Personalizing Medicine for the Future

A first-of-its-kind degree trains doctors and engineers to speak the same language

Computer Science 2.0

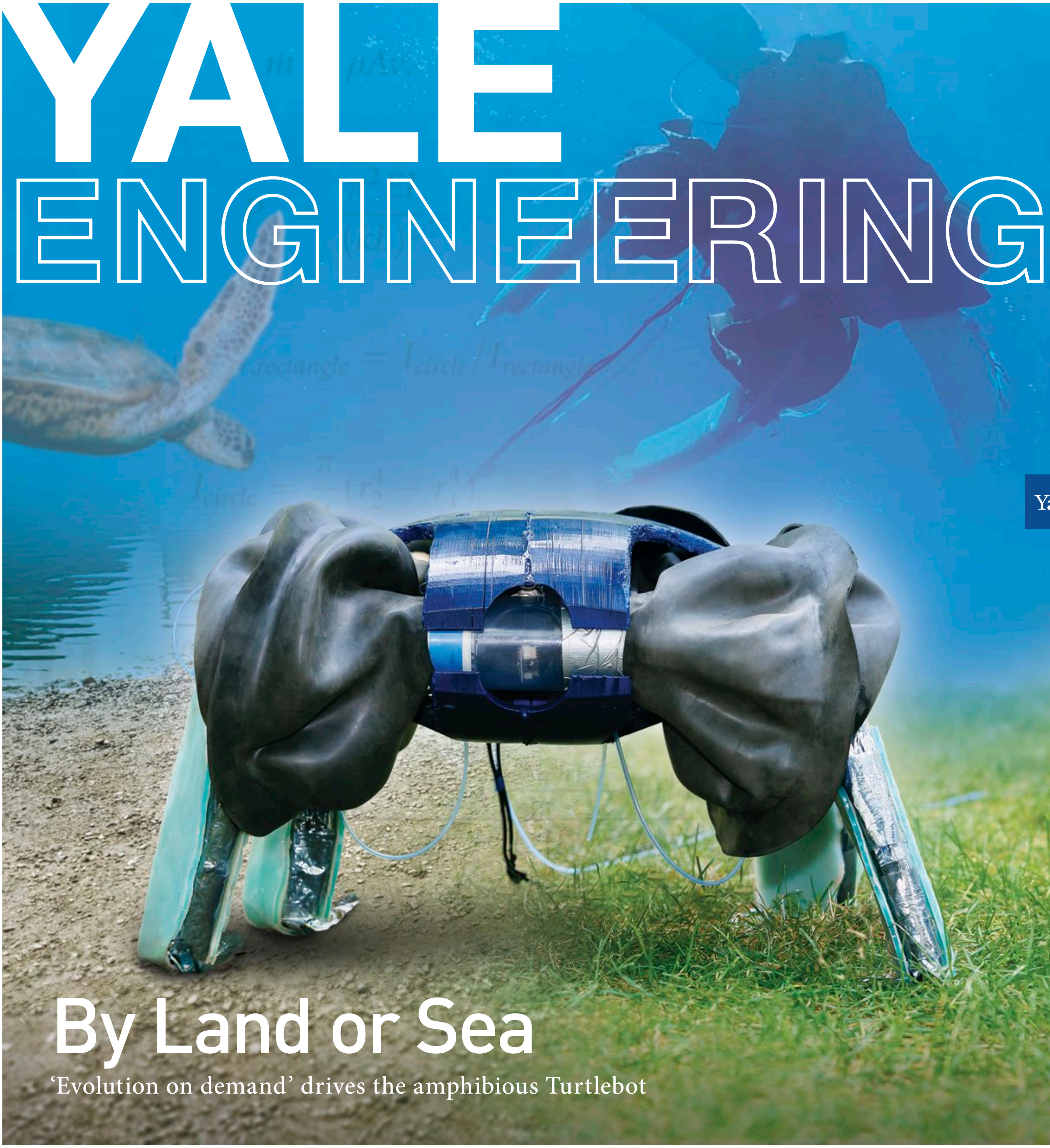
Explosion of faculty, courses, and research ushers in a new era for Computer Science at Yale

Entrepreneurship at SEAS

Faculty-led startups thrive, firing up the engine of innovation

2022-2023

YALE ENGINEERING



By Land or Sea

'Evolution on demand' drives the amphibious Turtlebot

Yale

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

In This Issue

YALE ENGINEERING 2022-2023

Front Cover: *Developed in the lab of Rebecca Kramer-Bottiglio, the Amphibious Robotic Turtle's limbs morph in shape, stiffness, and volume to transition between flippers and legs, allowing it to efficiently travel through water, land, and other terrains.* Photo: *Tony Fiorini*

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Message From the Dean

The past year marked a transformational moment in the history of Yale's School of Engineering & Applied Science, including the separation of SEAS as an independent faculty from the Faculty of Arts and Sciences. I am honored to lead the School as we realize our ambitious vision to build a culture of innovation, inclusion, and excellence.

It was in further recognition of the value and importance of our Strategic Vision that Yale recently announced the expansion of SEAS — both in faculty size and physical space — to unprecedented levels. The transformative impact this development will have on SEAS and on Yale underscores our School's importance as a destination for collaboration and innovation and as a portal for translational research.

As you'll read in this issue, progress towards our goals is already well underway. In the past year, we dramatically increased the size of our Computer Science faculty, onboarding excellence in cybersecurity, AI, machine learning, robotics and quantum computing, positioning SEAS to lead the development of society's critical technologies.

And it's not just in the lab that you can find our researchers' innovations. In this exciting volume, you'll learn of the amphibious turtle-inspired robot that could one day be assisting the military, the environment, or in a number of other fields, advancing our aim to become a world-leader in what we call "Robotics for Humanity."

On the 10th anniversary of the Center for Engineering Innovation & Design, we highlight the many achievements that exemplify our School's ethos of creativity. Along those lines, we feature successful SEAS startups specializing in everything from cryptocurrency security to heart disease.

SEAS' excellence attracts unique and cutting-edge partnerships from all corners of campus. These include the SEAS-School of Medicine collaboration on a first-of-its-kind degree in personalized medicine. Elsewhere at SEAS, you'll learn of scholars in the humanities working with computer scientists to unearth clues to a lost society.

Yale's forceful embrace of the centrality and importance of SEAS is nowhere clearer justified than in the creative and innovative solutions you see animated in these pages. Our future is bright, and our purpose and mission on behalf of our community and our home University has never been stronger.

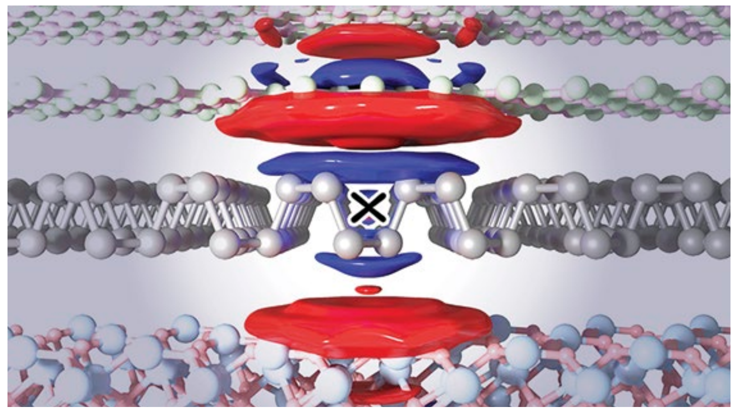
Jeffrey F. Brock
Dean, School of Engineering & Applied Science
Zhao and Ji Professor of Mathematics

Year in Review

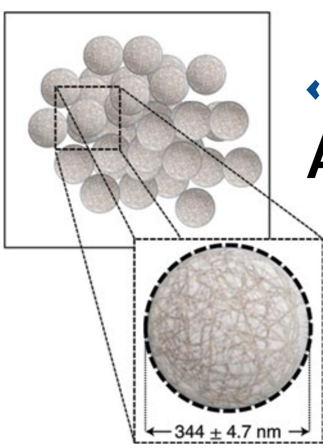
A look back at some of the news stories from the Yale School of Engineering & Applied Science over the last academic year

2021: October

Shedding Light on How Light Works



For her work in studying how matter absorbs light, Diana Qiu, assistant professor of mechanical engineering & materials science, won the Packard Fellowship in Science and Engineering. Qiu will receive $875,000 over five years to focus on excitons — an energy-carrying combination of an electron and a hole, which is a positively charged empty state caused by the absence of an electron. Her research has the potential to advance the fields of solar energy, quantum computing, and optoelectronics.



2021: November

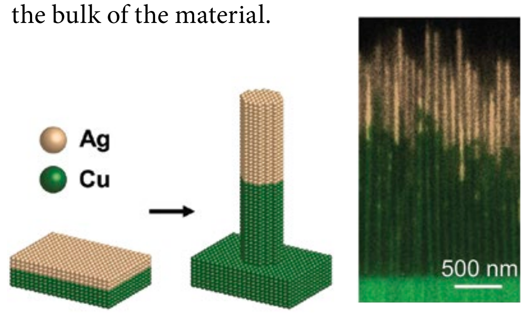
A Diabetes Drug that Does Double Duty

Yale researchers developed an oral medication to treat Type-1 diabetes that both controls insulin levels and reverses the disease's inflammatory effects. The research team, led by Tarek Fahmy, associate professor of biomedical engineering and immunobiology, created a drug with two critical advantages over standard diabetes treatments. It's taken orally, so it's much simpler for patients to stay compliant with their treatment. It also addresses three major issues with diabetes at the same time: it controls immediate blood glucose levels, restores pancreatic function, and re-establishes normal immunity in the pancreatic environment.

2021: December

Nanofabrication, Precisely

With a process known as thermomechanical nanomolding, a team of researchers led by Jan Schroers, professor of mechanical engineering & materials science, developed a highly precise method of nanofabrication. With this method, they can create nanowires of essentially any material. One application is for making inexpensive catalysts. Since the method is very effective at bringing precious metals to the surface of the material, less of these pricey metals are needed, while a cheaper metal can make up the bulk of the material.



2022: January

Quantum Power, with More Reliability

Shruti Puri, assistant professor of applied physics, won a $500,000 Faculty Early Career Development (CAREER) Award from the National Science Foundation to develop a quantum hardware system that will be more resource-efficient and better at correcting system errors. The project aims to fully harness the power of quantum phenomena by making a fault-tolerant quantum computer — that is, a system that reliably executes a quantum algorithm even if some of its constituent hardware components have failed.

2022 : February

Boldly Investing in Engineering's Future

Yale University announced a substantial investment in the School of Engineering & Applied Science that will allow the school to even more aggressively pursue opportunities for breakthrough research and collaborative innovation. SEAS will add 30 ladder faculty slots across the school's six departments, allowing SEAS to increase the size of the Department of Computer Science — the SEAS department with the most undergraduate majors. It will also allow the school to focus on initiatives in artificial intelligence, biological systems, materials science, mathematical modeling, and what it calls "robotics for humanity."

2022: March

A Gripping Advance

When we pick something up, we'll often jostle it around a bit to get the best grip. Researchers have now developed a robotic hand that does something similar — a breakthrough that could advance the field of assistive robots. In the lab of Aaron Dollar, professor of mechanical engineering & materials science and computer science, the team created a robotic hand that can fully rotate various objects even as its grippers occasionally break contact with the object. The device successfully manipulated objects with a variety of shapes, including a sphere, a toy car, a plastic bunny, and a plastic duck.

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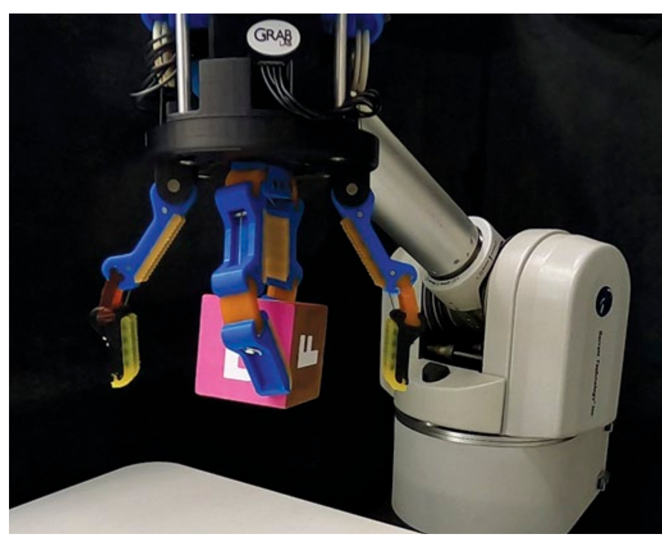


Year in Review

2022 : April

Sparking Innovation

A new initiative was launched to accelerate the SEAS engine of innovation, bolstering the process of bringing impactful faculty discoveries to market. Thanks to a generous gift from Yale alumnus Will Roberts ’90, the Roberts Innovation Fund will provide grant funding, mentoring, and business training to assist in the commercialization of breakthrough inventions that solve real-world problems. The fund’s focus will include technologies that show promise toward having an impact within the domains of artificial intelligence, blockchain, trustworthy computing, computational modeling, and more.

ROBERTS INNOVATION FUND

2022: June

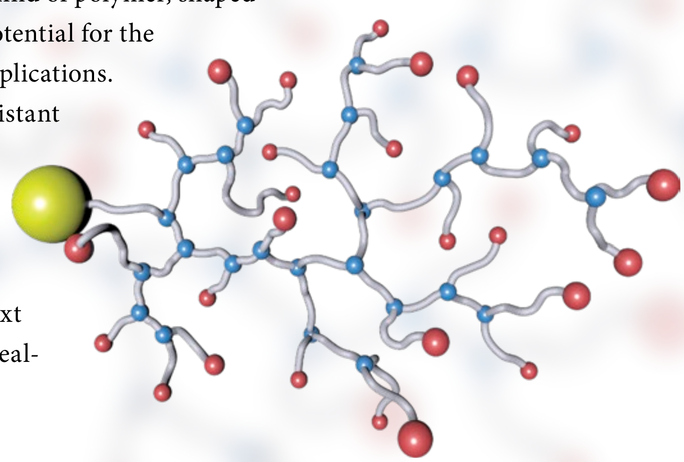
Safe Drinking Water, Brought by the Sun

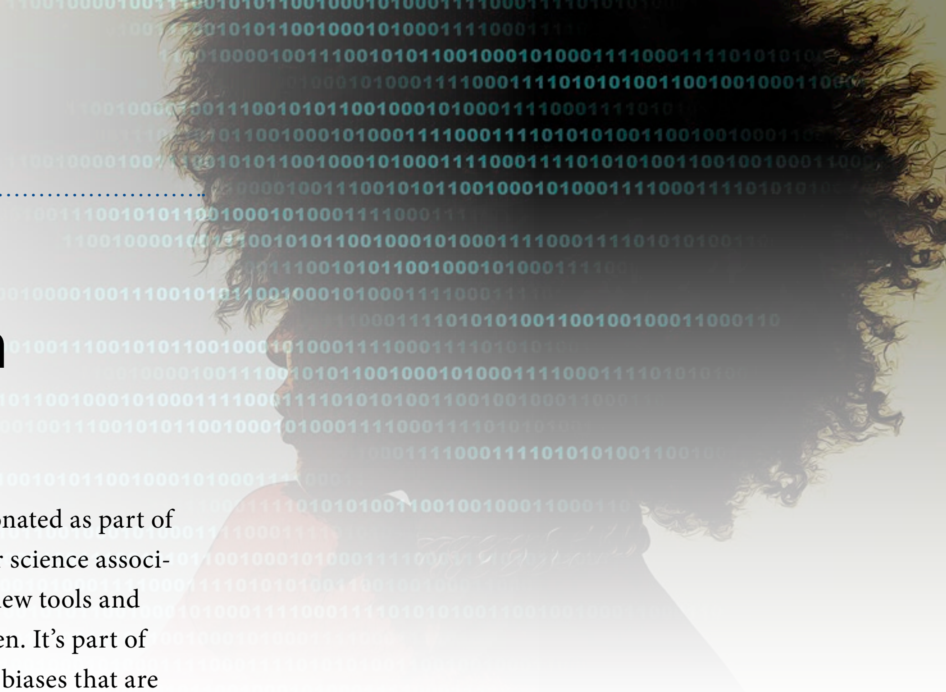
Poor access to safe drinking water is a major issue for a third of the world’s population. Because of the abundant sunlight in many regions most in need, solar disinfection technology has great promise — but it’s unclear which form would work best. In the first such analysis, Jaehong Kim, the Henry P. Becton Sr. Professor of Chemical & Environmental Engineering, led a research team in studying the pros and cons of five of the most common solar-based disinfection technologies. Solar pasteurization, the researchers concluded, may hold the most promise.

2022: May

Polymer Researchers Branch Out

Polymers, which are made of repeat units of small molecules to form a larger molecule, have various structures. One kind of polymer, shaped as if it has tiny tree branches, has significant potential for the biomedical field, nanoelectronics, and other applications. Researchers in the lab of Mingjiang Zhong, assistant professor of chemical & environmental engineering and chemistry, have developed a way to efficiently create these unique structures with a combination of mechanistic experiments and computer simulations. The next step, Zhong said, is putting these materials to real-world uses, possibly for water filtration.





2022: July

Inclusivity Through Algorithms

A $1 million gift from the Bungie Foundation, donated as part of Yale's For Humanity campaign, funded computer science associate professor Theodore Kim's project to develop new tools and algorithms to bring inclusivity to the digital screen. It's part of an ongoing effort to correct the racial and ethnic biases that are often written into the algorithms used to generate virtual humans in animation and graphic design. One focus of the project is to make it easier for software users to create more accurate representations of types of hair characteristic of different racial groups.

2022: August

A Cross-Disciplinary Kickstart for Blockchain

A $5.75 million grant from the Algorand Foundation funded the formation of a Yale-led cross-disciplinary team of experts working to advance blockchain systems, while exploring their connections to economics and law. PAVE: A Center for Privacy, Accountability, Verification, and Economics of Blockchain Systems is led by Charalampos Papamanthou, associate professor of computer science. The center is designed to accelerate the deployment and adoption of blockchain, a decentralized, communally maintained database designed to reliably store digital information.

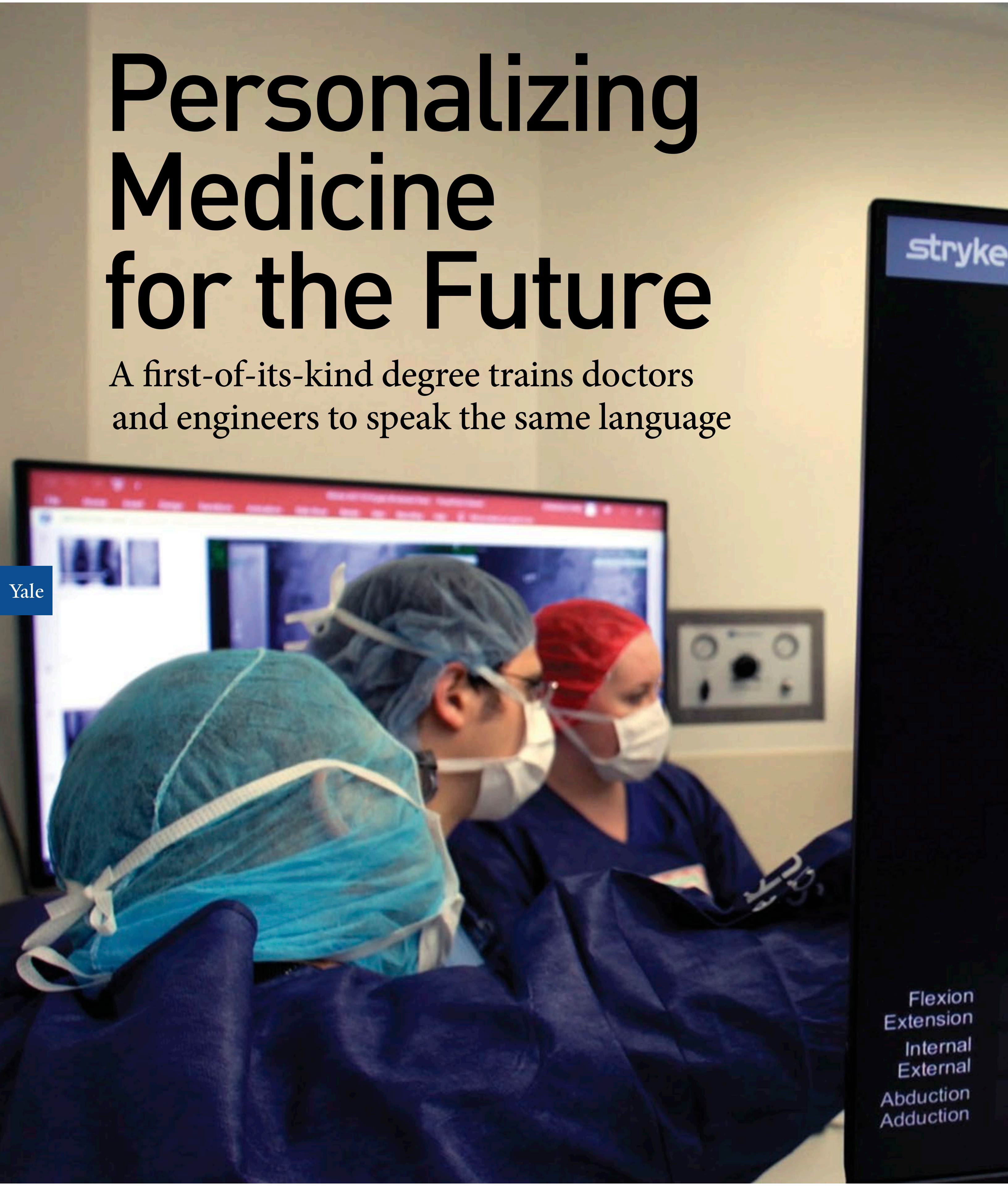
2022: September

Breakthrough Prize for Spielman

Daniel Spielman, the Sterling Professor of Computer Science, Statistics and Data Science, Mathematics and Applied Mathematics, won the Breakthrough Prize in Mathematics for "multiple discoveries in theoretical computer science and mathematics." The prize comes with a $3 million award. In addition to solving long-standing mathematical mysteries, Spielman's work has led to significant and very practical benefits in the fields of computing, signal processing, and engineering. The prize's founders — Sergey Brin, Priscilla Chan and Mark Zuckerberg, Julia and Yuri Milner, and Anne Wojcicki — created the prize to recognize game-changing discoveries in Mathematics, Fundamental Physics, and Life Sciences.

Personalizing Medicine for the Future

A first-of-its-kind degree trains doctors and engineers to speak the same language



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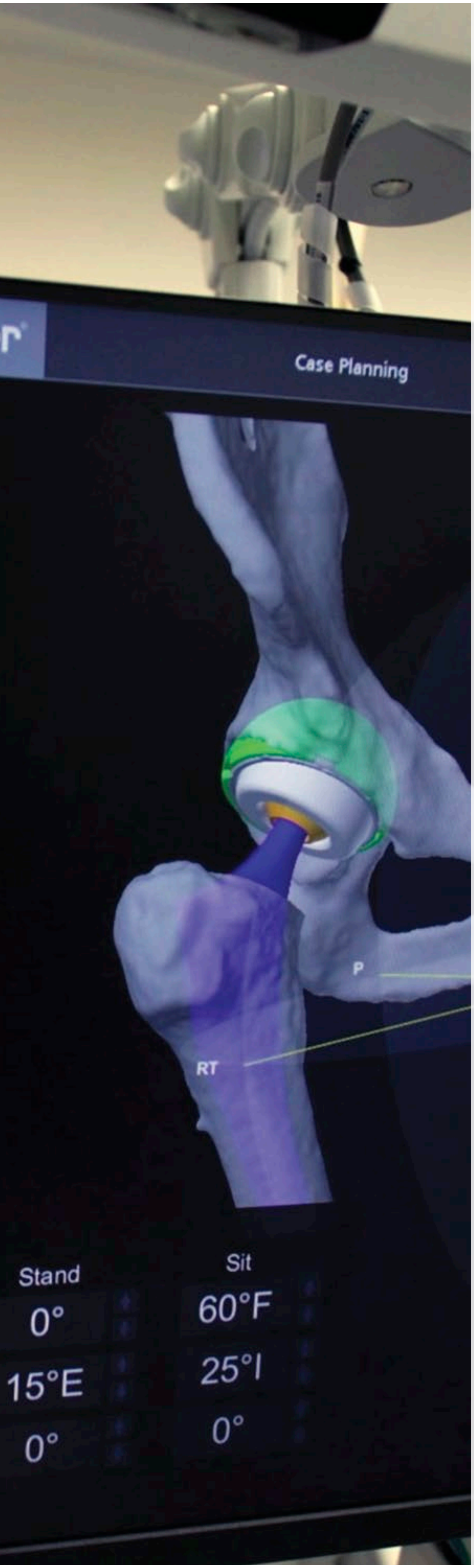

High-resolution imaging, 3D printing and modeling, and other technologies have radically changed healthcare and how some doctors are treating their patients. Certain cases that, in the recent past, would have automatically been paired up with a standard treatment are now being addressed with one-of-a-kind solutions.

For instance, Dr. Daniel Wiznia said, a patient might come to him with a defect in his or her bone structure.

"We can create a 3D model of that," said Wiznia, assistant professor of orthopaedics and rehabilitation and mechanical engineering & materials science. "We can figure out in a 3-dimensional space how we're going to reposition the bones, and how a plate is going to bring the two ends together. We can also print out custom instruments — I can create a 3D-printed guide that will lock onto the bone and guide me to where I put the drill or tell me where I cut the bone and create a specific little notch."

Wiznia's specialty is orthopedics, but this is a seismic shift in healthcare that cuts across disciplines — neurosurgery, for instance, or vascular surgery.

"In cardiology, we can create 3D models of a patient's heart and see what the pathology is," he said. "We can determine beforehand how we want to treat that pathology. We can look at different vascular patterns and see how best to access those sites."

That means, on a per-patient basis, a physician can tailor not only their techniques but the tools and implants themselves to the specific case and the specific patient's anatomy. This makes sense. After all, we aren't made up of parts mass-manufactured in a factory. Every person's physical make-up departs from the norm in some way.

So the technology for this type of personalized medicine is there. What's needed now is a generation of physicians and engineers who know what it can do, how to use it, and can speak the same language to each other.

To that end, the Yale School of Engineering & Applied Science and the Yale School of Medicine have launched the first-of-its-kind Master of Science in Personalized Medicine & Applied Engineering program. The one-year advanced degree program began this summer and it's designed to bring engineers, computer scientists, and medical professionals together to learn

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Yale

the new technologies in 3D medicine and imaging with the goal of improving patient outcomes. Students who go through the program will know how to — among other skills — generate high-resolution imagery, design and create 3D models of anatomy, use 3D printing to create customized medical instruments, and program surgical plans into robots and other computer-guided systems.

"They're going to come out of this with a good background in how to use and develop tools to improve treatment, diagnosis, and healthcare in general," said Steven Tommasini, research scientist at the School of Medicine.

All the principals involved in getting the program off the ground agree that Yale is the perfect setting for an entirely new kind of interdisciplinary degree. SEAS Deputy Dean Vincent Wilczynski noted that the university's culture of collaboration was a critical component.

"The new degree builds on the strong partnerships in research and education between the two schools and creates new opportunities to create innovative solutions for health care," Wilczynski said. "The combination of educators, practitioners, and researchers will certainly lead to the development of innovative medical devices and processes."

Above: *The first-of-its-kind degree program brings engineers, computer scientists, and medical professionals together to improve patient outcomes.*

The technology of personalized medicine brings engineering and medicine together. The program is designed to get both sides speaking the same language.

"The engineers need a background in anatomy that they don't have, and maybe a background in radiology and imaging that they don't have," said Lisa Lattanza, chair and professor of orthopaedics and rehabilitation. "The people coming from the School of Medicine side need to know how to segment images and how to work with computer-aided design drawings and things like that. The idea is that we want surgeons to come out who can do this, and we want engineers who can come out and do this."

Lattanza has been using 3D technology since 2012 and has conducted more than 250 surgical cases. She started out working with a 3D company in Belgium. That worked out great as long as she was assigned to a company engineer who was skilled in what she needed for her orthopedic work. That wasn't always the case. This is where the idea came from for the new degree.

"I mean, you can't just phone it in and send the images to the engineer and expect them to plan the operation," she said. "You have to be there, engaged, and know how you would get there without the technology and then know what the technology can and can't do for you."

Along the way, she also saw the technology surge in popularity among her fellow surgeons, not all fully understanding its capabilities and limitations.

"So if you paired up a new engineer with a new surgeon trying to do this, it's a disaster waiting to happen."

After she worked on an outline of the program with Wiznia, Tommasini, and Wilczynski, they then pitched it to SEAS and the School of Medicine. Everyone was 100% behind it right from the start.

"There's nobody that doesn't like it, and everybody sees the need for it," Lattanza said. "It's the proverbial basket of kittens."

To graduate, students will need to take two electives and six required courses, which include a Personalized Medicine Seminar, a course on biomedical 3D Printing, and one on Medical Device Design. Courses are taught by both clinical and ladder faculty from the School of Medicine and SEAS.

Above: *Physicians can tailor their tools and implants to a specific patient's anatomy.* Below: *3D printers are frequently utilized to create customized medical instruments, anatomy models for surgical planning, and more.*

As part of the program, the students spend the summer in a "clinical immersion" phase where they shadow physicians in various fields, observing surgeries and doctor-patient interactions. More than 40 healthcare workers from 11 fields, including orthopaedics, radiology, cardiology, and neurology volunteered to take part as mentors for the program.

"I think the summer program will help them get familiar with the medical environment, be able to speak the clinicians' language, and see what the clinical process is like, from the O.R. to just meeting with patients," Tommasini said.

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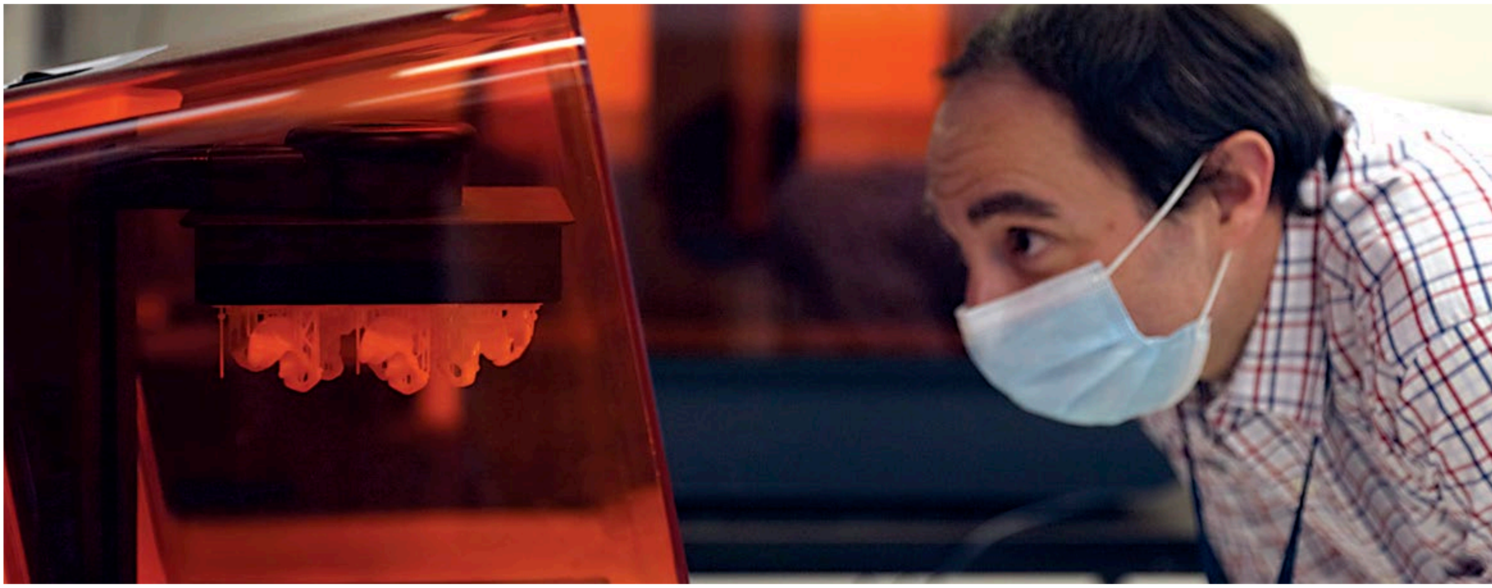
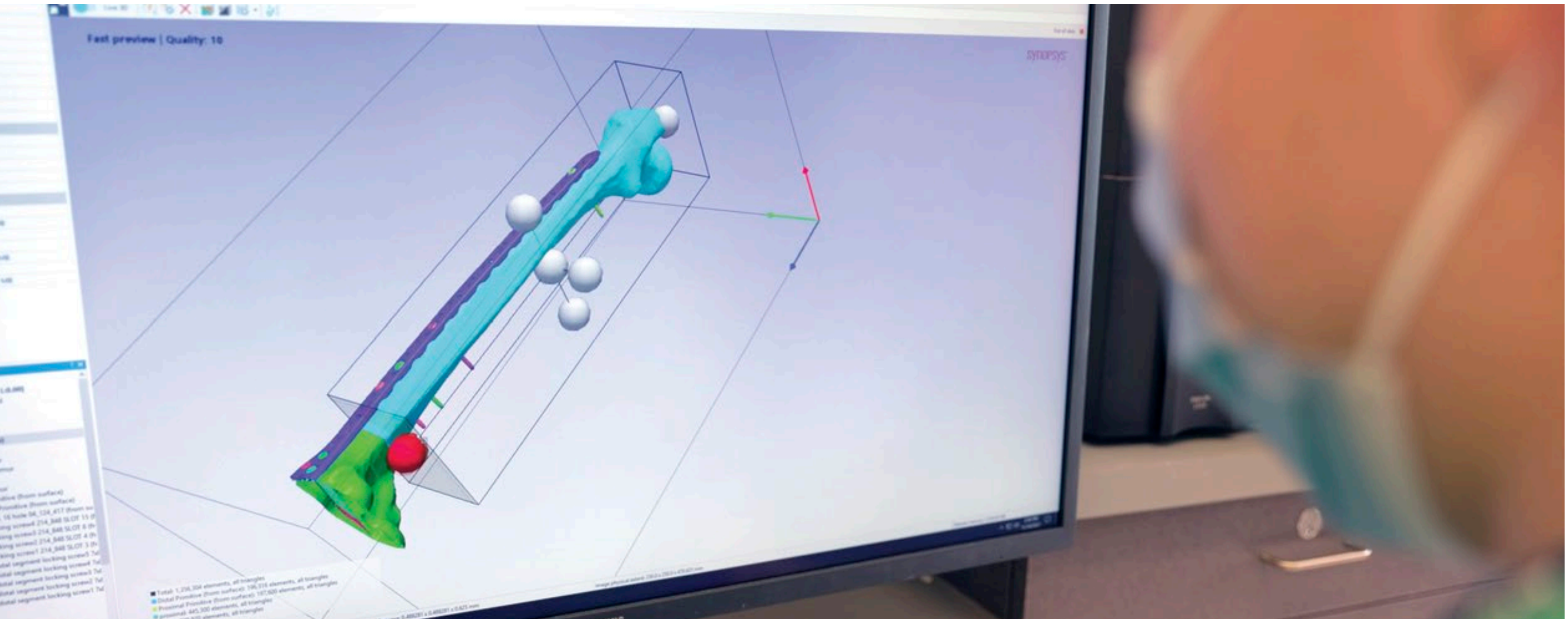




Left: *New technologies in 3D medicine have surged in recent years allowing doctors to better customize patient care.*
Right: *Derek DeMel '22 and Dr. Daniel Wiznia study a 3D model to discuss the best approach for treatment.*

Derek DeMel '22, who graduated in May with a bachelor's degree in biomedical engineering, says this phase of the program was invaluable.

"I think it's so important for the pre-med people in the program to learn about how these devices are engineered," he said. "And in the engineers' case, if we're going to go ahead and make these technologies, ultimately they're useless if we don't actually know what the doctors want and what the patients need."

Specifically, DeMel is interested in preventive medicine and the idea of being able to print organs and tissues rather than having to rely on just transplants. He's also open to working with medical devices more broadly. In either case, he sees the program giving him the boost in skills that he needs.

"With this program and the extra year as a grad student, you get so much more access and more closeness to the faculty. I really think this program is going to help teach me more of what I need to know."

After taking the School of Engineering's Medical Device Design course as an undergrad, Ashley Anthony '22 decided she wanted to do more hands-on engineering, particularly in a clinical setting.

"What appeals to me about the program is that I want to be able to help people, and I personally enjoy just solving problems," said Anthony, who also majored in biomedical engineering. "I think most engineers also have this kind of personality trait where they just like to be able to work through a problem and create something that fixes it."

As a student from Guyana, Anthony said the program has also gotten her thinking about how to make devices and personalized medicine more accessible to people living in a low-resource region.

"What are some of the ways that we can make things more cost effective?" she said. "What are some of the ways that we can make things not just available to larger swaths of people but also design devices that can be manufactured and made more accessible in places with fewer resources?"

And with a grant from the National Institutes of Health, the clinical immersion phase of the program is offered to up to five undergraduate students each summer. In the following spring semester, these students also take the Medical Device Design course taught by Wiznia and Tommasini.

"We use the summer program as a tie-in so they learn about different problems that exist, and then they can come up with ideas that could be used as projects for the device class," Tommasini said.

Among the three undergraduate students who took for the first summer immersion phase was Caroline Reiner, who is majoring in computer science and psychology.

"I've always been interested in health and medicine, but I also have this itch to innovate and create," she said. "When I found out about the program, it seemed like the perfect intersection between my interests. I get to be with the patients and also express my creative side. And in classes, we learned that there are a lot of AI applications in medicine and healthcare."

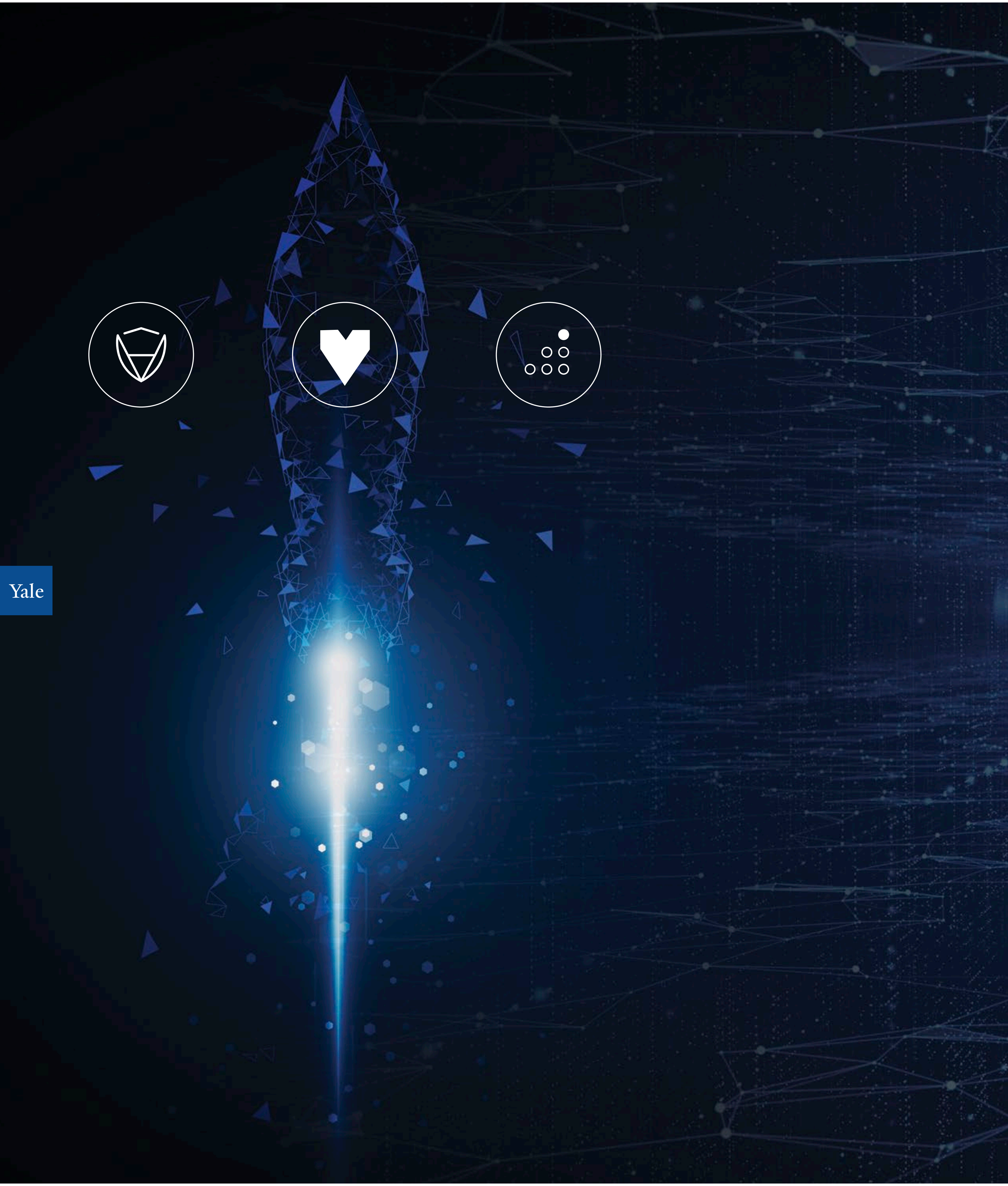
As part of the immersive program, she observed surgeries and doctor-patient interactions in the fields of urology, orthopaedics, and infectious diseases.

"The doctors that were in the room, they would always be pointing out things on the screen, teaching me things, and answering my questions," she said. "It was really helpful."

Like her fellow undergrads in the program, Reiner will be taking the Medical Device Design course in the spring. The summer program has her already thinking about potential projects, like redesigning a soft tissue biopsy gun commonly used to take tissue samples. She thinks it can be made more efficient and quieter (patients often complain about the noise it makes).

As much as the program is focused on bringing students up to date on the technology of personalize medicine, it's also about preparing them for the future of the field. Lattanza noted that the skills and knowledge that the students learn in the program are the kind that will increase because technology will continue to advance. As a result, the field of personalized medicine is going to quickly morph over time.

"Right now, we're talking mostly about 3D modeling and virtual planning of surgery, but eventually we might be talking about developing a 3D molecule that can be used in some way in the body, or the printing of bone and cartilage," she said. "We want to create the people who are going to solve those problems ten years from now. I don't want to hear that people are still putting in plastic and metal joints — I want to hear that people have figured out how to resurface cartilage and grow bone in a way that's necessary to solve some of these bigger problems."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Entrepreneurship at SEAS

Faculty-led startups thrive, firing up the engine of innovation

From blockchain security to revolutionary single-cell analysis, research at the School of Engineering & Applied Science has generated several very successful faculty-led start-ups, applying the breakthroughs from their labs to make a real-world impact.

Now, the School is taking further steps to foster more entrepreneurship and create a culture where researchers are not only conducting important work — as they always have — but also looking toward how it can be deployed for maximum effect. That includes providing the infrastructure and resources to help faculty-led start-up companies get up and running.

"Nothing we do will get in the way of our core mission of research at Yale, but it's not always the case that research should remain in the lab," said SEAS Dean Jeffrey Brock. "We're trying to make sure that if we have something that could have an application outside the lab that we give it the right kind of rails to get it out of the lab."

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ROBERTS INNOVATION FUND

Among other efforts, SEAS has recently established the Roberts Innovation Fund, a new initiative underway to accelerate the SEAS engine of innovation, bolstering the process that gets groundbreaking faculty discoveries to market. Thanks to a generous gift from Yale alumnus Will Roberts ’90, the Roberts Innovation Fund will provide grant funding, mentoring and business training to assist in the commercialization of breakthrough inventions that solve real-world problems with the greatest impact. The fund, overseen by the SEAS Dean’s Office, will also provide participants with valuable feedback from the fund’s director and from an external advisory board composed of industry veterans with a wealth of experience in technology ventures.

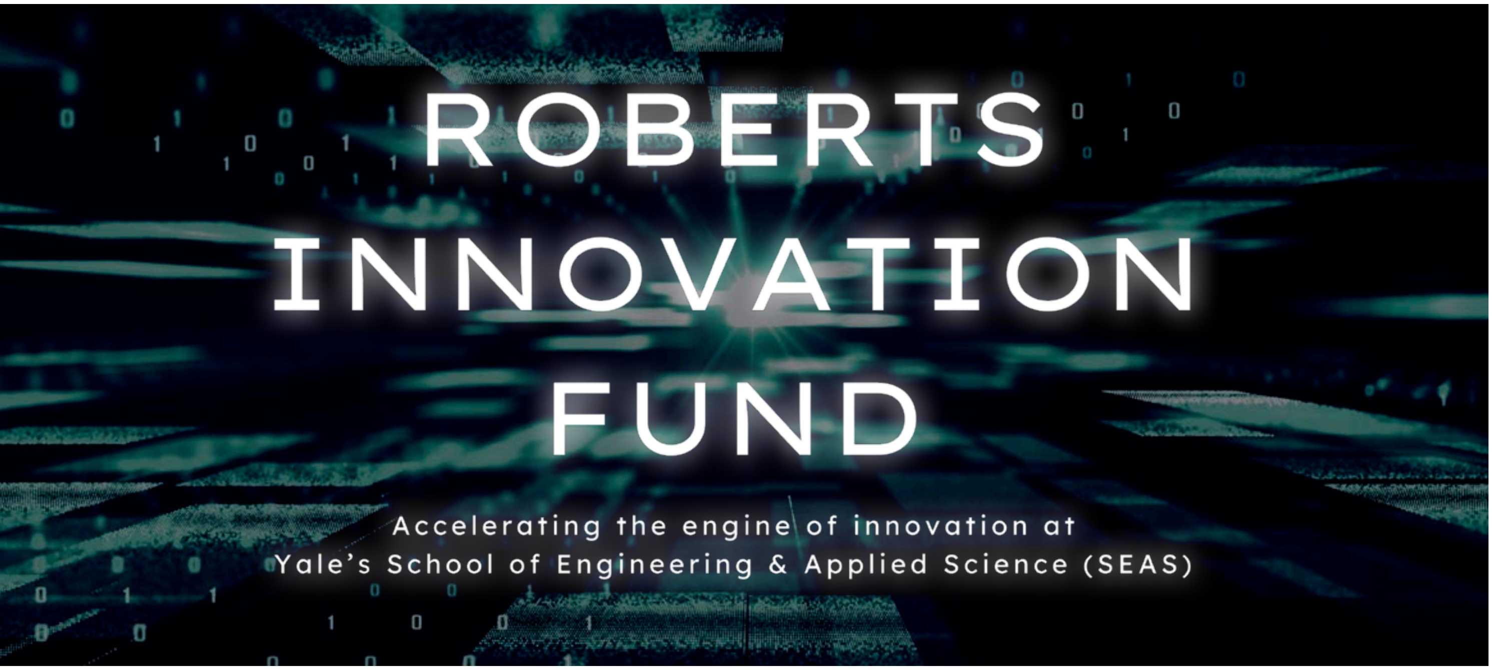
“Faculty will receive written support on everything from financial modeling, competitive analysis, landscape mapping, market research, to helping with communications and really understanding where the biggest problems and opportunities are,” said Claudia Reuter, the director of the Roberts Innovation Fund at Yale Ventures. “Our hope is that we’ll help bring all the amazing things going on at Engineering at Yale to life in the biggest and most impactful way that we can.”

Grants of up to $150,000 will be awarded to those selected. The money, though, is only one part of the Innovation Fund.

“I would say the bigger piece of it is that we have an amazing team at Yale Ventures that will help our faculty in the process of understanding and developing the model for whatever business they’re envisioning,” Brock said. “That team is really the key because, as a faculty member, you don’t arrive on campus with the training on how to do this.”

For instance, chosen participants will receive expert guidance on the potential risks and benefits, and “how to get past that zero-to-one phase of the process.”

“We want the Innovation Fund to encourage ambitious thinking, and to provide the infrastructure and resources to create a robust pipeline of start-up companies and partnerships with industry,” Brock said. “We have no shortage of great ideas; we just want to make the process of commercializing those ideas faster, better informed, and more targeted to where these innovations will have the most impact.”

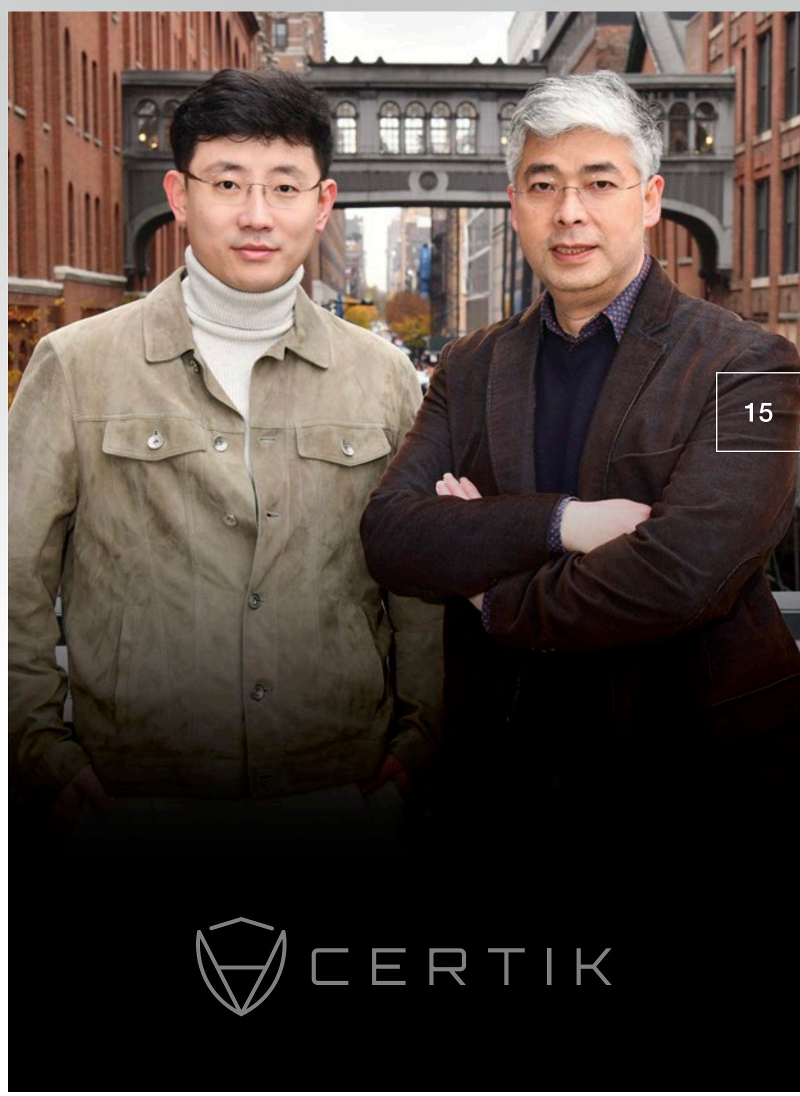


From medical applications to cutting-edge electronics, Yale SEAS faculty continue to not only produce ground-breaking ideas but are getting them out into the world via start-ups.

For instance, there's Saphlux, co-founded by Jung Han, the William A. Norton Professor in Technological Innovation in 2014. It produces innovative materials that enable next-generation, high-efficiency, high-power, low-cost LEDs and lasers that will be compatible with most applications. The company recently unveiled its NPQD R1 Micro LED chip, designed to improve the performance of display screens, and at a lower production cost. There's also Supercool Metals, a company founded by Jan Schroers, professor of mechanical engineering & materials science. This start-up is based on Schroers' research in bulk metallic glass to produce ultrahigh strength metals with exceptional, plastics-like processability.

From companies that are just getting off the ground to billion-dollar ventures that have gone public, SEAS faculty are leading a diverse array of start-ups. Here's a look at few of them, each at a different stage of development:

Below: *CertiK founders Ronghui Gu and Zhong Shao.*



CertiK: Securing the Future

Last year, $2.8 billion was lost in an increasingly common scam known as the rug pull. It involves a crypto developer promoting a new project that draws in investors, and then disappearing with all the money. Rug pulls have shown to be relatively easy to pull off, with a big potential payday for the scammers. Unless CertiK is on the case.

Co-founded in 2018 by Zhong Shao, the Thomas L. Kempner Professor of Computer Science, CertiK is a pioneer in blockchain security. It uses artificial intelligence (AI) technology, formal verification, and other safeguards to secure and monitor blockchains and smart contracts (agreements written in software that take effect automatically when all the conditions are met). Essentially, CertiK provides clients with what the company's founders call "a one-stop shop for all their security needs."

Continued →

Shao and co-founder Ronghui Gu, the Tang Family Assistant Professor of Computer Science at Columbia University (and former Yale researcher), saw early on the need for Blockchain security, and the company today is considered a leader in the field. The company is based on decades of research, particularly in the development of Shao's innovative certified operating system, known as CertiKOS.

CertiK has already earned industry recognition with numerous awards, including the CB Insights Blockchain 50 Award, and is listed as the only blockchain security firm.

Yale

And the need for the company's expertise is greater now than ever. The use of cryptocurrency has shot up dramatically in the last few years, which translates to a higher demand for security as well.

CertiK has also positioned itself as a security service for apps for Web3 — that is, a new, decentralized version of the Internet built with blockchains. The company recently launched a fraud investigation service known as "Know Your Customer," or KYC. Shao and Gu say that KYC is the "missing link" in preventing the malicious intent behind rug pull scams.

CertiK has already earned industry recognition with numerous awards, including the CB Insights Blockchain 50 Award, and is listed as the only blockchain security firm. It has also won the Globee Cybersecurity Global Excellence Award. In addition to Yale University, the company's investors include Goldman Sachs, Insight Partners, and Advent International.

To date, CertiK has protected over $300 billion worth of crypto assets for well more than 3,200 enterprise clients. As of April this year, the company was valued at $2 billion.

Propria: At the Heart of Innovation

A thin piece of stretchy cardiac tissue could be the key to faster and more efficient drug discovery.

That's the premise of Propria, a startup company founded by Stuart Campbell, associate professor of biomedical engineering. He started the company with the goal of making human engineered heart tissue more powerful and accessible to scientists. In just a few years, the company has shown significant growth, and its employees include two former students from Campbell's lab.

Below: *Propria founder and associate professor of biomedical engineering, Stuart Campbell.*

Propria provides scientists with a full set of reliable data, letting them know whether their treatments can make cardiac tissue more pliable, stronger, or any other property relevant to their research.

"We make fully functional, mature, machine-readable heart muscles that pharmaceutical companies can use to test their new heart drugs," Campbell said.

In essence, Propria's technology allows stem cell-derived human cardiac cells to be packaged into thin, beating muscle strips. With a cellular composition that closely resembles the muscle layer of the heart, these engineered tissues react to medications and conditions in a way that accurately reflects how a human heart would. Once the drug is applied, Campbell and his team perform numerous tests on the tissue that reveal key aspects of muscle function. For example, they can measure how the strength and speed of contraction are altered by drugs, as well as how treatments may affect the heart's ability to respond to exercise.

It's based on methods that Campbell developed in his lab, and his research team has since refined the technique, allowing them to reproduce high-quality tissue consistently and accurately.

A client can order specific tests to be conducted on the tissue. They can study the effect of a medication on a heart tissue over days or weeks, for instance, or monitor the chronic effect of an environmental toxin on the tissue and compare it to a control group tissue that has not been exposed. Or they can test a drug designed to modify in real time how the heart operates.

"Our system is actually very well-designed to be able to do that, to flow the drugs over the tissue and watch their behavior over time," Campbell said.

Propria provides scientists with a full set of reliable data, letting them know whether their treatments can make cardiac tissue more pliable, stronger, or any other property relevant to their research. Conversely, the results can also determine whether a drug could be detrimental — all of this in a human context but without the risk and expense entailed by clinical trials.

Continued →

IsoPlexis: Fighting Disease, One Cell at a Time

With a unique method of single-cell analysis developed in the lab of Rong Fan, professor of biomedical engineering, IsoPlexis is accelerating the fight against cancer and other diseases. Using extremely precise detection systems, the company's technology reveals unique immune biomarkers in small subsets of cells. By doing so, it can advance immunotherapies and develop highly accurate and personalized therapies.

"It tells us how to best use the immune system to save patients' lives," said Fan.

For all of its technological advances, the device itself is fairly simple to operate. An engineered immune cell sample is loaded into the microdevice. The cells are then scuttled to thousands of microscopic chambers to be analyzed individually. Users then read the data on a computer to understand the function of each immune cell and its anti-tumor capability.

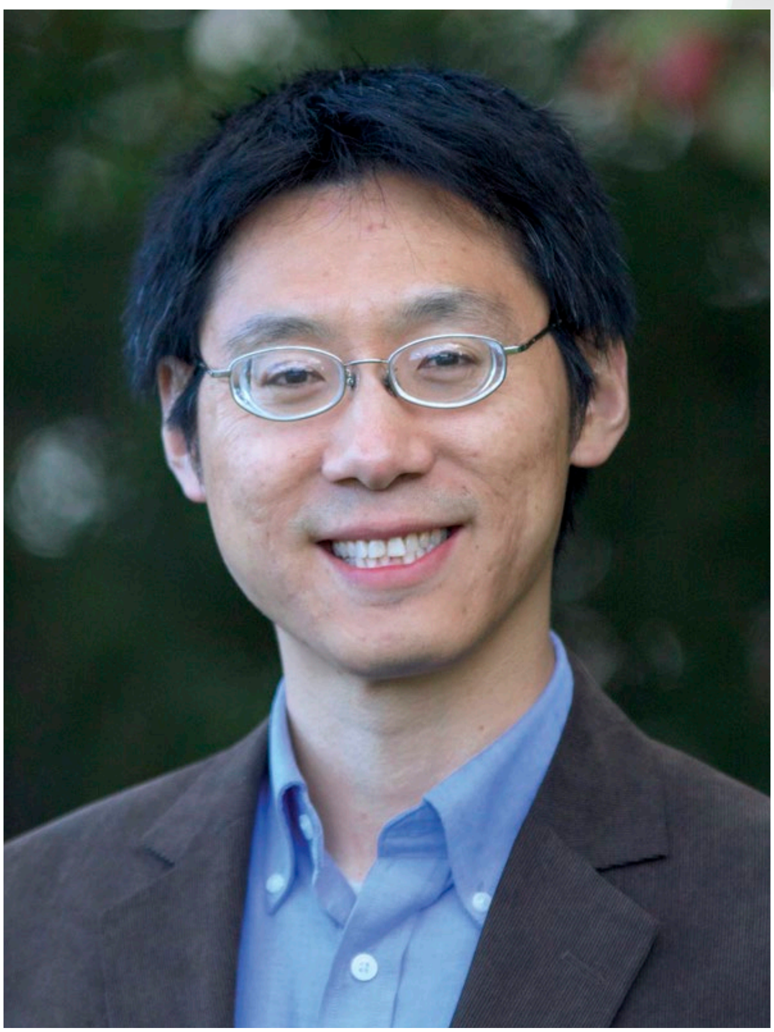
By capturing and analyzing large quantities of highly precise data per individual patient cell, the technology allows immunotherapy developers or health care professionals to determine which patients will benefit from certain cancer

Left: *The IsoPlexis technology details unique immune biomarkers in small subsets of cells to determine which patients will benefit from certain cancer therapies.* Right: *IsoPlexis co-founder and professor of biomedical engineering and pathology, Rong Fan.*

Without the level of detailed information that the IsoPlexis technology provides, the data of patients tend to look the same.

therapies. The technology analyzes the sample one cell at a time and provides doctors with information that allows them to decide in advance whether a particular treatment would be effective or toxic to that specific patient. It can also help guide decisions about combining different cancer therapies.

"It's proactive information with long-term impact," said Sean Mackay, who co-founded IsoPlexis with Fan and is a 2014 graduate of the Yale School of Management.



One of the company's first major milestones was showing that the technology could be manufactured and reproduced. The company now produces hundreds of the chips each week — mostly for pharmaceutical companies or cancer centers in the immuno-oncology field.

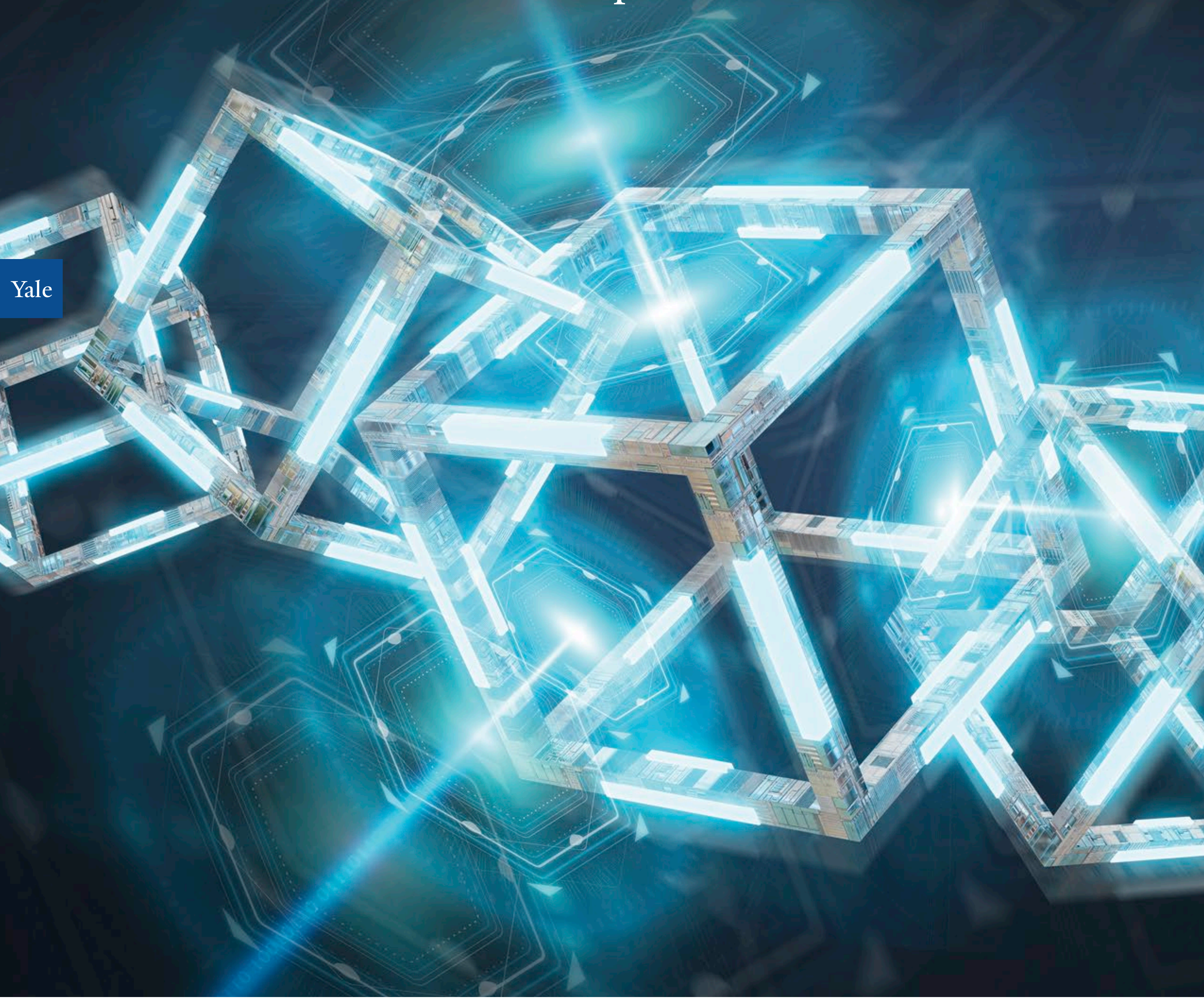
Similar technologies can analyze large numbers of cells at a time, but IsoPlexis's technology, licensed from Yale and the California Institute of Technology, reads each cell's true function individually. This distinction makes a big difference. It simultaneously measures up to 42 immune effector function proteins secreted from single cells. Without the level of detailed information that the IsoPlexis technology provides, the data of patients tend to look the same.

The company counts Bristol Myers Squibb, Genentech Inc., Merck & Co. and other major pharmaceutical companies among its customers.

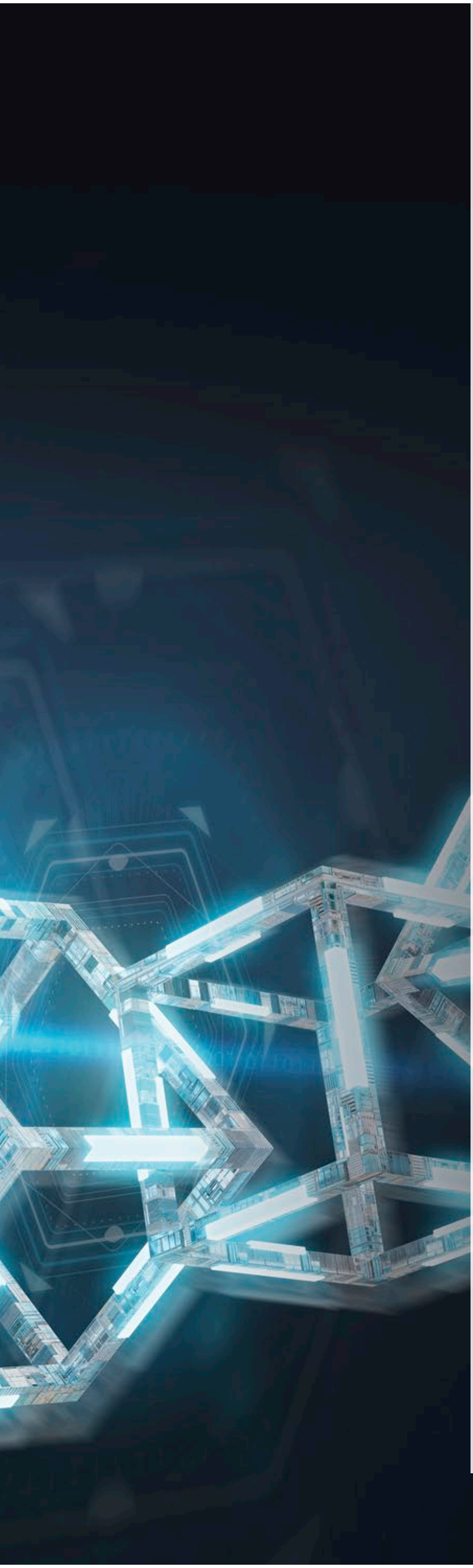
And IsoPlexis is doing good for the local economy as well. The company expanded from about 40 employees in 2017, adding hundreds more with plans to further grow its workforce in the next few years.

Computer Science 2.0

Explosion of faculty, courses and research ushers in a new era for Computer Science at Yale



Yale



When Yale's Computer Science Department was established in the early 1970s the videogame Pong had recently been invented, the 8-inch floppy disc had just been introduced, and the first portable calculators had just hit the stores.

All of which is to say that a lot has changed in computing. And at Yale, Computer Science is keeping apace. Robotics, machine learning, artificial intelligence, quantum computing, and blockchain are just some of the areas that will be bolstered by the department expansion. With numerous new courses, new faculty members, and a wider range of research fields, the Computer Science department is better positioned than ever to take on emerging challenges and to meet the needs of students and industry.

The department recently hired ten tenure-track faculty members and four teaching-track lecturers to its ranks. These hires are in addition to an earlier round of 11 new tenure-track faculty members and two lecturers hired in the last few years. The boost in hiring accomplishes a number of long-term goals, including expanding the department's areas of expertise.

Also, as Computer Science has emerged as the second-most popular major (just behind economics) at Yale, the boost in faculty will go a long way toward meeting students' curriculum needs.

"Our new faculty members were chosen for the excellence of their research, as well as for their fields that they represent, all of which have been in high demand by both our students and faculty on campus as well as the industry," said Zhong Shao, the Thomas L. Kempner Professor of Computer Science and department chair. "The range of their expertise addresses some of the most critical challenges that we face today."

SEAS Dean Jeffrey Brock said the new faculty will be critical to realizing the ambitious goals set out in SEAS' Strategic Vision, particularly in the areas of artificial intelligence and robotics, while building in key areas like cybersecurity and distributed computing.

"This exciting cohort of new faculty stands to transform our Computer Science department," Brock said. "During our recruiting season, they sensed Yale's momentum in computer science and in engineering, ultimately turning down excellent offers at other top schools to join our faculty. Their presence will allow Yale Computer

Continued →

Science to expand their course offerings, as well as to establish critical mass in core and cutting-edge research areas."

Many of the new faculty members, like Fan Zhang, cited the department's "fast growth in recent years." Others said that they were drawn by the collaborative environment at Yale, especially considering that Yale is ranked at or near the top in numerous research areas.

"These new faculty are working with faculty across departments and schools and are transforming the university— because computer science and AI are actually transforming every discipline, every sector of our lives," Shao said.

Daniel Rakita, for instance, said he's looking forward to working with colleagues at the Yale School of Medicine to see how our robotics solutions can possibly help in hospital or home care settings, as well as working with the Wu Tsai Institute on Brain-Machine Interface technologies.

"Many people I spoke with indicated that there are no boundaries between departments at Yale, and interdisciplinary research is not just encouraged here, but is a 'way of life,'" Rakita said.

Many of the new faculty have already engaged with key academic leaders around the campus, from medicine, to economics, to quantum computing.

As part of this boost in hiring, the department strategically targeted certain research areas, including artificial intelligence, trustworthy computing, robotics, quantum computing, and modeling.

This hiring season marks the first since the changes in organizational structure provided SEAS with more independence, as well as a substantial University investment in the School. Both enable SEAS to pursue opportunities even more aggressively for breakthrough research and collaborative innovation.

"Our independence and ability to seize valuable opportunities were key elements in our ability to realize this transformational growth of Computer Science at Yale," Brock said. "As Computer Science plays such a critical role in an increasingly broad range of disciplines, the size and breadth of Computer Science is crucial to our strategy for SEAS. I'm thrilled to be able to take the first step in realizing that vision for a SEAS that is well integrated within its host University and aligned with its mission."

A Curriculum to Meet the Needs of Students and Industry

Increasing the department's curriculum has also been in the planning stages for a while, a goal made possible by the recent hires of new faculty and lecturers. Shao said there was a concerted effort to meet the high demand in areas such as artificial intelligence, blockchain, machine learning, and introductory programming.

"Our students have been asking for these new courses for many years," Shao said. "This has been on the to-do list for the department for many years, but we just didn't have the manpower. And finally, with the new faculty hires, we can actually offer these courses."

Ben Fisch, for instance, is teaching a new course focused on blockchains for both graduate students and advanced undergraduates in computer science. The course, Frontiers of Blockchain Research, engages students with research problems related to such blockchain systems as Bitcoin and Ethereum, including the topics of scalability, verifiability, decentralization, interoperability, and economics.

Rex Ying is teaching Deep Learning on Graph-Structured Data, a field that Ying said has attracted "incredible attention" over the last three to four years. "I'm excited to present a systematic overview of graph learning and share what incredible applications we could build with this new technology," he said.

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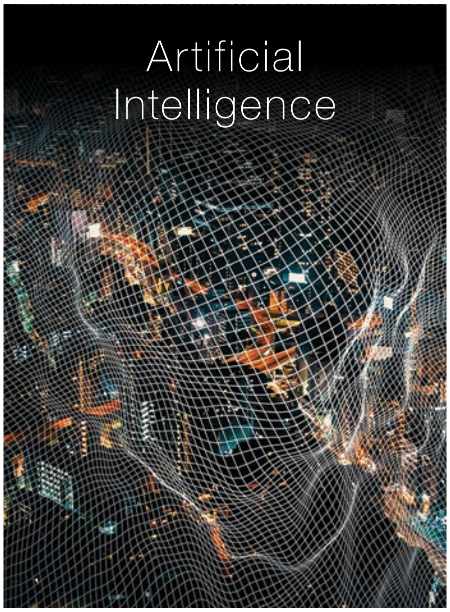
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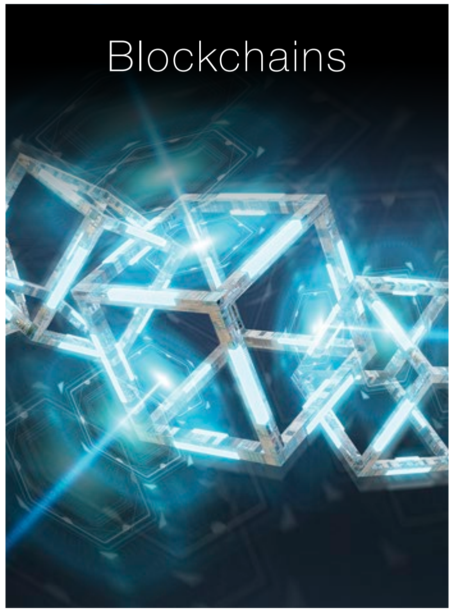
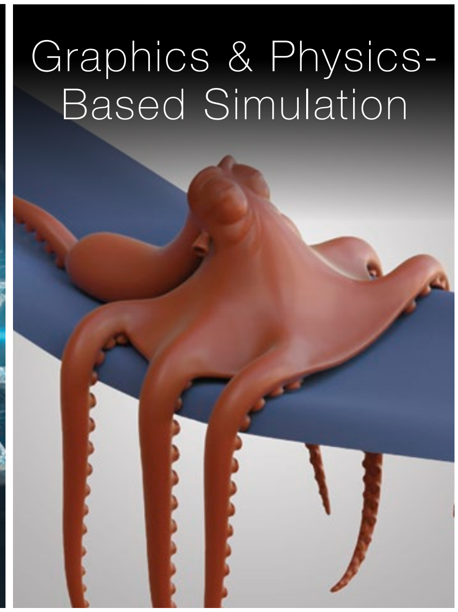
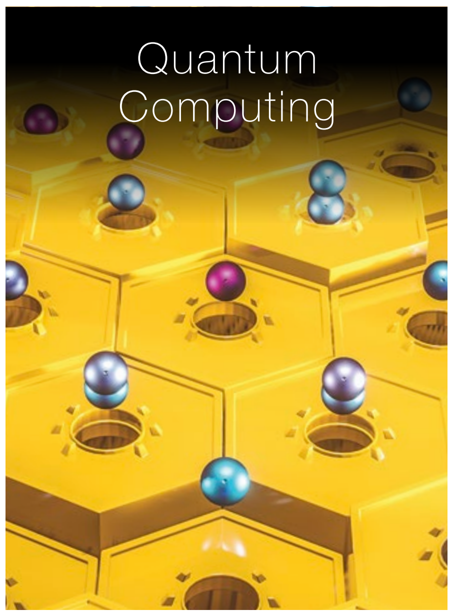
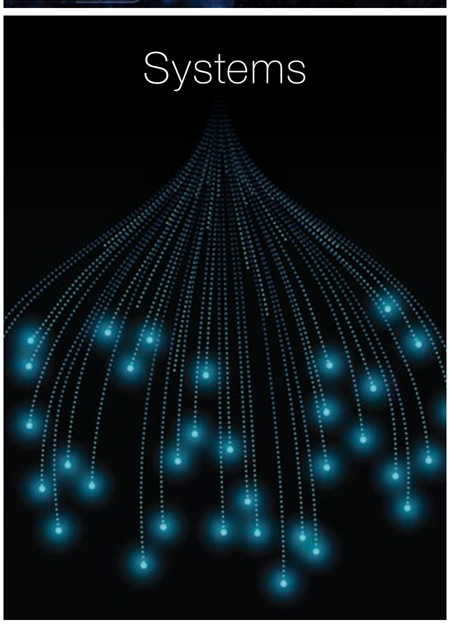

Blockchains


Graphics & Physics-Based Simulation

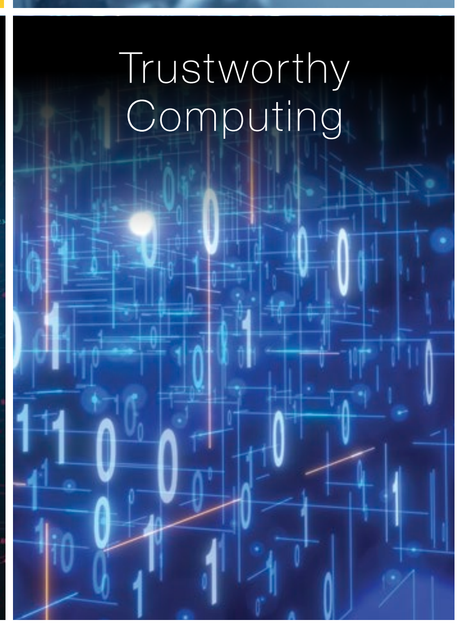

Machine Learning


Quantum Computing


Robotics


Systems


Theory


Trustworthy Computing

New Computer Science Tenure-Track Faculty

Leading the Computer Science Revolution

In the field of robotics, Tesca Fitzgerald introduced this fall a new graduate-level seminar on Interactive Robot Learning that explores methods for grounding machine learning problems in human-robot interaction. Students will take on a semester-long project that incorporates state-of-the-art methods for interactive robot learning.

Responding to industry needs, the department has also added courses focused on what's known as full stack web programming — that is, the set of skills needed to develop the interface as well as the coding behind building a complete web application. One of the department's most popular courses on software engineering will now be offered for both semesters of the year, instead of one. Both, Shao said, are specifically aimed at meeting the needs of industry and students.

According to Dr. Alan Weide, who's teaching the course on full stack web programming with Dr. Jay Lim, students in the course will learn industry-standard technologies

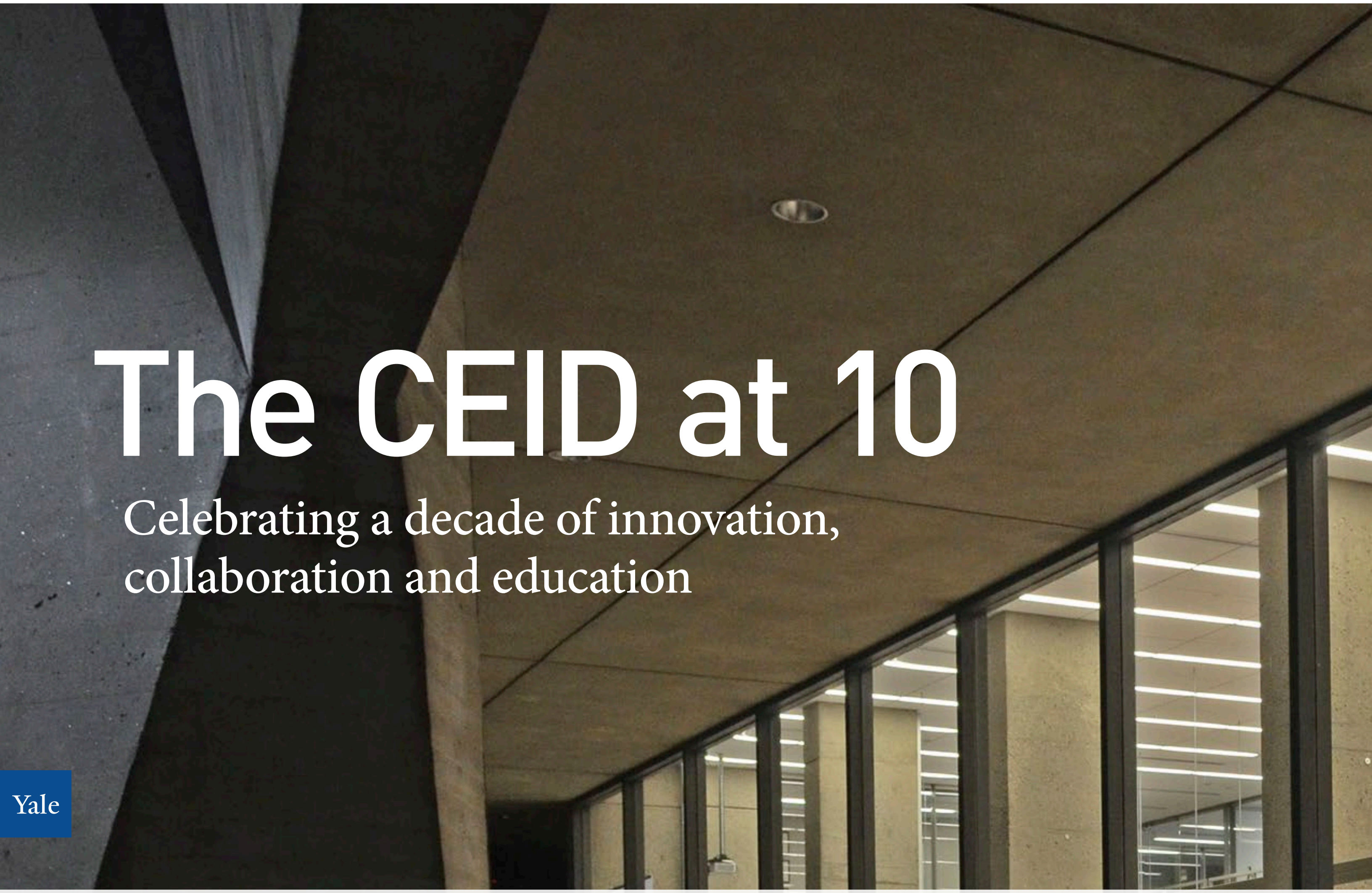
In the past four years, SEAS has doubled the number of Computer Science faculty to meet the significant demand of students and industry. We strategically targeted these new hires — all having demonstrated excellence in their fields — whose expertise often straddles multiple research areas. By doing so, we aim to address the critical challenges of today and position the department to lead tomorrow's technologies.

through a semester-long, team-based project in which they will develop from scratch a web-based application that not only solves a problem, but a problem that is important to them.

"Along the way, they will learn about the 'full stack' of components that goes into a web application: databases, servers, and user interfaces, giving students hands-on experience building the kinds of applications they use every day," he said.

These are just a few of the new courses available. Along with other changes in Computer Science, Shao said, they are part of the department's ongoing and ambitious goal of developing leaders in the field and being at the forefront of the current revolution in computer science and AI.

"As new challenges emerge, Computer Science at Yale will continue to adapt," Shao said. "We're excited about the future of our department, and these new additions to our faculty and our curriculum are going to be a major part of it."



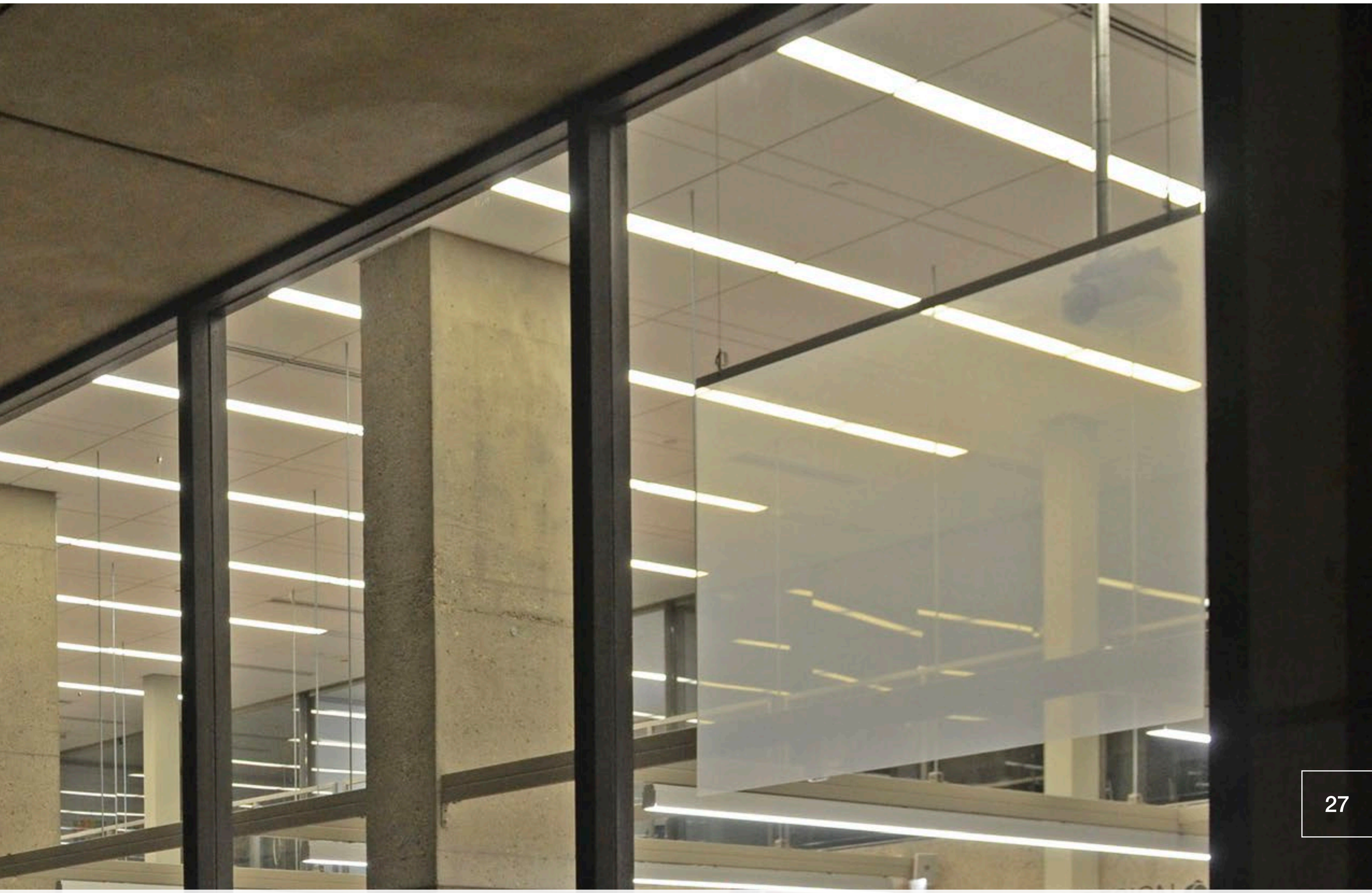
The CEID at 10

Celebrating a decade of innovation, collaboration and education

When the Center for Engineering Innovation and Design (CEID) officially launched in 2012 — 10 years ago! — it opened a whole new world of innovation for the Yale community. Countless SEAS majors began their engineering journey at the CEID. Perhaps they were invited by a friend or were curious about what they saw through the massive windows that line Prospect Street. Maybe they stopped in for one of the many workshops held at the CEID — hands-on explorations into everything from Arduinos to molecular gastronomy to motion graphics to ham radios and working with concrete.

With the CEID, Yale had for the first time a primary, centralized hub where people could generate ideas and produce prototypes. It quickly became a place where plans made their way from the whiteboard to the real world. Better ways to perform surgeries, make music, preserve art, and countless other innovations had their genesis at the CEID in the last 10 years.

The CEID acts as both an educational resource as well as a focal point for design and engineering on campus. Designed as a space to foster collaboration, its 8,700-square-foot John Klingenstein '50 Design Lab combines an open studio, lecture hall, wet lab, and meeting rooms. The studio is equipped with 3D printers, hand tools, electronics workstations, and a variety of materials for members to use. Typically, members have 24/7 access to the studio space, as well as to a state-of-the-art machine shop, wood shop, and wet lab during regular staffed hours. The CEID was one of former SEAS Dean Kyle Vanderlick's strategic priorities in 2010 when she led efforts to create and support the center's design, construction, and operations.



“My friends and colleagues from the CEID have gone on to earn Ph.D.s from top institutions and start businesses; and they are some of the first people I reach out to when I have questions or need advice,” said Glen Meyerowitz ’14, now the director of engineering for biodesign at UCLA Health. “It was a privilege to have access to a world-class facility filled with curious and enterprising students, staff, faculty, and community members.”

Students have used the CEID as a base for launching what would become million-dollar startup companies. Faculty have used it to bolster game-changing research. But the CEID has also wended its way into the nooks and crannies of everyday life, as students use the same space and resources to make presents for families or sculptures to mount on their mortarboards at graduation.

“I always felt welcomed by the CEID, and in turn I felt a sense of duty to make the CEID as welcoming as possible to anyone who entered,” Antonio Medina, ’19, a former CEID design fellow. “From theater majors to architects, surgeons to football coaches, everyone on campus knew that the CEID was the go-to spot to turn their ideas into reality.”

In its first 10 years, the CEID has made engineering, innovation, and technology more accessible to everyone. Guest lectures, tech talks, social events, undergraduate clubs, and hackathons have brought together folks from Yale and well beyond campus. To celebrate a decade of innovating and collaborating, we highlight 10 great things about the CEID:

Continued →

1
Where Engineering Meets Medicine

Since its beginning, the CEID has closely aligned itself with the Yale School of Medicine through numerous collaborations. The most recent example is the new Master of Science in Personalized Medicine & Applied Engineering (see story on page 6). One of its most fruitful collaborations is the course Medical Device Design (MENG/BENG 404). There, student teams work with "clients" from Yale Medicine to come up with an innovation to improve healthcare in some way. Results have included a balancing device that measures the recovery progress of head injury patients, a device to better transport donated organs, and a virtual reality platform to examine kidney biopsies. Some of these projects outlasted the course, with the clients and students continuing to iterate and improve on them. Others have become their own start-ups (more on that soon).

Glen Meyerowitz

Director of Engineering for Biodesign at UCLA Health

The CEID was established while I was a student at Yale, and its presence radically changed the course of my time at Yale. My first two years on campus were "pre-CEID" and the final two years were "post-CEID." The CEID had a very positive impact on me, serving as a nexus of innovation and collaboration, bringing together disparate groups of students, faculty, campus institutions, and more in ways that was difficult to do before. From working on class projects to student groups, I probably spent more time in the CEID than any other place on campus after it opened. The doors that were opened for me have propelled my personal and professional growth since then.

2 The CEID and the Arts

Completed in 1504, Michelangelo's David was remarkably well-constructed. But it's been more than 500 years, and time takes a toll on everything. Hairline cracks have been showing up in David's ankles. In the course Materials Science of Art, these tiny cracks served as a window into the artistic process and how a work changes over time. It also gave students a chance to engineer solutions to keep David from keeling over.

In other artistic pursuits, students have explored the chemical make-up of paints, and why certain photos will fade. A student group worked with Yale's Center for Collaborative Arts and Media (CCAM) to create an automated rotating sign that announces the organization's presence to all passersby on York Street. Courses on the artistry of light and spaces have also taken place here. And in a less structured role, the CEID has also been a go-to space for individual artists to come and hash out their own work.

3 Engineering a Better Athlete

The Yale lacrosse team won its first national championship since 1883 the same year it first started using the Lightboard, a device created at the CEID to help goalies hone their reaction times. A coincidence? Perhaps we're biased, but we're pretty sure there's a connection. The device has 15 circular lights, each a different color that the user hits upon flashing as fast as he or she can. It's a deceptively simple idea that improves players' reflexes and provides coaches with a heap of useful data. It was just one of the many CEID-based projects designed to boost athletics.

The Bulldog RepBox ensures that users are performing their push-ups, squats, sit-ups, and other exercises properly. As the flagship item in the Projects2Products (P2P) program, you might soon be seeing it in a lot of gyms. P2P is an undergraduate student innovation program that provides hands-on experience in all angles of entrepreneurship — product design, manufacturing, and marketing — to turn student projects into commercial products.

Other sporty innovations include a mat fitted with sensors to help tennis players improve the accuracy of their serves, and a weight training device known as the Velociraptor that measures the speed of the user's movements.

Continued →

4 Where Entrepreneurship Begins

Khushi Baby, a company that uses technology to improve community healthcare, was started as a student project at the CEID by Ruchit Nagar '16. It's now a global company with 50 employees that has screened more than 18 million people in Rajasthan, India's largest state. The company has developed a platform that stores medical histories, sends messages to beneficiaries, and provides health officials with critical data. Together, it ensures offline, informed, and accountable screening, referral, and follow-up care.

The CEID also spawned the start-up Arix, a company founded by Dianna Liu '18 and two recent SEAS grads Petter Wehlin '17 and Bryan Duerfeldt '17 that uses robotics to inspect pipes for corrosion — a much easier and safer way than conventional methods.

Wellinks, founded by Ellen Su '13 and Levi DeLuke '14 also came out of the CEID. The startup focused on a smart strap for scoliosis braces aimed at giving its users, especially children, a greater sense of independence.

Antonio Medina

Current student, Stanford University's Design Impact Program

I owe so many of the incredible experiences I had at Yale directly to my involvement with the CEID. In the span of one year, I got to write a paper with the United Nations, design and teach my own technical workshops, present at a musical invention competition, host a conference with instructors from makerspaces around the world, develop a product with a manufacturer in China, and give a tour to the president of a foreign nation, all while helping mentor students, work on my own side-projects, and apply to grad school.

Kayla Matheus

The first CEID design fellow, and now a Ph.D. student in the lab of Yale Computer Science Prof. Brian Scassellati

I remember it feeling very unique at the time, how interdisciplinary the center was. [Being a dual art and engineering major], it felt like there was this turning point where I was in these totally separate worlds and here was a place and a vision that was trying to pull people of different mindsets from different departments together. It was funded through SEAS, but anyone on campus could come and make things. That was absolutely amazing to me at the time and it still is. And I think in the last ten years, coming back now, it's shown that there are a lot more students that are thinking in this interdisciplinary way and are coming together.

Exhibits, curators, and scientists at some of the most prestigious museums in the U.S. have all benefited from the work of the CEID. Sometimes it's a matter of custom-making a machine to generate multi-colored lights for an exhibit at the Yale University Art Gallery. Or it could be to help preserve priceless and centuries-old artifacts from ancient Egypt. In that case, a student team devised a way to dampen vibrations that could potentially damage ancient wooden coffins in the Egyptian Art collection at The Metropolitan Museum of Art in New York.

Another group of students worked with officials at both the Smithsonian Institute in Washington, D.C. and Yale's own Peabody Museum of Natural History on a contactless microscope. It's now being tested for use in museums. Patrons operate the device, named the Hover, to get a more detailed look at some of the museums' artifacts.

Officials at the Yale Center for British Art have also worked with the CEID on projects ranging from better ways to clean paintings to setting up new exhibits.

Continued →

5 Assisting the World's Greatest Museums

6 CHIME: Collaborating in a Crisis

In the spring of 2020, the CEID doubled as the hub for the urgently formed Coalition for Health Innovation in Medical Emergencies (CHIME), a collaboration of engineers, physicians, nurses, and many others, to provide healthcare professionals with the tools they needed to combat COVID as it was first hitting the U.S. The team first identified the most crucial problems facing healthcare workers and the best ways to address them. This included a new technology to test non-certified face masks, alleviating a critical shortage of masks in hospitals.

Progress was quickly made on several other projects, including a device to measure the reliability of non-certified respirators, and efforts to allow ventilators to treat more than one patient at a time. A partnership with researchers at the School of Engineering & Applied Science and the School of Medicine resulted in a research journal paper on bench-top testing of masks and respirators allowing the work at Yale to be replicated around the world.

Yale

The CEID, which has been described by Yale SEAS Dean Jeffrey Brock as the “portal to the world for innovation at Yale,” has hosted several international guests and events. This includes the International Symposium on Academic Makerspaces (ISAM), which convened at Yale in 2019. The event was co-hosted by Olin College and attended by 350 maker educators, equipment manufacturers, and other enthusiasts from 156 universities from 14 countries. For three days, they talked shop, traded notes, and heard from leaders in the growing multi-disciplinary field.

The CEID also hosted a partnership between SEAS, the School of Architecture, and the Whitney and Betty MacMillan Center for International and Area Studies at Yale — all of whom worked with Afghan entrepreneur Roya Mahboob on designing the Dreamer Institute, a school to be attended by both boys and girls in Kabul.

Students taking the course Environmental Technology and the Developing World traveled to Nicaragua to collect data and run experiments designed to solve real-world problems related to water purification and air quality.

Most recently, the CEID hosted a weeklong workshop for Israeli high school students, where they learned the many aspects of turning student projects into commercial products.

7 From Prospect Street to the Rest of the World

Lauren Chapey

Manager,
New Markets Advisors

There were so many interesting projects and experiments going on, and I found a lot of inspiration from my peers and their work.

While the CEID is obviously an engineering-centric space, the most important skills I developed there were non-technical, like collaboration, communication, and public speaking. Even the most sophisticated engineering project loses its value if you can't show it to the world. All the hands-on courses and extracurriculars I participated in at the CEID taught me not only how to build interesting things but also how to explain them to my peers and to the broader world. I continue to use these skills in my everyday life today, fostering community wherever I go.

8
Collaborations You Probably Hadn't Considered

If you thought a 132-year-old French literary classic would be out of place in a tech-heavy hub of innovation, think again. Working with assistant professor of French Morgane Cadieu and her students, the CEID staff 3D-printed the train at the center of Emile Zola's 1890 novel "La Bête Humaine" ("The Beast Within") based entirely on descriptions from the book. Once the train found its way to Cadieu's classroom, it became the focal point of discussions on language, metaphor, and the nuances of translation.

Fictional trains are one thing, but can you 3D-print a neuron? Absolutely. With help from the CEID, Dr. Gordon Shepherd, professor of neurobiology became the first person in the world to do so. The 3D-printed neuron is approximately 1,000 times bigger than the actual neuron in the hippocampus. When holding the printed neuron, researchers said they could notice details of the flexible dendrites that they hadn't noticed from looking at models on the computer.

The makerspace has also contributed to Yale's vaunted tradition in the dramatic arts, thanks to the senior project of mechanical engineering major Sydney Garick '18. Working in the CEID, she built a giant LED panel – essentially, a floor with programmable lights – to be used in the Yale production of the musical "Fun Home."

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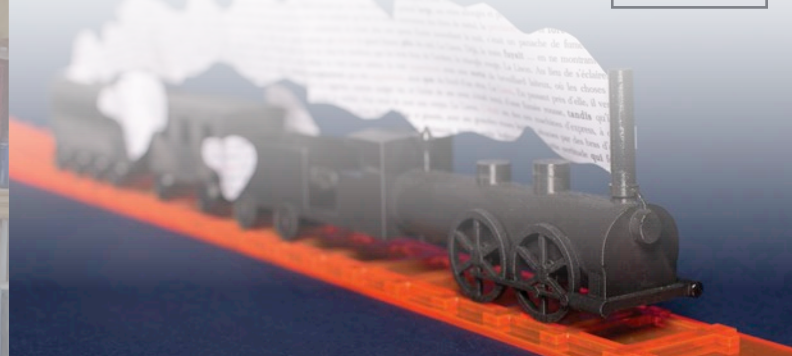


9

Air, Bones, and Other Faculty Research

However esoteric the subject, the CEID can help. That includes monkey bones. Dr. Robert Wyman, professor of molecular, cellular and developmental biology, took advantage of the CEID's resources to replicate the bones of extant specimens of the cercopithecoid primates, which include baboons and macaques. The 3D-printed replicas were used for comparisons to fossils and to study the degree of variations between the bones.

The CEID is also helping you breathe better air. Students in ENAS 118 worked with Drew Gentner, associate professor of chemical & environmental engineering and the environment on sensors for a study on the air quality of Baltimore. The devices measure particles and volatile compounds in the air in micrometers. Some were designed for portability, so that the study's subjects could carry them around all day.

When Dr. David Frumberg in Yale Orthopedics needed to fix an abnormal connection between two bones in a patient's leg, he knew X-rays and CT scans wouldn't give enough information for the tricky case. He went to the CEID to make a 3D-printed model of the joints. Having the model allowed him to see things he couldn't before. The operation was a success.

Yale

Jan Kolmas

Software Developer — Flight Control, Wingcopter

My favorite part about the CEID was the atmosphere — everyone there shared a passion for building things and was excited to tell about it. Plus, no matter when I passed by, there was always someone I knew.

I learned a lot of hands-on skills with mechanical design, prototyping, machining, as well as electronics. I also developed a love for whiteboards.

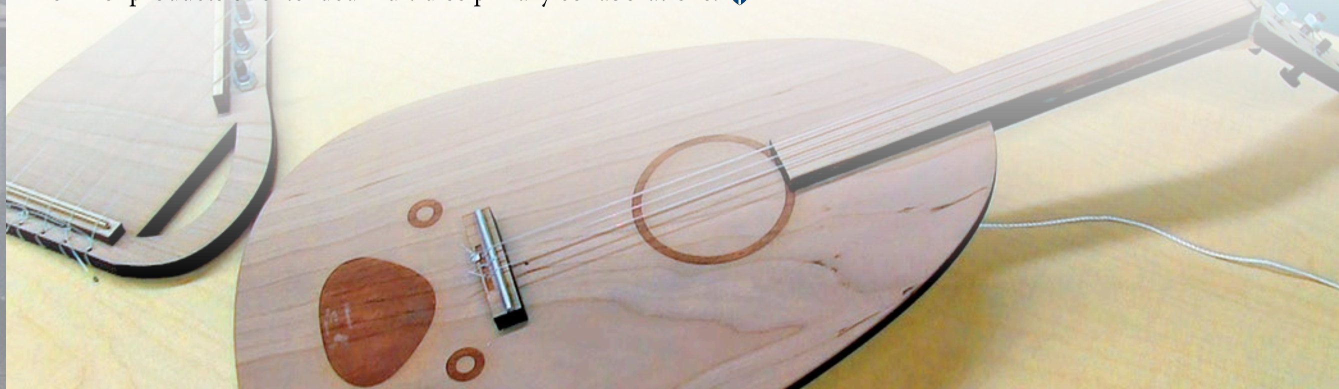
10 Years of Teaching Engineering in All Its Forms

Perhaps more than anything, the CIED is a place to lean. In its 10 years, the CEID has been a hub for forward-thinking, collaborative courses. In Engineering Innovation and Design, taught by Larry Wilen, a Yale senior research scientist and design mentor in the Center for Engineering & Design, and SEAS Deputy Dean and James S. Tyler Director of the CEID Vincent Wilczynski, students learn to work in teams across multiple engineering disciplines to develop a project for a guest client.

In Musical Acoustics & Instrument Design, students design and build entirely new musical instruments. Taught by Larry Wilen and Konrad Kaczmarek, a composer and lecturer in the Department of Music, the course has produced instruments that draw inspiration from everything from wine glasses and Ben Franklin to Tuvan throat singers.

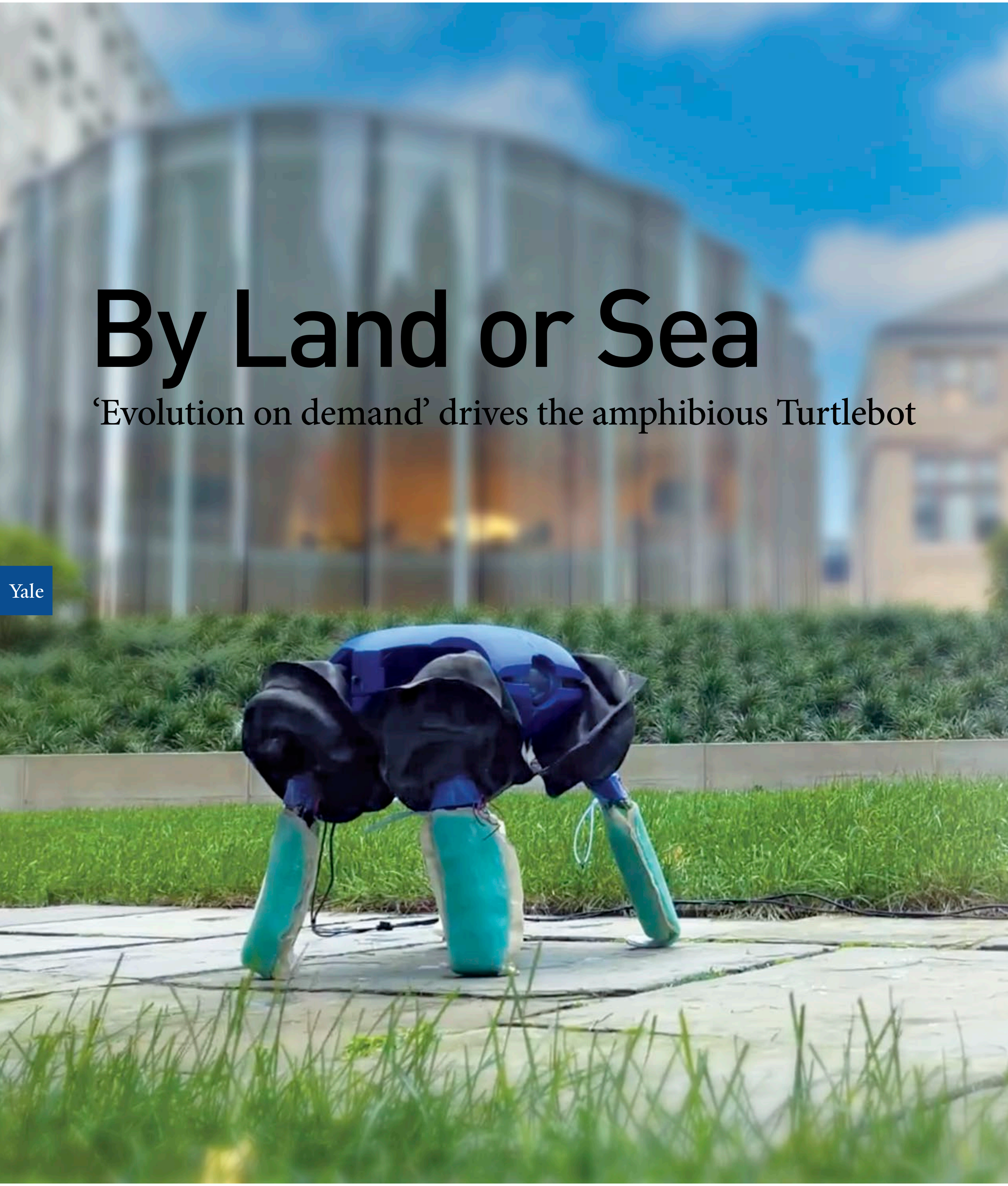
In Making It, taught by Joe Zinter, assistant director at the CEID, students take on the many facets of product design and development while simultaneously working to conceive and develop a marketable product and business.

The projects that come out of these often take on lives that go well beyond the courses themselves, in the form of products or extended multidisciplinary collaborations.



By Land or Sea

'Evolution on demand' drives the amphibious Turtlebot



Turtles may have earned a reputation as slowpokes on land, but they move through the water like pros. Conversely, tortoises are considered merely adequate when it comes to swimming, but surprisingly nimble on the ground.

And if you could combine the strengths of both? Then you'd have ART, more formally known as the Amphibious Robotic Turtle, developed in the lab of Rebecca Kramer-Bottiglio. While actual turtles and tortoises tend to spend most of their time where they move best, ART travels adeptly in both land and water at the shoreline. It differs from other amphibious robots in that it doesn't require multiple types of limbs for multiple terrains. For instance, some water-land robots will use retractable wheels for land and propellers for water. That means the robot is always carrying around unused parts regardless of what environment it's in.

In the case of ART, though, the same parts that act as flippers to swim through water adapt to become legs once the robot is on land. One key difference between turtles and tortoises is in the shape of their limbs. Turtles' limbs are long and flat like flippers, while tortoises have rounded, load-bearing limbs more suited to walking. (We're generalizing a bit when we talk about primarily aquatic turtles and primarily terrestrial tortoises; Kramer-Bottiglio noted that there are many variations in the turtle-tortoise world, including morphologies and skill sets.) With artificial muscles and materials of variable stiffness, the robot adapts its shape, stiffness, and movement patterns to the

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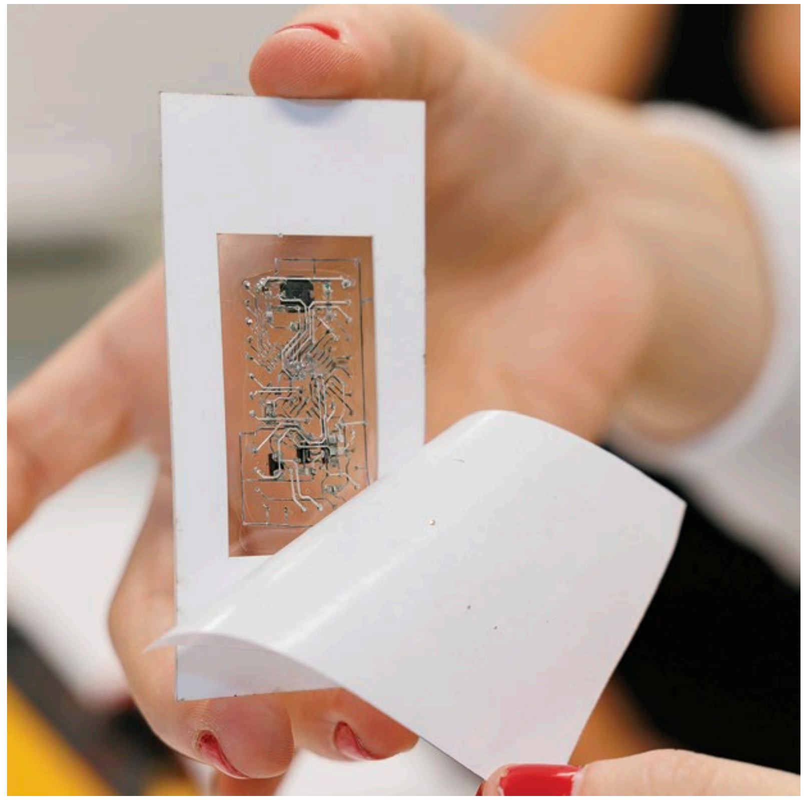
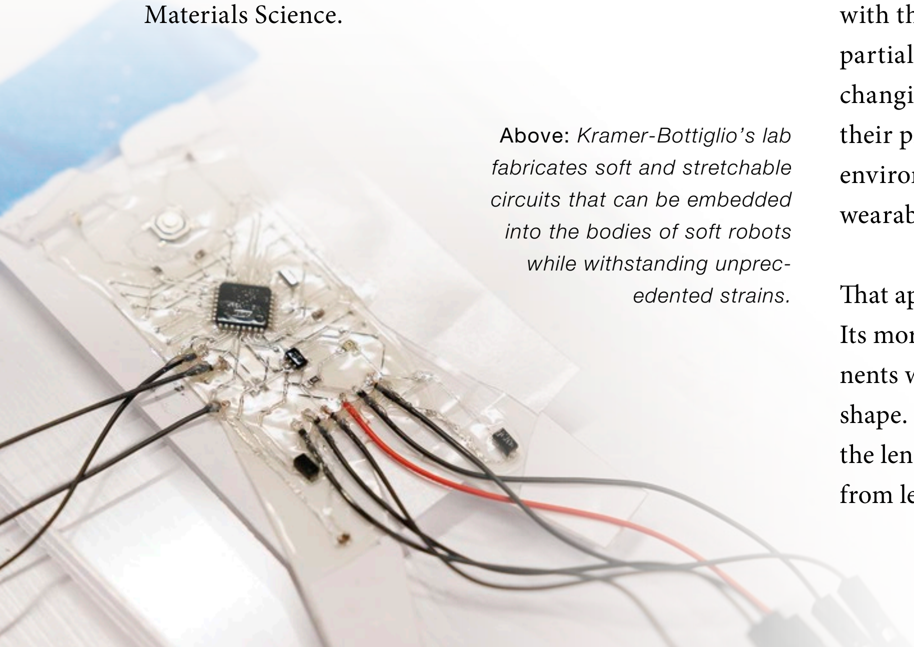


environment. In its legged state, ART traverses land with a variety of four-legged terrestrial gaits. When it reaches water, ART's legs morph into flippers, enabling it to swim with lift- and drag-based aquatic gaits. This design strategy, which the researchers call "adaptive morphogenesis," cuts down on the number of the device's parts allowing it to operate more efficiently.

"By using the same structural and actuation components for propulsion in both environments, we reduce the overall part count and expect efficiency gains for multi-environment locomotion," said Kramer-Bottiglio, the John J. Lee Associate Professor of Mechanical Engineering & Materials Science.



Above: *Kramer-Bottiglio's lab fabricates soft and stretchable circuits that can be embedded into the bodies of soft robots while withstanding unprecedented strains.*

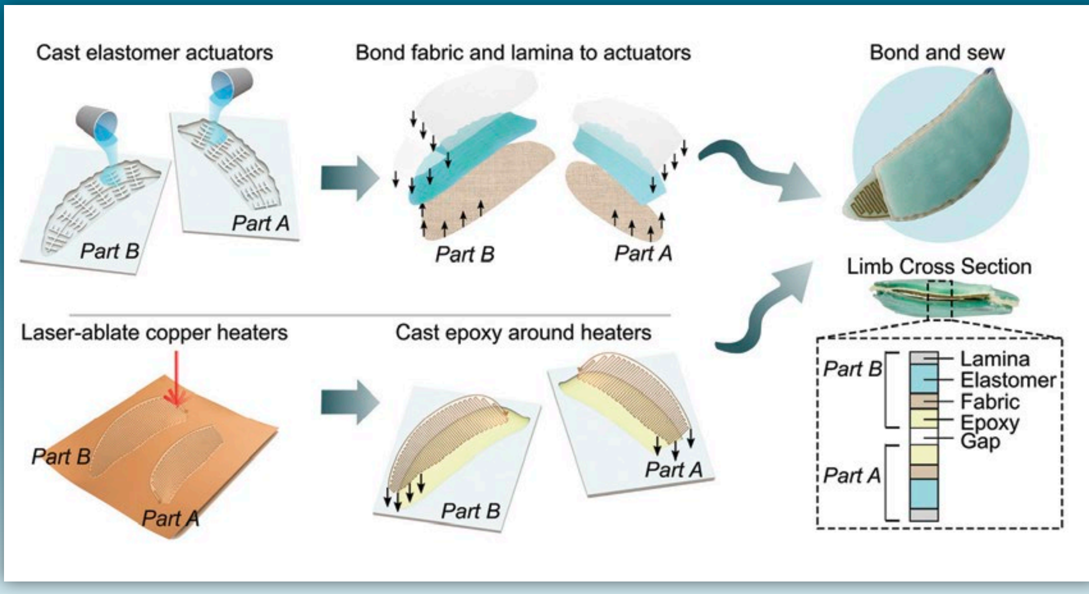
It's an innovation that's made a splash within the robotics community. When ART was recently featured on the cover of the journal *Nature,* Chief Physical Sciences Editor Karl Ziemelis compared adaptive morphogenesis to "a form of evolution on demand."

The word "robot" comes from the 1921 play *R.U.R. (Rossum's Universal Robots)* by the Czech writer Karel Čapek. It's a story of human-like robots made from soft materials. Since then, though, the popular image of the robot has been one of rigid and metallic devices. But as Kramer-Bottiglio points out, the natural world is filled with soft, adaptive systems capable of deftly interacting with their environments — in fact, all animals are at least partially soft. In her lab, they focus on developing shape-changing, soft robotic systems that allow devices to adapt their properties and shapes to take on different tasks and environments, which have numerous applications from wearable devices to self-deploying shelters.

That approach has been crucial to the development of ART. Its morphing limbs, which fuse traditional rigid components with soft materials, allow it to change its stiffness and shape. The lab-designed soft actuators are distributed along the length of the limb and drive the limbs' shape changes from legs to flippers.

Continued →

Above: *Kramer-Bottiglio and Ph.D. student Stephanie Woodman test their stretchable circuits that are capable of driving soft robots from onboard.* Below, left: *Ph.D. student Luis Ramirez tests the loading capabilities of a fabricated turtle limb.* Below, right: *Three robotic skins around a soft cylinder form a continuum arm and a fourth skin between two plates creates a gripper.*



Left: *Fabrication can be broken down into two main tracks: elastomeric actuators (top) and Joule-heating variable stiffness material (bottom). They are then combined via a sewed joint.*

To make these adaptable limbs, the researchers used a type of polymer that allows the limbs to change shapes and then remain in a particular state. With a combination of applying heat and then inflating it, for instance, the limb morphs from its default flipper state to adapt to land.

Yale

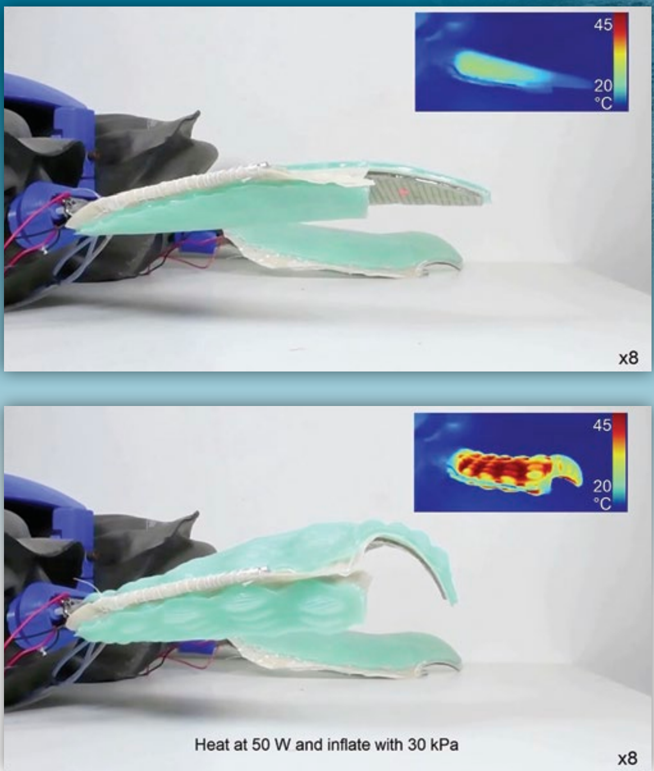
"It inflates and then cools in that inflated position, so it's able to hold a load-bearing, leg-like shape," said Robert Baines, a Ph.D. student in Kramer-Bottiglio's lab (known as the Faboratory) who contributed to the development of ART.

The researchers implemented specialized movements and limb shapes for water, land, and the transitional stage between the two. To better understand the animals' movements, Kramer-Bottiglio visited facilities where turtles are monitored and then released.

"We did unstructured experiments looking at turtles being released on the beach into the open ocean," she said. "We then did more structured studies looking at turtle hatchlings going up and down ramps at specific incline angles. We were looking for signatures in their amphibious locomotion strategies to inform the transition policies of the robot."

Frank Fish, a biologist from West Chester University who specializes in locomotion efficiency in certain animals,

$$I_{leg} = \frac{\pi}{4} r^4 \qquad I_{flipper} = \frac{bh^3}{12} \qquad P_{cr} = \frac{\pi^2 EI}{(kL)^2} \qquad \frac{P_{cr,\,leg}}{P_{cr,\,flipper}} = \frac{I_{leg}}{I_{flipper}} = \frac{\frac{\pi}{4} r^4}{\frac{bh^3}{12}}$$



Left: *The limbs can morph in shape, stiffness, and volume by applying heating and air pressure to transition between flipper and leg modes.* **Below:** *The underside of ART. The robot comprises four distinct subsystems: PVC chassis, shell, shoulder joints, and limbs.*

interpreted the video data and noted key elements of the animals' movements.

So, what do you do with a turtle- and tortoise-inspired robot? Potential applications for the robot include environmental monitoring, diver support, and carbon capture.

$$\frac{P_{cr,leg}}{P_{cr,\,flipper}} = 10.15$$

Below: *Crawling distributes ART's weight, allowing it to traverse sand and other substrates. When walking laterally, ART only has one limb off the ground at a time while incrementally pivoting its body to move forwards.*

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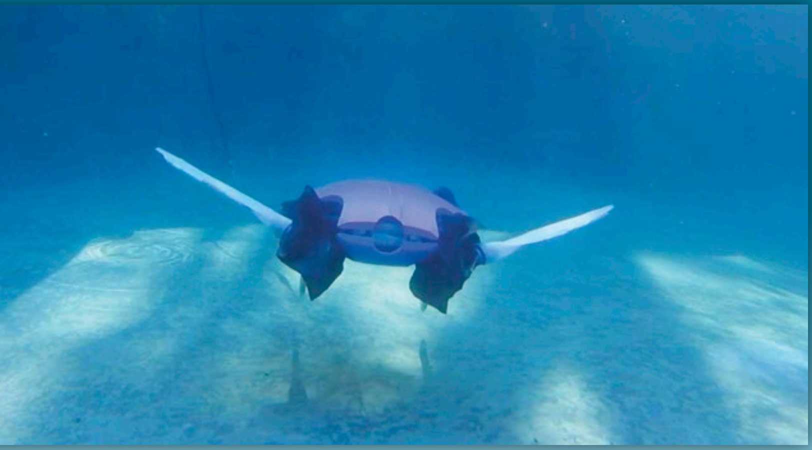
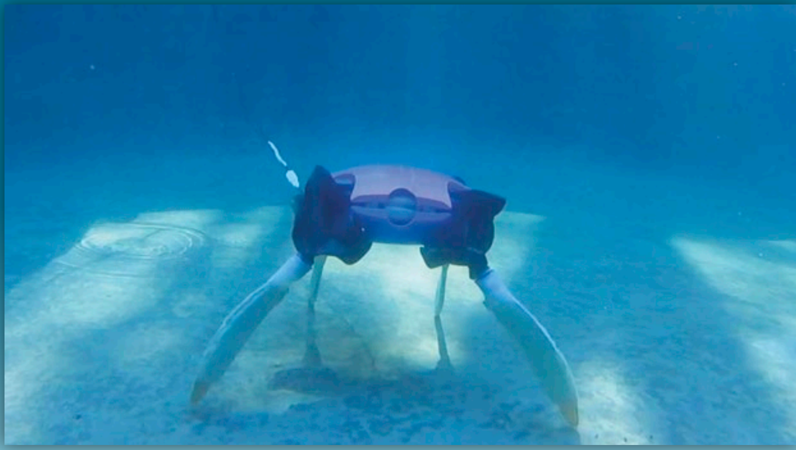




The research can also contribute to the field of biomechanics by gaining further insight into the mechanics of the animals' movements.

Looking for Water and Drawing a Crowd

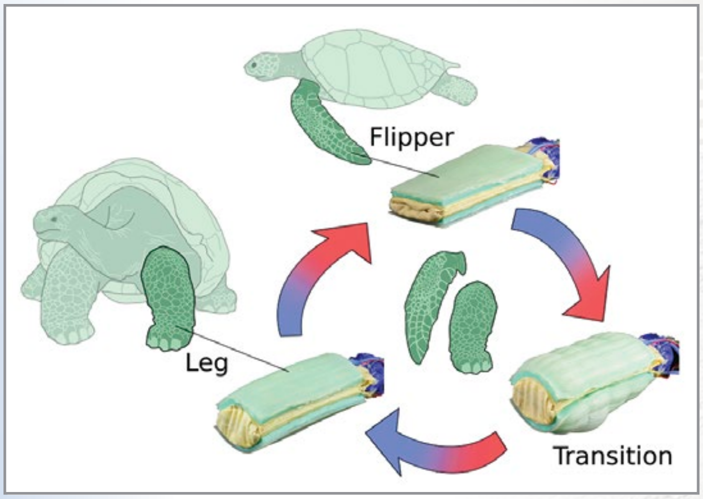
In addition to the controlled environment of the lab, Kramer-Bottiglio and her team were also able to find plenty of sandy, gravelly, and concrete terrains for test runs. Finding a place to operate it in water, though, proved surprisingly tricky. Initially, the pool at Yale's Payne Whitney Gym served as a testing site until it temporarily closed for COVID. For a while, an outdoor club close to Kramer-Bottiglio's home let them test early in the morning before it shut down for the season. At that point, they moved operations to the backyard pool of SEAS Deputy Dean Vincent Wilczynski, where they captured a lot of underwater video footage.

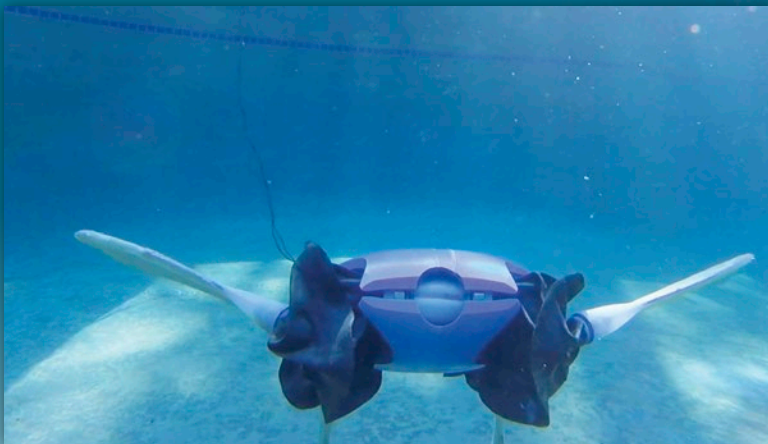
New Haven's East Rock Park also proved a valuable resource, as it has multiple terrains, including the transition between land and water. It's a convenient location, but it came with some complications. For example, testing the robot in the water of the park's canoe launch during the winter months, the cold temperatures caused some problems for the morphing of the limbs (future versions will correct this).

Also, it turns out that a robotic, turtle-like device will draw a lot of questions from passers-by.

"A lot of people are curious," Baines said. "I'd say 90% of people who walk by ask a question, which is great, but I think we need to make a sign because we're out there working and then if we're explaining to everyone what it is, it's like we're not working."

The University is currently building a state-of-the-art tank on West Campus for Kramer-Bottiglio and other roboti-





Left, below: *The researchers programmed movements and limb shapes to efficiently travel through water, land, and the transitional stage between the two.*

cists to conduct future testing. The 44 x 10-foot pool was designed with tunable wave energy and adjustable inclines, currents, and temperatures.

“For future iterations of the robot, we’ll be able to test amphibious locomotion strategies in this specialized facility, which doesn’t exist anywhere else,” Kramer-Bottiglio said. “We hope to gain a deep understanding of the physics of what’s happening and how the different variables in a surf zone play into locomotion strategies.”

Nature, an Expert Engineer

ART is hardly the first robot from the Faboratory to be based on the mechanics of living creatures. This makes sense — nature has proven to be particularly adept at finding the best and most efficient ways to move through the world and its many kinds of terrains.

When danger approaches, the Moroccan flic-flac spider takes the shape of a ball and rolls away to safety. Octopus tentacles can move in many directions, but also form stiff joint-like structures for more precise movements. Caterpillars can travel by using inchworm movements, as well as coil up and propel themselves away from predators. Such capabilities allow organisms to thrive in the natural, unstructured world. While she’s not trying to reverse-engineer animals, Kramer-Bottiglio has drawn inspiration from all of these creatures.

Her lab created robotic skins with embedded actuation and sensing, which are inspired by the multimodal sensing and adaptive abilities of animal skins. The robotic skins were made to be applied to random deformable objects to turn them into robots by “roboticizing” them from their surface. Another bio-inspired creation of hers is octopus-like tentacles with shape-morphing capabilities, enabled by variable stiffness fibers patterned around inflatable actuators. She’s also developed a number of multifunctional materials, for example, a self-coagulating conductive composite inspired by bodily hemostasis. In general, her lab develops new materials that, when embedded into robots, yield new behaviors such as shape change.

“We’re trying to create robots that can adapt their morphology and behaviors on demand,” said Kramer-Bottiglio. “We’ve found that changing both the body shape and the way it moves helps the robot to overcome obstacles or continue task performance despite changing terrains and environments.”

The Feedback Loop

Blurring boundaries to discover revolutionary materials

The discovery of new materials has long been key to technological advances that have transformed our lives. These include cell phones, medical devices, computers, and more efficient energy conversion. That said, new materials are often mysterious and truly understanding them takes a great deal of trial and error. At Yale, researchers on the experimental and theoretical sides of materials science have teamed up to take the guesswork out of their research and accelerate the progress of their field.

The value of this side-by-side partnership, referred to as a "feedback loop," has been recognized by the National Science Foundation and has become a model for researchers well beyond Yale.

"The two sides can now handshake on important quantitative details and thus answer the same questions about materials," said Sohrab Ismail-Beigi, professor of applied physics, mechanical engineering and materials science, and physics.

At Yale, Ismail-Beigi works on the theory side of materials discovery and collaborates closely with experimentalists Charles Ahn, the John C. Malone Professor of Applied Physics, Mechanical Engineering and Materials Science, and Physics, and with Frederick Walker, a senior research scientist in applied physics. And in the last year, Yu He, assistant professor of applied physics, has also joined the loop.

Essentially, the experiment side of the loop measures and characterizes a new material, and theorists work to understand it. The cycle closes when theorists suggest new materials based on the obtained understand-

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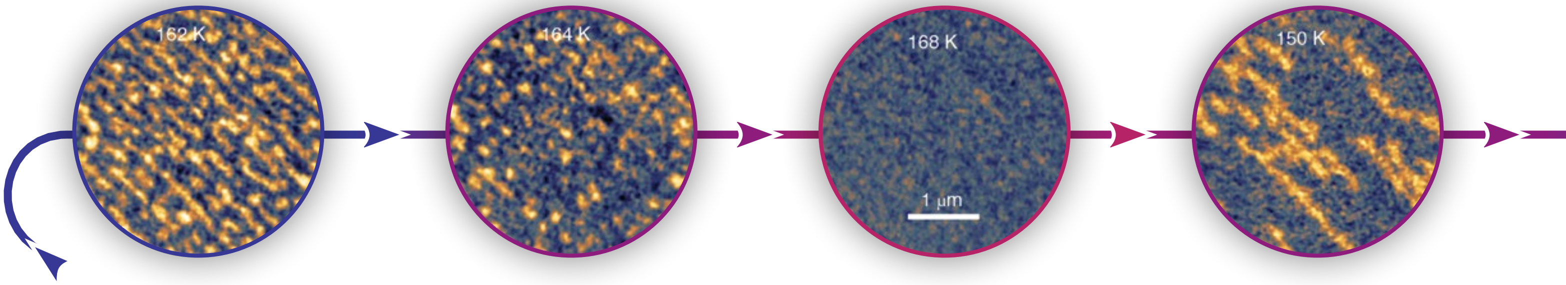


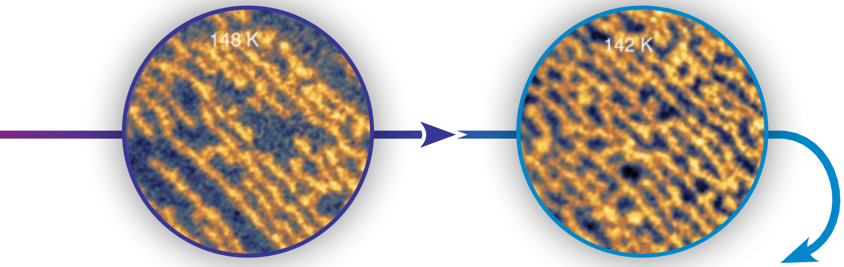
ing, and experimentalists then synthesize and measure the new materials to begin the next cycle.

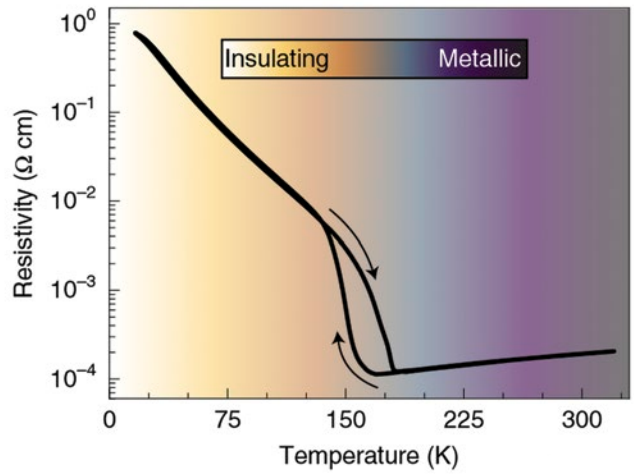
"The goal is to hopefully have impact on fundamental science or some application," Ahn said. "Sometimes experiment motivates the theory, and sometimes the theory drives experiment."

Experiments are needed to make cleaner, more ordered materials and to characterize them more critically at extremely high resolution in an atom-by-atom fashion. The complexity of many of these materials, however, had often outstripped the power of computers to create accurate models. But sometime between 2005 and 2010 that started to change, particularly due to computational hardware and algorithmic advances that have made calculations exponentially faster. For instance, predictions about a material's arrangement of atoms that would have once been beyond a supercomputer's capabilities can now be done with ease. And even as there are now instruments that can make extremely detailed measurements of a material's properties, today's computers can handle these mountainous volumes of data. The experiment-theory model of collaboration has been helped greatly by advances in various technologies. Once these improvements began happening, the Yale partnership could truly flourish.

"With better theoretical methods and more powerful computers, theory can now simulate the material's systems directly and produce results on them of an accuracy that allows direct comparison to an experiment in a quantitative fashion," Ismail-Beigi said.

Below, left and right: *Researchers in Ahn's lab measure and characterize new, complex materials at extremely high resolution in an atom-by-atom fashion.*





Above: *Metal-insulator transition in nickelates.* **Right:** *Resistivity versus temperature, revealing hysteresis, signature of a first-order phase transition.*

Those technological advances bring the theory and experiment sides to a much closer starting point.

"The kind of predictions that Sohrab has produced using first principles theory have become more believable," Walker said. "We've tested a lot of his predictions, and a lot of those predictions are very accurate. And it's that improvement and accuracy that really has led to an explosion of this kind of multidisciplinary collaboration."

The ability for the two sides to work together so well has been critical to reducing the role that chance plays in the field of materials science. This is no small feat, He points out. Even the simplest-seeming solid state materials — such as piezoelectric crystals in standard lighters, let alone the extremely cold superconductors beneath magnetically levitating trains — long amounted to a kind of "quantum voodoo."

"This is largely because alchemistic folklore often triumphed over simplistic theoretical predictions — until recent advances in both theory and

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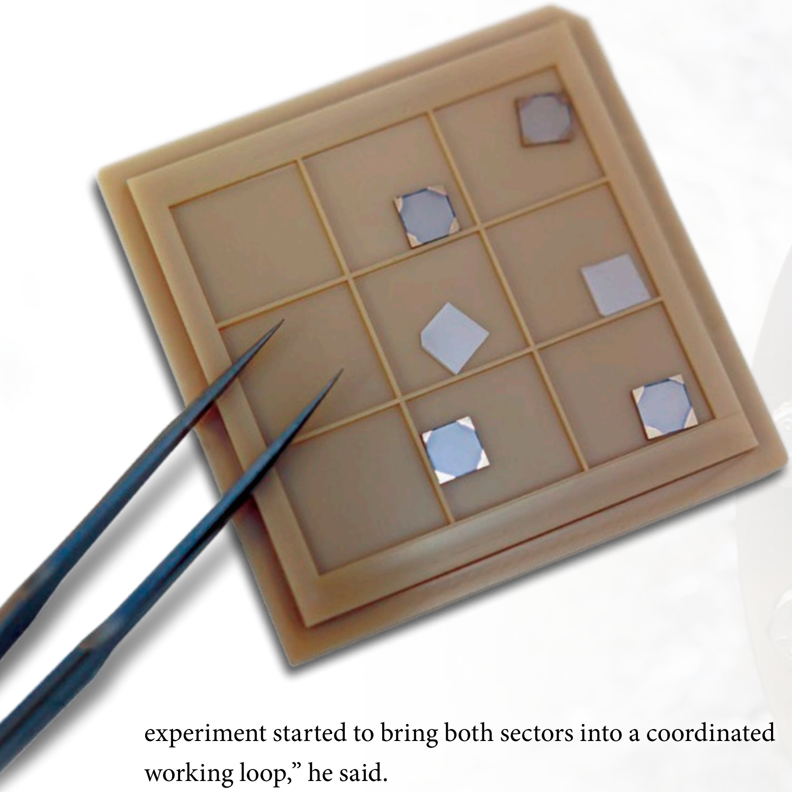


experiment started to bring both sectors into a coordinated working loop," he said.

Without this seamless relationship between the theoretical and the experimental, progress moves much more haltingly on either side. "In the typical situation," Ismail-Beigi said, "the process is remote or highly serialized."

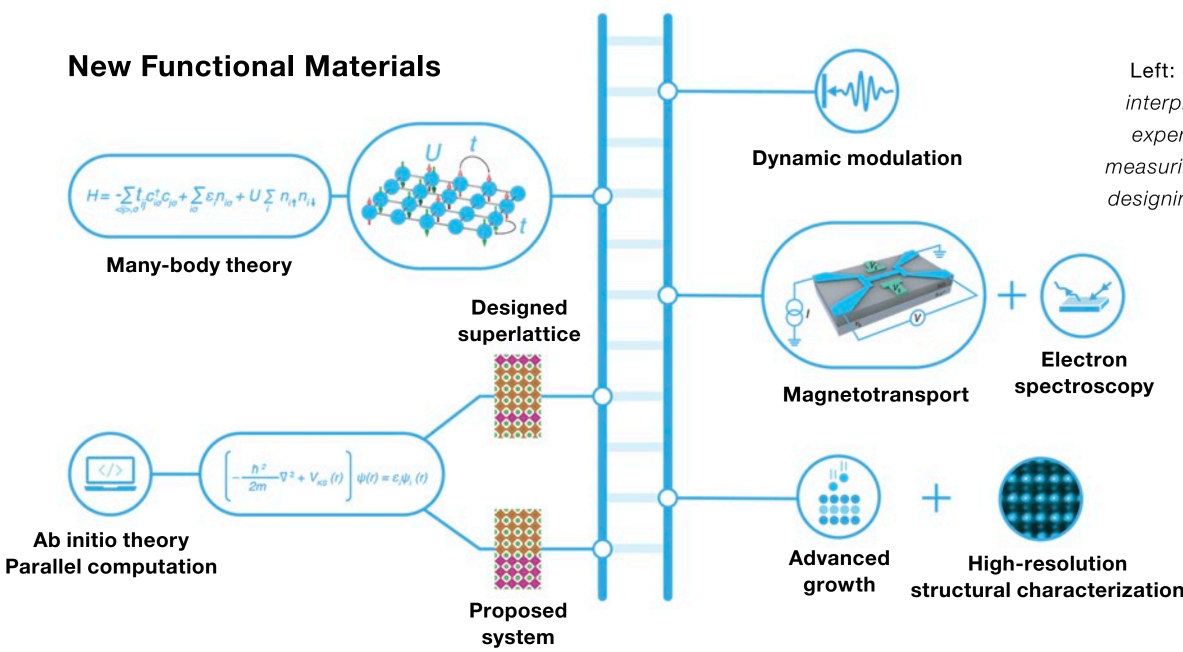
For example: Working alone, an experimentalist would typically publish their work or discuss it at a conference. A theorist working somewhere else may catch wind of this work and independently do computations based on it, usually to better understand the experiment or verify a theory. Rarely do the two meet up to advance the work together.

"I, personally, was more isolated in that I was doing theory on materials that were very interesting but did not have a close collaborator who made and measured them," Ismail-Beigi said. "And I certainly was not in a position to bounce ideas to innovate new materials quickly."

That changed about a decade ago, when Ismail-Beigi teamed up with Ahn and Walker to put their respective expertise to work on the same projects. One early success of this feedback loop is seen in their series of papers on materials known as nickelates (oxides of nickel). These are materials that have intrigued researchers for their potential as a superconductor that could operate close to room temperature, which could make energy transmission much more efficient and enable numerous game-changing applications.

Ismail-Beigi was one of the researchers intrigued by these materials, and his lab conducted a couple of studies to figure out what was going on with the material's systems. Typically, this would have been the end of his involvement, but one of his students noticed something

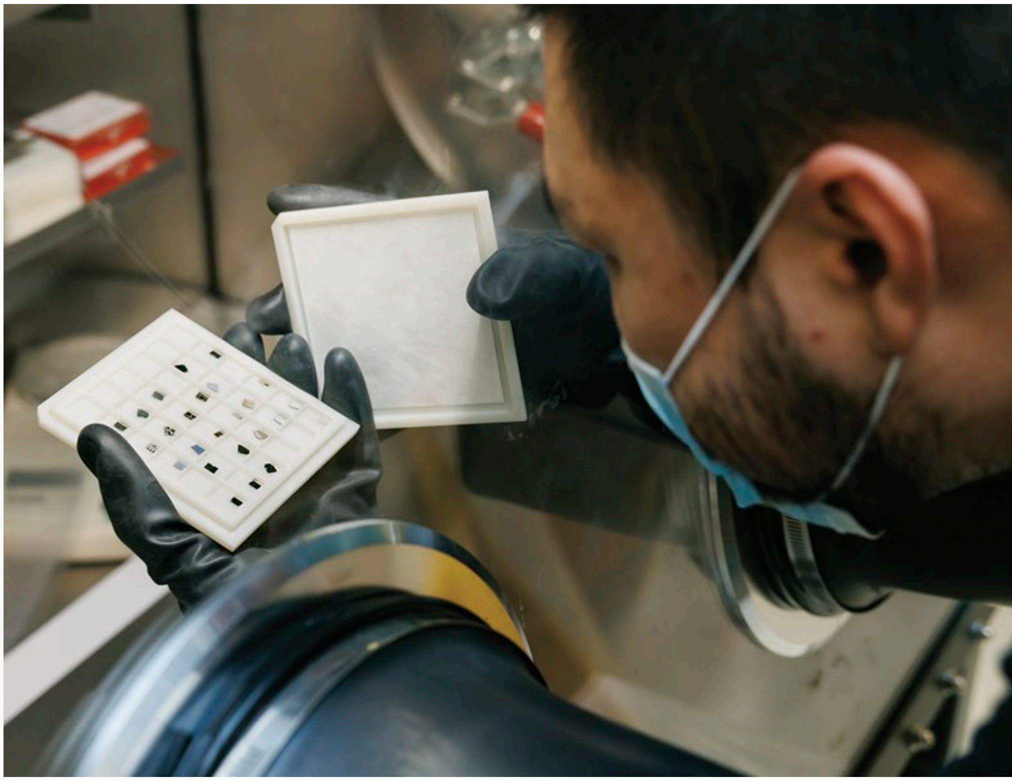
New Functional Materials



Left: *Schematic showing the interplay between theory and experiment when proposing, measuring, understanding, and designing electronic properties of quantum materials.*

unusual about the atomic orbitals of the nickel atoms on the surface of the thin nickelate films. It was potentially a key to engineering some electronic properties. With his interest further piqued, Ismail-Beigi's lab developed theoretical designs of some materials that incorporated this unusual feature in a 3D form.

"Charles's group then built a few materials variants that we proposed and measured them," he said. "We did a series of further calculations on variants and other chemical compositions, and we can now design 3D artificial layered materials incorporating this electronic feature."



Above: *Based on designs from the theoretical side of the feedback loop, experimentalists can build, measure, and better understand new materials.*

That led to another series of studies on another material, cobaltates, which set off another series of back-and-forth sessions. "New X-ray spectroscopy methods were used on these materials to better understand the electronic states at higher resolution, and now we are developing a new theory for that."

And the Applied Physics feedback loop appears stronger than ever. In the last year or so, He has teamed up with them as well. Recently, He lent his expertise in a technique known as angle-resolved photoemission spectroscopy (ARPES), for a study on superconducting iron selenide films that benefited from the experiment-theory loop.

"As a newly arrived spectroscopist to the scene, my specialty yields the electronic 'DNA' of a material," He said. "Now with Charles and Fred producing exciting new materials, and Sohrab making much more reliable predictions on the 'DNAs', it's a bread-and-butter operation to very efficiently resolve outstanding materials problems, old and new."

The exact process of how the two sides work together is in some ways more art than science. At one point, Ahn said, the Yale researchers worked with the NSF to diagram the feedback loop process, first creating a circular image to describe the process. But they realized the process is more complicated than that.

"Sometimes we'll be doing an experiment, we'll measure something, and then as part of some small, incremental step, we'll ask Sohrab, 'What do you think?' and he'll do some calculations," Ahn said. "This leads us to go back to grow some new material or do some new measurement. And then maybe we find some new property. And then we say, 'Oh, we could make a device out of this. It's passing ideas around a circle — it just bounces back and forth. Sometimes it's the other way around, with Sohrab initiating and asking us to do some experiment that drives the work forward."

Which is to say, it's not diagrammatic at all. The back-and-forth is baked into the process so that it's hard to parse it out in steps. In any case, keeping track of who contributed what to the study isn't a priority. It's all part of what Ahn calls "the soup of conversation."

"There's no formula, but you need people who work well together and who want to achieve a common goal," Ahn said.

Digitally Rebuilding a Lost City

Computer Science, Archaeology, and History team up to uncover long-lost clues

The ancient city of Dura-Europos, on the bank of the Euphrates River in present-day Syria, has long fascinated archaeologists and historians for its cultural diversity — Jewish, Christian, Mithraic, and other religious groups lived and worshiped close to each other. Even the graffiti that archaeologists uncovered revealed an impressive mix of languages — Greek, Latin, Parthian, Aramaic, Hebrew, and Middle Persian among them.

All of which makes it a rich area of study, especially since there are thousands of artifacts and documents from the site, which has been threatened by looting and conflict in recent years. The city, founded in 300 BC and abandoned in the third century AD, wasn't considered a major metropolis, but historians say its artifacts could tell volumes about the everyday lives of people from that time and region. But because these artifacts are located in numerous locations and are often unmarked or have multiple labels, it is extremely difficult for researchers to study them.

Holly Rushmeier, the John C. Malone Professor of Computer Science, and Anne Chen, a postdoctoral associate at ARCHAIA, an interdisciplinary program at Yale for the study of ancient and premodern cultures, are working to change that. They recently received a $350,000 grant from the National Endowment for the Humanities to develop a digital archive of materials related to the archaeological site of Dura-Europos. They will create a virtual data cloud known as "linked open data" to bring together the disparate materials from this region. This will create a user-friendly interface that allows researchers to access the data, as well as add their own contributions.

Continued →

"The linked open data will make it accessible, so you can search across all the collections and find the stuff that is really important," Rushmeier said.

The digital archive will also make it easier for researchers to find what they're looking for in the rather dense excavation records. For instance, they'll be able to map out the thousands of objects in Yale's possession and identify where on the site they were originally found.

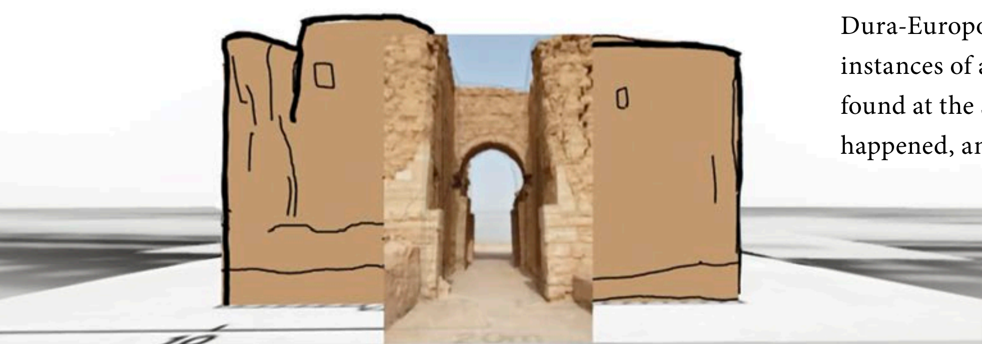
"Then, from that, scholars can start looking at interpreting what that means about everyday life," Rushmeier said.

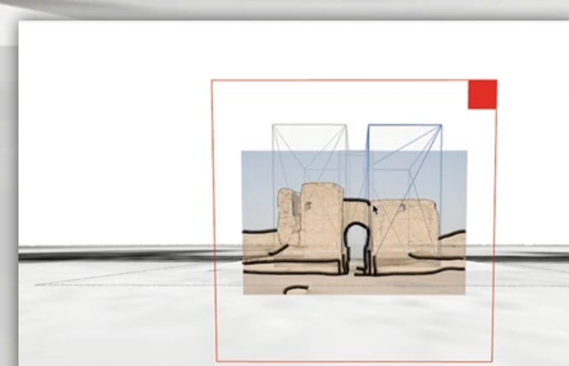
And they hope to eventually create 3D reconstructions of the city based on the many images they have. For instance, she said, reconstructing spaces of worship like the Mithraeum of Dura-Europos, the Baptistry, and the synagogue could help researchers better understand how they were used.

Part of the challenge with the current collection can be chalked up to the convoluted process of excavating the site, which began 100 years ago. There were three phases of the historic excavations. First, a British team came in to do some initial exploratory work but fled within 24 hours because it was a war zone at the time. A Belgian archaeologist headed up a French expedition a couple years later, but it again became a difficult place to work. And five years later in 1922, Yale researchers teamed up with French archaeologists for a more in-depth, collaborative excavation.

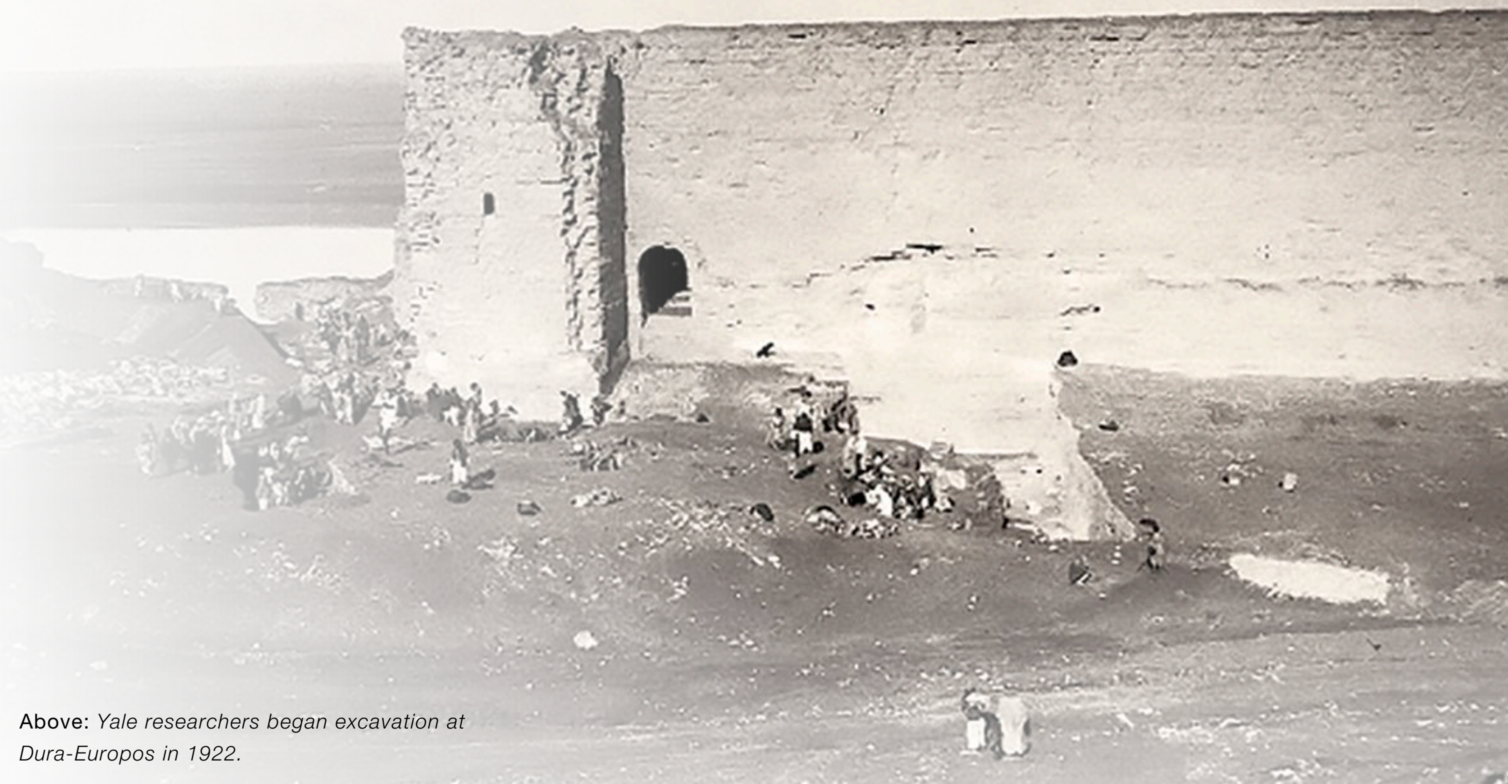
The collection is particularly valuable to history because much of what we know about it isn't through texts, but from the excavated artifacts. For instance, the director of the Yale excavation found evidence in the 1930s that Dura-Europos was the site of one of the earliest known instances of a gas attack. We only know this by what was found at the site, including a coin that revealed when it happened, and chemical tests done on excavated walls.

Yale





Top: *Raw image (left) is fed into the contour extractor to produce a bitmap (middle), which is then vectorized (right).* Bottom: *Image of the facade and its contours; sampled frames from reconstructed animation.*



Above: *Yale researchers began excavation at Dura-Europos in 1922.*

"They tunneled under the city, under the walls and set off gas that poisoned people," Rushmeier said. "So, it's an interesting place because a lot of what we know about it is from objects rather than written history."

At the time, institutions responsible for an excavation would often split the materials among themselves, so about half of the material came back to Yale. Much of the rest is in Damascus, and the Louvre in France has a relatively substantial collection. Other artifacts, mostly gifts from Yale, are scattered at various North American institutions. Yale's share of the collection is found at different campus locations. The Yale Art Gallery holds most of the objects and the historic photographs. Beinecke Library has about 100 of the objects. One cuneiform tablet that was found at Dura-Europos is in the Babylonian collection and can be found at the Peabody Museum.

"This is another reason why this is a great test case for linked open data, because even if we didn't go beyond the Yale aegis, we can demonstrate how for the first time, we could make Beinecke materials speak to Peabody materials, speak to Yale Art Gallery materials," Chen said.

Making things even more confounding for researchers is the turnover among curators over 100 years at all these locations, as well as all the different styles in record-keeping.

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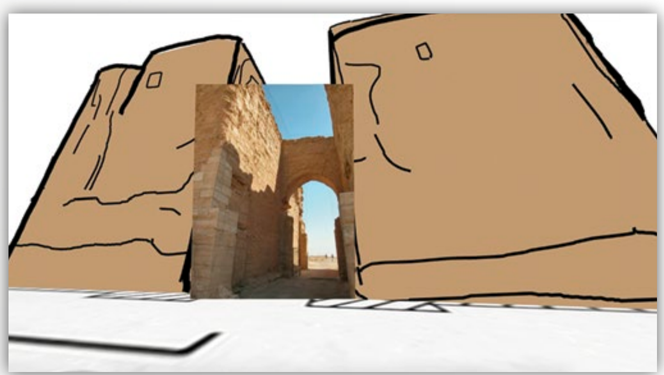
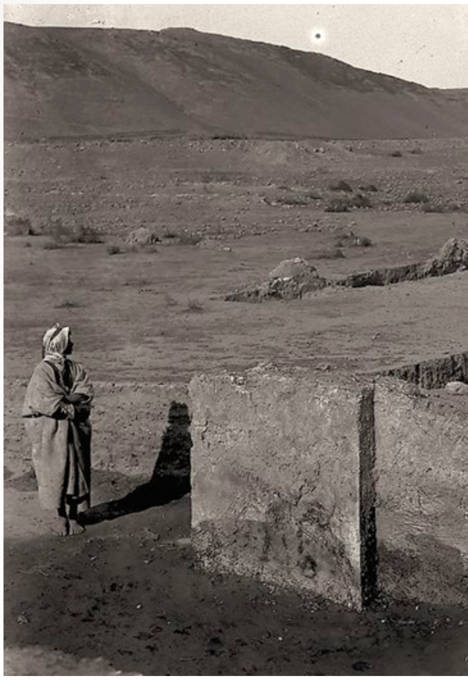




Right: *The digital archive will map out the thousands of objects in Yale's possession and identify where on the site they were originally found.*

And then there are sites with multiple names. For instance, the first building that was excavated at the site is a house of worship that's been known as the Temple of Bel, the Temple of the Palmyrene Gods, the Temple of Jupiter, and the Temple of the Oriental Gods. And that's just in English. None of the materials that are in Western collections have ever been searchable in Arabic.

In three years, they hope to make the full collection searchable, with Arabic translations throughout. They also want to create a user-friendly website that allows visitors to easily toggle between English and Arabic, allowing researchers all over the world access to the collection to contribute their own expertise to the site.

They're also aiming to use technologies developed in Rushmeier's lab to build 3D models and other forms of geospatial reconstruction from photographs in the archive.

"So, if my group could do something to kind of presort the material in a way that then Holly and her students could batch the material and process it for 3D modeling, then great things could happen," Chen said.

In addition to that project, Rushmeier and Chen also co-taught a course in spring of 2022, Introduction to the Digital Humanities for the Premodern World, which introduced students to various digital humanities methods and tools for studying the premodern world. Student teams created multidisciplinary projects related to the Dura-Europos site.

Left to right: *Artifacts catalogued by the researchers include the Coins of Antiochus I Soter, Seleucid King from Dura; the only known surviving example of the semicylindrical shield known as a scutum, used by Roman legionaries; and the Cult Relief of Mithras Slaying the Bull. All are in the Yale University Art Gallery collection.*

"We had a mix of computer science students and humanities graduate students taking the class together," Rushmeier said. "We can do these interesting interdisciplinary courses that we're really excited about in computer science, connecting things up to a lot of different areas."

The class broke into teams, each having students from both computer science and the humanities. A humanities graduate student would pose questions or suggest topics to study, and then the computer science students developed techniques to move the project forward."

One group developed a searchable database for the different examples of graffiti found at the site, with translation of the texts. Another group of students supplemented the content with information provided by the inscriptions for artifacts in museum exhibits. They also developed a QR code that visitors would scan with their phones and made use of the linked open data to access much more information about the items in the exhibit.

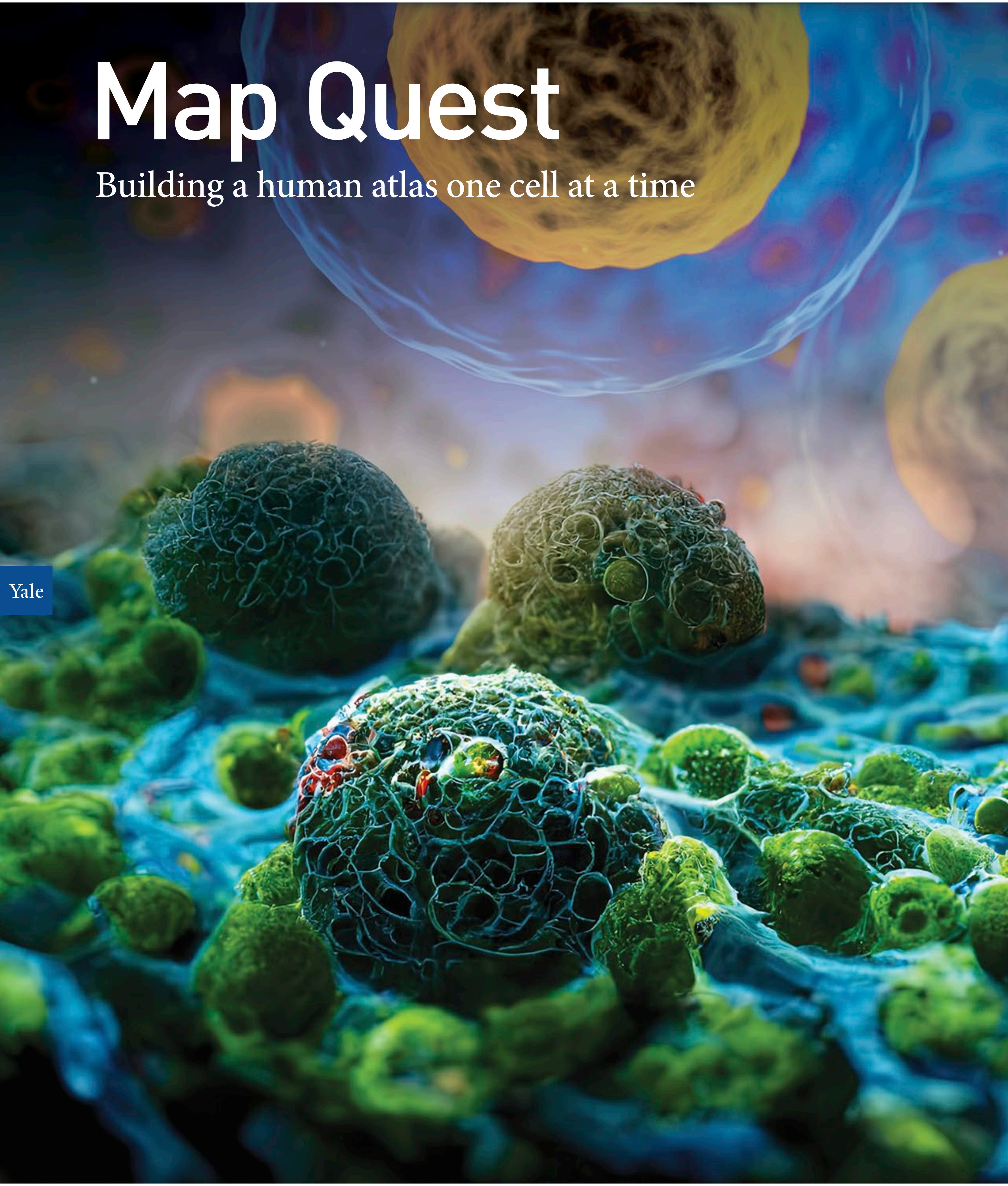
Strewn throughout the city of Dura-Europos were hordes of coins that residents hid whenever the city was attacked or some other crisis arose. A student team created a mapping device that shows their locations as well as some statistical analysis about the weights and origins of the coins.

Digitally organizing and reconstructing a collection from more than 2,000 years ago is an ambitious undertaking, but with the right technology and multiple disciplines working on it, Rushmeier is optimistic that it will soon be a valuable tool for researchers studying this remarkable site.

"With these multidisciplinary projects, we see how much we can push forward both to demonstrate things that can be done and surfacing these new questions that are opportunities for future research," she said.

Map Quest

Building a human atlas one cell at a time



When's the last time you used a map? Like, a real map — the kind that you cumbersomely unfold into a massive sheet that occupies the entire passenger side and then invades the driver's space? Thanks to GPS-based technologies, it's probably been a while.

Science, though, hasn't finished with maps yet. In recent years, researchers in multiple fields have been working to create an atlas of the cells in the human body. With more than 37 trillion cells, it's a massive undertaking (traditional cartographers have it comparatively easy, with a measly 65 million streets in the world to keep track of). But progress is being made.

Rong Fan, a professor of biomedical engineering and pathology, is among those contributing to the effort. He's leading the Yale Tissue Mapping Center for Cellular Senescence in Lymphoid Organs. It's funded with a five-year $6.5 million grant from the National Institutes of Health (NIH). It's one of eight centers supported by the NIH's Cellular Senescence Network, a new initiative of the NIH Common Fund program. It was created with the goal of identifying the various senescent cells in human bodies that play a significant role in disease such as cancer and cardiovascular disorders, as well as in aging.

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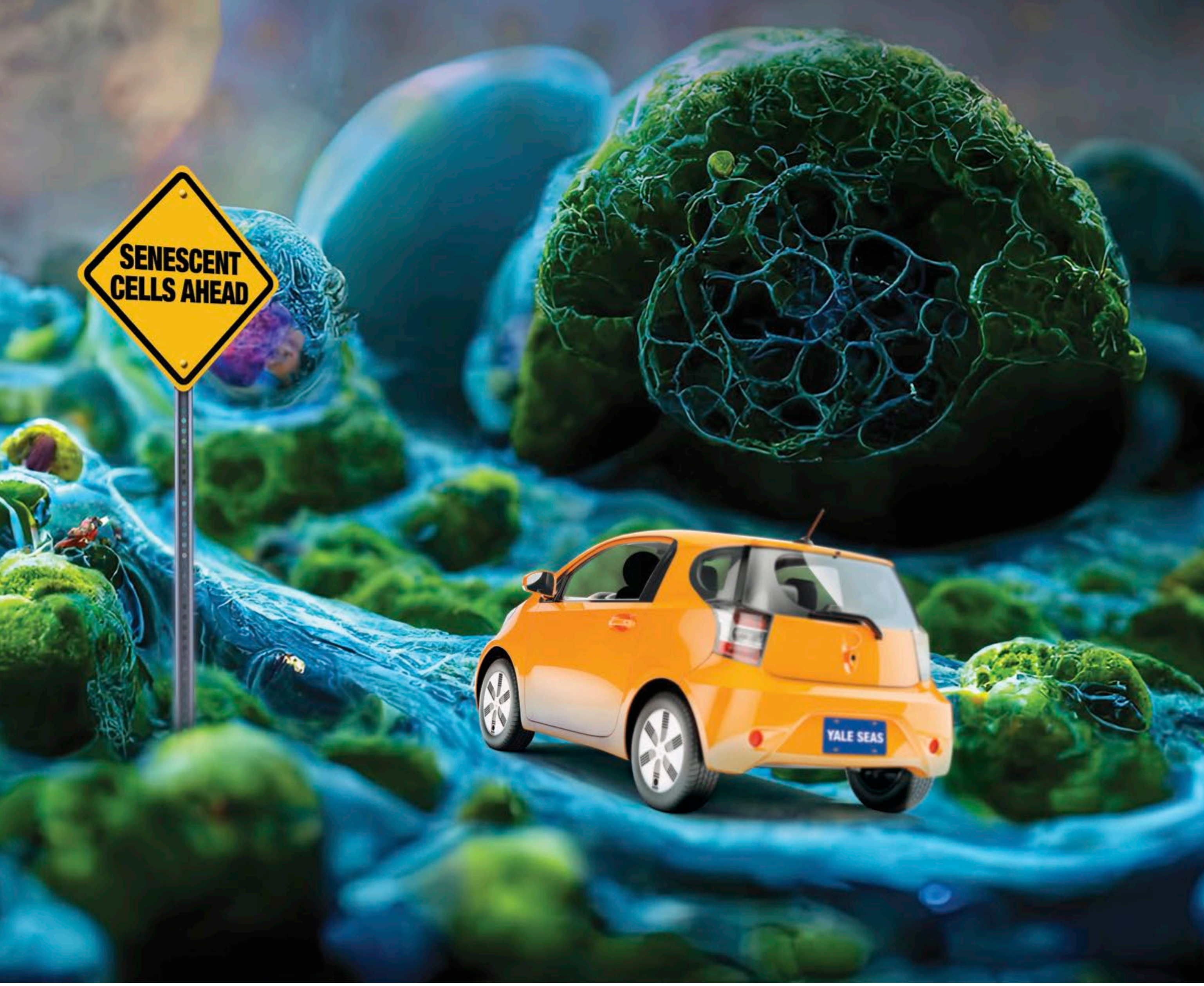
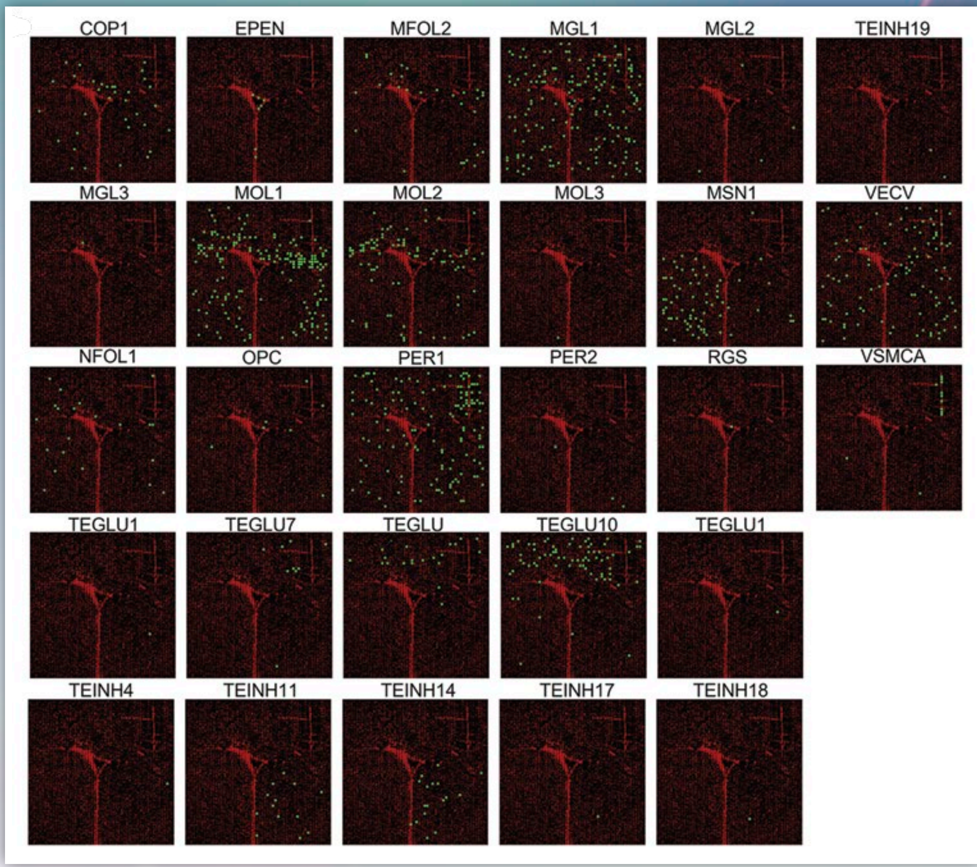


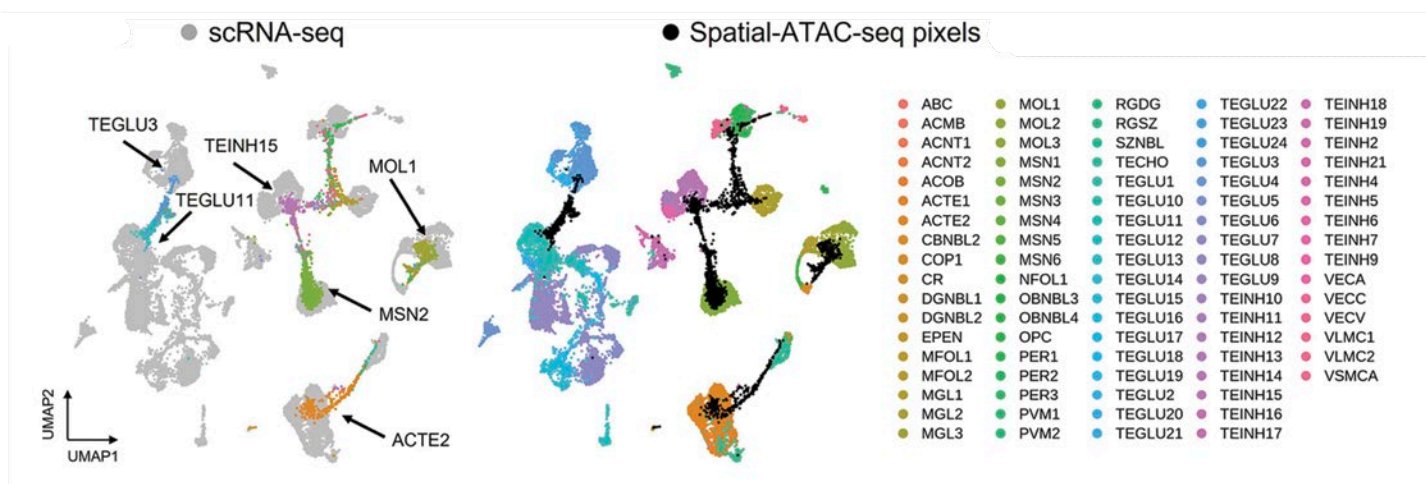


Yale

Left: *Integration of single cell sequencing from mouse brains and spatial sequencing data.*
Below: *Spatial mapping to identify cell types.*

When cells become senescent, they remain alive, but no longer divide. This lack of proliferation can be both helpful and harmful to human health. At the Tissue Mapping Center, Fan and a team of Yale investigators will build the first complete catalog of senescent cells in human lymph tissues, and map out how those senescent cells impact their local environments and tissue functions.

"We know lots of chronic diseases are associated with aging, and the senescent cells are shown to be implicated in the development or progression of those diseases," Fan said. "If you can identify the early signs in those bad senescent cells, maybe we can target those cells early on, either to treat or to slow down the progression of chronic diseases, like cardiovascular disease and diabetes."



"We will eventually integrate all that data together to build a whole book of different tissue maps — an atlas of tissue maps."

› Rong Fan / professor of biomedical engineering and pathology

Some senescent cells help heal wounds by accelerating the growth of blood vessels. But as people get older, they accumulate more senescent cells, and some of these cells may produce the factors that predispose certain types of tissue to a much higher risk of chronic diseases — cardiovascular disorders, pulmonary fibrosis, neurodegeneration, diabetes, and other disorders.

"Senescence in itself is a mechanism for the cells to prevent themselves from developing cancer, because if something is going out of control, the cells become senescent so they can't grow anymore — that's actually a defense mechanism," Fan said. "But it's well known that when those senescent cells accumulate, they create an inflammatory microenvironment, and an inflammatory microenvironment can drive and develop many diseases, including cancer."

Fan's efforts to map cellular senescence in lymphoid tissues expanded to mouse models with another grant from the NIH to launch the Yale Murine-TMC on Immune Cell Senescence Derived Inflammation. The principal investigator is Deep Dixit, the Waldemar Von Zedtwitz Professor of Pathology and Immunobiology, a world leader in aging research. Fan leads the biological analysis component to map senescence cells in murine lymphoid tissues to further complement the data generated from human tissues to deepen our understanding of cellular senescence in health, disease, and aging.

As part of both SEAS and the Yale Cancer Center, Fan is uniquely positioned to assume a major role in the national effort to better understand these cells. The multidisciplinary team of Yale researchers also includes clinicians, a pathologist, an immunologist, and a computational biologist.

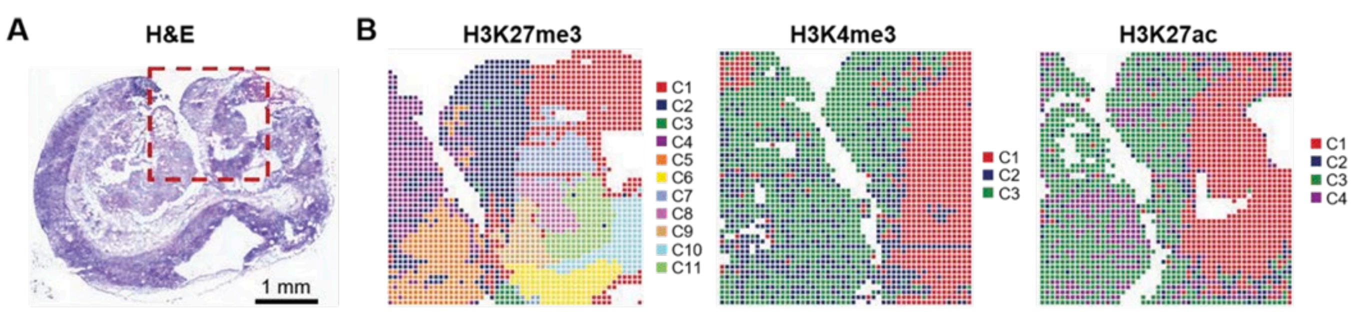
It's an ambitious undertaking that makes use of technology developed in Fan's lab. This includes a suite of spatial omics techniques — that is, ways to study biological molecules that form and guide organisms, and their locations within the tissue.

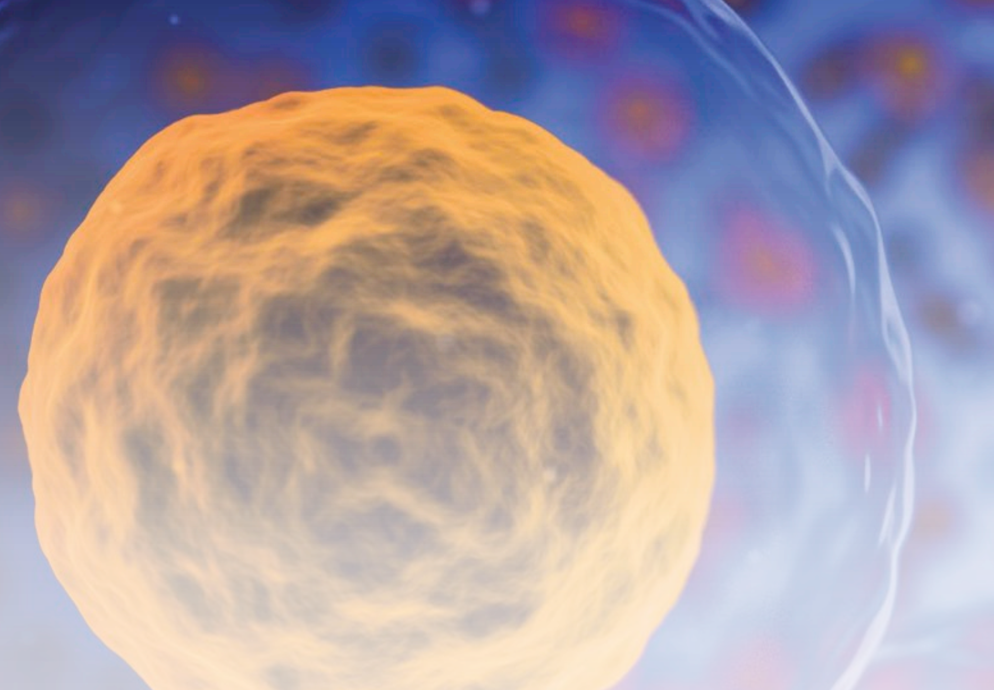
"We will eventually integrate all that data together to build a whole book of different tissue maps — an atlas of tissue maps," Fan said. "Then we can begin to understand how senescent cells develop over different lifespans and health spans."

To further refine their efforts, Fan recently developed a technology to define where the complex of DNA and proteins packed within the nucleus of a cell — known as chromatin — are accessible genome-wide in cells at specific locations in a tissue. Combining the ability to analyze chromatin accessibility

Continued →

Below: *Spatial epigenome mapping at cellular level: (A) H&E image of mouse embryo tissue. (B) Spatial distribution of each cluster of mouse embryo per histone mark.*





"Single-cell analysis has provided vital information that would have been impossible to obtain otherwise"

› Stephanie Halene / co-principal investigator at the Tissue Mapping Center

with the spatial location of cells is a breakthrough that can bolster our understanding of cells and the underlying mechanisms that determine the expression of genes in the development of different tissues or diseases.

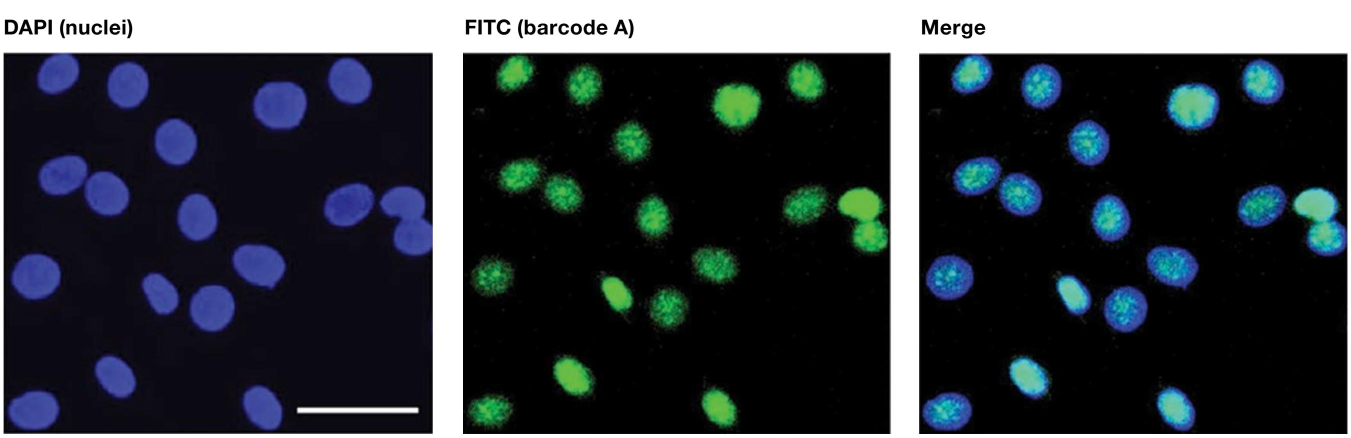
"Now we can identify the cell types to build a spatial cell atlas based on chromatin accessibility," Fan said.

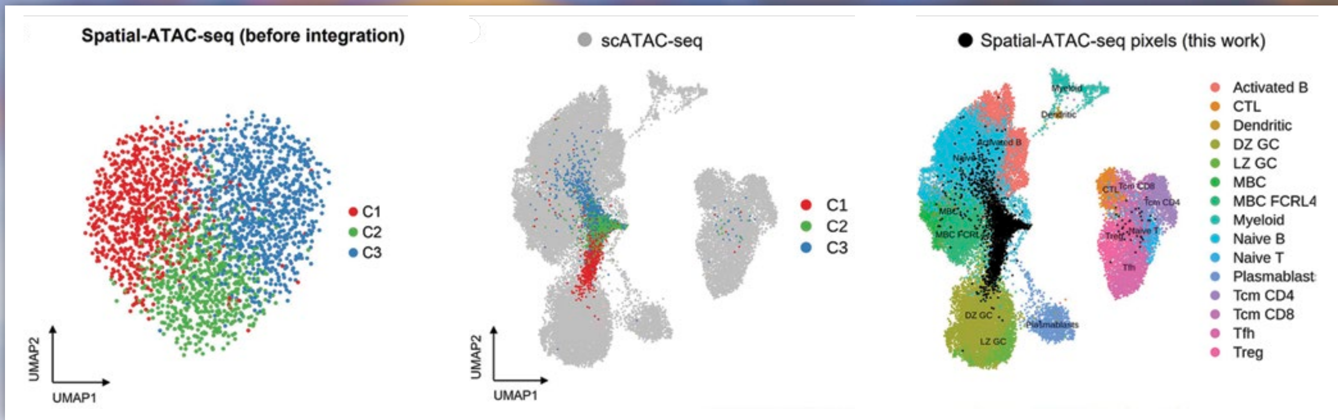
Lymphoid organs — the focus of the Tissue Mapping Center — play a vital role in producing blood cells and immune function. Researchers still don't know exactly what impact senescent cells have on these tissue environments, which makes it difficult to develop strategies to target senescent cells to battle aging, treat cancer, or promote normal tissue remodeling and repair.

The Tissue Mapping Center aims to determine the tissue context of cellular senescence — where those cells are in that tissue and what impact they generate on other cells in the microenvironment. In addition to analyzing senescent cells at single-cell level, they analyze those cells directly in the tissue section. They'll map those cells both in the lymph organs and in blood to identify the senescent immune cells. They can then begin to assess their wider physiological impact.

"Once the stromal cells there become senescent, they're going to produce many factors that can mess up the normal immune cell function," Fan said. "And the immune cells may become senescent as well, and then leave the lymphoid tissue and travel through blood circulation to every part of the body. Senescent cells developing in the lymph organs might have a systemic effect, affecting all different organs."

Below: *Validation of in situ transposition and ligation using fluorescent DNA probes.*





Above: *Spatial chromatin accessibility mapping of a human tonsil, highlighting before and after the integration of single cell and spatial sequencing.*

Single-cell analysis has provided vital information that would have been impossible to obtain otherwise, said Stephanie Halene, a co-principal investigator at the Tissue Mapping Center. Without it, examining tissue, bone marrow, or blood is comparable to looking at a smoothie, with all of its ingredients blended up together.

With single-cell analysis, "you can think about all the individual fruits that go into that smoothie," said Halene, associate professor of medicine and chief of hematology at Yale Cancer Center and Smilow Cancer Hospital. "It's provided so many insights into how normal hematopoiesis [the production of all blood cells] happens in the bone marrow and primary lymphoid organs. We now know what cells are in there – with spatial sequencing we can take it to the next level and study how cells interact and evolve together."

How cells function in tissue depends upon their local environments, so mapping their exact locations within a tissue is essential for a better understanding of disease. By generating a database, researchers can identify what senescent cells there are and start asking the right questions about what impact they have on their tissue microenvironments and functions. Which ones, for instance, help tissue recover from injury, and which ones drive the aging process?

"How do you differentiate that?" Fan said. "If you have that knowledge, maybe you can separate the good from bad senescent cells and target the bad ones to slow down aging — especially aging that's associated with human diseases."

Joseph Craft, the Paul B. Beeson Professor of Medicine and Immunobiology, is another researcher with the center. He and Fan began working together several years ago, using Fan's single-cell assays to define the nature of the immune cells in lupus patients. Now they hope to make the currently blurry picture of senescent cells a lot sharper. The benefit of Fan's technology is that not only can researchers observe the cells individually, but they can see them exactly where they're supposed to be. Craft compares the conventional way of observing these cells to looking at a cross-section of a multistory apartment building.

"You know that this is the couch and so forth, and you know that the couch is in this room in this apartment," Craft said. "And we're doing that at a tissue level, and Rong is certainly a pioneer in this."

In addition to the potential medical benefits, the research is simply providing valuable knowledge about us. Halene compares all the new insights about these cells to the new information about the universe that we're gaining from NASA's James Webb Telescope.

"I think something like that is going on in medical and biomedical science where we get these insights deep into the essence of life, and we're also understanding systems much better," she said.

From Hunters to Pitchers

Bringing Yale-style biomechanics to the big leagues

In the animal kingdom, the ability to throw fast and accurately is one of humans' specialties. In fact, it's been critical to our evolution. It allowed our human ancestors to disable or kill animals larger than themselves.

"Hunting requires not just speed in throwing, but accuracy," said Madhusudan Venkadesan, associate professor of mechanical engineering and materials science.

Obviously, finding rock-throwing hunters for Venkadesan's lab to study isn't easy. But there are still people whose livelihoods depend on their ability to throw fast and accurately. And within this group, professional baseball pitchers are a particularly promising subject for study.

That's where Dan Huynh '23 comes in. The avid baseball fan has been working with the lab on the biomechanics of throwing. And for the past two summers, he has interned with professional baseball teams, working as an applied sports scientist specializing in biomechanics. He monitors everything from the players' mental acuity to their on-field performances.

Huynh worked with the Washington Nationals this past summer and with the Tampa Bay Rays in 2021. Both summers, Huynh has worked out of Florida at his respective teams' training complexes. He's assigned to the Rookie-level Florida Complex League (the next level up is Single-A), so he works with the organization's youngest players, most of whom are usually just a few years younger than him. Many of them came up through baseball acad-

Continued →

emies in the Dominican Republic and have had very little, if any, sports science in their training.

"I apply sports science with a sole purpose: how can we make these players better, how can we get them to fulfill their potential and their goals and dreams of making it to the major leagues?"

A big part of his job with the team is hitting development. Much of the data that he works with comes from Blast Baseball sensors, placed at the end of a player's bat.

"They can tell me how fast they're swinging the bat, what angle their bat is both horizontally and vertically, what angle their bat is relative to their body," he said. "Metrics like that can give us insight into how their swing is working."

Photos courtesy of Dan Huynh

Right: *Huynh recently interned with the Washington Nationals, working as an applied sports scientist, monitoring everything from the players' mental acuity to their on-field performances.*

Although always a huge baseball fan and a player throughout high school, Huynh hadn't considered sports science as a field of study when he came to Yale.

"I was just a normal mechanical engineering major because I knew I wanted to do engineering, but I didn't know what type," said Huynh, who recently moved to Orlando, FL from the Washington, DC area.

When Covid hit in 2020, Huynh needed something to do for the summer. He secured an internship in biomechanics research at the United States Military Academy at West Point, where he worked on a study of the effect that hiking with loaded backpacks has on soldiers' postures.

The same summer that he worked at West Point, Huynh and his friend, Clark Klitenic (now a pitcher on the Yale baseball team), helped to build StatStak, an athlete data management system specifically geared for college baseball teams.

Right: *Huynh utilizes real time data to detect errors in a batter's swing or a pitcher's throwing mechanics.*

"The problem we found within the realm of college baseball is that all these teams have these fancy tools to collect these data points, but the coaches aren't data scientists or statisticians, so that data just goes into the void," he said. "The players don't get the benefit of it because they don't get their own data in a way that is actionable for them."

Essentially, users upload files to StatStak's online dashboard, which then generates graphs and other visual information that both players and coaches can access and use in real time.

Through his work at West Point, Huynh got the biomechanics bug. When he returned to Yale, Huynh found his way to Venkadesan's lab. At first, his role was mainly to observe and see how a lab operates. Then he began helping with grant applications and literature review for studies coming out of the lab.

"That was a really good kind of crash course and all of that," he said. "Being kind of a baseball fanatic and baseball biomechanics fan, that's what I really wanted to study," he said.

"A Perseverance and an Infectious Energy"

Huynh and Venkadesan discovered that they had a common interest in the mechanics of throwing, particularly in how humans can

Continued →

throw with such high velocity and still maintain accuracy. Although he's an avid fan of cricket, where fast and accurate hurling is also paramount, Venkadesan's interest in throwing mainly came through his research in evolution — particularly where it concerns mechanics and biology.

"One of the most attractive places to look for these high-performance systems is in biology, if you pay attention to which behavior and which animal," Venkadesan said. "That pairing matters a lot. If I want to look at throwing, I don't want to be studying a chimpanzee — I want to be studying a human."

Below: *Camera-based analysis technologies can capture an athlete's movement with precision and accuracy.*

Photos courtesy of Dan Huynh

Venkadesan has long been interested in throwing. His lab published a paper in 2013 on why humans are able to throw so fast, finding that much of it comes from the muscles lower in the body — and much less in the shoulder muscles than is commonly believed. Now his lab is concentrating on what allows humans to throw both fast *and* accurately.

"It's a well-known, age-old problem because the timing precision required to be as spatially accurate as a baseball pitcher is around a millisecond," Venkadesan said. "So if you let go of the ball a millisecond too late or a millisecond too early, you will end up completely missing your target."

Much of this work has been driven by undergraduate students in Venkadesan's lab. Previously, Petter Wehlin '17 worked on theories about the relationship between the muscles of the fingers, wrist, and arm, and its role in the release of the object being thrown.

Huynh's role tackles more of the experimental side of the research. Venkadesan put him in charge of working with the Institutional Review Board for an upcoming throwing study. He's also been an effective conduit between the science world and baseball world, particularly in explaining to potential participants how a study rooted in questions about evolution could somehow help their athletic abilities.

"Dan just has a perseverance and an infectious energy about pitching and baseball that's gotten a lot of others excited," Venkadesan said. "A lot of people say they love baseball, but

Above: *Prior to his partnership with the Washington Nationals, Huynh worked with the Tampa Bay Rays calling it a "life-changing experience."*

Dan takes it to the next level. He's reached out to teams and has really been part of this growth in data-driven training for athletes — in this case, pitchers and batters."

It was through Huynh's contacts, Venkadesan said, that the lab was able to secure the cooperation of a New Jersey training facility. In the winter, they'll set up experiments with multiple pitchers who have volunteered as subjects. Capturing the movements at the level of precision that the study calls for requires the latest technologies.

"We're going to be doing it Hollywood style," Venkadesan said. The researchers will attach reflective markers onto their arms and fingers to measure the movements of their body segments in 3D with "millimeter and sub-millimeter precision."

"Because this throwing is really fast and it's really accurate, you need what the state-of-the-art can offer," he said. Huynh's work with the Nationals and the Rays proved valuable in this area, and he keeps the lab updated on which camera-based analysis technologies are the best for their purposes.

The players will throw the standard distance from pitcher's mound to home plate aiming both for the standard strike zone, as well as more specific targets painted within the zone. The researchers will study a wide range of throwing styles and skill levels, from amateurs to professionals.

In the best scientific tradition, Venkadesan said, Huynh brings a "healthy skepticism" to the project, questioning how the various theories would play out on a real baseball diamond.

"We can't go in and say, 'This is how it works,' because we don't know how it will work," Venkadesan said. "It's a question of finding how it works."

Continued →

Above: *Huynh was recently assigned to the Rookie-level Florida Complex League working with prospects only a few years younger than him.*

Photo courtesy of Dan Huynh

A Turn of Events

Yale

Joining the Tampa Bay Rays for a sports science internship in the summer of 2021, Huynh said, was a "life-changing experience."

"One of the best things about it was that they gave me an incredible amount of responsibility and they exposed me to all realms of sports science," he said. Part of the job involved going over daily wellness questionnaires from the players and working with the medical staff and coaches on the best way to address any particular health or performance issue.

In terms of sports science and analytics, the Rays are among the most advanced in the league. The Nationals, the team he interned with this past summer, has traditionally lagged behind other teams in sports science. At the moment, his department only consists of himself and his supervisor, the team's Director of Player Development Technology & Strategy.

"I'm using the things that I learned with the Rays and trying to build upon them here to create an infrastructure, which is just a really exciting experience and a challenge for me," he said.

One of the projects he worked on with the Nationals over the summer involved the wearable sports technology called Catapult. Using a small GPS sensor that players wear on the back of their undershirts, coaches can monitor the running velocity, physical exertion, and other metrics related to the players' workload and performance. It helps optimize workouts, while reducing the chance for player injury.

"But it's a complicated system because it calculates so much," Huynh said. "So I'm trying right now to develop an automatic reporting system where we can run that data through various codes and it will tell us what we want to see, the visualizations that we want to see."

Even though Washington D.C. is his hometown, Huynh's favorite team growing up was the Houston Astros. Now, of course, it's the Nationals, he said. The Astros, though, share the training complex where he was working, and he'll sometimes see coaches or players that he remembers approaching for autographs as a kid.

"But now I'm working against them on the other side of the complex, which is definitely a weird experience — a turn of events."

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