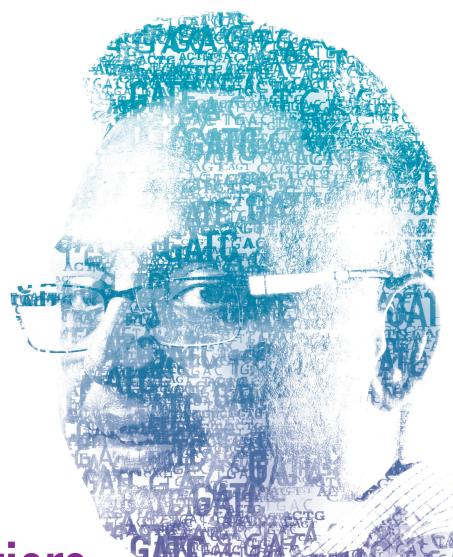
College of Engineering University of California, Berkeley Fall 2019

Fall 2019
Volume 16

Moments of untruth
Exposing digital deception

**Little earthquakes**Fault mechanics at nanoscale

# BerkeleyENGINEER



New frontiers in gene editing

Making headway against genetic disorders with CRISPR-Cas9

# A heart for students in engineering

The brilliance of Berkeley Engineering students attracted me to join the Berkeley faculty over 20 years ago, and it remains a source of inspiration for me today. Each of our students should be able to thrive and shine during their time here.

Ten years ago, the college set out to establish a more cohesive and comprehensive support system for our students. Student advising and co-curricular programs were brought together under one roof at the Bechtel Engineering Center, and Engineering Student Services (ESS) was born. Over the years, ESS has evolved into a vibrant center where students receive help, training and guidance to successfully navigate their college experience. This is one of the reasons why many students identified Bechtel as the "heart of engineering" in a facilities survey.

Recently, the college community marked the 10-year anniversary of ESS with more than 3,600 free Berkeley Engineering T-shirts for our undergraduate students and the inauguration of a new Welcome Center. Renovations to Bechtel included new flooring, paint, furniture and flat-panel displays installed at the entrance to ESS and in the Garbarini Lounge outside Sibley Auditorium. Additional renovations are planned to give students more places to study and collaborate.

The community event gave us the opportunity to highlight the important role that ESS plays in the success and well-being of our students. It offers a breadth of advising, academic support and professional development programs to help ensure that all students enrolled in our rigorous degree programs succeed. Remarkably, over 84% of Berkeley Engineering students who entered as freshmen graduate within four years; this is more than double the nationwide rate — but also shows that more can be done.

For this reason, the college sponsored a retreat last spring for the ESS staff and members of my leadership team to identify needs and opportunities for augmenting student support. As a result, a new ESS website is being developed and will be launched in early 2020 to make it easier for students to learn about and access the many resources available to support their success. The college will also fund the hiring of additional staff for ESS, including a learning specialist and psychological counselors.

I am confident that by fostering a more welcoming and supportive environment for learning and discovery, we can unlock the full potential of our students — and our collective potential as a community of scholars. This will distinguish Berkeley Engineering as the leader for empowering students to become global engineering leaders, working together toward a brighter future for the world.

By fostering a more welcoming and supportive environment for learning and discovery, we can unlock the full potential of our students.



— Tsu-Jae King Liu

DEAN AND ROY W. CARLSON PROFESSOR OF ENGINEERING



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COVER PHOTO: BIOENGINEERING PROFESSOR NIREN MURTHY; THE LETTERS IN THE IMAGE REPRESENT THE NUCLEOBASES THAT MAKE UP DNA: ADENINE, CYTOSINE, GUANINE AND THYMINE.

PHOTO AND GRAPHICS BY **ADAM LAU** 

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#### Roach-inspired robot

Cockroaches, known for their superior survival skills, are the inspiration behind the hardy, insect-like robot from the lab of Liwei Lin, professor of mechanical engineering. The robot, which weighs less than one-tenth of a gram, can withstand a weight of around 60 kg — about the weight of an average human — which is approximately 1 million times the weight of the robot. The size of a large postage stamp, the robot is made of a thin sheet of polyvinylidene fluoride, a piezoelectric material that expands or contracts with electricity. The sheet is covered with a layer of an elastic polymer, initially bent at an angle. The researchers added a front leg so that, as the material bends and straightens under an electric field, the oscillations propel the device forward in a leapfrogging motion. The resulting robot can move at a speed of 20 body lengths per second, a rate comparable to that of a cockroach and reported to be the fastest pace among insect-scale robots. It can also zip through tubes, climb small slopes and carry light loads, such as a peanut. Such tiny, resilient robots could play a role in search and rescue missions, squeezing into spots too small or dangerous for a dog or human to go.

CHEMICAL SCIENCES

## Separate ways

Actinides — the chemical elements with atomic numbers 89 through 103 — have a range of powerful applications, from medicine to nuclear energy. But first, scientists must purify these elements, which is a complex, multistep process that requires separating out contaminants and other elements. Now, a team of researchers, including Rebecca Abergel, assistant professor of nuclear engineering, has created a new and more efficient separation method that may accelerate the discovery of new elements, improve the reprocessing of nuclear fuels and ease the procurement of actinium-225, an isotope that has shown promise for treating cancer. The researchers demonstrated their method on actinium, plutonium and berkelium, and plan to research how this process can be used with other medical isotopes.

**DIAGNOSTICS** 

### Better eye screening

Diabetic retinopathy (DR) is the most common cause of vision loss among people with diabetes, and a leading cause of blindness. But thanks to cutting-edge machine learning techniques developed at the Risk Analytics and Data Analysis Research (RADAR) Lab, led by Xin Guo, professor of industrial engineering and operations research, millions of diabetic patients now have a cheaper and more accurate way to screen for eye disease.

of eye specialists to detect DR is 65%, the obvious cases, it is not that different PROBLEM Worldwide, about one-third of the estimated 415 million people with diabetes have DR. While blindness caused by DR is mostly preventable with early detection and treatment, it is difficult

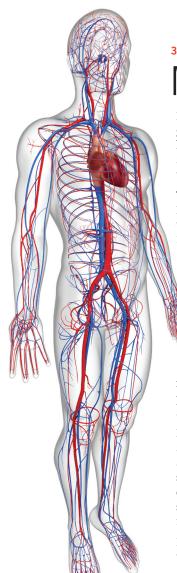
to diagnose, and many patients lack

access to eye specialists. Moreover, diag-

noses can be very inconsistent among

eye specialists.

"What is really needed, if you are thinking diagnose the cases in-between," said Guo.



3D PRINTING

## Mass-producing biomaterials

Researchers led by mechanical engineering professor Boris Rubinsky and graduate student Gideon Ukpai have developed a technique that may be key to the viability of bioprinting, an extension of 3D printing that could allow whole organs — as well as living tissue, bone and blood vessels to be printed on demand.

There have been two major hurdles standing in the way of organ printing. Because living cells and functioning organs require specialized temperature and chemical conditions to survive, cells deteriorate during the actual 3D printing of a large organ, as the process is too slow. And even if the

organ can be printed in 3D, the logistics of transporting it requires storage, which has always been a bottleneck for transplants.

To minimize cell death during the 3D printing of an organ, the researchers developed a technique that employs parallelization, in which multiple printers produce 2D layers of tissues simultaneously. These 2D layers are then stacked layer-by-layer to form 3D structures.

To overcome the storage problem of these manufactured organs, their technique freezes each 2D layer immediately after it is merged into the 3D structure. This process of freezing a single layer of cells provides optimal conditions for surviving the process of freezing, storage and transportation.

By printing tissues in 2D first and then assembling them into a 3D object at a different station, the team significantly sped up production. After the assembly line of bioprinters creates, in parallel, multiple 2D layers of tissue, a robotic arm — which was augmented by students from the master of engineering program — picks up each layer and carries it to another station. There, the tissues are stacked together to create a 3D object and fused via freezing.

In addition to bioprinting, this technique has other applications, such as the industrial scale manufacturing of frozen foods.



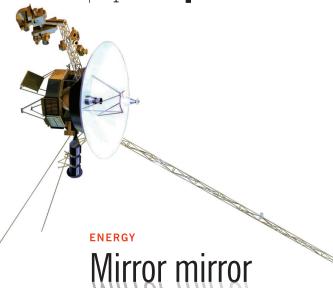
#### about prevention, is to "The average consistency and if you remove from flipping a coin."

**SOLUTION** Using machine learning techniques, Guo and her team developed algorithms to detect features in retinal images and help with diagnosis. To train their algorithm, they worked with hospitals in China that provided over 100,000 retinal images from patients. A team of expert doctors labeled the images as healthy or diseased.



**RESULT** The system can now detect DR with better than 97% accuracy, and researchers hope to apply these techniques to diagnosing other major eye

**IMPACT** Over 100 systems that assist doctors in diagnosing DR have been installed in some of the poorest rural areas in China. Up to 3 million people, most of whom had no access to regular eye checkups, have received free diagnoses from these systems since 2016. Guo is currently working to expand the remote diagnosis program into other regions.



Berkeley researchers led by Eli Yablonovitch, professor of electrical engineering and computer sciences, have broken another record in photovoltaic efficiency — an achievement that could lead to ultralight engines that power drones for days or deep space probes for centuries, as well as envelope-sized generators that power entire houses. In 2011, the researchers found that the key to boosting solar cell efficiency was not absorbing more photons, but emitting them. By adding a highly reflective mirror on the rear of a thinfilm photovoltaic cell, which assisted the light extraction, they broke all solar efficiency records at the time and have continued to do so with subsequent research. Recently, the team recognized that this mirror could also solve one of the biggest challenges in thermophotovoltaics, converting thermal radiation to electricity, and exploit the thermal photons that have too little energy to produce electricity. It turns out that the mirror provides a second function, reflecting those small photons to reheat the thermal source, providing further opportunity for high-energy photons to be created to generate electricity. This insight has allowed researchers to raise the efficiency of converting heat into electricity by thermophotovoltaics from 23% to 29%, with the aim of reaching 50% efficiency in the near future.

#### **GRADUATE EDUCATION**

## New master's degree programs

Because today's most pressing societal challenges cut across disciplinary boundaries, Berkeley Engineering is joining forces with the College of Environmental Design and the Haas School of Business to launch two new master's degrees in the fall of 2020.

The new Master of Design program is an innovative advanced degree that will be offered jointly by Berkeley Engineering and the College of Environmental Design. The three-semester program will focus on training students in design for emerging technologies. The Jacobs Institute for Design Innovation will play a key role in developing and delivering the core curriculum.

"This new degree program will educate designers with a deep understanding of the foundations of emerging technologies as well as their social implications, a perspective urgently needed today," said **Björn Hartmann**, faculty director of the Jacobs Institute and associate professor of electrical engineering and computer sciences.

With the Haas School of Business, Berkeley Engineering is offering a concurrent MEng/MBA degree program, which will allow students with sufficient undergraduate technical training to earn both degrees in just two years.

"This concurrent degree program is aligned with our college's mission to train graduate students who not only have expertise in their respective engineering subfields," said Dean **Tsu-Jae King Liu**, "but who also have the skills to succeed as entrepreneurs and as leaders in industries where technological innovation offers a key competitive advantage."

Both programs will begin accepting applications in the fall of 2019 for the inaugural 2020 cohorts.



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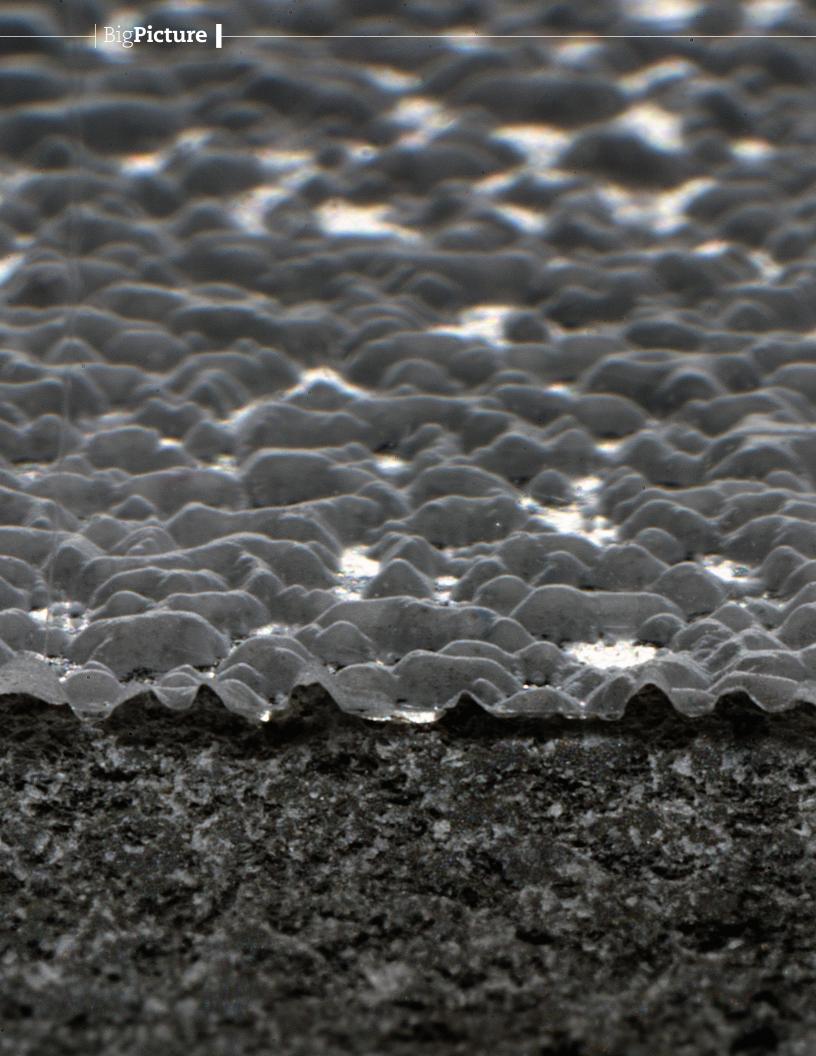
PUBLIC HEALTH

#### Get the lead out

at risk from water pipes that leach lead, which can cause brain damage, learning problems, premature births and high blood pressure, among other serious health effects. But the process for replacing entire municipal water systems can be very expensive and slow, as seen in Flint, Michigan, and more recently in Newark, New Jersey. Now, researchers led by **Ashok** Gadgil, professor of civil and environmental engineering, have devised a novel solution to this problem. The team found that when a low voltage power source, about 1V, is connected to a lead pipe filled with a harmless phosphate solution and to a conductive wire within the pipe, an insoluble lead phosphate layer rapidly forms on the inside surfaces of the pipe. In about two hours, the power source and the wire can be disconnected and removed. The newly formed protective scale results in a 99% reduction of lead leaching rates, according to preliminary laboratory experiments performed on lead pipes without any scale. While pipe replacement remains the best solution, this technology could be an important stopgap for communities where timely pipe replacement is not economically feasible.

MATERIALS A surprising twist Materials scientists two layers at a time, from Berkeley Engibut this work shows neering and Lawrence how to synthesize Berkeley National stacked structures -Laboratory have potentially millions created new inorof layers thick — in a ganic crystals made of continuously twisting stacks of atomically fashion. To create the thin sheets that unexstructures, the team pectedly spiral like a took advantage of a nanoscale card deck. crystal defect called Made of stacked laya screw dislocation, known as the Eshelby ers of germanium sulfide, a semiconductor Twist, that gives the material, these helical structure twisting crystals may yield force. By adjusting unique optical, electhe material synthetronic and thermal sis conditions and properties, including length, the researchsuperconductivity. ers could change Other researchers had the angle between successfully stacked the layers, creating a helical structure. This technique could likely be used with other materials that form similar atomically thin layers.

HOW DO I FIND OUT MORE? Find links to source articles and expanded coverage at **engineering.berkeley.edu/magazine**.



# At fault

A seismic rupture often occurs over a single asperity, an uneven area on a fault where friction causes it to be stuck. When an asperity slips, it produces seismic waves that can trigger additional movement along the fault, resulting in another earthquake. Civil and environmental engineering Ph.D. student Jes Parker, working in the lab of professor Steven Glaser, is part of a team that is taking research on asperities to a new level, studying fault mechanics at the nanoscale. "As far we can tell, friction behaves the same at all scales." Parker said. "So the energy signature of events in the lab can show a miniature version of full-scale tectonic earthquakes."

PHOTOS BY ADAM LAU

Parker applies different forces to a fault interface, made of an acrylic slider block and a base plate. When all or part of the fault can no longer hold up, it causes slippage — comparable to a mini-earthquake. Using acoustic emission sensors as seismometers, the researchers can measure which asperities fail, and when,

in a highly detailed way.

A close-up of the fault interface, as viewed through the slider block from a high angle. The white patches are the bottom surface of

the asperities. These were created

by laser cuts into the slider block

exterior, which rests against the

base plate, below.



STORY BY NATE SELTENRICH

Humans have been manipulating photos for as long as we've had cameras. But political and social forces have been using images to manipulate us for nearly as long.

By 1865, photojournalist Matthew Brady had already mastered the art of photo manipulation, as he demonstrated in a studio portrait of eight Civil War generals — including one who wasn't actually there. Later, a 1920 photograph of Vladimir Lenin addressing troops in Moscow was famously modified by Soviet censors to remove state opponent Leon Trotsky. Over the decades, we've seen a slew of altered images created by intelligence agencies and governments around the world, usually for dubious purposes.

But in recent years, something has changed. Now, virtually anyone can manipulate a photo well enough to go undetected, thanks to sophisticated, affordable and user-friendly editing tools. And, increasingly, they can do the same with video. With the broad reach of the internet and social media, this modified and misleading content can spread more quickly and have far greater impact than it did in the past.

The potential harm from this technology — to individuals, democratic elections and even the idea of truth itself — means that the stakes are higher than ever. But Berkeley researchers, using groundbreaking technologies, are taking a leading role in developing powerful techniques to analyze and authenticate visual media – tools that will allow us to better distinguish the fake from the real.

#### DETECTING DEEPFAKES

Many of us have watched as fake and modified videos have paraded across our social media feeds: actor Jordan Peele ventriloquizing President Barack Obama; House Speaker Nancy Pelosi slurring her speech; Facebook CEO Mark Zuckerberg boasting about using stolen data.

Like fake photos, digitally manipulated videos can be compelling enough to gain traction online. Yet modified videos

USING TECHNOLOGY TO EXPOSE DIGITAL DECEPTION

# OF UNTRUTH

are still relatively easy to spot — particularly those featuring high-profile people made to do or say something new.

But for how much longer? Videos synthesized through artificial intelligence (AI), commonly known as deepfakes, are improving in realism. There will likely come a time — perhaps not so far from now — when the naked eye can no longer tell an original video from a modified one.

That's where Hany Farid, professor of electrical engineering and computer sciences and at the School of Information, comes in. He's a pioneer and world expert in digital forensics — determining if photos, and increasingly videos, are real or fake. Over the past 21 years, he has developed mathematical and computational algorithms to detect tampering in digital media.

His job is getting harder all the time. Rapid advances in machine learning have made it easier than ever for average people to create seamless, believable fake photos and videos. "We know that this technology to create fake content and distribute it is developing very, very quickly. There's no question about that," Farid says. "That means that the threat is increasing."

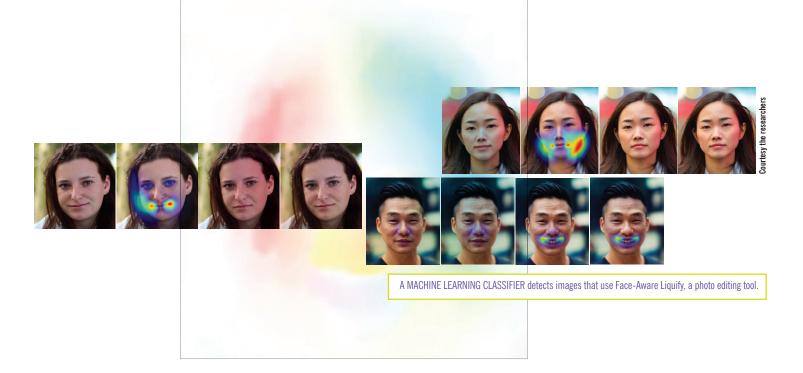
He's trying to stay at least one step ahead. The latest method out of his lab, for example, uses sophisticated modeling to detect deepfakes of U.S. politicians, including Donald Trump, Joe Biden, Cory Booker, Kamala Harris, Bernie Sanders and Elizabeth Warren.

By feeding a model with hours of authentic video footage, Farid and Ph.D. student Shruti Agarwal trained it to recognize each individual based on a frame-by-frame analysis of 18 facial movement and two head movement parameters, including how and when they raise and lower their eyebrows, wrinkle their nose

and tighten their lips. Because these facial movements represent "very particular glitches that cannot be replicated easily by AI tools," Agarwal says, the model uses them to verify if the individual depicted in a given video clip is the real thing or some sort of impostor.

"We saw the infamous Jordan Peele impersonation of Obama [in April 2018], and that video was really good quality at that time," she says. "We realized that with the development of new AI tools, this technique was going to improve, and it would be very difficult for an average person, or even an expert, to tell whether a video is a fake or a real one. That can be used for lots of nefarious purposes."

The detection technique isn't foolproof, Agarwal notes, but should stop most people from creating a passable deepfake — at least for now. Other approaches to detecting digital fakery involve searching for artifacts or signatures left behind by AI



tools, she notes, such as blurring in areas where manipulation has taken place, particularly around the face.

Farid has worked on many of these. But to retain an advantage in his corner, he keeps some of his tools under wraps, in a personal digital forensics arsenal he can deploy when called upon by news organizations, social media companies or others to detect a particularly highquality fake.

When publishing Agarwal's model, the pair decided not to release the actual data or code. "We don't want this thing getting operationalized against us," Farid says. "We will share it with very specific forensic researchers, but not everybody."

Detecting fakery is a task he takes seriously. But he also believes that in the long run, technology will never solve the bigger problem of misinformation. Preserving our faith in legitimate news organizations, democratic elections and the concept of truth itself will take policy, regulation and education, too. "Once we enter a world where everything can be faked, then nothing's real," he says, "and everything has a sense of plausible deniability."

#### "A COMPETITIVE COLLABORATION"

Farid, of course, is not the only one fighting this battle. He's joined by professor of electrical engineering and computer sciences Alexei Efros, whose lab works on synthesizing as well as detecting fake content simultaneously - and sometimes in the same paper.

Efros believes a healthier orientation with the truth can be found somewhere between the poles of real and fake. "The nature of science is a marketplace of ideas," he says. "You need to have multiple points of view, and you need to have them clash, and you need to have them challenged. In that sense, doing work on both sides of synthesis and detection is what propels the sides forward. It's a competitive collaboration, because in science it's really all about finding the truth."

To wit, consider three recent advances out of his lab: a method for detecting the use of a facial-manipulation tool in Adobe Photoshop, then reverting back to the original; a technique for transferring dance movements from one person to another, plus another for detecting if such a manipulation has been performed; and an approach toward learning individual styles of conversational hand gestures that could be used both to detect deepfakes, in a similar manner to Agarwal's approach, or to synthesize them, by animating realistic hand gestures to go along with modified speech.

The Photoshop paper, authored by Efros, postdoctoral researcher Andrew Owens, undergraduate researcher Sheng-Yu Wang and two colleagues from Adobe, presents a novel way of detecting if a photograph has been modified by a photo editing tool called Face-Aware Liquify.

Using a simple but powerful interface, this tool allows users to alter a subject's facial expression by changing their eyes, mouth and other features. Just last year, the Kremlin released an image of North Korean leader Kim Jong Un smiling and

shaking hands with Russian Foreign Minister Sergey Lavrov — when really Kim was scowling. That's Face-Aware Liquify at work, Efros says. The team's innovation was to use the script behind this trick to train a machine learning classifier to detect and deconstruct fakes.

Caroline Chan, an undergraduate student at the time, was the lead author of the second paper, "Everybody Dance Now," which describes a method for transferring video motion from one person to another. Given a source video of a person dancing, the researchers showed they could digitally transfer the same moves to another individual — someone who wouldn't have been able to pull off the challenging ballet or hip-hop routines — after just a few minutes of the target subject performing some standard motions for a camera.

"Although our method is quite simple, it produces surprisingly compelling results," the authors write — so compelling, they say, that they developed a companion forensics tool to test whether a given clip has been produced using their

The research on conversational gestures employed machine learning and hours of video footage to sync ten individuals' speech patterns and hand arm movements, then generate appropriate gestures to match new audio. The team, led by Ph.D. student Shiry Ginosar along with Owens, published their work, "Learning Individual Styles of Conversational Gesture," in June. Jitendra Malik, professor of electrical engineering and computer sciences, was the principal investigator on this paper.

The paper came paired with a large video dataset of person-specific gestures for talk-show hosts John Oliver, Seth Myers, Ellen DeGeneres and others. In a similar fashion, the dance paper came bundled with a first-of-its-kind opensource dataset of videos that can be used for training and motion transfer. For Ginosar, who also contributed to the dance work, sharing this allows other researchers to better understand motion transfer and identify videos where it's in use.

#### THE COUNTERFEITER VS. THE INVESTIGATOR

The research coming out of Efros' lab takes advantage of a relatively new concept in machine learning known as generative adversarial networks, or GANs. These systems use the interplay between synthesis and detection to produce more realistic synthesized images.

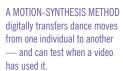
Think of it as pitting a counterfeiter against a police investigator, Efros says. GANs include both a generator, trying to make counterfeits, and a discriminator, like a detective, trying to spot them. The two sides optimize each other in an automated one-upmanship that is a boon to those looking to synthesize realistic digital content — and an adversary for those looking to detect hidden fakes.

Theoretically, this technology could reach a state of equilibrium where generated























content becomes virtually indistinguishable from real content. For now, the detectors are ahead. But if an equilibrium is reached, Efros says, we'll need to adapt by modifying our expectations about digital images and videos, akin to how we came to scrutinize scam letters created by laser printers back in the 1990s.

"Things that people trusted in the past, they realize that they cannot trust anymore," he says. "I would argue that their trust in photographs has always been misplaced. It was never the truth. It was always what the photographer wanted you to see. So in some sense this is good that people are getting more awareness of this now, because photography and even film were always subjective, in many different subtle and not-sosubtle ways."

Both Farid and Efros agree that the greatest risk we face as a society is not the proliferation of foolproof deepfakes per se, but rather the argument that anything could be fake, without the weight of a trusted voice - such as a news organization or social media company — to counteract it.

"To me, that is the broader threat here," Farid says. "As we become a more polarized society, as we enter a world where more and more people get their news on Facebook, which of course is manipulating what you see, we are all going to have our own set of facts. Something will come out damaging for a candidate, that candidate will tell you it's fake, the people who are opposed to the candidate will say it happened, and where are we left as a democracy? If we can't agree on basic facts of what happened and didn't happen, we're in trouble." BE



#### MAKING HEADWAY AGAINST GENETIC DISORDERS WITH CRISPR-CAS9

STORY BY ANN BRODY GUY • PHOTOS BY ADAM LAU

For babies with Duchenne muscular dystrophy, development starts out normally. They might be slow to start walking, but it's not until the age of 2 or 3 — when they fall frequently, or struggle to run and jump — that their parents realize something's amiss. The prognosis is grim: Children with Duchenne experience a progressive weakening of all of their muscles, need a wheelchair by around age 12, and face a drastically shortened lifespan due to weakened heart and lung muscles. A lifelong steroid regimen is one of the only available treatments to slow the inevitable progress of this disease.

Duchenne is caused by an absence of dystrophin, a huge protein on the X chromosome that helps the body form healthy muscle tissue. When some of the protein's genetic sequence is missing, it causes muscular dystrophy, which like other X-linked diseases, primarily affects boys. Duchenne is the most severe form; there's zero dystrophin protein present in the cell, so the outcomes are the worst.

With the disease built right into a person's DNA, the treatment focus for Duchenne has been on managing symptoms. CRISPR-Cas9, a gene-editing tool discovered at Berkeley in 2014, has been shaking up therapeutics from cancer to heart disease and has offered the promise of targeting the mutated dystrophin gene itself. But efforts thus far have fallen flat because, while the CRISPR tool excels at deleting defective genes, it is less efficient at correcting mutations. Now, Berkeley bioengineers think they have cracked the stubborn barriers to correcting the Duchenne gene mutation, potentially optimizing both treatment and diagnosis. If they're successful, their work could have implications for nearly every genetic disease.

CRISPR, short for the genomic pattern "clustered regularly interspaced short palindromic repeats," and the Cas9 enzyme, DNA "scissors," function as bacteria's natural system to expel viruses by cutting an offending sequence from its genome. The CRISPR-Cas9 gene-editing tool — the groundbreaking innovation first identified by Jennifer Doudna, professor of biochemistry and molecular biology, and her colleague Emmanuelle Charpentier — allows scientists to aim Cas9 at any sequence in a person's genome, modifying genes to remove mutations or fight disease.

When researchers want to use CRISPR to correct, not remove, a mutated gene, they first must send the unmutated sequence, or wild type "blueprints" — called donor DNA — into the cell. And because genetic mutations are present in every cell in the body, CRISPR must repair the DNA of a large number of cells to successfully treat disease.

The challenges of genetic disease also create its greatest promise. Unlike cancer, for example, where the causes are often murky, "genetic diseases are one of the few types of diseases where we exactly know the mechanism," says bioengineering professor Niren Murthy. "That means if you had a way of correcting that sequence you have a very high chance of actually curing that disease."

Murthy, like many biomedical researchers, targets Duchenne because of the large patient population, large unmet medical need and non-invasive access to muscle tissue. "What CRISPR does really well is it cuts DNA," he explains. "But with most genetic diseases, you don't actually want to cut DNA — you want to correct the mutation." Ideally, he says, that means restoring the wild type gene.

Correcting a gene mutation is more akin to a precision-timed transplant than CRISPR's typical routine surgeries. Scientists must deliver three components into each cell: guide RNA, a map to the target location; the Cas9 enzyme to cut the DNA; and donor DNA — the correct sequence. If these elements can reach a cell at precisely the same time, it triggers a natural process called homology directed repair: Cas9 cuts the DNA then swaps in the donor gene for the mutated one, "tricking" the DNA that the new gene belongs there.

The current standard is for the components to ride into cells on benign viruses. But viruses present problems. It's a one-shot effort; once a virus enters the body, antibodies form so the body rejects that virus in future encounters. The process is expensive and can lead to off-target DNA damage.

Murthy and bioengineering professor Irina Conboy, whose lab focuses on biomedical stem cell therapies, think getting the homology directed repair components to cells more efficiently will have huge implications for Duchenne muscular dystrophy and other genetic diseases.

"I absolutely think it's just a delivery problem," Murthy says. Gold nanoparticles are a promising delivery vehicle, according to a 2017 study co-authored by Murthy, Conboy, Doudna and others.

"It's really easy to coat DNA onto gold," Conboy says. Gold bonds easily with sulfur, and sulfur-attached DNA is a common lab product. Then the Cas9 enzyme and guide RNA naturally bind to each other and onto that core. When these locked-andloaded gold particles were delivered to mice, the components hit their target cells simultaneously.

The study's findings were highly promising: A single salinebased injection of CRISPR-Gold particles doubled strength and agility in Duchenne mice compared to control groups. The wild type gene increased by up to 5 percent, several percentage points higher than any previous results. Five sounds like a small number compared to drug treatments, which generally must inhibit at least 50 percent of their target to be effective, Murthy notes. But because Duchenne patients start with no dystrophin protein, he says, "When you go from nothing to something, you're going to see very dramatic health benefits."

Moreover, adds Conboy, unlike viruses' single-use problem, the body does not form antibodies to gold. That enables continued saline infusions of these nanoparticles, which "can gradually keep repairing the DNA so the muscles stop dying and eventually even repair the defective dystrophin gene back to the wild type."

Minute as these nanoparticles are, too much gold can be toxic to the body. So the team's next step is to make more biodegradable, less toxic formulations. Murthy and Conboy have a National Institutes of Health grant supporting that work.

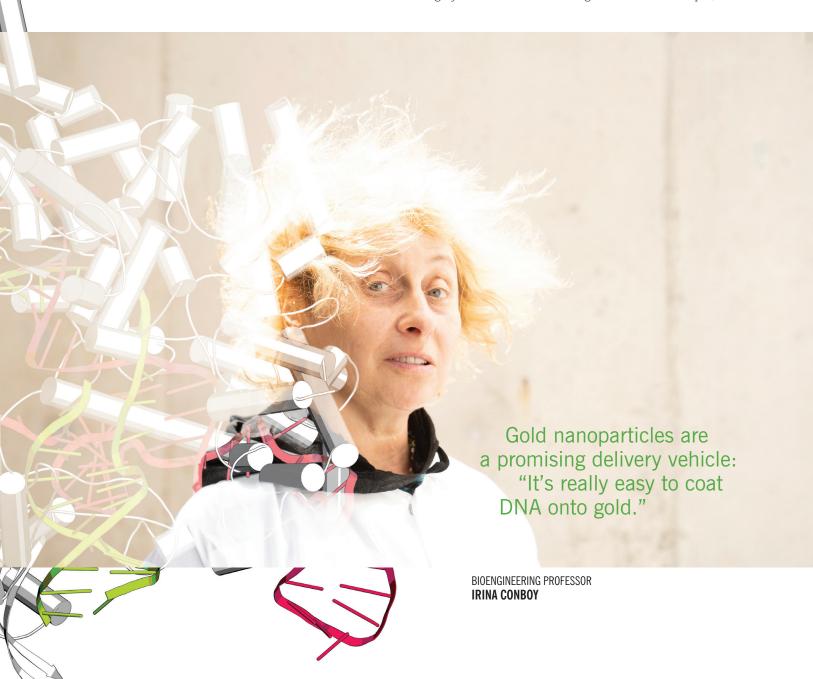
These successes are tempered by dissimilarities between mouse and human biology, which can lead to disappointments when lab research moves to clinical trials. While there are promising indications that gene editing will avoid some of those issues, no one really knows how effective homology directed repair is going to be in humans.

Still, Murthy and Conboy expect to see clinical trials of their nanoparticle therapy as soon as five years from now, especially if they appeal for "compassionate consideration," an expedited process. "It's not like you're competing against some other therapeutic," Murthy says, "There's really nothing out there."

"What we have now is not adequate" says Alex Fay, a pediatric neurologist and neuromuscular specialist at UCSF Benioff Children's Hospital San Francisco, who treats muscular dystrophy patients. "There's an urgent need for treatments that are going to dramatically alter the course of the disease." Even for families willing to take on added risk, therapies often come too late to be meaningful. "The ideal time to treat these patients is when they're infants or babies," Fay says — long before symptoms appear.

#### DISRUPTING DIAGNOSTICS

Kary Mullis won the 1993 Nobel Prize in Chemistry for developing a laboratory process that finds a specific location on the roughly 3 billion-letter human genome. The technique, called



polymerase chain reaction, or PCR, has been refined in labs over many years, but it is still prone to errors.

As a postdoc in both the Conboy and Murthy labs, Kiana Aran created a tool that uses CRISPR to perform similar tasks to PCR, but digitally — like Google for genomes. Users place a drop of purified DNA, extracted from a simple swab sample, directly onto a chip containing thousands of tiny CRISPR-programmed graphene transistors. Then, using Duchenne guide RNA as the "search term," the transistors scan the genome for target sequences and deliver the search results electronically.

The quick, inexpensive and portable technology, called CRIS-PR-Chip, could be used for diagnosis and for ongoing monitoring of patients' gene-therapy progress. Aran's current chip tests for Duchenne, but her team can load guide RNA for other genetic diseases, including sickle cell anemia and Huntington's, and her lab is developing more sensitive technologies to detect other types of genomic material, like infectious-disease indicators.

A direct comparison to PCR doesn't apply, Aran says. "We are starting a new process of making genomics digital. We've been developing high-tech instruments and gadgets, and we haven't been using these technologies for healthcare applications." CRISPR-Chip is one step toward what she sees as the inevitable digitization of all medicine.

NIREN MURTHY

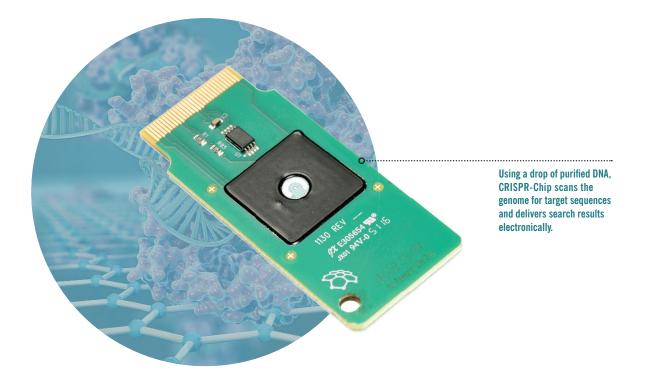
Aran, now an assistant professor of medical devices and diagnostics at the Keck Graduate Institute, didn't start out with this visionary agenda. "I did not enjoy electrical engineering as an undergrad," she recalls. "How could I connect with real-world problems by just designing transistors and circuits?" When she discovered biomedical engineering, her attitude changed. Now, as the chief science officer at Cardea, which recently merged with Nanosense, a company she co-founded with industry partners, she's focused on getting her solutions into the world by first commercializing the device for lab-based quality-control while she completes the long regulatory process for medical uses.

#### "IT'S GOING TO BE REVOLUTIONARY"

Better diagnostic tools can't come soon enough for Fay, who thinks it's time to add creatine kinase, the muscle-damage test, to neonatal testing protocols. And if technology like Aran's could provide easy in utero testing, he's for it.

But as researchers develop these powerful technologies, they must also grapple with the ethical quandaries and unforeseen





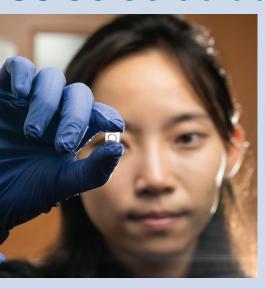
consequences of their work. For example, while gene therapies currently under development can't be inherited, CRISPR also enables germline editing, which creates inherited changes permanently altering human DNA — an ethical rabbit hole so deep that it is formally prohibited in more than 30 countries, including the United States.

Despite these attendant societal concerns, CRISPR gene editing continues its march from labs to implementation. For medical professionals and patients with genetic diseases, this opens a future of possibilities.

"I think it's going to be revolutionary," Fay says of the potential for Duchenne. "The whole mentality of the field is going to change from a supportive care model to a treatable disease model, and it's going to increase the urgency of early genetic testing."

Aran says the key to successfully implementing CRISPR to treat genetic disease — and other applications from cancer to agriculture — will be addressing the engineering, societal and safety challenges step by step, worldwide. "The U.S. must maintain a position of technical and ethical leadership," she says. And, she adds, stepping back isn't an option. "History has shown that you cannot fight advances like this. We cannot stop it from moving forward." **BE** 

#### KEEPING EDITED CELLS HEALTHY



Editing T-cells with CRISPR-Cas9 can improve immunotherapy outcomes and shows promise for treating diseases such as cancer. To avoid the numerous problems with virus-based delivery systems, researchers often use an electric charge to open holes in cells to deliver the Cas9 molecule. But T-cells are sensitive, and about half break apart from the procedure. Now, postdoctoral fellow Yuhong Cao has developed a new technique that doubles the effectiveness of the process. In a recent study co-authored by chemistry and materials science and engineering professor Peidong Yang, Doudna and others, Cao demonstrated the effectiveness of using inexpensive lab equipment to deliver macromolecules into cells.

"Cells are precious — if you kill too many, you won't have enough cells for therapy," Cao says. So, using a common laboratory filter, she created a gentler method to open holes, with a nearly 100% cell survival rate. When cells are loaded onto the filter, its pores serve as a physical template, effectively stenciling tiny, controlled openings into the cell membrane when an electric field is turned on. The voltage also pulls macromolecules placed on the filter through the pores and into the cell. Turn off the electricity and the pores close up. "That's how we keep the cell heathy," she says.

The technique, called nanopore-electroporation, or nanoEP, is already being adopted in other labs. Medical applications will require scaling up from about 10,000 cells to millions. Sizing up by that magnitude creates challenges like keeping the electric field uniform across a much larger membrane. "This is an engineering problem," Cao says.



#### Streets named Pew **Scholar**

Aaron Streets, assistant professor of bioengineering, is one of 22 early-career researchers joining the 2019 Pew Scholars Program in Biomedical Sciences. This honor comes with four years of funding for exploratory research to advance human health and tackle some of biomedicine's most challenging questions. Streets will explore how obesity leads to unhealthy changes in the cellular, molecular and structural composition of adipose tissue.

PHOTO BY BRUCE COOK

Alexis Abramson (Ph.D.'02 ME) is the new dean of the Thayer School of Engineering at Dartmouth College. Previously, she was a Case Western Reserve University professor, specializing in sustainable energy technology.

Materials science and engineering adjunct professor Joel Ager and Yanwei Lum (M.S.'15, Ph.D.'18 MSE) are co-authors of a study in Nature Catalysis showing that a simple copper-based catalyst can be used to recycle carbon dioxide into valuable chemicals and fuels, economically and efficiently.

Maria Artunduaga (MTM'18 BioE) took home the first prize in the Big Bang! Business Competition at UC Davis. Her company, Respira Labs, is developing a wearable device that uses acoustic sensors, data signal processing and artificial intelligence to predict and prevent chronic obstructive pulmonary disease (COPD) attacks.

Anil Aswani (M.S.'07, Ph.D.'10 EECS), assistant professor of industrial engineering and operations research, has received a CAREER Award from the National Science Foundation to investigate

personalized chronic disease management.

Matthew Avery (B.S.'01 MSE) was recently promoted to partner at Baker Botts LLP, where he is an intellectual property attorney. He also serves as an adjunct professor at UC Hastings, where he teaches courses on patent prosecution and food and drug law.

Pamela Bhatti (B.S.'89 BioE) has been appointed the associate chair for innovation and entrepreneurship at Georgia Tech's school of electrical and computer engineering.

Professor Jeffrey Bokor is the new chair of the Department of Electrical Engineering and Computer Sciences, taking over for outgoing chair James Demmel. Professor John Canny will succeed Bokor as the department's associate chair and Demmel as chair of the computer science division.

Civil and environmental engineering professor Jonathan Bray (Ph.D.'90 CEE) and graduate student Daniel Hutabarat were awarded the Outstanding Paper Award by the International Society for Soil Mechanics and Geotechnical Engineering.

Danny Broberg (Ph.D.'19 MSE) started a one-year term as the 2019-20 Optical Society and Materials Research Society congressional fellow. "I look forward to applying the lessons learned in my research on semiconductor materials to science-informed policymaking on energy and climate issues," he said.

Assistant professors Alvin Cheung and Anca Dragan of electrical engineering and computer sciences and associate professor Javad Lavaei and assistant professor Barna Saha of industrial engineering and operations research have been awarded the Presidential Early Career Award for Scientists and Engineers, the highest honor bestowed by the U.S. government to scientists and engineers in the early stages of their careers.

Professor emeritus Leon Chua in the Department of Electrical **Engineering and Computer Sciences**  has been named the 2019 Celebrated Member by the Electron Devices Society of the IEEE.

Meryll Dindin (MEng'19 BioE), **Thomas Galeon** (MEng'19 BioE) and Pierre-Louis Missler (MEng'19 CEE) were the winning team at the first Code and Response Codeathon for their creation of AsTeR, a platform for collecting and prioritizing information to facilitate decision-making during natural disasters.

Jordan Edmunds, a Ph.D. student in electrical engineering and computer sciences, was named a 2019 Hertz Fellow. He specializes in the fabrication of neural interfaces.

Chelsea Finn (Ph.D.'18 EECS) has won the prestigious ACM Doctoral Dissertation Award, given for the best doctoral dissertation in computer science and engineering.

Mark Godwin (B.S.'04, M.S.'07, Ph.D.'11 ME) is the co-founder of Boxbot, which recently unveiled a new system for delivering packages to consumers using self-driving vehicles and a new hub that can automatically load delivery vehicles with packages.

Civil and environmental engineering professor Allen Goldstein received the Yoram J. Kaufman Unselfish Cooperation in Research Award from the American Geophysical Union for advancing scientific understanding of Earth and its planetary health.

Nadia Heninger (B.S.'04 EECS) has won the 2019 Borg Early Career Award, given to a woman in computer science and/ or engineering who has made significant research contributions and who has contributed to her profession, especially in the outreach to women. She is currently an associate professor of computer science and engineering at UC San

Mark D. Hill (M.S.'83, Ph.D.'87 CS) has won the ACM-IEEE CS Eckert-Mauchly Award, considered the most prestigious award in the computer architecture community. He is a professor at the University of Wisconsin-Madison.

Professor **Sanjay Kumar** is the new chair of the Department of Bioengineering, taking over from outgoing chair **Dan Fletcher**.

Carl Lampert (B.S.'74 EECS, B.S.'74, M.S.'77, Ph.D.'79 MSE) received an Outstanding Contribution Award from Elsevier Publishers for 38 years of service as editor-in-chief of the journal Solar Energy Materials and Solar Cells, as well an award from the Society of Vacuum Coaters for his service as technical director.

Two electrical engineering and computer sciences professors have won awards from the IEEE Technical Committee on Cyber-Physical Systems: **Edward Lee** (Ph.D.'86 EECS) won the Technical Achievement Award and **Sanjit Seshia** won the Mid-Career Award.

Michael Lieberman, professor emeritus of electrical engineering and computer sciences, has won the 2020 IEEE Marie Sklodowska-Curie Award from the Nuclear and Plasma Sciences Society for his groundbreaking research in the physics of low-temperature plasmas and their application.

Jitendra Malik, professor of electrical engineering and computer sciences, has been given the IEEE Computer Society's 2019 Computer Pioneer Award for his leading role in computer vision research.

Tahir Masood (M.S.'86, Ph.D.'90 CEE) has been named the president and managing director of National Engineering Services of Pakistan, the largest state-owned consulting engineering company in Pakistan.

Samantha McBirney (B.S.'12 BioE) was featured on NPR's *All Things Considered* for her graduate work on an inexpensive magnetic detector for malaria.

Shane Mortazavi (B.S.'75, M.S.'77 IEOR) has been named vice president of operations at Vitrium, a solutions provider of industrial solid-state drive and memory solutions.

Civil and environmental engineering professor **Scott Moura** (B.S.'06 ME) received an NSF Career Award for his project "Estimation and Control of Electrochemical-Thermal Battery Models: Theory and Experiments."





Crace Cu

Raluca Ada Popa

## Two faculty named top innovators

Two Berkeley assistant professors — mechanical engineering's **Grace Gu** and electrical engineering and computer sciences' **Raluca Ada Popa** — were included in MIT Technology Review's 2019 list of "35 Innovators Under 35."

Gu is advancing 3D printing applications to create novel materials with enhanced mechanical properties. Her research uses machine learning algorithms to identify new and better composite structures based on natural materials.

Popa is one of the co-founders of Berkeley's RISELab, and her research focuses on secure systems and applied cryptography. She has developed encryption systems that provide security without the use of firewalls, but still allow for complex calculations on data.

PHOTOS COURTESY GRACE GU AND RALUCA ADA POPA



## Alum honored as MEMS pioneer

Kurt Petersen (B.S.'70 EE) has been awarded the 2019 IEEE Medal of Honor, the organization's highest award, "for contributions to and leadership in the development and commercialization of innovative technologies in the field of MEMS." He first made his mark in 1982 as the author of "Silicon as a Mechanical Material," a review paper that is considered foundational to microelectromechanical systems (MEMS) research. The paper, which described the mechanical properties of integrated circuit materials and envisioned future electro-mechanical applications, aided researchers scattered throughout the MEMS field, ultimately accelerating the development of MEMS technologies.

Petersen also led IBM's micromachining research group and eventually co-founded six successful companies, including NovaSensor, Cepheid, SiTime and Profusa. The MEMS technologies that he helped develop — including pressure sensors and oscillators, as well as a PCR biodetector that screens all United States mail for anthrax — were key advancements in the commercial application of MEMS.

He currently advises a number of startups and is part of the Band of Angels, Silicon Valley's oldest angel investment group. A member of the National Academy of Engineering, he has published over 100 papers and been granted more than 35 patents.

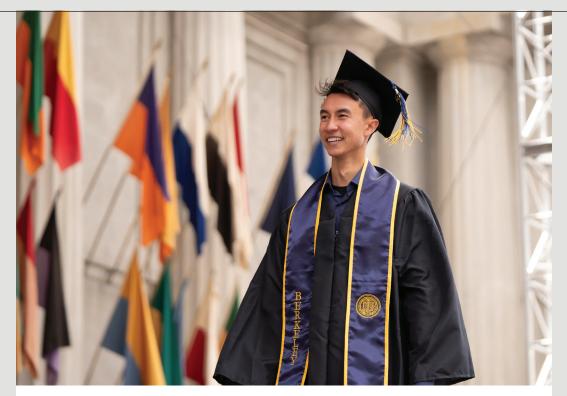
PHOTO COURTESY KURT PETERSEN

#### Vasuki Narasimha Swamy

(M.S.'15, Ph.D.'18 EECS) has been honored with a 2019 Marconi Society Paul Baran Young Scholar Award for her work in designing robust wireless protocol frameworks for ultra-reliable low-latency communications.

Electrical engineering and computer sciences assistant professor **Aditya Parameswaran** has won the Very Large Data Bases Early Career Award for developing tools for large-scale data exploration, targeting non-programmers.

Electrical engineering and computer sciences professor emeritus **David Patterson, Zhangxi Tan** (M.S.'08, Ph.D.'13 CS) and **Lin Zhang**of the Tsinghua-UC Berkeley
Shenzhen Institute (TBSI) have been chosen to co-direct the new RISC-V International Open Source Laboratory, a nonprofit research lab launched by TBSI to expand and elevate the capabilities of reduced instruction set computer microprocessors.



Tyler Chen (B.S.'19 BioE/MSE) was this year's winner of the University Medal, Berkeley's highest honor for graduating seniors. He leaves campus with a succession of impressive scientific and technological breakthroughs, plus a near-perfect GPA of 3.96. In addition to co-founding and mentoring the Berkeley Hyperloop team, he worked in the Streets Lab, designing microfluidic devices to manipulate individual cells for RNA sequencing. Among other achievements, he helped develop carbon nanotube-based biosensors to track the health of astronauts. And, during a campus makeathon, he led a successful effort to build gripping devices for a person with quadriplegia. As part of the University Medalist honor, Chen delivered a speech to thousands of his peers at the campuswide commencement ceremony in May.

PHOTO BY ADAM LAU

Stuart Russell, professor of electrical engineering and computer sciences, was named a 2019 Carnegie Fellow in recognition of his artificial intelligence work.

Lee Schruben, professor of industrial engineering and operations research, retired this year after 19 years on the Berkeley faculty. He has been a key figure in the department, serving as chair and helping to launch the Center for Entrepreneurship in Technology.

Zu-Jun "Max" Shen, professor of industrial engineering and operations research and of civil and environmental engineering, has published a paper with UCLA assistant professor Auyon Siddiq

(M.S.'14, Ph.D.'18 IEOR) that shows how smart placement of defibrillators may help save lives for victims of cardiac arrest.

Scott Shenker, professor of electrical engineering and computer sciences, has been elected to the National Academy of Sciences, one of the most distinguished scientific organizations in the country.

M. Vali Siadat (B.S.'67 EECS) of Richard J. Daley College, one of the city colleges of Chicago, has been named the recipient of the 2019 American Mathematical Society Award for Impact on the Teaching and Learning of Mathematics for his many contributions to mathematics education at both the pre-college and college levels.

Michal Siwiński (B.S.'97 EECS) is the new corporate vice president at Cadence Design Systems, which develops computational software

Pivot Bio, founded by Karsten Temme (Ph.D.'11 BioE), was named to Fast Company's 2019 "The World's Most Innovative Companies" list in the food sector. Pivot Bio makes the world's first nitrogen-producing microbial that grafts onto corn to act as a sustainable fertilizer.

Mechanical engineering professor Masayoshi Tomizuka has been selected to receive UC Berkeley's Carol D. Soc Distinguished Graduate Student Mentoring Award. Electrical engineering and computer sciences professor Claire Tomlin (Ph.D.'98 EECS) is one of nine Berkeley faculty honored with membership in the American Academy of Arts and Sciences for 2019.

Rachel Vandenberg (B.S.'86 CEE) has been promoted to senior vice president at Dewberry, where she has overseen the growth and expansion of its ports and intermodal practice across the East and West coasts.

David Wagner (M.S.'99, Ph.D.'00 EECS), professor of electrical engineering and computer sciences, was awarded the prestigious USENIX Test of Time Award for research on computer security completed when he was a Berkeley graduate student.

Teresa Williams (M.S.'14, Ph.D.'17 AS&T) is finishing up a year in Washington, D.C., as an AAAS congressional science and engineering fellow working on policy related to electric vehicles, workforce development, toxic chemicals and energy efficiency on the Energy and Commerce Committee in the U.S. House of Representatives.

Undergraduate students Caleb Wright, mechanical engineering, and Charles Yang, materials science and engineering and electrical engineering and computer sciences, won a competition co-hosted by the MIT Climate CoLab and the United Nation's Environment Program, which sought ideas for achieving the U.N.'s sustainable development goals by 2030. Working with fellow Berkeley student Dan Ma, they were the only undergraduate team in the competition, beating out 69 other teams to take first place.

Mechanical engineering professor Paul Wright received the Berkeley Citation, awarded to individuals whose contributions to UC Berkeley go beyond the call of duty and whose achievements exceed the standards of excellence in their fields

Elwyn Berlekamp, professor emeritus of electrical engineering and computer sciences and of mathematics, died in April at the age of 78. He was internationally renowned for his work in mathematics, coding theory and game theory. In the early 1970s, he founded Cyclotomics, a firm that developed error-correcting codes that were used by NASA for space communications. He later branched out into cryptography and the financial market, as well as the theory of combinatorial games. He was the author of seminal book Algebraic Coding Theory, held more than a dozen patents and was a member of the National Academy of Engineering and the National Academy of Sciences.

Sally Floyd (M.S.'87, Ph.D.'89 CS) died in August at the age of 69. Known for her work on congestion control, she was one of the inventors of Random Early Detection, an algorithm used to manage internet traffic during times of overload. Following graduation, she joined the Network Research Group at Lawrence Berkeley National Laboratory, then worked as a research scientist at the International Computer Science Institute.

Victor Gretzinger Jr. (B.S.'44 CE) died in May at the age of 94. He served in the U.S. Navy during World War II, then spent much of his career in California's gold country, where he ran his own engineering business. He later moved to Alaska, working in Anchorage and then as public works director in Palmer.

Jean Paul Jacob (M.S.'65, Ph.D.'66 EECS) died in April at the age of 82. An acclaimed expert on informatics, he was the first founding member of CITRIS as well as a faculty-in-residence at the Department of Electrical Engineering and Computer Sciences since 1971. He also had a 42-year career at IBM, where he was instrumental in creating scientific centers around the globe. He received Berkeley's Distinguished Alumnus Award in Computer Science and Engineering and the University of California's Research Leadership Award.

Kenneth King (B.S.'58 CE) died in July at the age of 83. He worked as a civil engineer for 50 years, designing water recreation areas at Disneyland, Wild Rivers and Raging Waters.

John Lindblad (B.S.'52 Agricultural Eng.) died in July at the age of 88. After serving in the U.S. Army during the Korean War, he embarked on a career in public service. He worked as an engineer for the Napa County Public Works Department, then as the public works director for the city of Napa for 28 years. After retirement, he consulted on a system to relieve downtown Napa from frequent flooding.

Carol Major (B.S.'13 BioE) died in August at the age of 28. She was a technical program manager at Apple and had previously worked at St. Jude Medical.

Robert "Bob" Matthews (B.S.'49 ME) died in May at the age of 95. After serving as a Navy pilot in World War II, he completed his degree and began a wideranging career that culminated in the founding of SeaTel, a leading marine satellite antenna firm. An avid Berkeley supporter, he funded numerous scholarships for undergraduate engineering students with financial need.

Charles "Chuck" McIlvain
(B.S.'97 EES) died in September at the age of 44. A visual effects designer, he was known for his work on movies, including Watchmen, Spider-Man and Green Lantern. He was working at Netflix and had previously been employed at Walt Disney Imagineering and Sony Pictures Imageworks.

Povindar Kumar Mehta (D.Eng.'64 MSE/Mineral Eng.), professor emeritus of civil and environmental engineering, died in August at the age of 88. A faculty member from 1963–93, he was a world-renowned expert in sustainable concrete and cement manufacturing. He received many prestigious awards over the course of his career, including the Berkeley Citation, one of the university's highest honors.

Jerome Singer, professor emeritus in the electrical engineering and computer sciences and the biophysics departments at Berkeley, as well as of radiology at UCSF, died in July at the age of 97. His research centered on quantum electronics and magnetic resonance imaging (MRI), and with his graduate students, he was credited with developing and constructing the first practicable MRI apparatus. He was also a prolific inventor and entrepreneur — having more than 20 patents, including two for MRI technology — and was the founder or co-founder of eight technology companies.

Wei Tan (MEng'19 IEOR) died in September at the age of 26. She had recently launched her career as a data scientist at Evidation Health.

**Colin Um,** a mechanical engineering and chemical engineering undergraduate student, died in June at the age of 22. He had worked as a researcher in the Berkeley Biomechanics Laboratory, where he performed computational studies of spinal discs.

Raymond Wong (B.S.'50 CE) died in January at the age of 91. He worked for the California Department of Transportation in San Jose before serving in the Korean War, and then at the Department of Water Resources for 37 years.









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