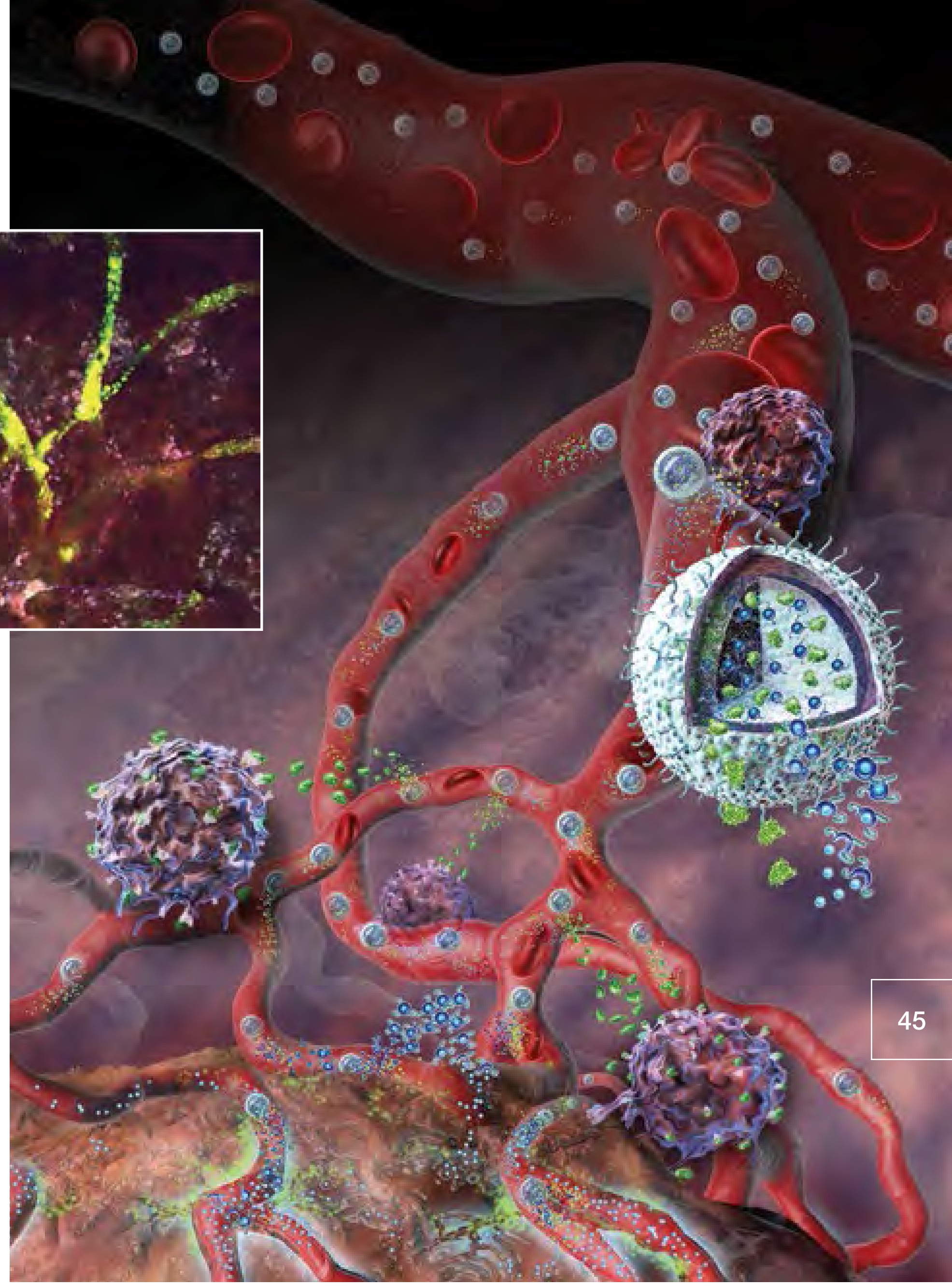
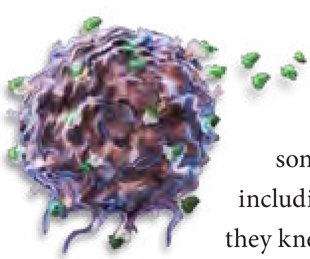




Left: *Demonstration of nanolipogel diffusion within the subcutaneous tumor.* Right: *Illustration of nanoparticles that target and suppress immune cells that induce inflammation.*

The sunblock from Saltzman's lab doesn't pose these risks because it doesn't penetrate skin. And because the nanoparticle is covered with a hydrophilic layer, it essentially locks in the active ingredient, a hydrophobic chemical called padimate O.

The idea for the sunscreen came while they worked on a nanoparticle for intravenous injections that wouldn't attract proteins, which leads to a dangerous uptake in the liver. Then they tried something that had the opposite effect. They gave the nanoparticle a polymer-based coating rich in aldehyde groups, which "stick tenaciously to proteins."



They couldn't use it for intravenous drugs, but figured that something so bioadhesive had to be good for something. So they tried a few things, including applying it to skin. That's when they knew they were on to something.

Tarek Fahmy, whose lab is right next to Saltzman's, is using nanoparticles for a therapy that would attack cancer microenvironments with a nanoparticle loaded with two drugs. One is interleukin-2, or IL-2, which T-cells secrete as a sort of alarm to the body's immune system. The other is an inhibitor of tissue growth factor beta, or TGF-beta, a protein that all cells in the body secrete.

"TGF-beta is a sign of 'Hey, I'm part of the body, don't attack,'" said Fahmy, associate professor of biomedical engineering and immunobiology. Cancer cells "learn" that signal and they express TGF-beta as well. So if you can inhibit TGF-beta in the tumor microenvironment, you can expose cancer cells as foreign elements.

This combination of agents should be devastating to a tumor, but traditional drug delivery would wreak havoc on the body. That's why Fahmy wants to deliver them inside a nanoparticle right

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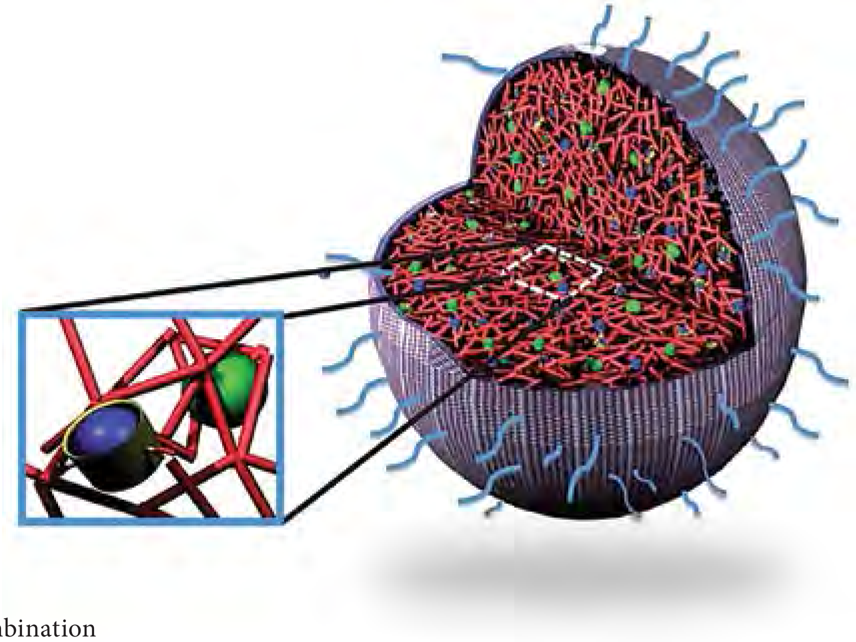
Right: *Fahmy's nanoparticle is loaded with two different drugs that target the tumor environment rather than a single cell.*



to the tumor site. But the two drugs make for an odd couple: TGF-beta drugs are small hydrophobic molecules; IL-2 is a protein 34 times bigger and hydrophilic.

To engineer a way to house them together, he developed a nanogel that encases both with a combination of two polymers, polyactic acid (PLA) and polyethylene glycol (PEG). The researchers then shine a UV light on it to crosslink the agents.

Fahmy excitedly ticks off the benefits of the nanogel. Additional molecules can be added to it (Fahmy compares the system to Legos). It also works in concert with other therapies, making them more effective. Most importantly, it targets the tumor environment rather than a single cell.

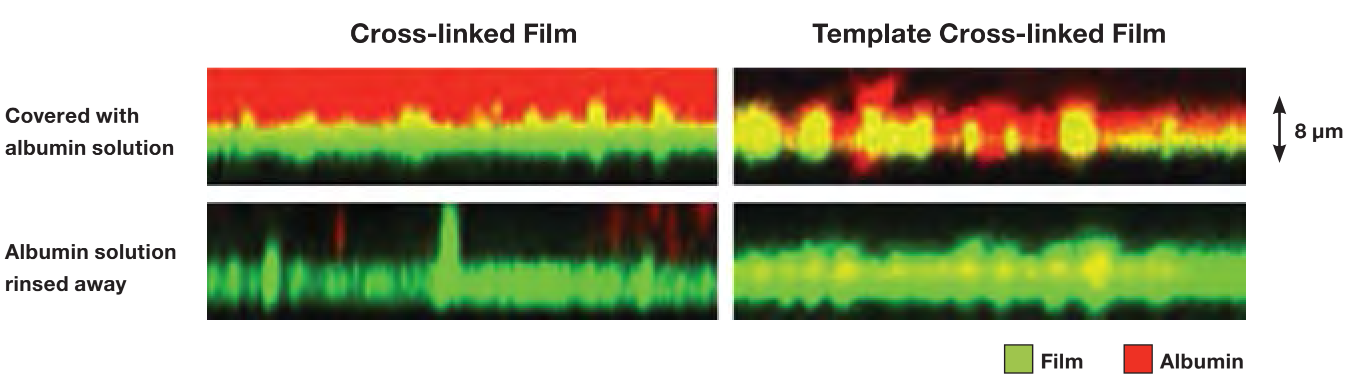
While molecules can pass through the dense tangle of blood vessels that form at tumor sites, the biodegradable nanoparticle that Fahmy's research team created is big enough to get stuck there. He compares it to a large truck getting stuck in a busy intersection.

"We load the nanogel with the TGF-beta inhibitor and the IL-2, we inject it intravenously, and they accumulate in the microenvironment," he said. "And it works spectacularly well."

The Living and the Synthetic, Working Together

The challenge of designing materials that function with biological materials is an ongoing one in the field. Paul Van Tassel, professor of chemical & environmental engineering and biomedical engineering, is well familiar with this. His lab is honing the development of nanofilm biomaterials — multilayered films that serve as the communicator between living tissue and synthetic materials.

Below: *Laser scanning confocal microscopy images of cross-linked films, without (left) and with (right) nanoparticles removed via tetrahydrofuran exposure.*



Van Tassel and his research team build the films layer-by-layer, each the opposite charge of the next, so it all sticks together. Layers of polymers provide the film's backbone, and bioactive species — usually proteins — interact with living tissue. Working out the mechanics of these films is tricky because they tend to be soft. That's great for housing bioactive species, but in many cases, cells aren't adhesive and can't integrate well with such soft material.

Van Tassel and his research team correct for this by chemically bonding the polymer layers, a process known as cross-linking that stiffens the film and makes just the right mechanics for the cells to attach and adhere. But there's a catch: doing so also traps the bioactive species inside the film, preventing interaction with the living tissue.

One promising solution that Van Tassel is working on involves manipulating the pH of the solution in contact with the nanofilm, which diminishes the degree of electrostatic attraction holding the film together. That expands the nanofilm almost to the breaking point. The solution's pH is then returned to the original value, increasing the electrostatic attraction, which causes the film to rapidly contract. Such stresses result in a partial break-up and the formation of pores. Once stabilized, these pores take on bioactive species capable of interacting with living tissue, even after the films have been made rigid through cross-linking.

Van Tassel's lab is applying this technology in his current collaboration with a group of researchers in France. Specifically, they're working on bone replacements, but Van Tassel says his lab's approaches have a broad range of potential applications. Certainly, he said, the demand for this science isn't going away.

"These issues are bigger now than ever," he said. "We fight wars, we play sports and we're wanting to do more things when we're older. So there is a need and there's probably going to be an even bigger need."

About 25 years ago, Kyle Vanderlick, Dean of SEAS, turned her studies of thin films and surfaces toward biology. Doing so gave her lab another set of tools to work with — a cell membrane, after all, is just another thin film.

"I said 'I'm an engineer, and someone's giving me this box of Tinkertoys,'" said Vanderlick, also the Thomas E. Golden, Jr. Professor of Chemical & Environmental Engineering. "What kinds of new things can I make?'"

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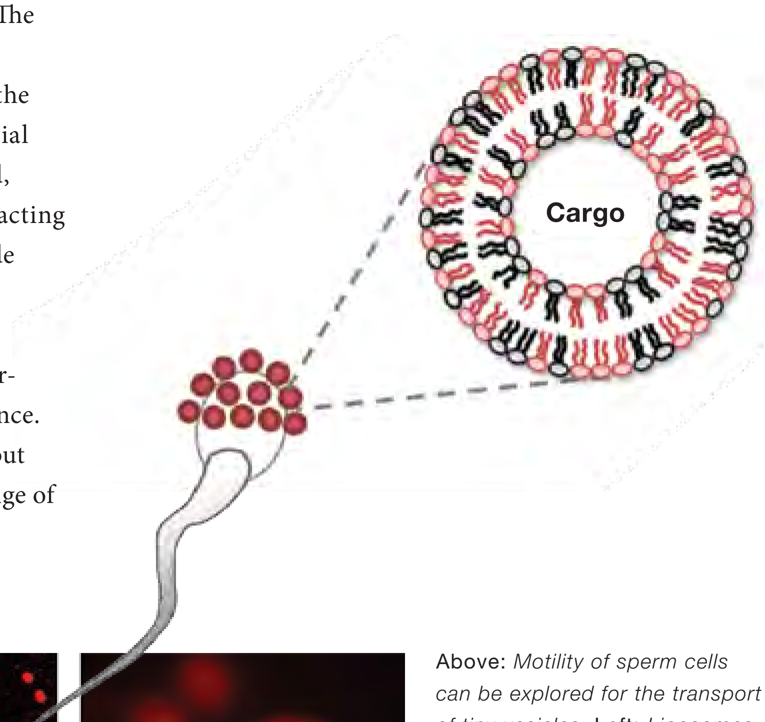
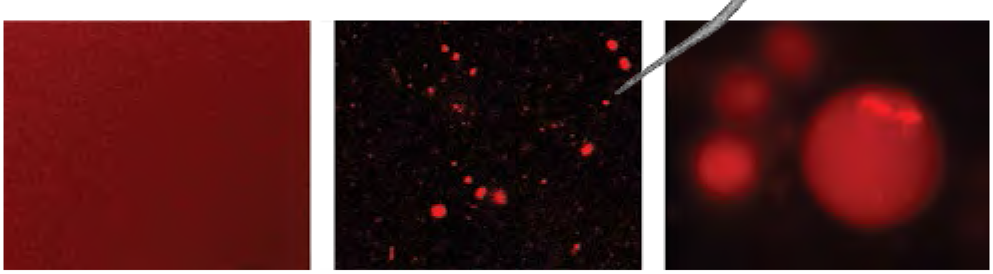
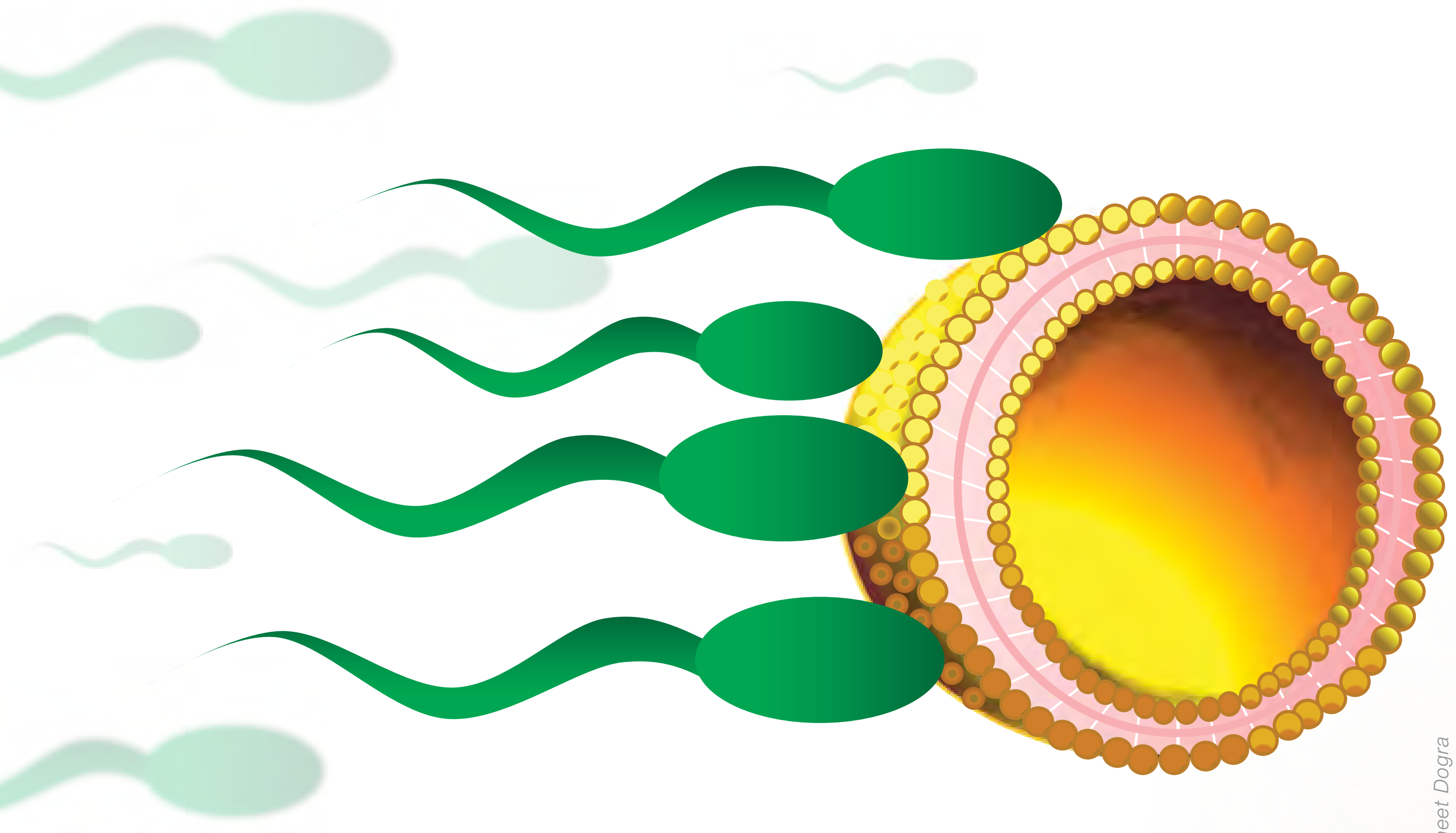




Credit: Navneet Dogra

Above: *Motility of sperm cells can be explored for the transport of tiny vesicles.* Left: *Liposomes can be prepared in multiple sizes. Figure depicts fluorescence micrographs of small, large, and giant vesicles (from left to right).*



Credit: Navneet Dogra

Motile cells can be used as micro-motors to transport cargo vesicles. Above illustration depicts sperm cells transporting vesicles.

A lot, it turns out. Her lab is making good use of tiny cargo systems known as vesicles. These man-made membrane-enclosed sacks are attractive to researchers for a number of reasons. Their structure allows them to carry both hydrophobic and hydrophilic molecules, and they can be made to mimic human cells close enough to manage the immune response. But they lack self-propulsion, so they need a motor to get anywhere.

They found great success with the sperm cell, which is non-toxic and has potential applications for fertility, contraception and preventing sexually transmitted diseases. The first challenge for the researchers was creating a lipid composition of the vesicles' membranes that would attach to spermatozoa. After a few experiments, they used two uncharged lipids that each attach to sperm because of their structural similarities to hyaluronic acid, which is known to bind strongly to sperm.

With that accomplished, the researchers then had to make sure that the sperm would still function as a sperm. "After you find a way to link these vesicles to the sperm, you realize there's a possibility that the sperm might be really angry and decide not to swim anymore," Vanderlick said.

"But that didn't happen. The sperm's behavior was minimally altered by the attached vesicles, and its swimming ability wasn't hindered."

Most important of all, the attached vesicles do not prevent a sperm from fertilizing an egg. Using eggs and sperm from mice, the researchers found that vesicle-laden sperm could fertilize as well as any other sperm. The researchers could also see — thanks to a phosphorescent cargo — that the vesicles had penetrated the egg's membrane along with the sperm.

Using vesicles, the spermatozoa in the Yale team's research could deliver virtually any molecule that can be dissolved in water, making it a cargo-transporting system with numerous potential applications. Vanderlick's lab is now exploring other tiny and promisingly useful motors to see what other advances they can make with biology's seemingly endless box of Tinkertoys.

The Once Lowly Polymer Gets Its Due

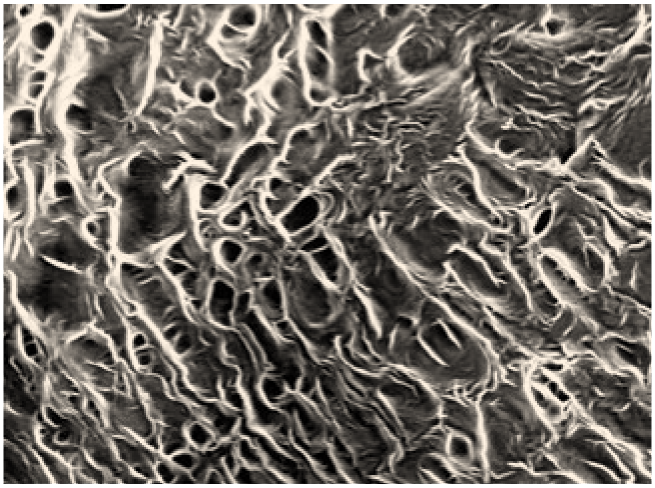
The German chemist Hermann Staudinger, who pioneered polymer research in the 1920s, suffered the barbs of fellow scientists for studying "such disgusting and ill-defined compounds." The prevalence of polymers today makes it hard to imagine life without these materials, which are characterized by their macromolecular structures. And there's certainly no longer any question about their value to researchers.

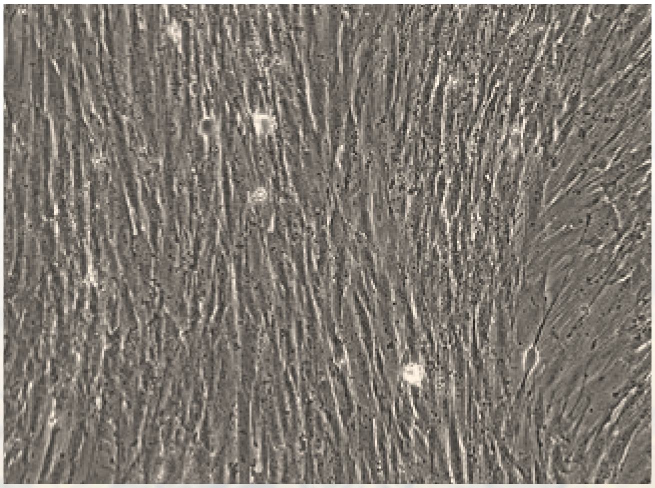
Anjelica Gonzalez, the Donna L. Dubinsky Associate Professor of Biomedical Engineering, uses polymers in conjunction with human cells to make a better model of the vascular system and show that pericytes — a much-overlooked cell — play a bigger role in inflammation than anyone thought.

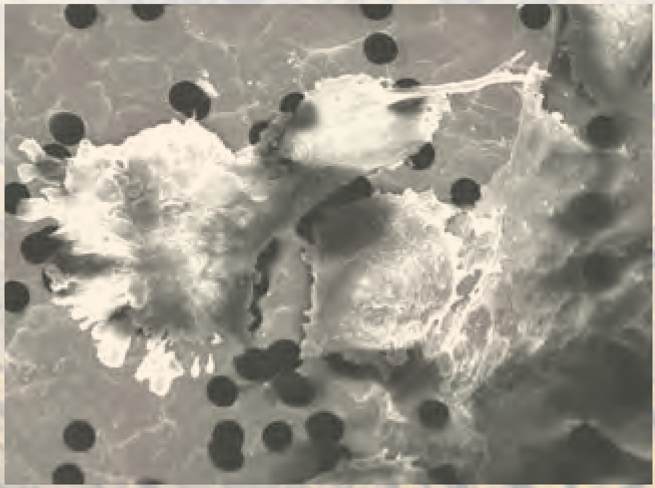
Pericytes are difficult to isolate from humans, which limits researchers' ability to closely examine them. They've mostly been considered little more than structural support to the small blood vessels that they wrap around. But Gonzalez and her collaborators have come to understand that they can also create an extracellular matrix, which Gonzalez describes as the material that both supports cells and tells them where to go.

Her lab is creating models of the human extracellular matrix that look and perform as those created by pericytes. Like other researchers, Gonzalez uses a polymer hydrogel to build the matrix scaffold. Gonzalez's lab goes one step further by creating pores in the structure — much like the architecture of the real thing — by instilling soluble crystals that leave tiny holes after dissolving.

Realism is important because Gonzalez is making the extracellular matrix biologically functional by creating an infrastructure that allows her to add vascular cells to it. Those cells can attach to the scaffold and start migrating across and through it to create little tubes that will





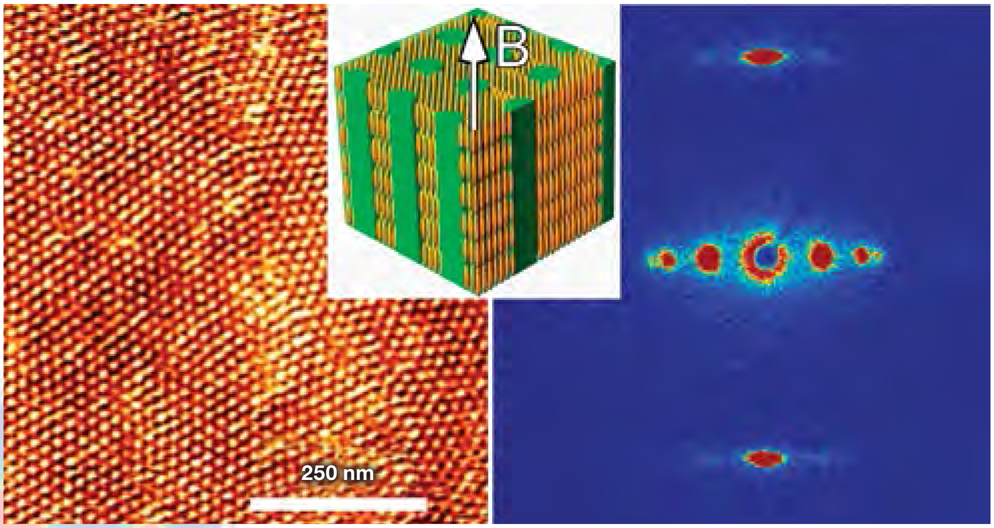


Top: *Salt leached polyethylene glycol hydrogel model of extracellular matrix.* Middle: *Human cells grown on synthetic extracellular matrix model.* Bottom: *Pericyte developing on a porated polycarbonate transwell.*

Continued →

ultimately be vessels. "We're getting much closer to mimicking the smallest human vessels than people have before," Gonzalez said.

By getting a closer look at what the pericytes are doing, Gonzalez has found that these cells contribute significantly to the shape and properties of the extracellular matrix. That means they're influencing the formation of blood vessels, and that certain pericytes potentially play a significant role in inflammation. The body's attempt to heal itself, inflammation is what happens when white blood cells gather to the site of injured tissue. It's a good thing in most cases, but it can sometimes lead to fibrosis, the scarring of tissue.



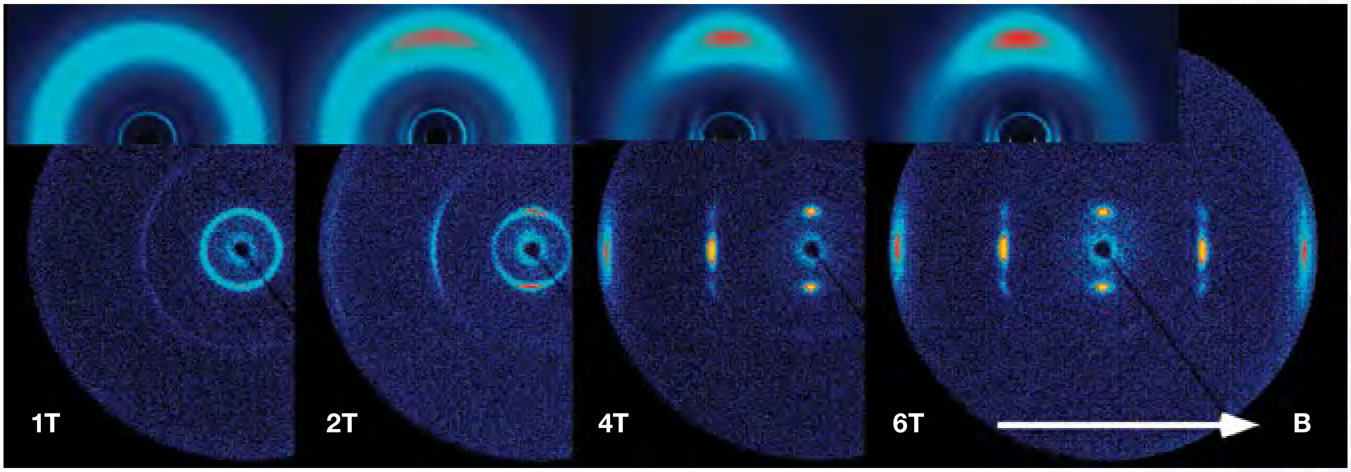
She wants to use this information about pericytes to treat inflammation before it becomes fibrotic disease. Her lab is now studying drugs recently approved to treat pulmonary fibrosis to see what effect they may have on pericytes.

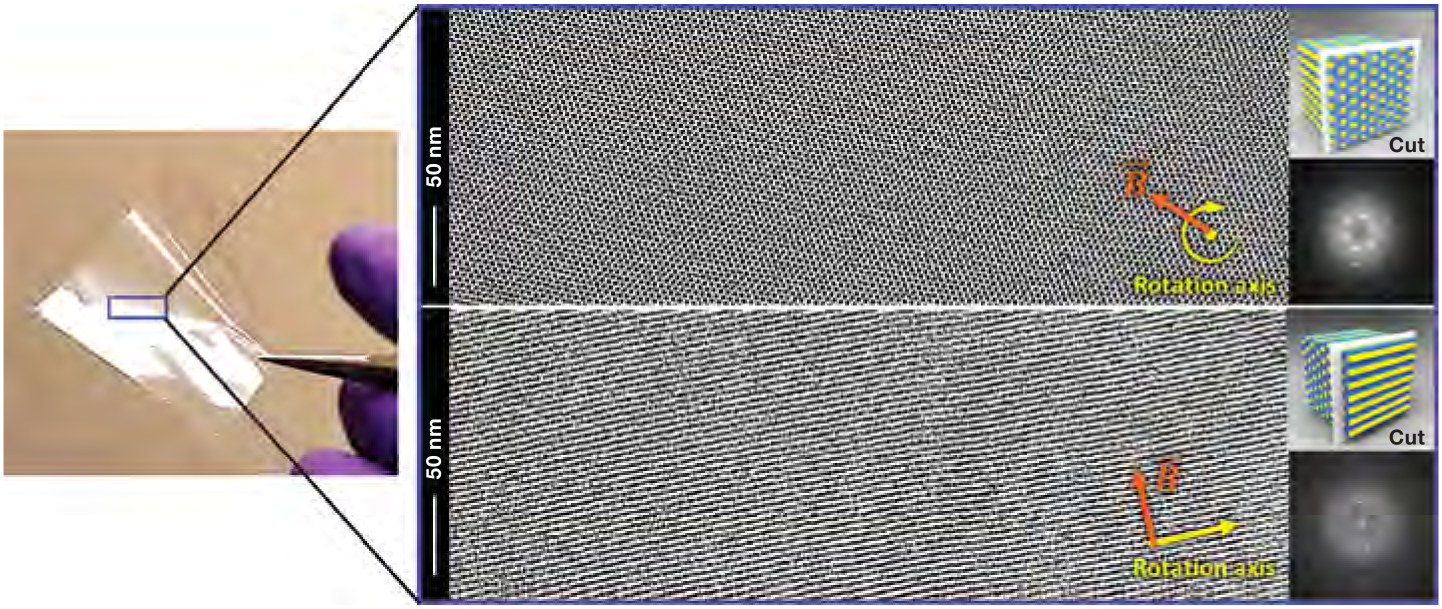
Block copolymers, self-assembled nanostructured materials made from blocks of chemically dissimilar polymers, have long been useful for making things like comfortable shoe soles and hand rests. Chinedum Osuji, associate professor of chemical & environmental engineering, has bigger plans for them.

Top: *Atomic force microscopy (left) and X-ray scattering data (right) illustrate magnetic field control of the orientation of self-assembled nanostructures.* Bottom: *X-ray scattering data shows progressive alignment of nanostructures with increasing field strength.*

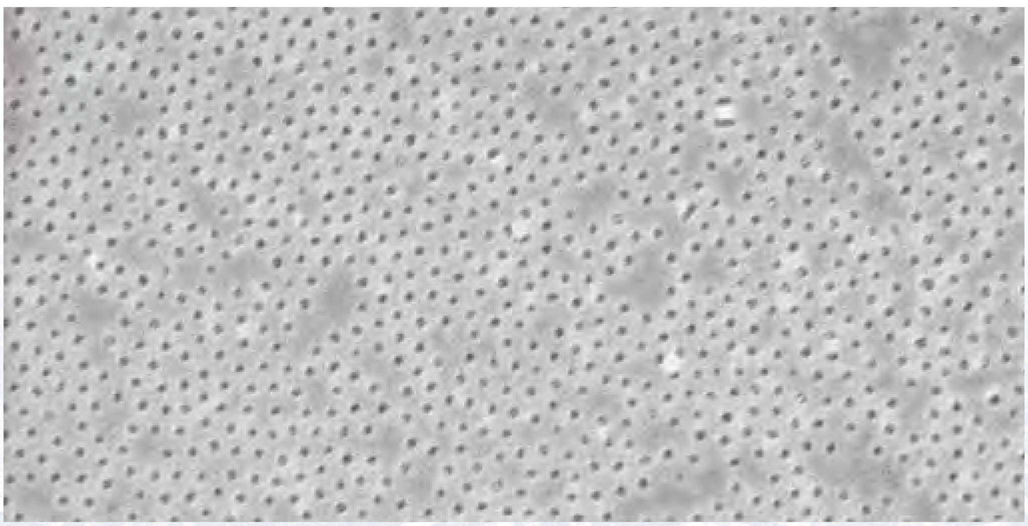
With what's known as directed self-assembly, his lab transforms these nanostructured materials into something new, with novel properties that lend themselves to applications that could bring us everything from cleaner water and more efficient solar energy, to improved drug delivery methods and the next generation of computing.

Specifically, he's developing ways to accomplish this in thin films over large areas. It's one thing to control and transform the structure of a material; doing so on a scale large enough and making something useful from it is a whole other issue. Scientists have done so to great success with silicon, for





Top: *Surface and magnetic field alignment create highly ordered, densely packed and vertically aligned nanopores in a thin polymer film.* Right: *Electron microscopy image of aligned nanoporous block copolymer films.*



instance. But soft matter systems, such as block copolymers, have proven surprisingly difficult in this regard.

Osuji is working on a few promising solutions to this; one involves magnetic fields. Cylinder-shaped structures, known as microdomains, form during the self-assembly of block copolymers within a certain composition and temperature range. While the shape of the resulting microdomains is well-defined, their orientation over large length scales is not. Left to their own devices, the microdomains point every which way. To make a high-performance filtration membrane using the microdomains as pores, Osuji said, all of the microdomains must be aligned in the same direction and perpendicular to the surface of the film. This enables fluid or any other permeant moving through the membrane to do so in a straight line

To make this happen, Osuji uses a magnetic field to orient and align microdomains to form membranes; the effect is similar to a compass needle's alignment. And by using a novel type of block copolymer chemistry, the researchers can use temperature to tune the dimensions of the pores on the fly, and determine what particle size — if any — is allowed through. Among many other applications, that's useful for ion removal for water-softening, or the removal of organic dyes from water.

"Our work lends itself to applications in devices relevant to clean water and clean energy generation," Osuji said. "And we can do that in a way that is categorically different than how it's currently done."

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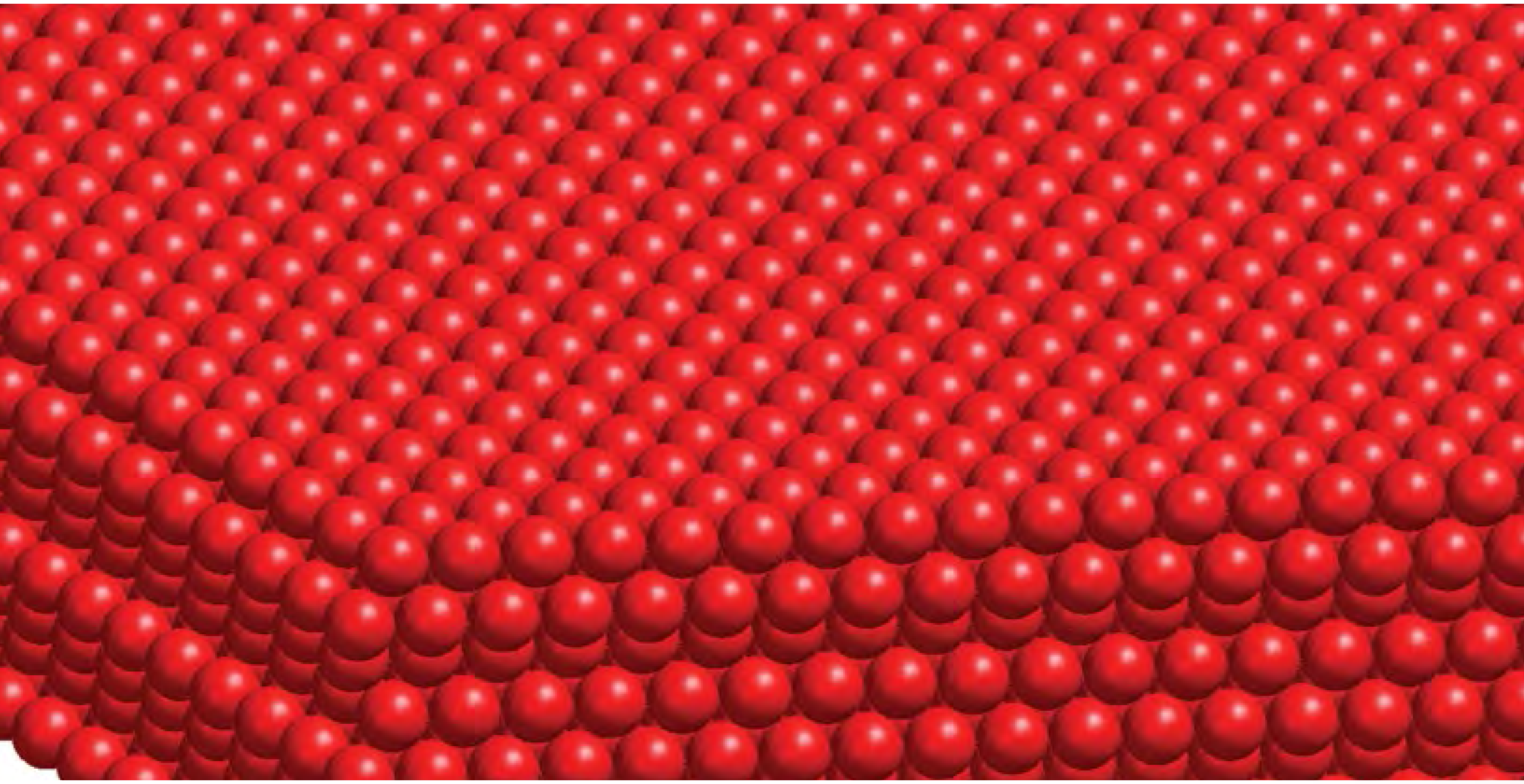
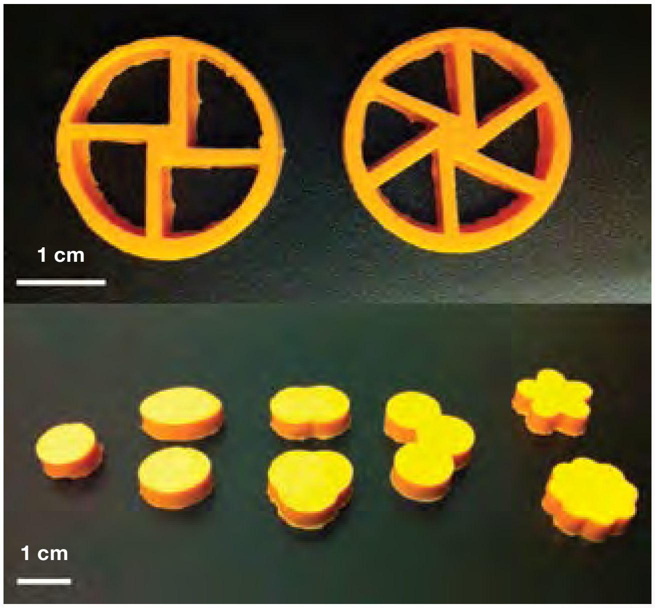


The Science of Jamming, from Earthquakes to Cornstarch

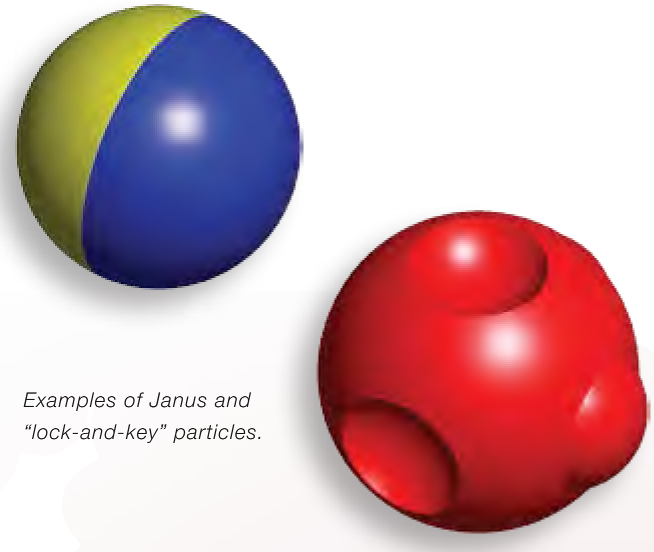
Science has solved countless long-standing questions, from those at the molecular level to the surface of Mars. Yet the exact mechanics of why jellybeans jam up at the mouth of a jar still confounds. It's a phenomenon aptly known as "jamming," and is part of an area of soft matter research that deals with everything from fine powders to collections of rocks.

Corey O'Hern, associate professor of mechanical engineering & materials science, physics and applied physics, notes that it takes only a few macroscopic quantities such as pressure and temperature to fully characterize the behavior of atomic and molecular systems. That's thanks to Josiah Willard Gibbs' fundamental contributions to statistical mechanics and thermodynamics here at Yale in the 19th century.



Top: *Surface reconstruction of a 3D magnetic resonance image of a face centered cubic granular crystal created layer-by-layer in experiments of packings of silica beads.* Bottom: *Silicone rubber particles with different shapes and material properties created using 3D printed mold.*

But many recent studies have shown that relationships between macroscopic quantities, such as pressure and temperature, don't hold for systems composed of macroscopic particles. That's why there are still so many ques-



Examples of Janus and "lock-and-key" particles.

tions about what triggers an avalanche or earthquake, why birds' nests are so sturdy, or what causes riverbed erosion — all phenomena that O'Hern's lab has explored.

"Earthquakes are caused by slips, so you're trying to figure out how much load a certain fault zone can withstand before slipping, and then determine the frequency of the slips of each size," O'Hern said.

To do that, he develops computational models of grain-to-grain contacts, performs simulations of large collections of grains, and calculates the applied force needed to make them flow, a process known as yielding or unjamming. He starts with simple models, grains that are spherical and smooth. For subsequent studies, he adds new complexities to the models by including non-spherical particle shapes with rough surfaces.

He can then determine how each property — the roughness or shape, for example — contributes to the yield strength of the material, bringing him a little closer to understanding the mystery of these materials' behaviors.

"When granular materials begin to flow, we don't know when they will stop," O'Hern says. "And when they are at rest, we don't know the size of the perturbations that will cause them to flow."

Just as researchers seek to understand how granular materials flow, they're also

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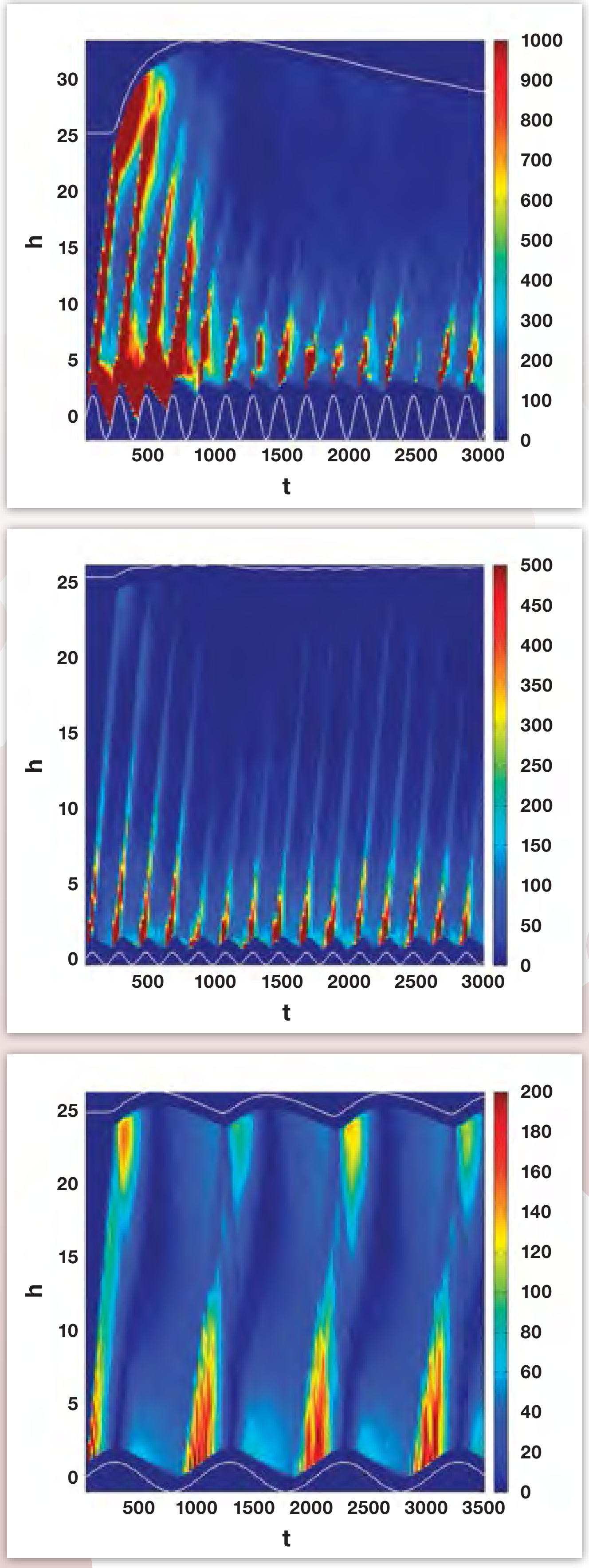


Contour plots of the kinetic energy as a function of height and time after vibrations were introduced in numerical simulations of inelastic hard disks confined within a box.

High-speed camera captures of various objects impacting suspensions of cornstarch and water demonstrating its solid-like properties. Clockwise: Bowling ball bouncing, foot running on the surface, raw egg bouncing, and a laboratory test displaying cracks in the fluid.

looking at the reverse — when flowing particles jam into a solid-like state. Eric Brown, assistant professor of mechanical engineering & materials science, is seeking answers in a lab filled with high-tech equipment and Argo cornstarch containers.

The combination of water and cornstarch offers a fascinating phenomenon. Fill a pool with this liquid and then run on it. Keep running, and you might as well be on a hard floor. Stop running, though, and you sink right in. That's because it's really good at responding to impact, for reasons that aren't entirely understood.

Brown suspects that the impact causes the particles to collide and form solid contacts, similar to a jamming effect. To better measure this material's unique response to impact, Brown and his team have developed a special rheometer to measure the effect. A high-speed camera captures what happens when a rod is jammed into a container of the solution. One thing they noticed is that it actually causes cracking. "Fluids don't crack, so that's one of the things that tells us it's behaving like a solid," he said.

But only for a few seconds; then it goes back to a fluid state. The potential for this is huge. Crack a bike helmet, and you have to get a new one. But what if it were made from material that heals itself? Understanding the phenomenon could lead to a very flexible material used to make better bulletproof vests and sports padding.

Brown said they're about "halfway there," to finding real uses for this quirky phenomenon.

"The thing we don't understand still is, how does it transition into a solid?" he said. "We can tell that it does, but don't know exactly what's happening at the microscopic level, so that's something we're still trying to understand. That's one of the open research questions."

Butterflies and Bacterial Motors

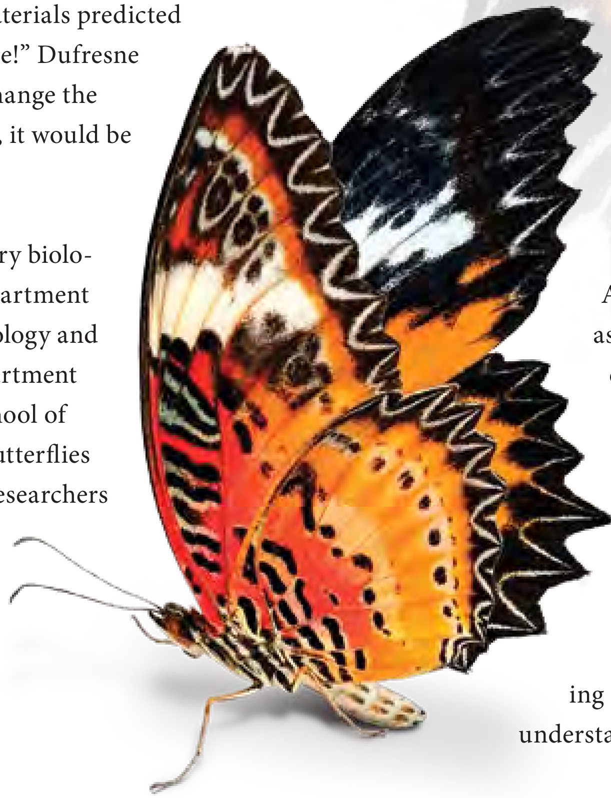
"Engineers can build awesome things out of traditional materials, but none of those things are as cool as what evolution has made out of soft materials," says Eric Dufresne, associate professor of mechanical engineering & materials science, biomedical engineering, cell biology and physics. For proof of this, just look at the butterfly.

About 30 years ago, researchers predicted something known as photonic bandgap materials, which would essentially serve as a semiconductor for light. It's even been proven that these materials can be made — and that would usher in a new era in the field of optics. Actually making them in sufficient quantities, though, is no easy trick.

Various strategies have been tried, without much success. Butterflies, though, have renewed researchers' hope. Dufresne was part of a team a few years ago that discovered structures in butterflies called gyroids. They're 3-dimensional, curving, crystal nanostructures that selectively scatter light and are responsible for how butterflies get their colors.

Gyroids interest Dufresne because they're almost — but not quite — one of the materials predicted decades ago. "It's, like, so close!" Dufresne says. "And if you could just change the material properties a little bit, it would be one of these materials."

He's working with evolutionary biologist Richard Prum in the Department of Ecology & Evolutionary Biology and Pietro De Camilli in the Department of Cell Biology at the Yale School of Medicine to figure out how butterflies make this structure — then researchers can copy what the butterflies are doing.



And that could lead to such advances as better optical devices and more efficient solar cells. It's one more reason Dufresne is convinced that nature's stock of materials is still the gold standard.

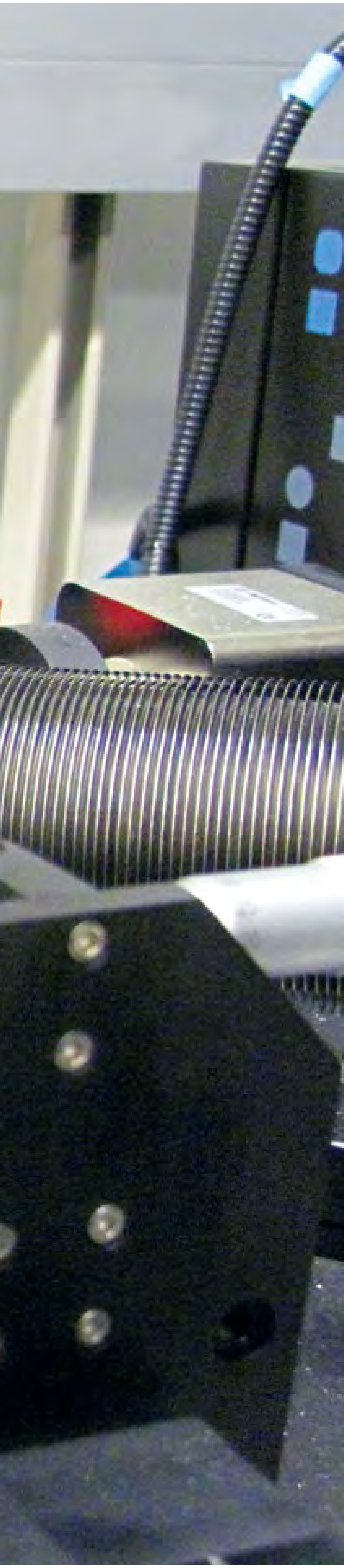
"Most living things are made out of soft materials," he says. "Engineers aren't capable of designing anything like that because we don't understand how they work."

Yale

TECHNOLOGY

An Old Material Made New

Fengnian Xia explores the bright future of black phosphorous



Black phosphorus was once a material ahead of its time. In the early part of the 20th century, it piqued the curiosity of physicist Percy W. Bridgman, who was the first to publish on its properties. Bridgman went on to great acclaim for his investigations into matter under high pressure and won the Nobel in Physics in 1946. Black phosphorus, on the other hand, was swept into the dustbin of history. Mild interest in it returned in the 1980s, when researchers looked at it for its potential use in electronics. By that time, though, the prevalence of silicon didn't leave much room for black P (as it's sometimes known). And once again, it was pretty much forgotten.

But if the world of allotropic elements was ever in need of a great comeback story, black phosphorus is in good position to answer that call. Fengnian Xia, assistant professor of electrical engineering, is confident that it could happen. He has spent his two years at Yale so far concentrating on black phosphorus, and his group is among the first to make transistors with the material. His group was also the first to explore the unique optical properties of monolayer and thin film properties and reveal their potential in various applications, such as imaging and optical communications.

Technology and our needs have now caught up with what black phosphorus has to offer. That's largely because the race to make electronic components even smaller continues, while the ability to do so with silicon is reaching its limit. Black phosphorus could potentially be used to make transistors with a thickness of just a few atomic layers. If it's everything researchers hope, we could soon have faster transistors, better imaging devices and more sophisticated night vision technology. It could also usher in a new generation of smaller devices and flexible electronics.

At IBM, where Xia worked before coming to Yale, he focused on graphene. A very popular two-dimensional material, researchers began to look at it seriously around 10 years ago. The high mobility of the material's carriers (the electrons or electron holes) made it a promising candidate for electronics and photonics.

The major problem with graphene is that there's no bandgap — an energy range that electrons can't get into. "The reason we need bandgap is so that we can switch the transistor to the on-state or the off-state," Xia said. "We also want a very solid off-state so that power consumption can be minimized."

Black phosphorus has a mobility of about 1,000 centimeters squared per volt-second at room temperature. That's only about one-tenth of graphene's mobility, but it's still pretty fast. In fact, of the 100 or so known layered materi-

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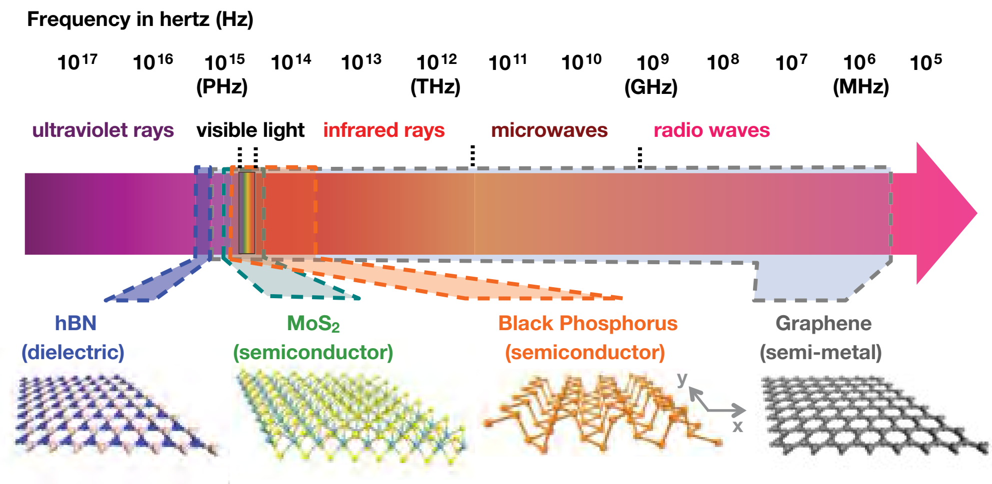


Two-dimensional materials can cover photonic applications in a very broad wavelength range from microwave to ultraviolet.

als, black phosphorus has the next highest mobility after graphene. But unlike graphene, it has a bandgap, which makes it very valuable.

An Investment in the Future

The field of low-dimensional materials and devices is an extremely competitive one, said Hong Tang, professor of electrical engineering, physics and applied physics. Tang chaired the search committee that hired Xia, and noted that Xia was chosen out of a pool of more than 200 candidates. It's a hot area of research right now, Tang said, but many are in it only until the next big field of research comes along.

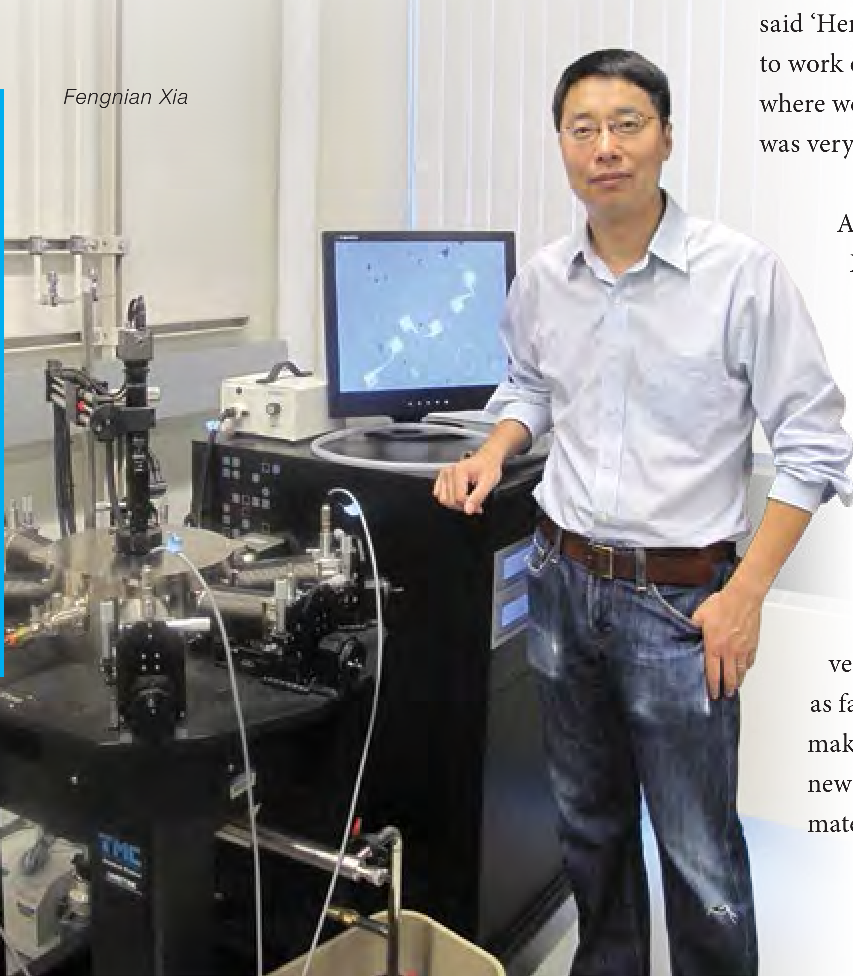
"I think with Fengnian, it's long-lasting — it's not something temporary," he said. "We saw that he came with a very solid semiconductor background, so that really distinguished himself."

Tang recalls an early meeting his committee had with Xia. "I remember he went to the white board, and he said 'Here's the state of the art, here are the ideas I want to work on, here's the space I want to occupy, and here's where we can take a leadership role in the field.' So that was very impressive."

And in the short time he's been at Yale, Tang said, Xia has secured many grants in a field where they're not easy to come by. He's also received several major awards, including the Young Investigator Award from the Office of Naval Research, which he won this year.

Until now, Tang said, Yale hadn't done much as far as researching low-dimensional materials. But the state of semiconductor technology called for a change. "We look at it as a future investment," Tang said. "Today, we are really cornered as far as semiconductor technology — you cannot make smaller and smaller chips, you have to look for new solutions. We think the new materials will play a big role."

Fengnian Xia



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A Lesson Comes Alive, Thanks To a Can

Combine some inventive teaching minds and an empty Arizona Tea can, and you have the makings of a good lesson plan.

The students of EENG 203, co-taught by Hong Tang and Fengnian Xia, learn how to make a radio transmitter out of an aluminum can. Specifically, they build circuits that can receive a signal from an iPod, which then turns that signal into the equivalent of an AM radio station. That AM radio signal is sent out via antenna — which is where the aluminum can comes in.

The idea for the lab experiment came from research support specialist Kevin Ryan, who assists SEAS faculty with electronics and electrical engineering systems like those used in this lab.

"An antenna can really be just a piece of wire," Ryan said. "But connecting that piece of wire to a can gives the antenna more surface area, thereby increasing the area and shape of the transmitted signal. The same sort of technology is used in wireless transmission, so the radio receiver is essentially a wireless speaker."

In the end, the students were able to apply the theoretical and mathematical concepts they learned in class, while picking up some soldering skills.

Tang and Xia thought it was a great idea.

"Lectures can be very boring," Tang said, laughing. "We just wanted something new. We wanted students to see more than just the circuit board."

The two professors say they'll make it a permanent part of the course, which is required for all Electrical Engineering majors. "One big thing we really want to do is enhance the lab components, so the students have a chance to really play with the circuits," Tang said.

For Xia, working with Tang has been a big part of his introduction to teaching. Coming from IBM, Xia's work had been strictly research, and he had never taught before. When he arrived at Yale, he knew that there would be greater freedom to pursue certain research projects.

"I think the most attractive thing in academia is the freedom," he said. "You don't need anyone's approval before you decide to work on something."

But the teaching part of his job, it turns out, has also proved rewarding. "Teaching is interesting," he said. "If you spend time, devote yourself, you'll get good results. You just focus, try your best, and then you will have confidence teaching."

And by explaining certain ideas to his students, he ended up getting new ideas for his own research.

"One of the courses I taught, about microelectronic circuits, kind of inspired me to write one of my proposals to the Navy," Xia said, adding that his early research on black phosphorus focused mainly on photonics. "So I taught this course, and thought it was a good idea to expand it to black phosphorus electronics. I wrote this proposal, and fortunately, it got funded. And that's one of the directions we're trying to explore."

Top: *Cheng Li, a first-year graduate student in Xia's lab, measures transistors made from new materials.* Bottom: *Heterostructure light-emitting diodes can be constructed using different two-dimensional materials.*

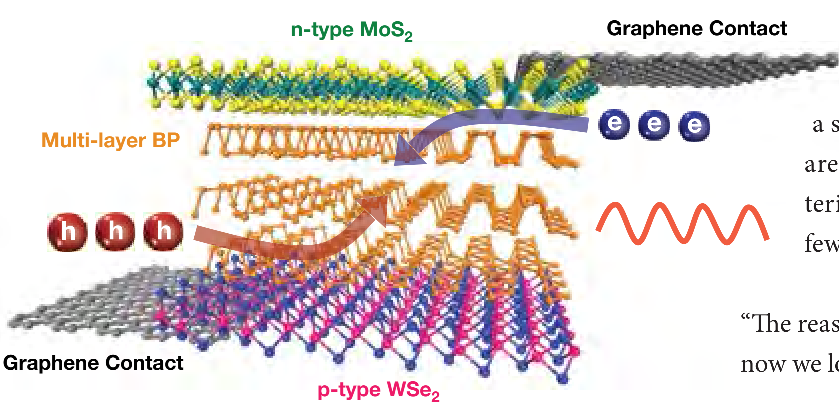
Making the Old New Again

Graphite and phosphorus have been around forever, but advances in researchers' capabilities can make new use of them.

"What's new is that people can extract a single layer or a few layers from the graphite," Xia said. "When we do that, the properties of these materials become very, very different from their 3D parental materials due to the quantum confinement along the direction perpendicular to the layered planes."

Traditional 3D materials, like silicon, are tightly bonded throughout, so it's impossible to extract individual layers from it.

Xia and his research team found some unusual optical properties when they looked at a single layer of black phosphorus. In layered materials, the electrons usually move in different directions, but the electrons of black phosphorus move in one direction, due to the material's crystalline symmetry.



To explore this further, they shined a light on a single piece of black phosphorus. "We excited the material with some high-energy photons — then, we looked at the emission of photons, the photoluminescence," he said. "Regardless of the polarization of the light we used to excite the material, the emitted light from the material is always polarized along one direction. So this is something very unique."

That opens up other possibilities, such as using the material to make a polarized light source for an integrated photonics chip.

Xia is also working on how to prepare black phosphorus on a large scale. He and a team of researchers recently succeeded in using very high pressure to convert red phosphorus to black phosphorus. There's still work to go, but it's a significant step toward making the material usable for realistic applications.

Black phosphorus itself isn't any different from what it was 100 years ago when Bridgman wrote about it. But a lot of other things have changed, and quantum mechanics has a lot to do with it.

"The quantum confinement of carriers within a single layer of atoms makes a difference — they are no longer explored as a bulk, 3-dimensional material," Xia said. "Instead, we focus on their single, few-layer, and thin-film formats.

"The reason all of these materials get popular again is that now we look at them from a very different perspective."

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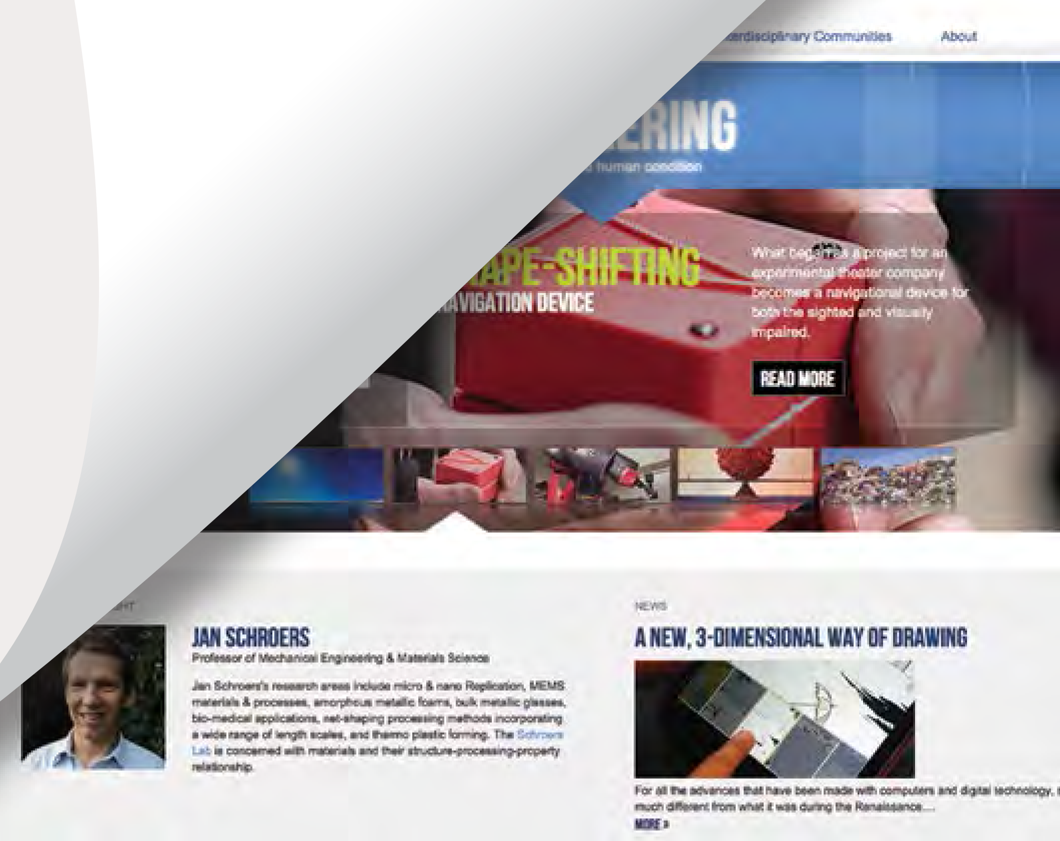

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