Year 2021 | Volume 19 | Health | Natural Science | Technology | Social Science | Humanities | Business

Research at Penn

An Invisible Foe Inspires Innovation

Year 2021 | Volume 19 | *www.upenn.edu/researchdir*

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Research at Penn

Advances in Knowledge from the University of Pennsylvania

Research at Penn is produced by the University of Pennsylvania's Office of University Communications

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ON THE COVER: A year ago, SARS-CoV-2 was little-known to science. Now, it's at the center of an array of research projects at Penn, aimed at uncovering the secrets of the virus in order to help prevent and treat the disease it causes.

Penn's Research Enterprise

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It is impossible to talk about 2020 without talking about the coronavirus. The pandemic afflicted the entire world, causing millions of deaths and a war-like marshalling of resources.

Researchers at Penn have been battling COVID-19 since the early days of the pandemic. This 2021 edition of *Research at Penn* includes a small selection of the diverse ways the University is responding to the crisis.

At the Perelman School of Medicine, faculty formulated a new clearing-house to coordinate coronavirus-related research: the Center for Research on Coronavirus and Other Emerging Pathogens. Scientists at the School of Veterinary Medicine have investigated the effects of the coronavirus on lung cells. A Wharton professor studied why some countries respond to pandemics better than others, and social scientists examined the pandemic's impact on older youth in and aging out of foster care.

Groundbreaking, non-COVID-related research findings are included in these pages as well—innovative discoveries from each of Penn's 12 schools.

Penn Medicine's uterine transplant team has completed three uterine transplants to date, most recently in October 2020. Specialists at Penn Vet are designing the sustainable farm of the future. Researchers from the Penn Museum discovered the oldest known remains of *Homo sapiens* in Europe. Fittingly, a historian investigated how the Mediterranean quarantine system of early 19th-century Europe reshaped British public health policy.

Known throughout the world for its interdisciplinary approach to scholarship, Penn is one of America's top research universities, with more than $1 billion in annual research and development expenditures.

To stay abreast of all University research, visit Penn's research website: www.upenn.edu/researchdir.

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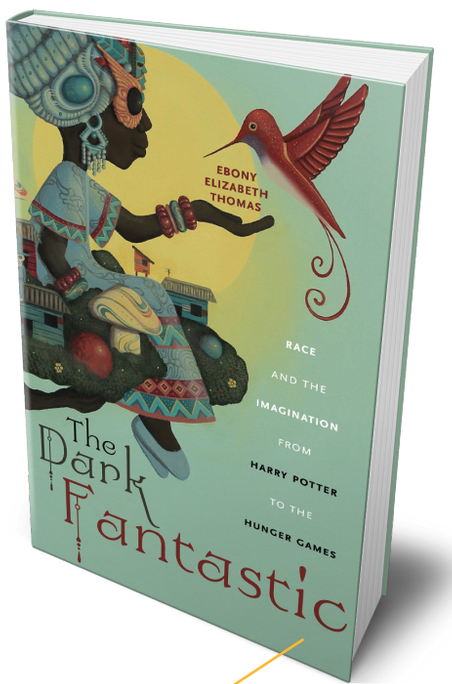

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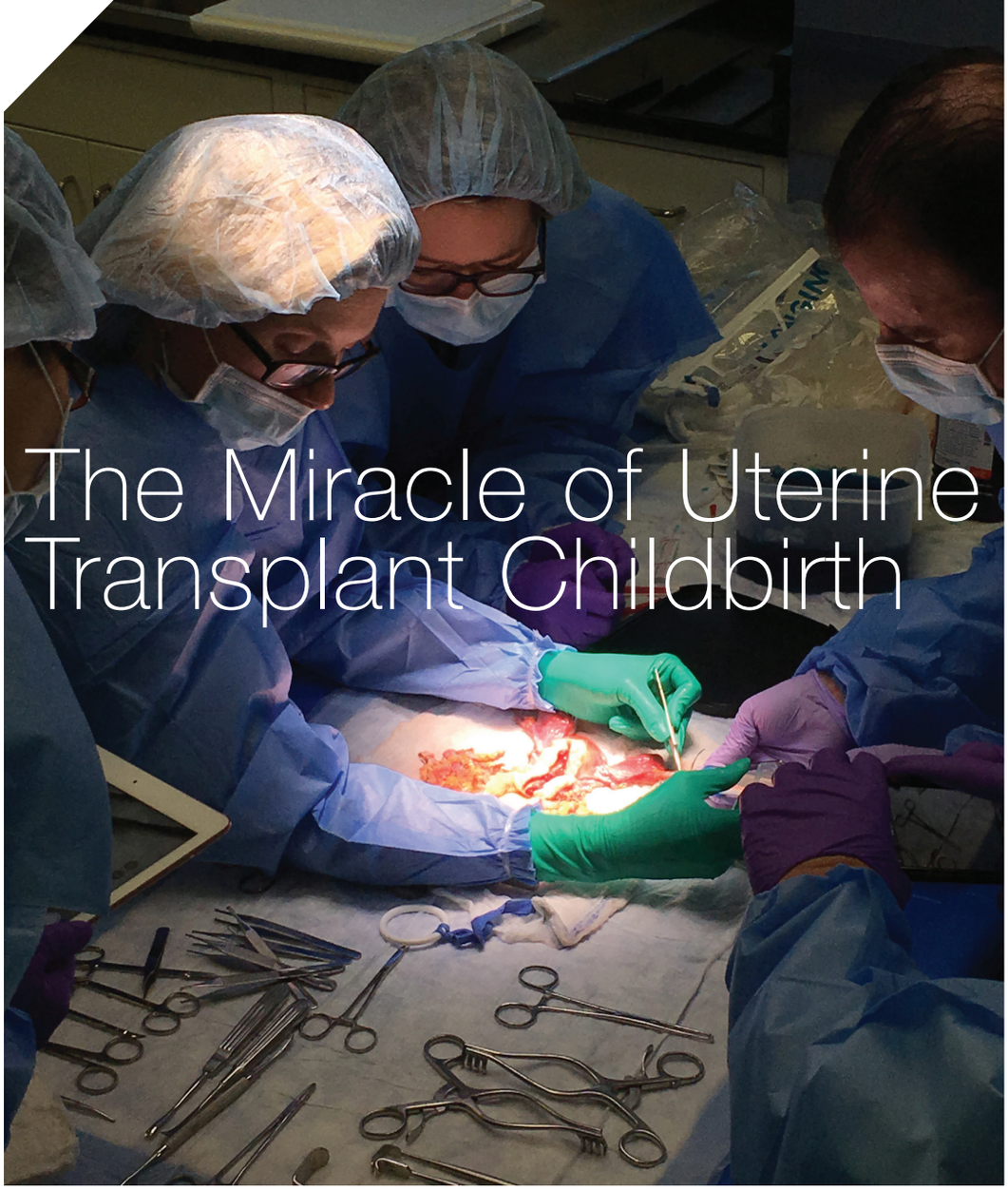
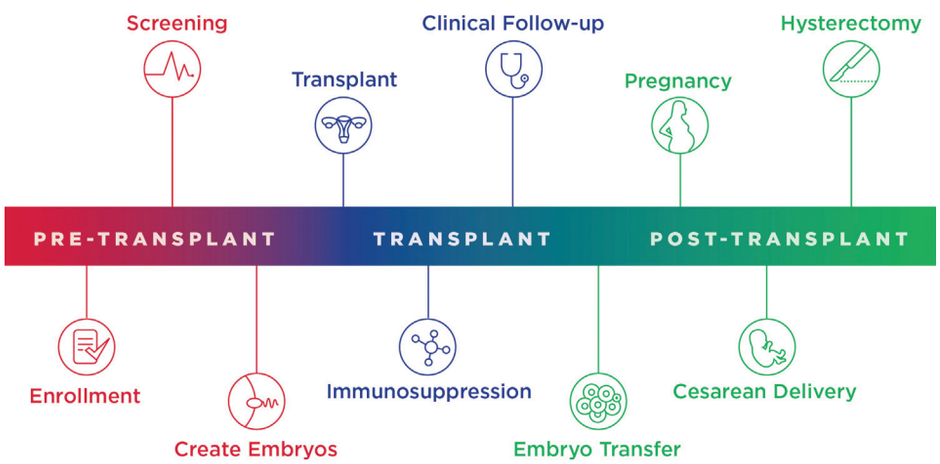




For someone with uterine factor infertility (UFI), which affects up to 5% of women worldwide, the possibility of a healthy pregnancy can seem unattainable. But in November 2019, Jennifer Gobrecht, who was born without a uterus, gave birth to a baby boy named Benjamin after a uterine transplant at the University of Pennsylvania.

Gobrecht is part of a clinical trial spearheaded by the Perelman School of Medicine's Kathleen O'Neill, an assistant professor of obstetrics and gynecology, and until recently, transplant surgeon Paige Porrett, formerly at Penn but now at the University of Alabama.

The team—which includes more than 150 people—has done three uterine transplants to date, two from deceased donors, one from a living donor. A second healthy baby was born in October 2020, and the third transplant recipient is undergoing IVF to get pregnant. O'Neill and colleagues are aiming for two more transplants in 2021.

"The idea was always to start with five," O'Neill says. "When you're doing innovative, high-risk, high-reward research like this, you don't want to let failures completely stop the work."

For a woman going through this, the process is complex. Her eggs get harvested and fertilized, and the collected embryos frozen. Then, following a standard organ-transplant evaluation and clearance, she undergoes major surgery for the transplant. At that time, she starts immunosuppressant medications to keep her body from rejecting the uterus. After six months of recovery, a single embryo is transferred. The ultimate goal is a healthy child.

Despite all those steps, an influx of individuals expressed interest when O'Neill and Porrett opened enrollment for the Uterus Transplantation for Uterine Factor Infertility trial in 2017.

At that time, O'Neill had been at Penn a year, pursuing research and seeing patients. For those with UFI, she had alternatives to achieving parenthood she could offer, but no treatments.

Paige Porrett (left), formerly of Penn Medicine, and Kathleen O'Neill led the uterus transplant clinical trial. (Pre-pandemic photo)

She approached the division director about a uterine transplant program. "I saw this incredible clinical need and an incredible model to explore some of the fundamentals of reproduction, implantation, and pregnancy."

With support from the OB/GYN Department, the Penn Transplant Institute, and Hospital of the University of Pennsylvania CEO Regina Cunningham, O'Neill started building an interdisciplinary team that included maternal-fetal medicine physician Eileen Wang, gynecologic oncologist Nawar Latif, and others. In 2018, that team completed its first surgery, and just

"I saw this incredible clinical need and an incredible model to explore some of the fundamentals of reproduction, implantation, and pregnancy."

two years after program conception, delivered its first baby. Despite a pause due to COVID-19, there's plenty of momentum to keep it moving.

"This program highlights what people are willing to go through, both as recipients and donors," O'Neill says. "For some reason, people view reproduction as optional, but I think the vast majority of individuals who have families would agree it's one of the most important parts of their life."

Ishmail Abdus-Saboor (right) and research technician William Foster go over a still image from a video of a mouse reacting to a stimulus. (Pre-pandemic photo)

A NEW PLATFORM TO EVALUATE PAIN

The touch of a feather, the itch of a mosquito bite, the prick of a needle: The body is capable of distinguishing and responding to all of these sensations in a near instantaneous relay, from skin to brain and back again.

"Our brain is constantly computing these things, and in healthy people it never gets it wrong," says Ishmail Abdus-Saboor, the Mitchell J. and Margo K. Blutt Presidential Assistant Professor in the Department of Biology, whose work focuses on the nervous system pathways involved in this relay, with a particular focus on acute and chronic pain.

In a paper in *Cell Reports,* he and colleagues reported on a novel technique to measure pain in mice, a platform that could be used to screen new drugs or even help clinicians one day evaluate their patients' discomfort in a much more rigorous way than is currently available.

The technique uses high-speed videography, capable of capturing 1,000 frames per second.

"Taking lessons from other model systems, mainly fruit flies and zebrafish, people have been using high-speed cameras to slow down behaviors that we can't see with the naked eye," says Abdus-Saboor. "I had the hypothesis that if we did this, maybe there was a lot more information we could extract that could inform us and teach us about what the animal is experiencing. And that turned out to be the case."

Processing frames from these recordings manually, which is how the researchers initially completed the study, was a tedious task. But working with biostatisticians, computational biologists, and machine-learning specialists, Abdus-Saboor and members of his lab were able to streamline the process. In collaboration with departmental colleague Joshua Plotkin and the Perelman School of Medicine's Gregory Corder, they've successfully automated the video frame-by-frame analysis, sharing their findings in the journal *eLife.*

Abdus-Saboor is also collaborating with other Penn researchers to apply the platform in clinical settings to objectively evaluate the patients' pain and prescribe painkilling drugs appropriately.

"We're not there yet, but these are conversations we're starting to have," says Abdus-Saboor. "If this technology could evolve into the clinic, that would be a wonderful thing."

A Single Episode of Vaping Can Damage Blood Vessels

Smoking e-cigarettes, or vaping, has been marketed as a safe alternative to tobacco cigarettes, and is rising in popularity among non-smoking adolescents. However, a single e-cigarette can be harmful to the body's blood vessels—even when the vapor is entirely nicotine-free—according to a study by researchers at the Perelman School of Medicine.

> ***"We have found that dangers exist, independent of nicotine."***

To study the short-term impacts of vaping, the researchers performed MRI exams on 31 healthy, non-smoking young adults before and after vaping a nicotine-free e-cigarette. Comparing the pre- and post-vaping MRI data, a single episode of vaping resulted in reduced response in blood flow following a brief period of obstruction of the femoral artery, which supplies blood to the lower extremity. The data suggest the vaping insult causes transient impairment of the endothelium (lining of the blood vessel).

Their research, supported by the National Heart, Lung, and Blood Institute, was published in the journal *Radiology*.

Felix W. Wehrli, the study's principal investigator and a professor of radiologic science, says while e-cigarette liquid may be relatively harmless, the vaporization process can transform its components into toxic substances.

"Beyond the harmful effects of nicotine, we've shown that vaping has a sudden, immediate effect on the body's vascular function, and could potentially lead to long-term harmful consequences," he says.

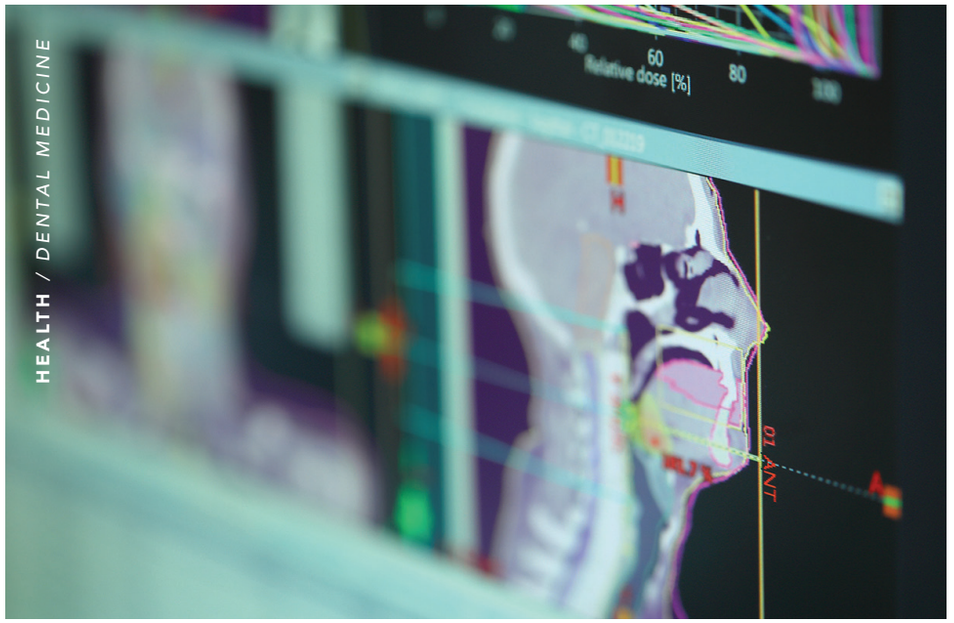
Study lead author Alessandra Caporale, a postdoctoral researcher in the Laboratory for Structural, Physiologic, and Functional Imaging, says their findings suggest vaping can cause significant changes to the inner lining of blood vessels.

"E-cigarettes are advertised as not harmful, and many young e-cigarette users are convinced that they are just inhaling water vapor," she says. "But the solvents, flavorings, and additives in the liquid base, after vaporization, expose users to multiple insults to the respiratory tract and blood vessels."

Wehrli says more research is needed to address the potential long-term adverse effects of vaping on vascular health, but he predicts that e-cigarettes are potentially much more hazardous than previously assumed.

"I would warn young people to not even get started using e-cigarettes," he says. "The common belief is that the nicotine is what is toxic, but we have found that dangers exist, independent of nicotine."

Leveraging Science in the Dental Clinic



Patricia Corby (center) is collaborating on a clinical trial with (left to right) Katherine France and Takako Tanaka (far right) of Penn Dental Medicine and John Nicholas Lukens, Samuel Swisher-McClure, and Alexander Lin of Penn Medicine. (Pre-pandemic photo)

Over the last two years, Patricia Corby, associate dean of translational research at the School of Dental Medicine, has built an entirely new clinical and translational research program with enthusiastic support from Morton Amsterdam Dean Mark Wolff.

"The school had a very strong basic science research program, but now we have a support system for researchers interested in human subject research as well," says Corby, who directs the recently launched Center for Clinical and Translational Research, which shepherds faculty projects from the earliest pilot studies and grant writing to carrying out clinical trials on site.

One of the trials in full swing at the Center? Corby's own.

Prior to coming to Penn, Corby led clinical research operations at the New York University College of Dentistry. She noted how radiation therapy, commonly used in patients with head and neck cancer, could wreak havoc on the oral cavity. Oral mucositis, when radiation triggers painful ulcers that make it difficult or impossible for patients to eat and function normally, is a common but debilitating effect of treatment.

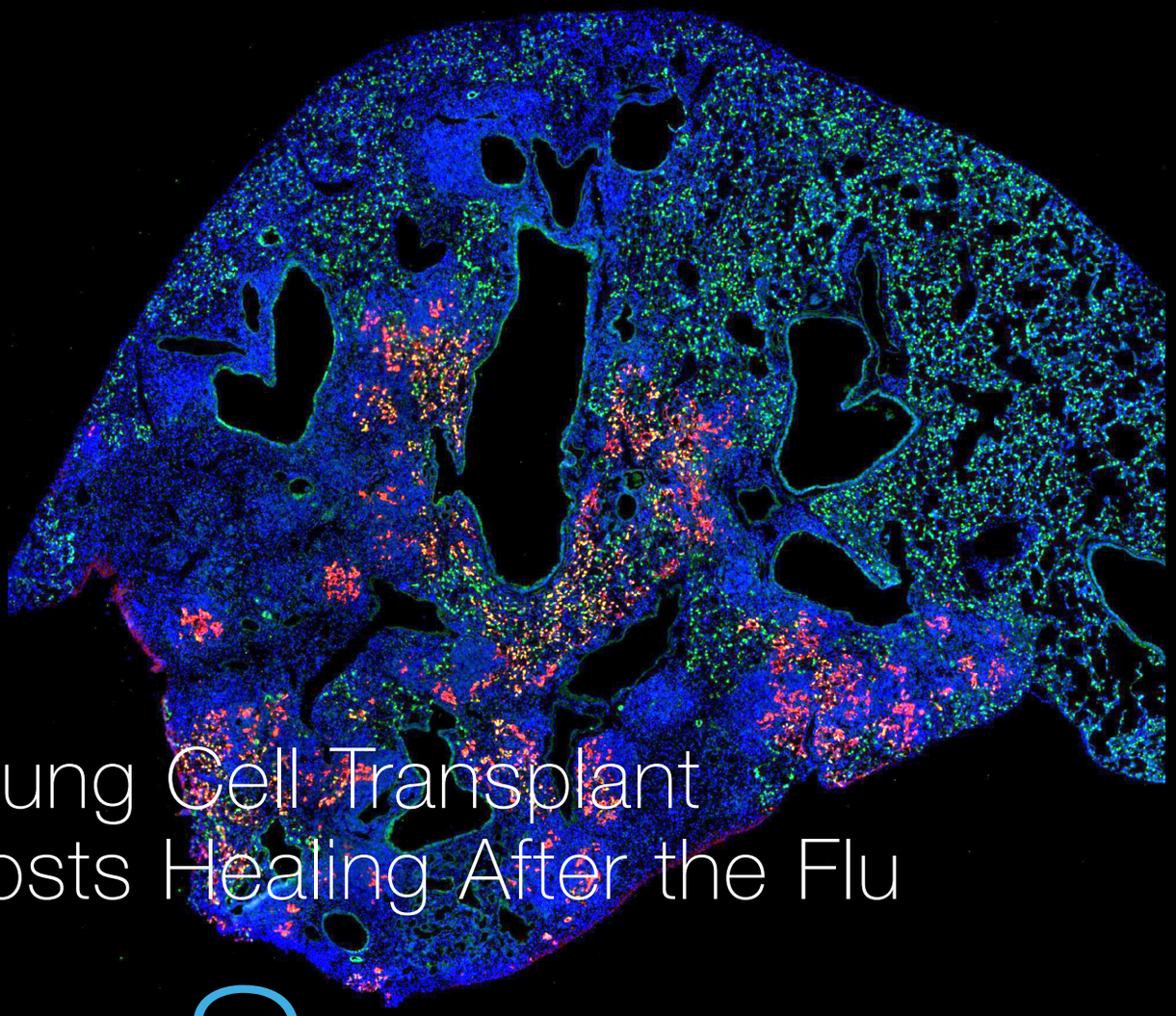
"It can affect the whole oral mucosa, the tongue, the throat, even the esophageal and gastrointestinal tract," says Corby, "and it's a disaster. Severe cases place patients at risk for secondary infections and even sepsis due to open sores in the mouth. In the worst cases, treatment can't continue."

Corby wondered whether a new oral health protocol that introduces professional cleaning of patients' mouths during radiation therapy, aimed at preventing the colonization of "bad" bacteria, could help reduce or even prevent this side effect of cancer care.

That thought led to a small, successful pilot study, which has since grown into an $8 million National Institute of Dental and Craniofacial Research-funded project. The trial is currently enrolling patients in collaboration with a team of investigators from the Perelman School of Medicine: Alexander Lin, Samuel Swisher-McClure, and John Nicholas Lukens.

In Corby's view, with the National Institutes of Health supporting more translational research than in the past, there hasn't been a better time to pursue this type of work.

"If you're in health care, you can't progress without clinical and translational research," she says.



Researchers successfully transplanted a special type of lung cell called AT2 cells (in green) from healthy mice into mice that had experienced a severe flu infection. The AT2 cells that engrafted (in red) appear to have helped the animals recover more robustly.

A Lung Cell Transplant Boosts Healing After the Flu

Some cases of the flu are so severe they cause lasting injury to the lungs. Research led by Andrew Vaughan, an assistant professor in the School of Veterinary Medicine, aims to one day offer protection against this damage.

Vaughan, graduate student Aaron Weiner, and colleagues found that transplanting a type of lung cell called alveolar type 2 (AT2) cells from healthy mice to those that had been injured by an influenza infection could improve healing. The transplant—achieved by allowing sick mice to simply breathe in AT2 cells taken from healthy animals—led to improved blood-oxygen levels.

"Can we make them better? Can we improve lung regeneration?"

"We took this really simple approach," says Vaughan, senior author on the study, published in *Regenerative Medicine* and funded by the National Institutes of Health, "and asked if we could supplement back these AT2 cells into injured mice, can we make them better? Can we improve lung regeneration?"

AT2 cells produce surfactant, a substance that lowers surface tension in the lung's alveoli to ensure proper function. But AT2 cells can also take on a stem cell-like activity, able to both self-renew and to give rise to alveolar type 1 (AT1) cells, which are responsible for gas exchange in the lungs.

Vaughan and colleagues decided to take advantage of this latter ability of AT2 cells to see if the researchers could aid healing by isolating roughly a million AT2 cells from healthy mice, and transplanting them to sick animals. Two weeks later, the AT2 cells had expanded in number and differentiated into AT1 cells. Mice that got the transplant of primary AT2 cells had significantly higher blood-oxygen saturation than mice that received a mock transplant of saline solution, a sign of a stronger recovery.

The team found similar success in two other models of lung injury: acid inhalation and drugs used for chemotherapy known to harm the lungs.

In follow-up work, Vaughan and his collaborators are investigating the molecular signals that may be encouraging the transplanted cells to stick around and contribute to healing. And they're looking to other factors that influence recovery from infections like flu—or even COVID-19—including how blood vessels act to help repair lung tissue, work led by postdoctoral researcher Gan Zhao that the group recently shared in the journal *Science Advances*.

HEALTH / NURSING SCIENCE

Why Some Black Men Seek Help After a Traumatic Injury

Therese Richmond of the School of Nursing has been trying to better understand the psychological effects of trauma and, more specifically, why traumatic injury and violence disproportionately affect Black men. With funding from the National Institutes of Health, she and colleagues collected data on 623 Black men hospitalized in a Level 1 trauma center following an injury.

"We looked at factors like childhood adversity, prior mental health challenges, and pre-injury health," says Richmond, the Andrea B. Laporte Professor of Nursing. "These factors all came together in a complex picture, contributing to more severe acute psychological reactions leading to poorer outcomes. Outcomes were worse for men with violent injuries."

Digging into those findings, Richmond and collaborator John Rich of Drexel University wanted to know what might encourage someone to seek professional help after such an experience. Through quantitative and qualitative data from 32 of the original study's participants, they discovered three common scenarios, findings they published in the *Journal of Traumatic Stress.*

"First, high levels of depression and financial worry alone were sufficient for Black men to want to get help," she says. "High depression and post-traumatic stress disorder (PTSD) symptoms together—because they can co-occur—were also sufficient to seek help."

The third pathway stood out to Richmond and Rich.

They found that a combination of financial worry, PTSD symptoms, and the experience of having faced even moderate discrimination over the course of a lifetime also motivated study participants to seek professional assistance.

"That's important because it shows us that Black men are not a monolith," she says. "We need to recognize that factors beyond the injury itself, such as experiences with discrimination, are important in needing and seeking assistance."

From here, Richmond says it will be important to disentangle what else might be contributing to these pathways. Ultimately, the aim is to ensure that those who have suffered a violent trauma get the help they need.

"As clinicians," she says, "we need to identify people at risk and get them help to fully recover. That's the bottom line."

REDUCING TONGUE FAT IMPROVES SLEEP APNEA

Researchers in the Perelman School of Medicine have discovered that improvements in sleep apnea symptoms appear to be linked to the reduction of fat in one unexpected body part: the tongue.

Twenty-two million Americans suffer from sleep apnea, a serious health condition in which breathing repeatedly stops and starts, causing patients to wake up randomly throughout their sleep cycles.

"Most clinicians, and even experts in the sleep apnea world, have not typically focused on fat in the tongue for treating sleep apnea," says Richard Schwab, chief of the Division of Sleep Medicine. "Now that we know tongue fat is a risk factor, and that sleep apnea improves when tongue fat is reduced, we have established a unique therapeutic target that we've never had before."

The new study included 67 participants with mild to severe obstructive sleep apnea who were obese—those with a body mass

index greater than 30. Through diet or weight loss surgery, the patients lost nearly 10% of their body weight, on average, over six months. Overall, the participants' sleep apnea scores improved by 31% after the weight loss intervention, as measured by a sleep study.

Using magnetic resonance imaging to measure the effect of weight loss on the upper airway in obese patients, researchers found that reducing tongue fat is a primary factor in lessening the severity of obstructive sleep apnea. The findings were published in the *American Journal of Respiratory and Critical Care Medicine.*

The authors believe that tongue fat is a potential new therapeutic target for improving sleep apnea. They suggest that future studies could be designed to explore whether certain low-fat diets are better than others in reducing tongue fat, and whether cold therapies—like those used to reduce stomach fat—might be applied to reducing tongue fat. However, Schwab notes, these types of interventions have not yet been tested.

Designing the Sustainable, Humane Farm of the Future

According to Thomas Parsons, a professor of swine production medicine at the School of Veterinary Medicine, a sustainable pig farm must be both socially acceptable and economically viable.

"For most farmers, farming is not a livelihood, it's a lifestyle," Parsons says. "And so if they lose that social license to farm, not only do they lose their livelihood, but they lose their lifestyle."

To help farmers sustain both, Penn Vet's Swine Teaching and Research Center, which Parsons directs, offers a model of sustainable agriculture. With humane conditions and efficient resource use, its research stands to reshape the environmental and social impacts of raising swine.

Implementing alternatives to gestation stalls has been a key step in defining more socially acceptable swine farming. Individual gestation stalls eliminate feed competition between sows, but also preclude many of their natural behaviors. Sows at the Swine Center, in contrast, are raised in groups without behavioral restrictions, and receive personalized, private meals upon entering a specialized electronic feeder.

The Penn Vet farm uses solar panels to generate electricity, and is certified organic, which requires that animals receive feed raised without herbicides or pesticides, and that antibiotics use is limited.

The Swine Center's impact is now felt across the state. Roughly 60% of sows raised in Pennsylvania are no longer confined to gestation stalls, more than any other state except where the crates have been legislatively banned. The Center is now researching new solutions to meet the augmented animal welfare expectations of California's Proposition 12, which stand to affect farming practices nationwide by 2022.

To catalyze new knowledge and practices, Penn Vet, together with the Stuart Weitzman School of Design and PennPraxis, has recently launched a series of dialogues around the concept of "the farm of the future."

"What I'm excited about here at Penn Vet is to be able to better formalize, 'What is sustainability?'" says Gary Althouse, associate dean of sustainable agriculture and veterinary practices. "Being able to address this topic beyond just looking at an animal, but more so looking holistically at the process, and to provide this insight through the training to our veterinary students and outreach."

Thomas Parsons (above, left), director of Penn Vet's Swine Teaching & Research Center, Gary Althouse, associate dean of sustainable agriculture and veterinary practices, and colleagues have worked for years to improve animal welfare and environmental sustainability at the swine unit, and with recent improvements, are setting a new standard for the industry. (Pre-pandemic photos)

HEALTH

First-in-Human Trial Finds CRISPR-Edited Immune Cells Safe and Long-Lasting in Cancer Patients

Penn Medicine researchers have shown how the genetic editing tool known as CRISPR can be safely used to fight cancer in the first clinical trial in the United States to test the approach in humans.

A team reported in 2019 that genetically editing a cancer patient's immune cells using CRISPR/Cas9 technology, then infusing those cells back into the patient, appeared safe and feasible.

The research team, led by Carl June, the Richard W. Vague Professor in Immunotherapy and director of the Center for Cellular Immunotherapies and the Parker Institute for Cancer Immunotherapy at the Perelman School of Medicine, and Edward A. Stadtmauer, section chief of hematologic malignancies at Penn, infused three participants—two with multiple myeloma and one with sarcoma—and observed the edited T cells expand and bind to their tumor target with no serious side effects. Penn is conducting the study with the Parker Institute for Cancer Immunotherapy and Tmunity Therapeutics.

"Can we edit T cells in this specific way? Are the resulting T cells functional? And are these cells safe to infuse into a patient?"

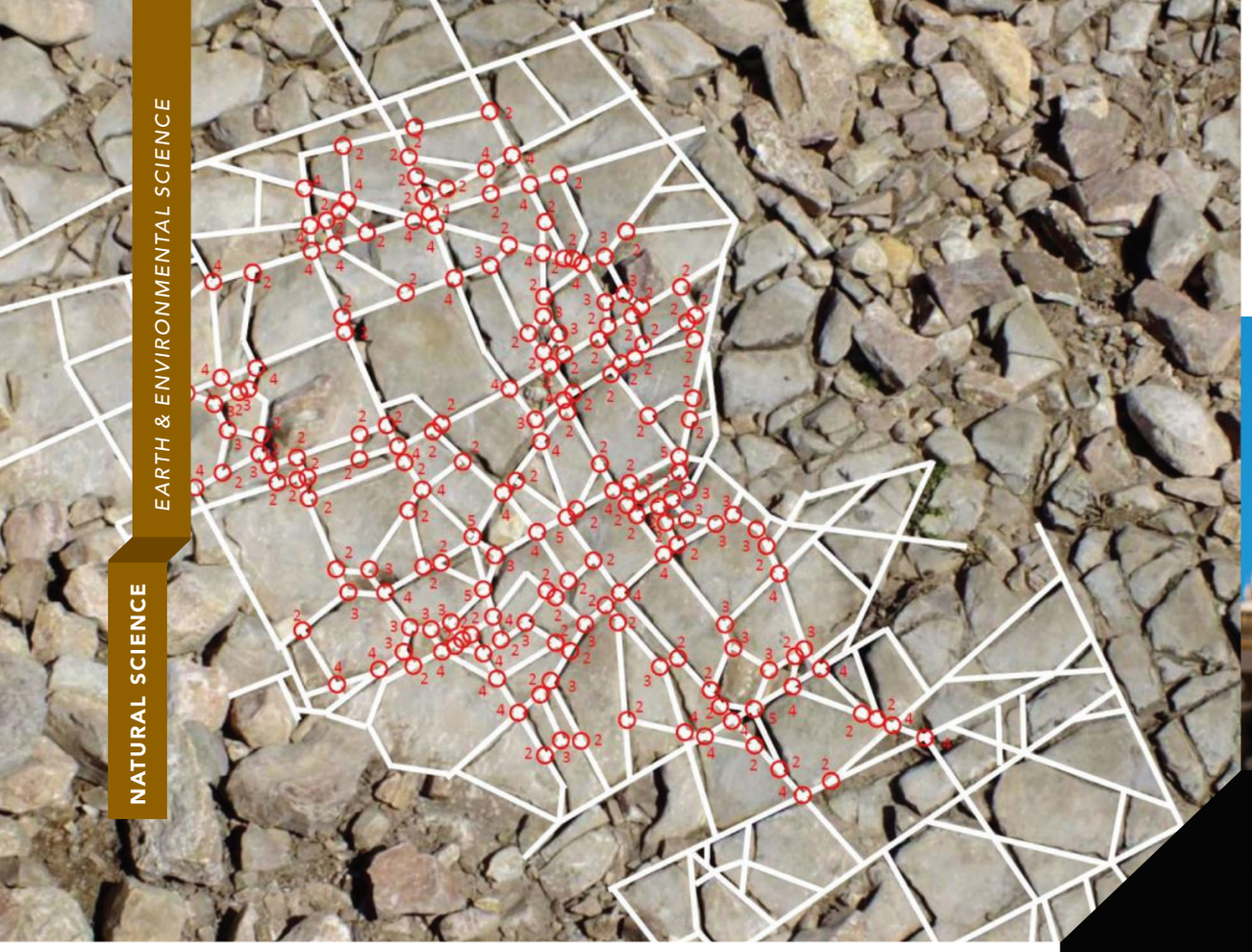
"This trial is primarily concerned with three questions: Can we edit T cells in this specific way? Are the resulting T cells functional? And are these cells safe to infuse into a patient?" says Stadtmauer. "This early data suggests that the answer to all three questions may be yes."

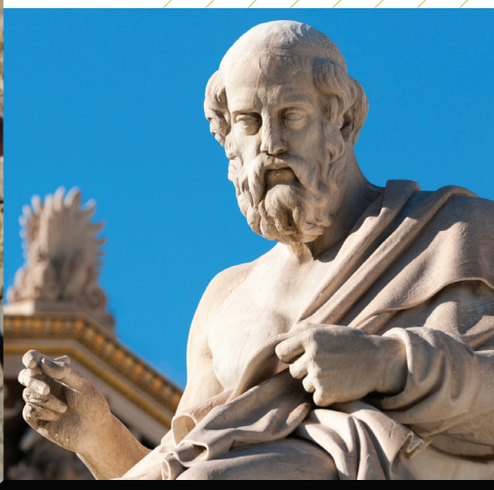
Four months later, in February 2020, they presented in the journal *Science* how those genetically edited immune cells can persist, thrive, and function months after a cancer patient receives them. The team also showed cells removed from patients and brought back into the lab setting were able to kill cancer months after their original manufacturing and infusion.

The approach is closely related to CAR T-cell therapy, which engineers patients' own immune cells to fight their cancer—but does have some key differences. Just like CAR T, researchers begin by collecting a patient's T cells through a blood draw. The team first uses CRISPR/Cas9 editing to remove three genes that eliminate a T cell's natural receptors to make sure the immune cells bind to the right part of the cancer cells, and remove PD-1, a natural checkpoint that sometimes blocks T cells from doing their job. A lentivirus is used to insert an affinity-enhanced T cell receptor, which tells the edited T cells to target a cancer antigen called NY-ESO-1.

"We leaned heavily on our experience as pioneers of the earliest trials for modified T-cell therapies and gene therapies, as well as the strength of Penn's research infrastructure at the Abramson Cancer Center, to make this study a reality," says June.

While it's still early in the ongoing trial, the findings help illustrate the potential of this technology to treat many diseases that were previously not able to be treated or cured.





The research team analyzed fragmentation patterns of rocks on Earth (above left), as well as from around the solar system, such as on Jupiter's moon Europa (above).

PLATO'S CONJECTURE, COME TO LIFE

"The solar system is littered with ice and rocks that are ceaselessly smashing apart. This work gives us a signature of that process that we've never seen before."

Plato, the Greek philosopher who lived in the 5th century B.C.E., believed that the universe was made of five types of matter: earth, air, fire, water, and cosmos. Each was described with a particular geometry, a "platonic shape." For earth, that shape was the cube.

Science has steadily moved beyond Plato's conjectures, looking instead to the atom as the building block of the universe. Yet Plato seems to have been onto something, researchers have found.

In a paper in the *Proceedings of the National Academy of Sciences,* Douglas Jerolmack, a professor of earth and environmental science in the School of Arts & Sciences, and colleagues use math, geology, and physics to demonstrate that the average shape of rocks on Earth is a cube.

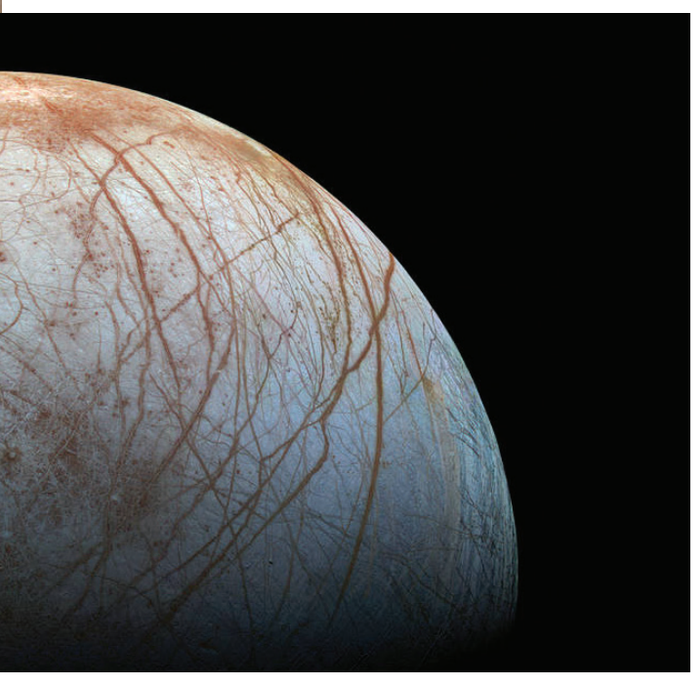
The group's finding began with geometric models developed by mathematician Gábor Domokos of the Budapest University of Technology and Economics, whose work predicted that natural rocks would fragment into cubic shapes. Domokos pulled two Hungarian theoretical physicists into the loop: Ferenc Kun, an expert on fragmentation, and János Török, an expert on statistical and computational models. The researchers took their finding

to Jerolmack to work together on the geophysical questions; in other words, "How does nature let this happen?"

The team measured hundreds of rocks that they collected and thousands more from previously collected datasets. No matter whether the rocks had naturally weathered from a large outcropping or had been dynamited out by humans, the team found a good fit to the cubic average.

Remarkably, they found that the core mathematical conjecture unites geological processes not only on Earth, but around the solar system as well.

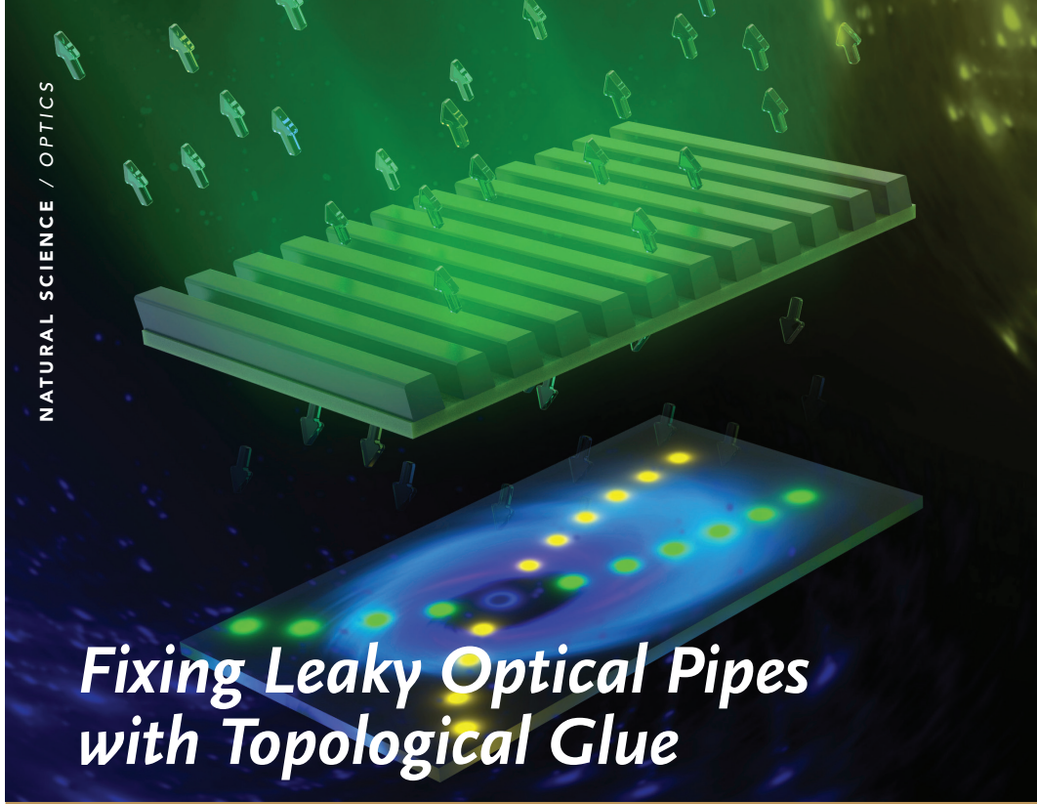
"The solar system is littered with ice and rocks that are ceaselessly smashing apart," Jerolmack says. "This work



gives us a signature of that process that we've never seen before."

Part of this understanding is that the components that break out of a formerly solid object must fit together without any gaps, like a dropped dish on the verge of breaking. The only one of the so-called platonic forms—polyhedra with sides of equal length—that fits together without gaps is cubes.

"When you pick up a rock in nature, it's not a perfect cube, but each one is a kind of statistical shadow of a cube," adds Jerolmack. "It calls to mind Plato's allegory of the cave. He posited an idealized form that was essential for understanding the universe, but all we see are distorted shadows of that perfect form."



Fixing Leaky Optical Pipes with Topological Glue

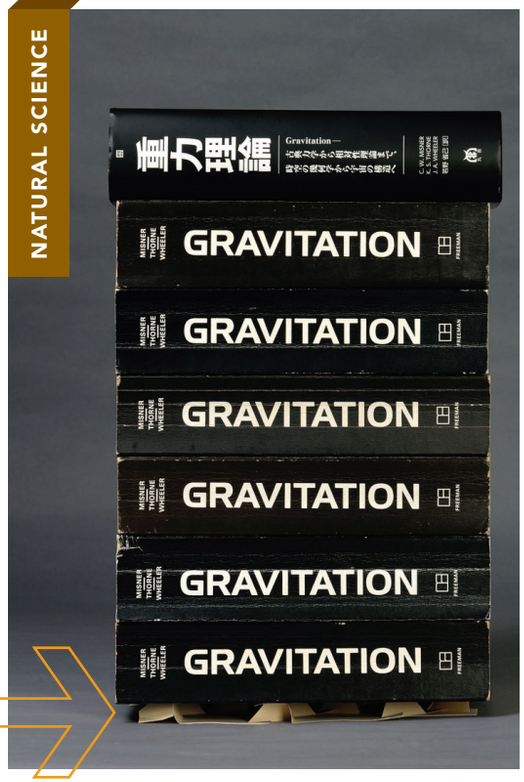
Research published in *Nature* describes a new design for an optical material that can radiate light in a single direction. Using a combination of theoretical and experimental results, a team of physicists demonstrated how insights from topology can help reduce energy consumption in optical devices. The work was conducted by Ph.D. student Jicheng Jin, assistant professor Bo Zhen in the School of Arts & Sciences, and researchers at Peking University and the Massachusetts Institute of Technology.

Single-sided radiation is important in optical fibers, which are used to transmit information in data centers, because of the amount of energy lost. Because optical fibers operate in a single direction, like water flowing through a pipe, the loss of light at "leaky" points, where fibers connect to chips or where signals are generated, can quickly multiply in data centers that are often comprised of large networks of nodes.

After finding that breaking symmetry in a chip could reduce radiation loss to zero, the researchers developed a new theory based on a concept known as topological charges.

"Imagine it as two-part glue: By breaking the left-right symmetry, the topological charge is split into two half charges, and the two-part glue is separated so each part can flow," says Zhen. "By breaking the up-down symmetry, each part flows differently on the top and the bottom, so the two-part glue combines only on the bottom, eliminating radiation in that direction. It's like a leaky pipe has been fixed with a topological glue."

The researchers then came up with a design to test in the lab, fabricating a chip made of a series of slanted bars that break left-right and up-down symmetries at the same time. After developing a novel etching method, by placing silicon chips on a wedge-like substrate, the researchers were able to confirm the reduced energy loss that was predicted by their theory. This new system is practical and simple to make, and the team is now working on refining their approach to be compatible with existing industrial fabrication processes.



Kirigami Designs Hold Thousands of Times Their Own Weight

Using kirigami, a variant of origami that allows materials to be cut and reconnected with adhesives, researchers describe a new set of motifs for creating lightweight, strong, and foldable structures. These structures can support thousands of times their own weight and can easily be flattened and refolded. The research was published in *Physical Review X* and conducted by former visiting graduate student Xinyu Wang, Randall Kamien, the Vicki and William Abrams Professor in the Natural Sciences in the School of Arts & Sciences, and Simon Guest from the University of Cambridge.

Wang, who came to Penn with an interest in the mechanical properties of kirigami, was asked to try out some new designs using the Kamien group's previously established set of rules. Shortly thereafter, Wang showed Kamien a kirigami triangle that had tilted walls, and Kamien was surprised that she had left the flaps from the cuts in place. "The usual kirigami route is to cut that off and tape it," says Kamien, adding that Wang "found that, in this particular geometry, you can get the flaps to fit."

While a single triangle wasn't particularly strong on its own, the researchers discovered that several arranged together in a repetitive design could support 14,000 times their own weight. The tilted, triangular design was strongest when the flaps were undamaged and untaped, and it was also stronger than the same design with vertical walls.

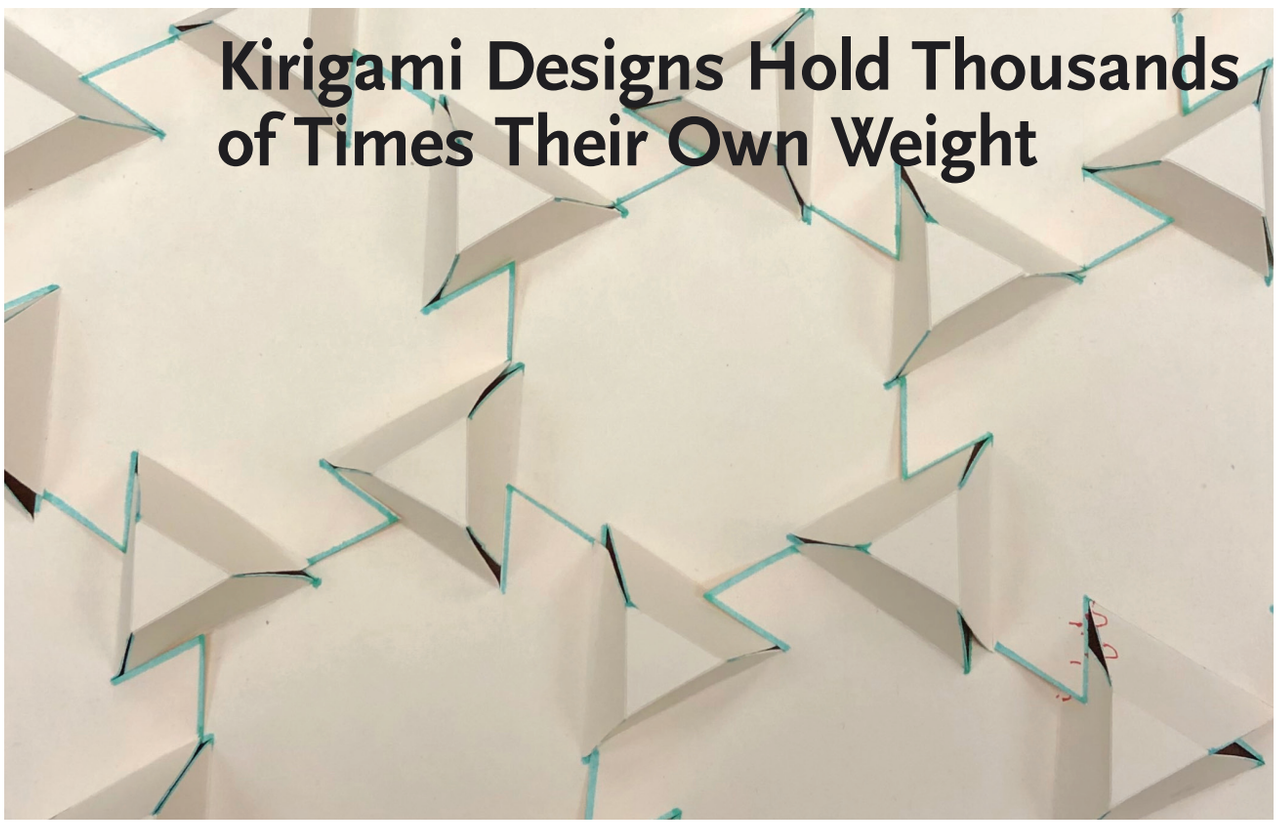
With the help of Guest, Kamien and Wang found that two deviations from the kirigami rules were key to the structure's strength. When the walls of the triangles were angled, any force applied to the top could be translated into horizontal compression within the center of the design. They also found that the paper-to-paper overlap from leaving the cut flaps in place allowed the triangles to press up against their neighbors, which helped distribute the vertical load.

Their findings provide a new approach for making strong, rigid objects out of soft materials.

"We figured out how to use materials that can bend and stretch, and we can actually strengthen these materials," says Wang. She says future applications could include lightweight and deployable structures, such as temporary shelters.

ABOVE: The team collected the largest books they could find from across the Department of Physics and Astronomy. They found that seven copies of the five-pound "Gravitation" textbook could be supported by a single kirigami sheet.

RIGHT: A close-up view of the weight-bearing kirigami structures created by Xinyu Wang while working in Randall Kamien's lab. Each raised triangle platform is supported by neighboring flaps (shown outlined in blue) that work together to hold the structure in place without tape or adhesive.



USING MAGNETS TO SUSTAINABLY SEPARATE RARE EARTH METALS

NATURAL SCIENCE / CHEMISTRY

Seventeen of the periodic table's 118 elements are known as rare earth metals, critical components of phones and computers that require toxic, environmentally damaging procedures to extract. Now, chemists at Penn have demonstrated a new approach for separating mixtures of rare earth metals with the help of a magnetic field. The study, published in *Angewandte Chemie International Edition,* was conducted by postdoctoral researcher Robert Higgins and Eric Schelter, a professor of chemistry in the School of Arts & Sciences, and represents a key starting point toward achieving a cleaner, more circular rare earth metals economy.

The standard method for separating mixtures of rare earth metals is to use a solution of acid and an organic compound, where metal ions slowly move into different phases of the solution based on their chemical properties. However, because chemical properties are similar in this group of elements, the separation process requires a lot of time and energy. What is different between rare earth metals, however, is their paramagnetism, or how attracted they are to magnetic fields.

In this study, the researchers were able to combine a magnetic field with a decrease in temperature in a way that caused certain metal ions to selectively crystallize. The study shows a "100% boost" compared to the same method without a magnet, showing that a 50/50 mixture of lanthanum and dysprosium could be separated to achieve 99.7% pure dysprosium in a single step.

The researchers hope that their systematic yet simple approach can take metals separation technologies to something more controllable, competitive, and cost-effective.

"If you could rationally design ways to improve metals separation, that would be a huge advantage," says Schelter.

Higgins, whose work is supported by The Nature Conservancy, sees these types of fundamental chemistry studies as an important step toward making rare earth metal recycling more sustainable.

"The faster we can find new ways of performing separations more efficiently, the faster we can improve some of the geopolitical and climate issues that are associated with rare earth mining and recycling," says Higgins.

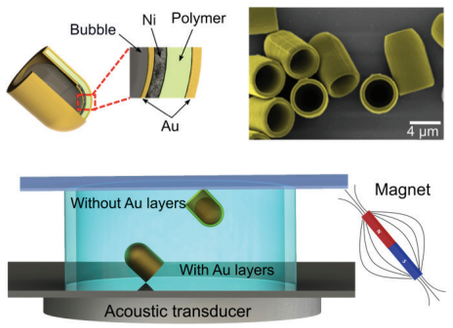
NATURAL SCIENCE / NANOTECHNOLOGY

Microscale Rockets Can Travel Through Cellular Landscapes

A team of chemists has developed microscale "rockets" that can travel through 3D landscapes of cells and particles. Powered by acoustic waves and an onboard bubble motor, these tiny, maneuverable rockets can be steered using an external magnetic field. Published in *Science Advances,* the research was led by Vagelos Professor in Energy Research Thomas Mallouk of the School of Arts & Sciences as part of a collaboration between Penn, University of California, San Diego, the Harbin Institute of Technology in Shenzhen, China, and Pennsylvania State University, where the study was initially conducted.

Progress in developing nano- and microscale vessels was previously limited by the toxicity of the chemicals required for powering the vessels. Then, an "accidental" discovery made by the researchers showed that high-frequency sound waves could be used to move these vessels, which led the team to explore new ways that they could be powered using ultrasound.

The resulting rockets are made of a 3D-printed, round-bottomed cup that's 10 microns in length and 5 microns wide (about the size of a particle of dust), and contain an outer layer of gold and inner layers of nickel and a polymer. Treatment with a hydrophobic chemical after casting causes an air bubble to form and become trapped inside the cup's cavity, which can then be excited by high-frequency oscillation at the water-air interface. Using magnets to steer, the tiny rockets are able to travel up microscopic staircases and can swim freely in three dimensions with the help of special fins. And by increasing or decreasing the amount of acoustic "fuel," the researchers can also control their speed.

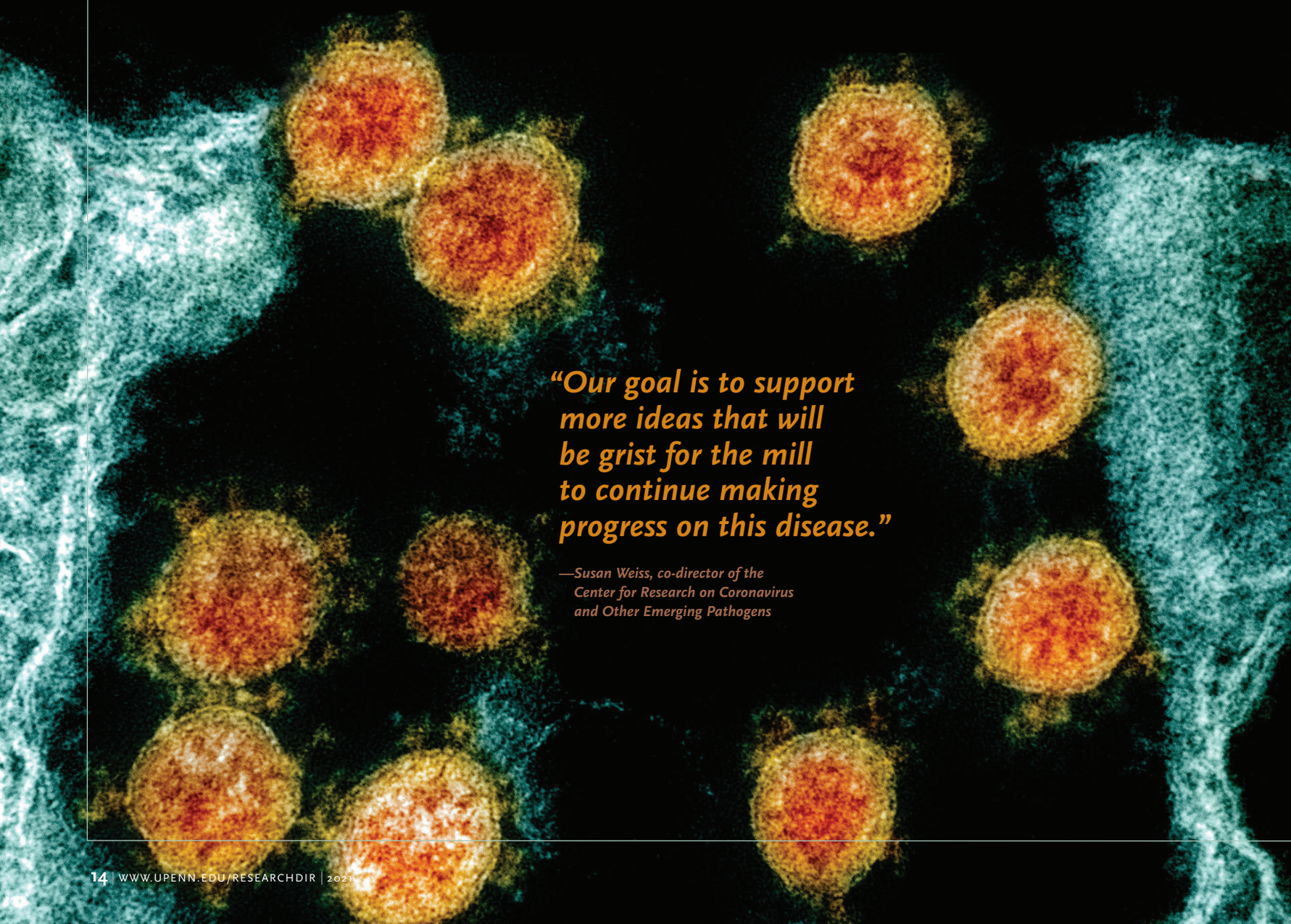


A schematic showing the structure of the microrockets, which are 3D printed and contain a trapped air bubble (top left), and how they look under scanning electron microscopy (top right). The acoustic fluidic chamber where they can be driven in three dimensions is shown on the bottom.

Mallouk and his lab are already exploring a number of areas of further research, including ways to actuate the rockets with light and making even smaller rockets that would be faster and stronger for their size. They have already developed new processes to make bubble motors that are up to five times smaller and in larger batches. Future collaborations with engineers and roboticists at Penn could also help make these rockets "smart" by outfitting the vessels with computer chips and sensors to give them autonomy and intelligence.

"We'd like to have controllable robots that can do tasks inside the body: deliver medicine, rotor-rooter arteries, diagnostic snooping," says Mallouk.

An Invisible Foe Inspires Innovative Penn Science



"Our goal is to support more ideas that will be grist for the mill to continue making progress on this disease."

—Susan Weiss, co-director of the Center for Research on Coronavirus and Other Emerging Pathogens

Breakthroughs in science happen, but they are rare. More often, researchers chip away at scientific problems through steady, incremental progress.

In John Wherry's lab at the Perelman School of Medicine, postdoc Amy Baxter, graduate student Zeyu Chen, and others have been working through the pandemic to study how different patients' immune systems respond to infection with SARS-CoV-2.

A worldwide pandemic, however, has demanded a different approach. The need to understand the SARS-CoV-2 virus and COVID-19, the disease it causes, has brought a new urgency to the scientific enterprise. And Penn researchers have risen to meet the challenge.

"I think this is a moment that's really highlighted the underlying strengths of the Penn community," says Senior Vice Provost for Research Dawn Bonnell. "When faced with this real emergency it was very gratifying to see people coming together from all over, and to see the underlying compassion on the part of the researchers, with people's lives and health at stake."

Given what she knows about the research community, Bonnell says, "It's inspiring to see this response, but it's not surprising."

Committed from the Get-Go

In mid-March, at the same time as many research labs were going dark and campus was emptying out in an attempt to contain the early stages of the pandemic, faculty in the Perelman School of Medicine's Department of Microbiology were formulating a new clearinghouse to coordinate coronavirus-related research: the Center for Research on Coronavirus and Other Emerging Pathogens, co-directed by Susan Weiss and Frederic Bushman.

Funded by the University and generous private donors, soon the Center was soliciting research ideas, facilitating exchange of reagents and methods, and holding seminars. Now it serves as an umbrella organization for roughly 100 projects that range from tackling the fundamentals of virology and immunology to developing more expedient diagnostics. And a new program to support additional pilot studies is in the works.

"We're reaching out to people from all over campus," says Weiss. "Our goal is to support more ideas that will be grist for the mill to continue making progress on this disease. The pilot study results will also hopefully allow researchers to recruit more funding from outside sources, like the National Institutes of Health."

Weiss and Sara Cherry, a microbiologist at the medical school, were among the first to receive samples of live virus, which they and members of their labs have been working with in Penn's Biosafety Level 3 (BSL-3) laboratory. While Cherry's own studies have entailed screening huge libraries of molecules for potential antiviral activity, and Weiss's focus on the host immune response, the researchers have also distributed reagents, such as inactivated virus, to colleagues to conduct their own studies outside the confines of the BSL-3.

Data from the Clinic

Meanwhile, as Penn Medicine hospitals began to admit patients with COVID-19, physician-scientists Ronald Collman, Nuala Meyer, and Daniel Rader organized a massive effort to have nurses acquire informed consent to collect blood, saliva, microbiome, and other samples. These samples are being catalogued in a biobank, supporting a host of investigations at present and more to come in the future.

"That's been a huge spine of our effort here," says Bushman, whose own projects in collaboration with Collman have examined the role of the lung microbiome in influencing COVID severity.

Leveraging Penn's strength in the field of immunology, John Wherry and Michael Betts are among researchers using these samples to track immune responses in patients. In September, together with pulmonologist Meyer, they reported in *Science* the presence of three distinct immune profiles in hospitalized patients, trajectories that could be used to help predict each patient's disease and guide treatment choices.

Data has also come in from tests performed in hospitals, a community-based testing site at Sayre Health Center, and pop-up testing sites in West Philadelphia and beyond. Test results have shed light on the unequal burden of COVID in the wider Philadelphia community, such as a study by Penn Medicine's Scott Hensley and Karen Marie Puopolo of Children's Hospital of Philadelphia showing that Black and Latina pregnant women were five times more likely to have been exposed to SARS-CoV-2 than white and Asian women.

"Pregnant women are fairly representative of community exposure, and these data provide more evidence, on top of what we already know with

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COVID-19, that health and socioeconomic equity are inextricably linked," Hensley says. "Hopefully, this will help lead to policies that address these inequities."

Getting Clinical Trials Up and Running

Scientific insights can mean lives saved, and clinical trials are where many of those ideas get tested. Numerous trials went into full swing throughout the spring and summer of 2020. By April, trials on treatments such as remdesivir and convalescent plasma were up and running, and soon after, Penn served as a site for a Phase 1 trial of a DNA-based vaccine from Inovio, based on research that David Weiner, now of The Wistar Institute, performed at Penn.

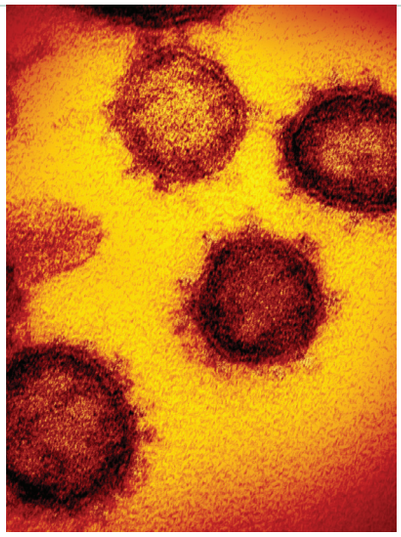
The biological insights underlying at least three other COVID-19 vaccines trace back to innovations from the Penn labs of Drew Weissman and Katalin Karikó. The mRNA-based innovation is being employed in vaccines from Moderna and BioNTech/Pfizer that received emergency use authorization in December, as well as one in a preclinical stage of development in collaboration between Weissman's lab and Thailand's Chulalongkorn University. Data from clinicals trials indicated that the Pfizer vaccine is 90% effective against the novel coronavirus and Moderna's is 94.5% effective.

"Drew and Katie [Karikó] had the key observation that if you take messenger RNA and modify it in the right way, it isn't recognized by the cellular immune system, so it isn't kicked out of the body," says Bushman. "That's been terrific as a platform for many vaccine technologies."

The School of Dental Medicine's Henry Daniell plans to use his patented plant-based protein therapy platform to create novel therapies for COVID, with support from a grant of more than $800,000 from the Commonwealth of Pennsylvania. "We are hopeful that we can do this all in a way that dramatically lowers treatment costs normally associated with protein drugs, delivering shelf-stable capsules that people could receive at home to treat this disease," Daniell says.

Treatments and Tests

Therapeutics can make a difference in the severity of disease. Making use of the High-Throughput Screening Core, Cherry and colleagues reported findings in August that, among other FDA-approved drugs, the immunosuppressant cyclosporine could inhibit COVID-19 infection while also suppressing an overactive immune response in human lung cells,



"If you take messenger RNA and modify it in the right way, it isn't recognized by the cellular immune system, so it isn't kicked out of the body. That's been terrific as a platform for many vaccine technologies."

which can lead to poor outcomes in acutely ill patients. Emily Blumberg and Carl June have been testing the safety and efficacy of this drug in COVID patients in a clinical trial at Penn.

"That rapid, high-throughput screening of thousands of compounds is a special capability at Penn, and Sara Cherry and her team were really on top of it and getting it done," Bonnell says.

And while trials and drug development take time, adequate testing was something that Penn was able to push for much faster, the University leading in efforts to develop new tests that can be deployed rapidly and easily.

Many scientists around Penn have contributed to making a saliva test a reality. Executive Vice Dean and Chief Scientific Officer Jonathan Epstein of Penn Medicine issued a challenge to faculty to create one early in the pandemic. The result was a test that uses an alternative DNA amplification method to the traditional PCR tests. Using this technique, the testing program COVID SAFE rolled out at the start of the fall semester, giving essential staff of the School of Medicine the option of getting tested quickly, right on campus.

Other faculty around campus have made contributions to testing innovations, including the School of Engineering and Applied Science's Haim Bau, and César de la Fuente and Ping Wang of the medical school. Wang, for instance, built on her past experience of crafting highly sensitive, specific, point-of-care tests for other biomarkers and rapidly turned toward developing a similar assay for SARS-CoV-2, in partnership with faculty from the engineering and dental schools.

Being Nimble and Shifting Focus

Indeed, in nearly every corner of campus, one can find researchers applying their expertise to the problem of COVID. Early on, massive efforts to share PPE and, at the engineering school, even putting 3D printers to work to manufacture it, underscored the community's generosity. And as many labs have directed attention to COVID-19, their questions and approaches are revealing its ingenuity.

A number of basic scientists at the School of Veterinary Medicine, including Andrew Vaughan and Montserrat Anguera, shifted gears early in the pandemic to study the effects of the novel coronavirus on lung cells and sex disparities in severity, while virologist Ronald Harty has been applying his background in developing inhibitors for other viruses, such as HIV and Ebola, to curtail the effects of SARS-CoV-2.

Similarly, at the dental school, Robert Ricciardi has been harnessing insights from his long experience identifying treatments for other viral diseases, such as a pox virus closely related to smallpox, to developing an antiviral for COVID.

At Penn Vet, some, too, are focusing on the disease's "One Health" aspects. "One really important aspect of this disease is that it's not just a human disease," says Elizabeth Lennon, a small animal veterinarian. "It affects animals and can be passed back and forth between species."

With funding from Penn Vet for pilot research, Lennon is testing cats and dogs seen at the school's Ryan Veterinary Hospital for COVID to get a sense of infection rates in the pet community. She's also in the early stages of a community-based testing study of pets in Philadelphia to reach more pet owners.

Another vet school scientist, Eman Anis, is studying the animals believed to have enabled SARS-CoV-2 to make the jump to humans—bats—as a way of assessing the presence of the virus in the wildlife population and identifying risks to wildlife rehabilitators.

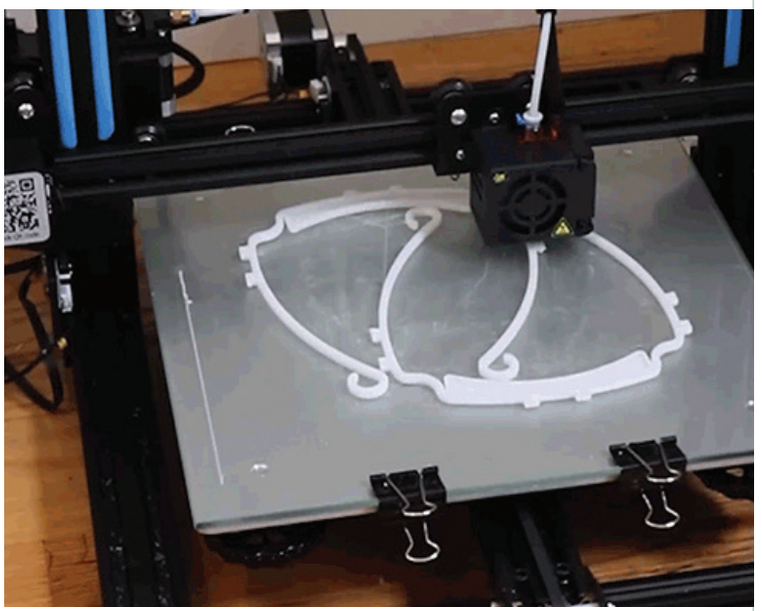
The Long Haul

Most experts agree: COVID-19 is going to be with us in some form for a long time. "We're going to be studying COVID for the rest of our lives," says Jason Moore, director of the Institute for Biomedical Informatics at Penn Medicine.

RIGHT: Using the Creality CR-10s, engineers from the Penn Electronic Design Shop, housed under the School of Arts & Sciences, can print up to 18 face shield mounts per day.

BELOW: Poncho, a Labrador retriever, is one of the dogs in Penn Vet's study to see if dogs can identify an odor unique to COVID-19.

BOTTOM: Courtney Comar, a graduate student in Susan Weiss's lab, has been studying SARS-CoV-2 in Penn's Biosafety Level 3 laboratory to understand how it interacts with the immune system.



To inform work moving forward, emerging database platforms are enabling Penn scientists to share the data they are generating from clinical and laboratory studies openly with researchers around the world, who can mine them for patterns and use the platforms as a springboard for new collaborations.

Work will continue apace on vaccines, therapeutics, and testing technologies. And as the pandemic stretches into a second year, researchers are looking for ways to resume other research efforts—safely.

"A big focus of ours is creating a safe work environment, so we can get work done not only on COVID, but on the other diseases that are continuing to occur amid the pandemic," says Epstein.

This, like the task of taking on COVID-19 from every conceivable angle, has and will continue to be a team effort.

"I've worked at so many levels in this institution," says Emma Meagher, vice dean and chief clinical research officer at Penn Medicine, "And what I never get tired of is our incredible innovation. With COVID, we have come at it from so many different fronts, we've been on the cutting edge of antibody technology, on the cutting edge of convalescent plasma, we've leveraged our institution's history on vaccine development. I think this level of innovation is likely unmatched in any other academic institution in the country."

COVID-19 Research at Penn

INNOVATION AT PENN

TIMELINE

2020

March 13

Nonessential staff of the University are asked to **work remotely**, effective March 16.

March 20

Drive-through testing sites open in West Philadelphia at 41st and Market streets, and in Radnor Township. Physicians, nurses, and advanced practice providers collaborated to open the sites within a week.

April 7

Penn Medicine announces its participation in the **Phase 1 clinical trial** of INO-4800, a DNA vaccine delivered intradermally to prevent COVID-19. The trial was conducted in collaboration with vaccine developer Inovio, based in Plymouth Meeting, Pennsylvania.

April 17

Penn Medicine launches its **convalescent plasma study**, examining the use of plasma from people who have recovered from COVID-19 in those who are moderately or severely ill.

April 29

Penn serves as the site for the **National Institutes of Health's remdesivir clinical trial**, the first clinical trial launched in the U.S. to evaluate an experimental treatment for COVID-19. Data indicated those who received the drug recovered faster than those who received a placebo.

June 1

The University moves to **Phase 1 of research resumption**. On-campus research continued for COVID-19, as well as projects and activities that needed to be initiated before others could work.

June 19

Sara Cherry, a professor of microbiology at the Perelman School of Medicine, publishes results of **antiviral compounds tested for effectiveness** in treating COVID-19. The study, led by Cherry, found nine drugs that inhibit infection of the novel coronavirus in human lung epithelial cells. This included cyclosporine, which suppresses an overactive immune response and blocks infection.

June 30

Inovio releases results from its Phase 1 trial and announces plans to **move forward to Phase 2**.

July 13

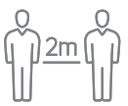
The University moves to **Phase 2 of its research resumption plan**, increasing density from 20% to 50% compared to pre-pandemic. Some social science human subject studies resume, as does some field work.

Late Aug

Penn Medicine begins **Phase 3 of the Moderna vaccine** clinical trial.

Aug 30

The University transforms Houston Hall's Hall of Flags into a testing space. Those on campus, whether students, faculty, or staff, were asked to participate in **PennOpen Pass**, a daily symptom tracker for the Penn community.



Sept 15

The University moved to the **Fall Semester Phase of Research Resumption**, which built on Phase 2, changing the density restriction to that determined by social distancing requirements and streamlining some approval and monitoring processes.

Sept 16

The Research Recovery Program launches, recognizing that impacts are not distributed equally among projects shut down during the pandemic. The program offers a variety of targeted grants aimed at assisting research disciplines that were disproportionately affected.

Nov 9

Pfizer and BioNTech announce interim results that show their experimental vaccine is more than 90% effective, and a week later, Moderna shares their own interim results, indicating that their vaccine candidate is 94.5% effective. Both use **messenger RNA** to instruct the body to begin defending itself against COVID-19—a key breakthrough that was made 15 years ago in the lab of School of Medicine Professor Drew Weissman, in collaboration with Katalin Karikó, a faculty member at the time.

Dec 7

Penn launched a **University-wide recurring saliva-based screening program** with the capacity to conduct 40,000 saliva-based tests every week.

A Superstrong, Reversible Adhesive That Works Like Snail Slime

Researchers have developed a strong, reversible adhesive that uses the same mechanism as snail slime. The study, which was published in the *Proceedings of the National Academy of Sciences,* was led by Shu Yang, a professor in the departments of Materials Science and Engineering and Chemical and Biomolecular Engineering in the School of Engineering and Applied Science. The team included former postdoctoral researcher fellow Hyesung Cho, former Ph.D. student Gaoxiang Wu, current Ph.D. students Jason Christopher Jolly and Yuchong Gao, and collaborators from Lehigh University.

This work is a starting point for designing new adhesives, with applications ranging from reusable grippers to gravity-defying boots and wound-dressing patches.

Yang's lab has a history of bringing nature's creations to life, developing nanoscale materials inspired by giant clams, butterflies, lotus leaves, cephalopods, and pollen. The breakthrough for the latest discovery came when Wu was working on a separate project using polyhydroxyethylmethacrylate (PHEMA), a polymer that has the unusual property of being rubbery when wet but rigid and glassy when dry.

The researchers realized that this unusual property also made it a potential strong, reversible adhesive: When wet, PHEMA conforms to all of the small grooves on a surface; then, as PHEMA dries, it becomes rigid but doesn't shrink, and the material hardens into the cavities and fastens itself to the surface. These are the same properties of a snail's epiphragm, a slimy layer that hardens to keep its body from drying out. This also allows the snail to hold itself in place for long periods of time, but can be reversed once it is ready to move again.

The team ran tests to see how well PHEMA could hold weight and how long it would take for water to reverse its grip, with their results showing that PHEMA acted remarkably similarly to the snail epiphragm. They found that PHEMA was 89 times stronger than gecko adhesion, even strong enough to hold up Jolly using a postage-stamp-sized patch, but its hold was also easily broken when wet. These results make PHEMA the strongest known candidate for reversible adhesion.

"When it's conformal and rigid, it's like super glue. You can't pull it off. But, magically, you can rewet it, and it slips off effortlessly," says Yang.

This work is a starting point for designing new adhesives, with applications ranging from reusable grippers to gravity-defying boots and wound-dressing patches. The next steps are to develop similar materials that don't use water so they could be used outdoors. The team is also aiming to develop new types of adhesives that could respond to cues such as pH, specific chemicals, light, heat, or electricity.

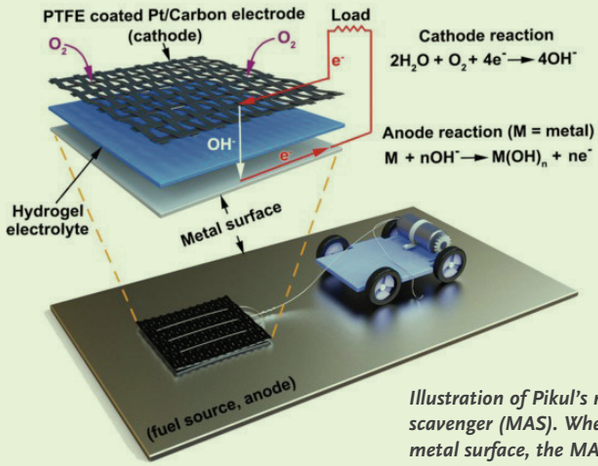


Illustration of Pikul's metal-air scavenger (MAS). When placed on a metal surface, the MAS oxidizes the metal and reduces environmental oxygen to generate energy.

NEW 'METAL–AIR SCAVENGER' TECHNOLOGY ALLOWS ROBOTS TO 'EAT' METAL FOR ENERGY

A "metal-air scavenger," created by a team of engineers, combines the best of both batteries and energy harvesters. The study highlighting the scavenger's capabilities, published in *ACS Energy Letters*, was led by James Pikul, an assistant professor in the Department of Mechanical Engineering and Applied Mechanics in the School of Engineering and Applied Science, along with group members Min Wang and Unnati Joshi.

Electronic devices can be powered using either batteries or energy harvesters. While batteries can store large amounts of energy, they are heavy and not long-lasting. On the other hand, energy harvesters, such as solar panels, can collect energy from the environment, but only work under certain conditions and are often unable to convert energy into usable power very quickly.

Like a traditional battery, the metal-air scavenger (MAS for short) has an anode and cathode wired to the device it's powering. In a battery, the anode and cathode are stored inside the battery housing and the battery stops working when they run out of energy. In the MAS, the anode and cathode are metals and oxygen in the environment, so the MAS can keep providing power as long as there are more metals and oxygen available. At the center of the MAS is a slab of hydrogel, a spongy polymer that moves ions between the metal surface and the cathode, allowing chemical bonds to break and electrons to flow between the electrodes like a battery.

To demonstrate the efficiency of their approach, the researchers had a MAS-powered vehicle drive in circles on an aluminum surface, with a small reservoir of water to prevent the hydrogel from drying out, and found that the MAS has 10 times more power density than the best energy harvesters, and 13 times more energy density than lithium-ion batteries.

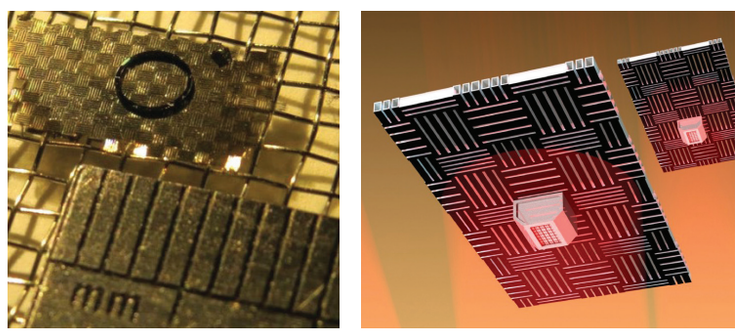
That power density means that the MAS is competitive against batteries, says Pikul. "It's using battery chemistry, but doesn't have the associated weight, because it's taking those chemicals from the environment."

In the future, the MAS could be the basis for a new paradigm in robotics, where machines keep themselves powered by seeking out and "eating" metal, breaking down its chemical bonds for energy like humans do with food.

'Nanocardboard' Flyers Could Be Used as Martian Atmospheric Probes

Researchers in Penn's School of Engineering and Applied Science have developed a novel approach for exploring the skies of other worlds: a fleet of tiny aircraft, each weighing as much as a fruit fly and with no moving parts. Published in *Advanced Materials,* the study, led by Igor Bargatin, the Class of 1965 Term Assistant Professor in the Department of Mechanical Engineering and Applied Mechanics, demonstrates the flying and payload-carrying abilities of "nanocardboard" in a Mars-like environment. Former graduate student John Cortes, fellow lab members Christopher Stanczak, Mohsen Azadi, Maanav Narula, Samuel M. Nicaise, and Professor Howard Hu, also in Mechanical Engineering and Applied Mechanics, contributed to the study.

The Bargatin group has been developing these nanocardboard materials, a hollow plate of aluminum oxide only a few nanometers thick, since 2017. The corrugated pattern of channels that span the plate, which are designed to enhance its bending stiffness and



LEFT: The researchers used silicone rings as mock payloads for their nanocardboard flyers. RIGHT: In this artist's conception, fleets of flyers could be launched from ground-based rovers and steered with lasers to collect samples.

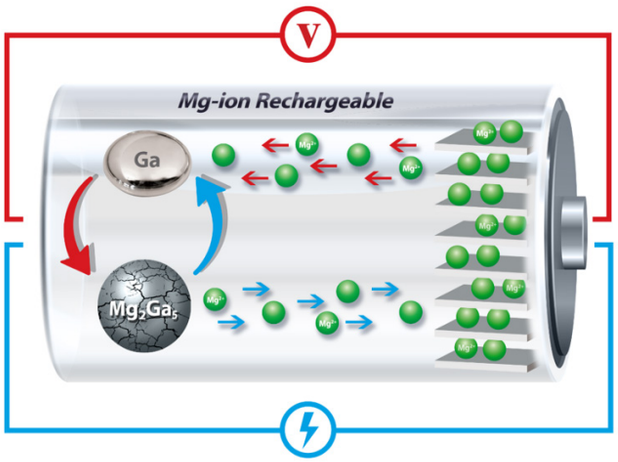
prevent cracks from forming, also allows nanocardboard to levitate under bright light—as one side of the plate heats up, the temperature difference causes air to circulate through its hollow structure and shoot out of the channels, thrusting it off the ground.

Their latest paper focused on measuring the flyers' ability to lift mock payloads, in the form of silicone rings attached to the top of the plates, an important first step for vetting nanocardboard's potential as a material for atmospheric probes. It's hypothesized that, because of the thinner atmosphere and weaker gravity on Mars, the nanocardboard flyers could gain an extra boost that would enable them to carry payloads 10 times as large as they are.

Bargatin is now collaborating with other researchers on how to miniaturize chemical sensors that could detect water or methane, potential signatures of life on the red planet.

"In addition to carrying sensors," Bargatin says, "our flyers could simply land and have grains of dust or sand passively stick to them, then transport them back to the rover so it doesn't need to travel as far."

Self-Healing Liquid Metal Electrode Extends Life of Battery Alternative



In the researchers' new anode design, gallium repeatedly melts and solidifies, "healing" the cracks that would otherwise gradually decrease the battery's ability to hold a charge.

An alternative to lithium-ion batteries, created by a Penn engineering team, doesn't require expensive or difficult-to-fabricate nanoscale materials.

While lithium-ion batteries are a staple of everyday life, they have a limited lifespan because the materials in the electrodes expand, break, and lose electrical contact with each use. These batteries also require cobalt, which can only be supplied by a handful of countries. While magnesium-based batteries have been a promising alternative for efficient, rechargeable battery electrodes, materials that can store magnesium are still highly susceptible to degradation during use.

In this study, researchers led by Eric Detsi, the Stephenson Term Assistant Professor in the Department of Materials Science and Engineering in the School of Engineering and Applied Science, and graduate students Lin Wang and Samuel Welborn, in collaboration with Vivek Shenoy, the Eduardo D. Glandt President's Distinguished Professor, describe a new approach that incorporates gallium in the anode of a magnesium-ion battery. Gallium starts out in a solid form because it is alloyed with magnesium in micron-sized particles. Then, because gallium melts and solidifies with each charge and discharge cycle, the anodes "heal" the cracks that form.

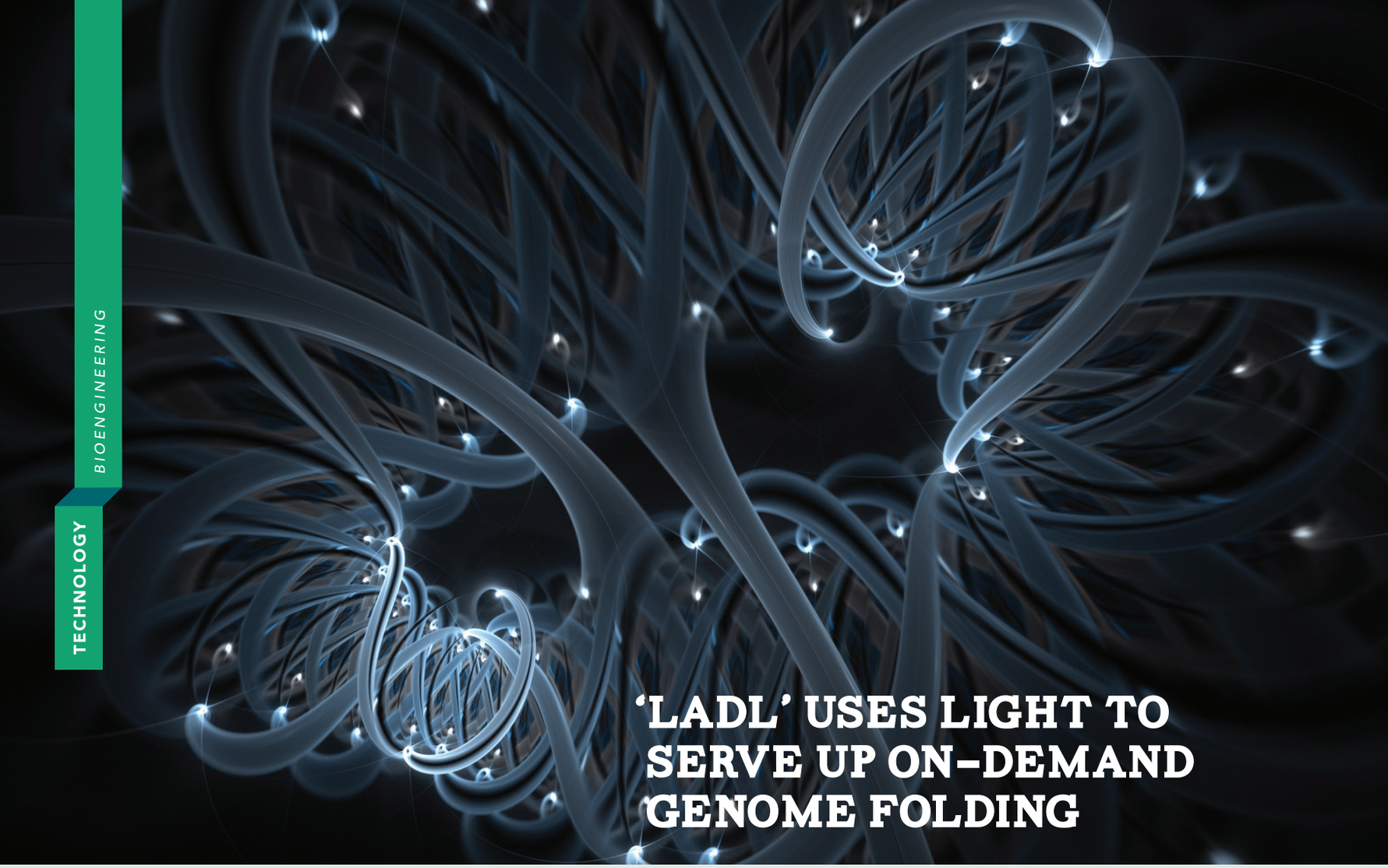
"Instead of a transformation from one type of solid into another, the original solid material transforms into a liquid. This inhibits the cracking and pulverization because the stresses associated with the normal solid-solid transformation are no longer present," explains Welborn.

"In order to electronically connect these particles," Wang says, "we put them into a conductive network of carbon fibers, carbon black, and graphene, which is all tied together with a binder. When the electrode goes from solid to liquid, it does not move around like you might expect a liquid to do."

The researchers used X-rays to examine the crystal structure of the materials inside the battery to prove that the solid-liquid phase transformation was occurring, and showed that the experimental battery withstood more than 1,000 charging cycles—five times the cycle life of the current state-of-the-art magnesium-ion battery.

"The thousand cycles demonstrated in this work represents a significant improvement," Detsi says of the work, published in *Advanced Energy Materials,* "but our dream is to take advantage of this unique self-healing behavior to design a battery that can be charged and discharged forever."

Because their design is simple and does not require any new types of nanomaterials, it's an approach that could someday be incorporated into industrial fabrication methods.



'LADL' USES LIGHT TO SERVE UP ON-DEMAND GENOME FOLDING

Penn engineers have established a new technique for quickly creating specific folding patterns of genomes on demand using light as a trigger. Known as light-activated dynamic looping (LADL), the approach is a promising new tool for studying gene regulation in detail. Published in *Nature Methods,* the study was led by Jennifer Phillips-Cremins, an associate professor of bioengineering in the School of Engineering and Applied Science, and lab members Ji Hun Kim and Mayuri Rege in collaboration with Jacqueline Valeri, Aryeh Metzger, Katelyn R. Titus, Thomas G. Gilgenast, Wanfeng Gong, Jonathan A. Beagan, Arjun Raj, and Margaret C. Dunagin.

The genome can be pictured as beads on a string, with each bead representing a different gene. While an individual's genome is identical in every cell, how these beaded strings are packed and twisted within cells, and how that packaging can lead to variation in a gene's expression, is not yet well understood.

"Although we are now capable of mapping and visualizing the topological structures, there is a critical gap in knowledge in how genome structure configurations contribute to genome function," says Phillips-Cremins, a pioneer in the field of "3D epigenetics."

Phillips-Cremins and her team have now found a way to use light to force both ends of genomic strings into spatial proximity by combining the power of two previously developed tools: CRISPR/Cas9 and optogenetics. The resulting LADL method allows researchers to fold the genome into specific shapes so that certain genes, or beads, are in physical contact with each other. By controlling which genes are touching, the researchers can study how a variety of configurations lead to different combinations of genes being expressed.

Previous research from the Phillips-Cremins lab discovered genome misfolding patterns in several key neurological diseases, and the researchers are now working on studies to correct the topological miswiring patterns with LADL, with the idea that pathological gene expression patterns could be reversed after correcting DNA misfolding.

By controlling which genes are touching, the researchers can study how a variety of configurations lead to different combinations of genes being expressed.

"The engineering of genome topology with light opens up new possibilities to understanding the cause and effect of DNA's structure on how the sequence directs cellular phenotype, which is a fundamental problem in biology where engineering approaches can make a major impact," says Phillips-Cremins. "Moreover, we anticipate that, over the long term, the use of light will allow us to target specific human tissues, and even to control looping in specific neuron subtypes in the brain."

POLITICAL SCIENCE

SOCIAL SCIENCE

The Political Influence of 'The Loud Minority'

A follow-up to the "The Political Power of Protest," his 2013 book about the influence of protest on policymakers, Daniel Gillion's new book, "The Loud Minority," published in March 2020 by Princeton University Press, expands on this dialogue by examining voter responses to protest. The title is a callback to the language of former President Richard Nixon, who in 1969 appealed to the American people on why he should keep troops in Vietnam.

The term made a surprising comeback in 2015 at the onset of former President Donald Trump's campaign. This prompted Gillion, a professor of political science in the School of Arts & Sciences, to look at what was really motivating voters.

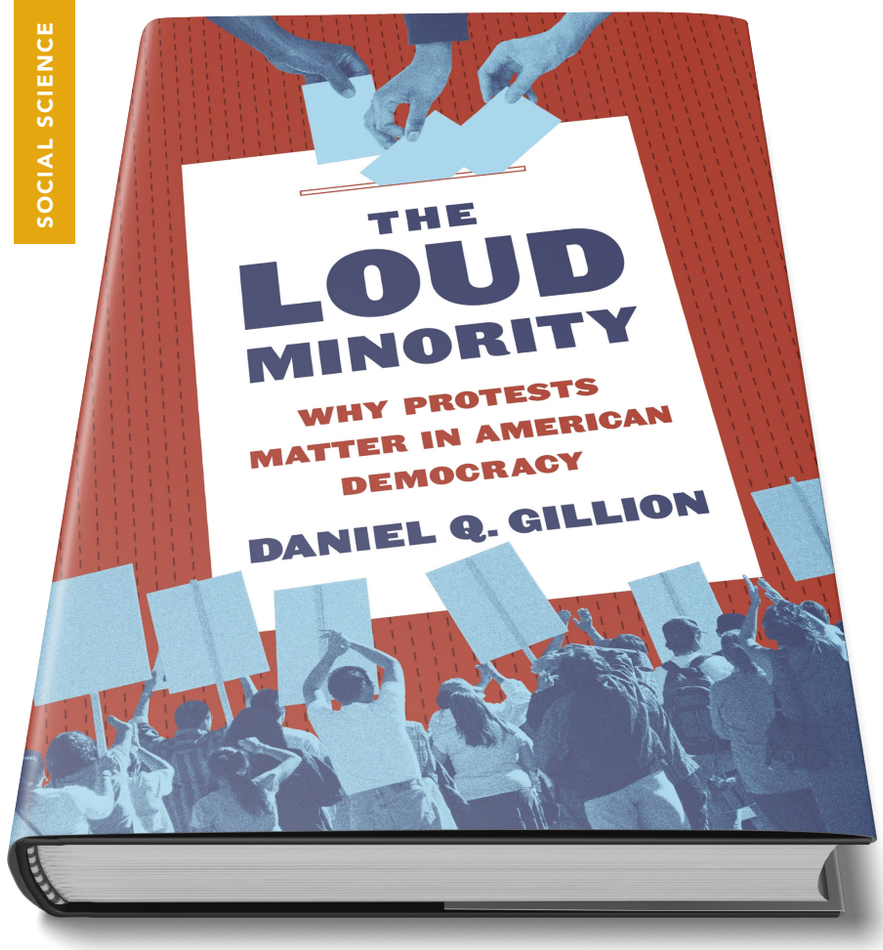
"The idea is that there is a group of society who is not protesting, who sees the issues completely differently, that there is a line drawn in the sand. In my book, I show that that line drawn in the sand is a fallacy," Gillion says. "It is the boogeyman underneath the bed that does not exist. These individuals are not seeing things in different perspectives, but, rather, the loud minority is speaking to the silent majority, informing individuals of what's transpiring in America."

Through analysis of statistical data, historical evidence, and detailed interviews about protest activity since the 1960s, Gillion demonstrates the very tangible effects of protests on the electoral process, in particular, the tendency of this activity to increase voter turnout in districts with high levels of activism. He shows that politicians were able to raise more money when aligning with the views of protesters, and that protests encourage new faces to rise up and challenge incumbents facing reelection. This is borne out in analysis of electoral results during the Civil Rights Movement in the early 1960s, as well as after the Tea Party protests in 2010.

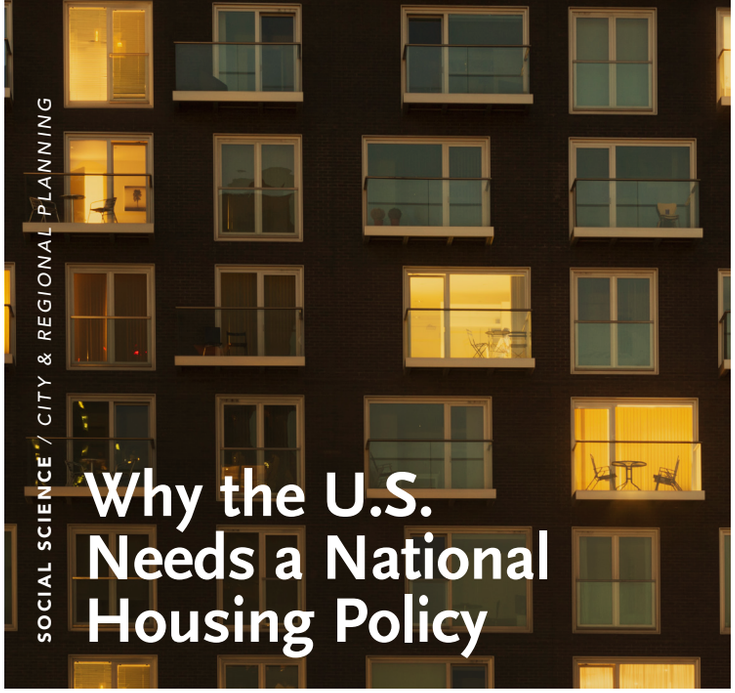
With the Black Lives Matter racial justice movement gaining prominence in 2020, Gillion's research happens to resonate in an even bigger way.

"The point of these protests is to bring about change," he says. "I think that's one of the most important aspects of what we're seeing right now; we're seeing the beginning stages of change in America. And that is a hopeful notion.

"One thing that the book is able to indicate is that protests are instruments of democratic change," he adds. "They are the beginning stages of how the government pays attention and how citizens come to the table."



"The loud minority is speaking to the silent majority, informing individuals of what's transpiring in America."



SOCIAL SCIENCE / CITY & REGIONAL PLANNING

Why the U.S. Needs a National Housing Policy

In many ways, Vincent Reina says the current U.S. housing market challenges are "unprecedented."

"Rents, and rent burdens, are at all-time highs, house prices are out of reach for many households, the available stock of for-sale units in many markets remain low, and there is uncertainty about what homeownership rates will look like for future generations," he writes in a policy brief, "The U.S. Needs a National Vision for Housing Policy," published through the Wharton Public Policy Initiative.

Reina's opinion comes from years of studying housing challenges and solutions. An assistant professor in the Department of City and Regional Planning in the Stuart Weitzman School of Design, his work spans various aspects of housing.

One study funded by Penn's Kleinman Center for Energy Policy, and published in the *Journal of the American Planning Association*, found that majority-minority neighborhoods experience higher energy cost burdens than their white counterparts.

A book Reina co-edited with Penn Provost Wendell Pritchett and Wharton Professor Susan Wachter, "Perspectives on Fair Housing," published by the University of Pennsylvania Press, complements several articles he produced that show how fair housing is one of the most critical policy issues of our time.

Reina is the faculty director of the Housing Initiative at Penn, which is based out of PennPraxis, and is working with a number of cities to monitor the success of rental assistance programs funded by the federal CARES Act. The aim is to prevent tenants from becoming homeless, being evicted, or incurring insurmountable debt.

In the Wharton brief, Reina writes that recent demographic changes—specifically, an increase in single-person households, especially among those over the age of 65, as well as racial disparities in homeownership—underscore the need for a new U.S. housing policy vision.

He offers solutions that are buoyed by his years of field experience, including supporting new and existing affordable housing. But he says his recommendations are not a replacement for a broader housing vision and strategy.

"We're at a point where we have a well-documented housing affordability problem, and we have a significant body of interventions around housing affordability," Reina says. "But it's kind of amazing to think how much we still don't know, and how much we're learning about the ways that housing is connected to so many facets of our neighborhood and micro- and macroeconomic progress."

SOCIAL SCIENCE / SOCIOLOGY

HOW DNA ANCESTRY KITS CAN BE HARMFUL

Millions of people complete DNA kits to learn about their family history. But what consumers might consider a lighthearted exercise worried Wendy Roth, an associate professor of sociology in the School of Arts & Sciences.

To her mind, such tests had the potential to inadvertently reinforce genetic essentialism, an archaic concept that says genes determine race and race determines abilities. "Even before any data, social scientists were saying these tests could revive this harmful view," says Roth. "I shared those concerns, but I wanted to answer this question empirically."

She and colleagues from the University of British Columbia and elsewhere designed a randomized control trial, enrolling 802 non-Hispanic, native-born white Americans who had no family results from a genetic ancestry test, and who had never taken such a test themselves—but wanted to. "This wasn't a sample of all whites, or even all non-Hispanic, native-born whites," she says. "It was a sample of people willing to take these tests."

Over about a year, participants completed two surveys intended to reveal their understanding of the relationship between genes and race. A control group took no DNA tests. A treatment group took two, one with results shown as a pie chart of ancestries, a second that traced maternal lineage. The researchers also used a scale they developed to measure belief in the idea that genes determine race.

In a paper in *PLOS ONE*, they showed that such DNA tests do not lead more people to believe that race is purely genetic; these tests increase belief in racial essentialism for some and decrease that belief for others, so the effect averages out.

The researchers also found that genetic tests influence people differently. "What seems to make the biggest difference is how much someone understands about genetics going in," Roth says. People with a better initial grasp of the subject end up more skeptical of racial essentialism. Those who understand genetics less believe in essentialism more by the study's end.

The work has important societal implications, Roth says. "There are people out there buying these tests as a lark. They're not really thinking about the kind of impact they could have."

U.S. DRUG OVERDOSE DEATHS ARE SEVERELY UNDERCOUNTED

"The drug epidemic is a major American disaster," says demographer Samuel Preston, a professor of sociology in the School of Arts & Sciences. "We keep annual reports on the number of deaths from drug overdose, but that's only part of the picture."

With funding from the National Institute on Aging and data from the National Center for Health Statistics, Preston and Georgetown's Dana Glei built models to assess the mortality rates for males and females in all 50 states for 15 age groups and 18 calendar years. The full dataset represented more than 44 million deaths, with 667,196 coded as drug-related, a grouping that includes overdoses and some mental and behavioral disorders.

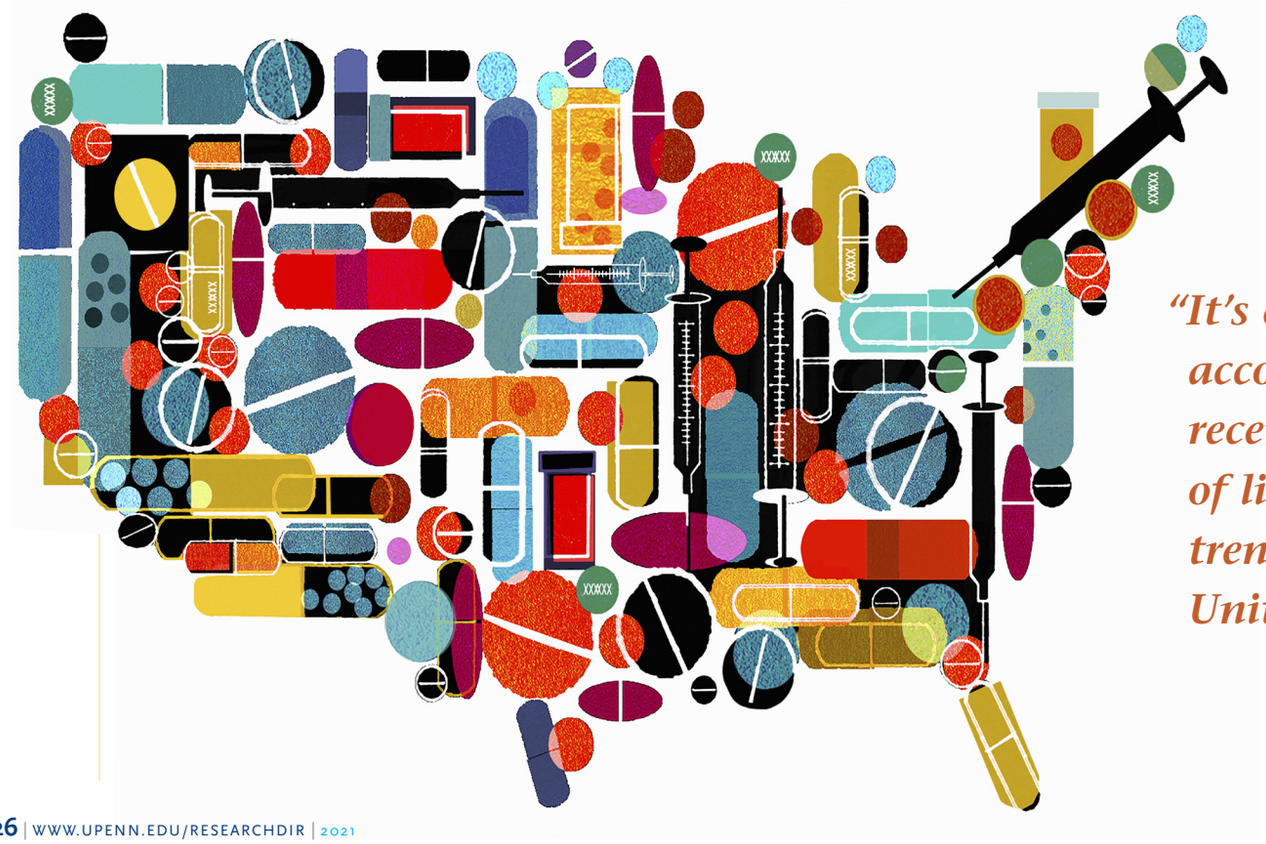
Using these models, Preston and Glei found that in 2016, for 15- to 64-year-olds, drugs accounted for some 142,000 deaths in the United States—more than twice the 63,000 death certificates that listed drug poisoning and related terms as the underlying cause.

"Drugs kill in other ways than overdose," Preston says. "Infectious disease like HIV/AIDS and hepatitis, impaired judgment, suicide, circulatory disease—these are all affected by drug use. Perpetual drug users have much higher mortality in general."

In addition to the undercount, the researchers found that, on average, drug use decreased life expectancy after age 15 by nearly a year and a half for men and three-quarters of a year for women. "That may not sound like a lot, but it's a big effect," Glei says. "It's enough to account for the recent reversal of life-expectancy trends in the United States."

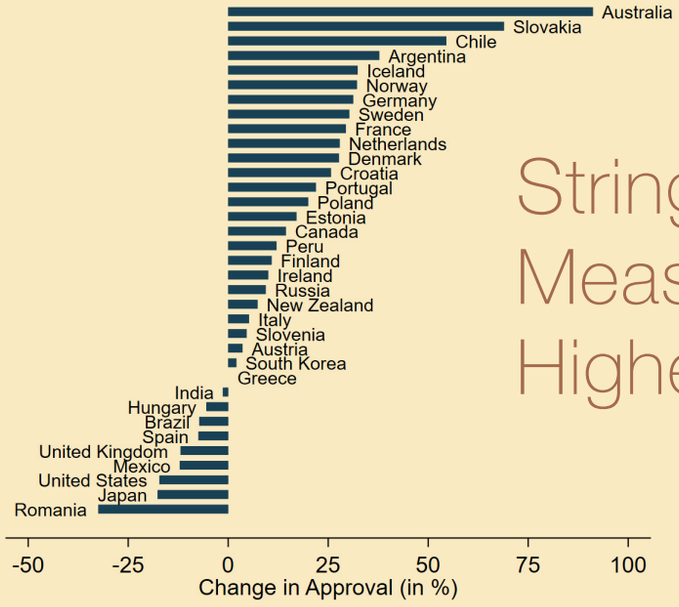
West Virginia, known to be the opioid crisis epicenter, with high drug overdose rates, fared worst, with drug-associated deaths hitting 39% for males and 27% for females. Nebraska fared best for both sexes. Variation in regional patterns helped the researchers see pockets of drug-related mortality that could easily have been missed, Preston adds.

Though this work, which they published in *PLOS ONE*, recalculates the magnitude of the U.S. drug problem, it doesn't get at root causes. That could potentially come in future research.



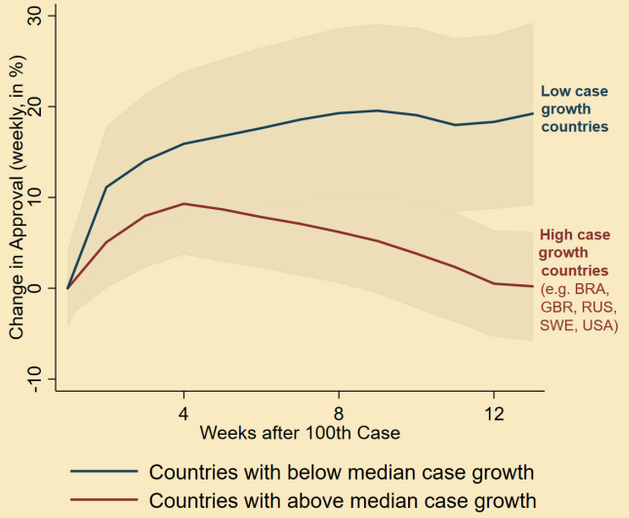
"It's enough to account for the recent reversal of life-expectancy trends in the United States."

Stringent COVID Measures Lead to Higher Approval Ratings



LEFT: The percentage change in government approval from February to July 2020 for the 35 countries in the researchers' sample.

BELOW: The change in government approval in percentage points on a weekly basis after the outbreak of the COVID-19 pandemic.



Macroeconomist Guillermo Ordoñez studies how financial crises arise and affect the economy. "As part of that agenda, I recently started looking into how politicians make decisions around such crises and how their approval evolves," says Ordoñez, a professor of economics and finance in the School of Arts & Sciences.

When COVID-19 hit, he and colleagues began assessing weekly data for 35 countries—20 advanced economies and 15 emerging markets, accounting for 65% of global GDP—to understand how a leader's popularity was influenced by the policies that person implemented during the pandemic.

In a working paper published in *Covid Economics,* the researchers show that governments that adopted strict virus-containing measures fared best politically, gaining up to 7 percentage points in approval when they successfully limited infection numbers, and not losing approval points even when unsuccessful. Conversely, governments that took a less stringent approach experienced a drop in approval, particularly when COVID-19 cases rose.

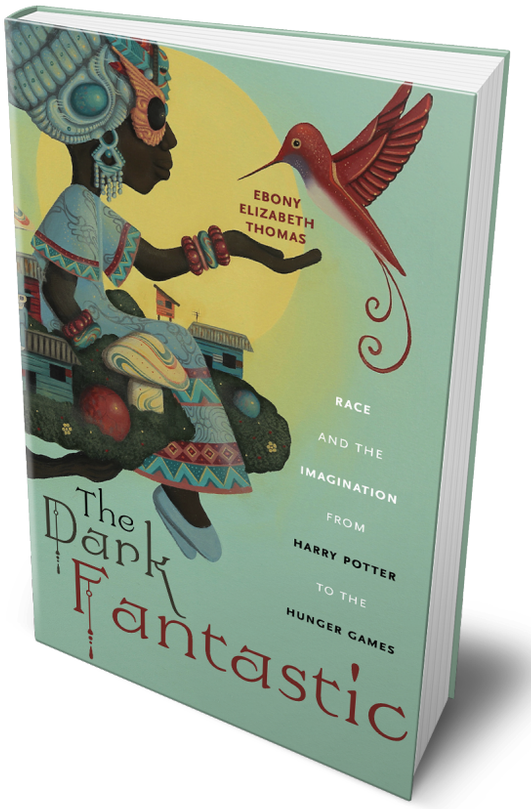
"If you see, for example, a 60% increase in the weekly growth rate of cases—from duplicating cases in a week to duplicating cases every three days—you can see a 4% decline in the approval rate of the government from the starting point before the pandemic," Ordoñez says. "That's quite sizeable and a much higher change than you'd typically observe."

This holds regardless of economic activity, he adds. "We find that people do not reward the government for relaxing restrictions if, at the same time, you have an uptick in cases. In other words, there's no tradeoff between health and economy. There is a pecking order."

Ordoñez and colleagues did note a rally-around-the-flag effect, a concept coined in the 1970s to signify when citizenry comes together around a hard time, like a war. "Immediately after big shocks, there tends to be support for the leader," Ordoñez says. The pandemic was no exception. In all countries in the study, regardless of policy practices, leadership approval increased the first four weeks after the outbreak.

How this will ultimately play out remains to be seen, especially given the unprecedented nature of the pandemic, but it's something economists like Ordoñez will continue to watch.

SOCIAL SCIENCE / EDUCATION



The 'Dark Fantastic Cycle' of Black Girl Characters

As a young schoolteacher in Detroit, Ebony Elizabeth Thomas, an associate professor of literacy, culture, and international education in the Graduate School of Education, was an avid "Harry Potter" fan-fiction writer. And while she enjoyed being immersed in that community, even building a name for herself among that fandom, it ultimately made her question why all the popular fantasy stories—especially ones meant for youth—left out people of color in these imagined new worlds, or one that belonged to the future.

"My experience 15 to 20 years ago really led me to want to think about how people were seeing characters of color—Black folks, in particular—in speculative narratives for young people," she says.

That questioning, all this time later and after five years of writing and research, culminated in the 2019 release of "The Dark Fantastic: Race and the Imagination from Harry Potter to the Hunger Games." The book, published by NYU Press, examines how Black girl characters are commodified in fantasy stories written for young people. In it, Thomas analyzes Rue from "The Hunger Games," Gwen from the BBC version of "Merlin," Bonnie Bennett from "The Vampire Diaries," and Angelina Johnson from "Harry Potter." She selected these zeitgeisty series intentionally, arguing that some fantasy narratives—ones like "Harry Potter," for example—become *the* fantasy narratives.

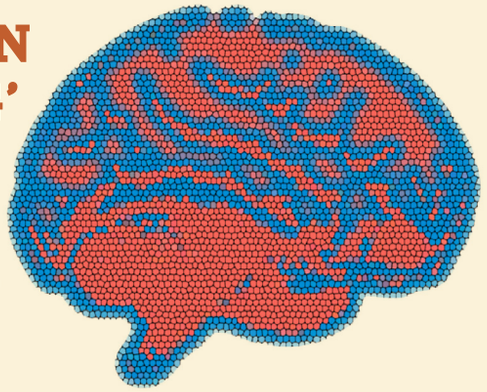
"My experience 15 to 20 years ago really led me to want to think about how people were seeing characters of color—Black folks, in particular—in speculative narratives for young people."

"Analysis of those commodified media matters, because those are the texts everybody reads," she says, explaining why she opted not to study texts like those from acclaimed Black science fiction writer Octavia Butler. "So, we need to look at what's going on with the Black characters in those stories."

"The Dark Fantastic" establishes the "dark fantastic cycle," which she describes as what happens to the characters in the narrative itself. The idea is that the characters she examines all are similarly positioned in the collective imagination in ways that are in service to others.

The book has since been nominated for a World Fantasy Award, British Fantasy Award, and Ignyte Award. She's eventually planning to write a follow-up to the book, and is currently preparing the release of "Harry Potter and the Other: Race and Justice in the Wizarding World," and her as-yet-untitled debut young adult novel.

WHY 'INFORMATION GERRYMANDERING' IS A THREAT TO DEMOCRATIC DECISION-MAKING



SOCIAL SCIENCE / NETWORK SCIENCE

The centuries-old practice of electoral gerrymandering, in which political districts are drawn to favor one party, can bias elections. In a study led by biologist Joshua Plotkin of the School of Arts & Sciences and the University of Houston's Alexander J. Stewart, it's not geographical boundaries that confer a bias but the structure of social networks, such as social media connections.

Reporting in the journal *Nature,* the researchers first predicted the phenomenon, which they've termed "information gerrymandering," from a mathematical model of collective decision-

Self-Reporting Treaties, Human Rights, and Women's Rights

Every country in the world has ratified at least one core international human rights treaty, which protect civil, political, economic, social, and cultural rights.

The treaties are administered by reviewing bodies that receive reports from the member states on their human rights practices. Recent research has shown that state reporting to human rights monitoring bodies is associated with improvements in rights practices, casting doubt on earlier claims that self-reporting is inconsequential. Yet little work has been done to explore the theoretical mechanisms that account for this association.

In their article, "The Proof is in the Process: Self-Reporting Under International Human Rights Treaties," published in the *American Journal of International Law*, Beth A. Simmons, the Andrea Mitchell University Professor in Law, Political Science, and Business Ethics at the University of Pennsylvania Carey Law School, and Cosette D. Creamer of the University of Minnesota Law School, systematically document—across treaties, countries, and years—four mechanisms through which reporting can contribute to human rights improvements: elite socialization, learning and capacity building, domestic mobilization, and law development.

Simmons and Creamer draw from their investigation of these mechanisms to provide a number of recommendations for reform, including encouraging greater participation; ensuring dialogue is a balanced, genuine deliberation; providing guidance on delegation composition; and making the dialogue interactive and geared toward problem-solving.

In a separate study, "The Dynamic Impact of Periodic Review on Women's Rights," published in the *Journal of Law and Contemporary Problems*, Simmons and Creamer marshal empirical evidence to demonstrate for the first time that self-reporting processes within international human rights treaty regimes generate positive domestic policy changes, again challenging the conventional wisdom that self-reporting serves no useful purpose.

Simmons and Creamer focus their study on the Convention on the Elimination of All Forms of Discrimination against Women (CEDAW). Under CEDAW's self-reporting regime, ratifying states must submit reports every four years on measures adopted to protect women's rights.

Using data from Latin American countries that have ratified CEDAW, the researchers found that self-reporting "encourage[d] domestic actors to demand and implement change" on women's rights issues.

Ultimately, Creamer and Simmons conclude, although the reporting system has weaknesses, the evidence suggests that self-reporting and dialogue between state representatives and international experts generates new ideas, advice, and domestic pressure for change in practice on issues related to women's rights.

"Far from finding that no one pays attention to this process outside the halls of Geneva, it turns out that in Latin America at least the review process literally piques the media's, and potentially the public's, interest," Simmons and Creamer note.

making, and then confirmed its effects by conducting social network experiments with thousands of human subjects. Finally, they analyzed a variety of real-world networks and found examples of information gerrymandering present on Twitter, in the blogosphere, and in U.S. and European legislatures.

"People come to form opinions, or decide how to vote, based on what they read and who they interact with," says Plotkin, the Walter H. and Leonore C. Annenberg Professor of the Natural Sciences. "And in today's world we do a lot of sharing and reading online. What we found is that the information gerrymandering can induce a strong bias in the outcome of collective decision, even in the absence of 'fake news.'"

In more than 100 online games conducted with 2,500 human subjects, the researchers' analysis revealed that information gerrymandering could easily produce biases of 20%. In other words, in a group that was evenly split into two parties, an outcome could render itself as a 60–40 decision due solely to information gerrymandering.

"The idea is akin to electoral gerrymandering, where one party can gain an advantage not by sheer number but by organization or structure," Plotkin says.

He and colleagues see this work as the beginning of a new avenue of study focused on how social networks impact collective decision-making, which they have been pursuing more recently in the context of the 2020 election.

"Right now, we need research on how social media affects the health of liberal democracies," Plotkin says.

Aging Out of Foster Care During the Pandemic

SOCIAL SCIENCE / SOCIAL POLICY

Older youth in and aging out of foster care are bearing the heavy burden of COVID-19's economic and social consequences, according to the Field Center for Children's Policy, Practice, and Research. Researchers Johanna Greeson, an associate professor in the School of Social Policy & Practice, Sara Jaffee, a professor of psychology in the School of Arts & Sciences, and Sarah Wasch, program manager for the Field Center, surveyed 281 people ages 18 to 23 in foster care or aged out in 32 states and the District of Columbia in order to gain a clearer understanding of the challenges facing this marginalized group during the pandemic.

The Field Center team worked with national foster care organization FosterClub to develop the survey questions. Participants reported negative impacts of the COVID-19 pandemic, including under- and unemployment, education disruption, homelessness, food insecurity, and physical and mental health concerns. Cisgender women and youth already aged out of foster care were particularly vulnerable.

The greatest impact was to their personal finances, with 72% reporting that they had only one month's worth of expenses covered. This had a ripple effect in other areas, including food and housing insecurity.

Greeson, managing faculty director of the Field Center, says the child welfare system needs an emergency response plan to address issues in times of disaster or crisis on a national level.

"This is a watershed moment for thinking about system reform," she says. "It brings to light how many holes are in the safety net for vulnerable populations."

Jaffe, co-faculty director of the Field Center, says measures taken to assist at-risk young adults would benefit society at large.

"The fact of the matter is that young adults who are homeless and young adults who are suffering from depression, anxiety, and substance abuse problems are not young adults who are economically productive and contributing to the financial health of our country," she says. "If you don't like the argument that we have a moral obligation to support vulnerable youth, then perhaps you are more persuaded by the argument that there are significant costs to society in not addressing these issues. Prevention would go a long way toward minimizing those costs in the long run."

SOCIAL SCIENCE / COMMUNICATION

How do space limitations on social media platforms affect political rhetoric and polarization? It's a question Annenberg School for Communication professor Yphtach Lelkes has been aiming to answer.

"Online, there's quite a bit of hostility and incivility that may feed into what we see happening at the ballot," he says. "We thought one way to tone it down might be to design social media differently, incentivizing better discussion."

Lelkes hypothesized that less space leads to more brusque behavior and crassness because people lack the room to fully lay out an argument. When Twitter increased its character limit from 140 to 280 in November 2017, Lelkes, Annenberg doctoral candidate Alvin Zhou, and Kokil Jaidka of Nanyang Technological University saw a built-in way to test the theory.

They looked at direct Twitter replies to 536 U.S. congressmen and congresswomen between Jan. 1, 2017 and Mar. 30, 2018, building a dataset of more than 358,000 tweets. Using machine learning and automated content-analysis tools, they coded how uncivil, negative, and deliberative the tweets were before and after the character-limit switch.

"We found that having more space led to more civility and higher discussion quality in general," Lelkes explains, a conclusion the researchers published in the *Journal of Communication*.

Though the Twitter work focused specifically on politics, Lelkes says it can likely generalize to other forms of debate.

"We think this is almost a kind of basic psychological feature," he says.

To push the work further, the research team has created a custom-made social media platform, where participants can engage in political discussion via chat. One recent experiment focuses on how anonymity influences civility in conversations about polarizing subjects like gun rights. Another allows participants to give a thumbs up or like a comment rather than engage directly, testing what effect this has on the discourse.

"My colleagues and I have built a whole research program around creating better social media platforms using evidence-based designs," Lelkes says. "So far, our results show that if you make use of the space given to you and elaborate on ideas rather than just respond abruptly and quickly, the quality of discussion generally increases."

RESEARCHERS DISCOVER EARLIEST EUROPEAN HOMO SAPIENS

In a cave in Bulgaria, the Penn Museum's Zeljko Rezek and colleagues discovered the oldest known remains of *Homo sapiens* in Europe, dating back nearly 46,000 years. That's about 5,000 years older than the previous recordholder, and points to a time when Neanderthals still existed in the region, meaning the two likely overlapped for several thousand years.

What's more, based on preserved mitochondrial DNA, the researchers found that this group of *H. sapiens* seems not to have contributed genetically to later *H. sapiens* in the region.

> *"Such high-resolution results of ancient DNA analysis do not happen often."*

"Nuclear DNA analysis is in progress, but if this is the case, contrary to popular belief, our species was not able to survive every time and in all environments," Rezek says. The research team published its findings in *Nature* and *Nature Ecology & Evolution*.

Bulgaria's Bacho Kiro Cave had been excavated twice before, in the 1930s and 1970s. Although the latter work yielded stone and bone tools and ornaments made of animal teeth, no reliable dating came from the finds, nor was it clear which hominin species left the record. In 2016, Rezek and others returned to the cave, where they collected more than 1,200 bone fragments.

In the lab, they removed the fragments' outermost layer of bone and investigated the composition and form of their collagen, the protein found in skin and bone. Five, including a fully intact second lower molar, were human remains, with the tooth and one bone coming either from the same person or two maternally related individuals. The other three were from different individuals.

"Such high-resolution results of ancient DNA analysis do not happen often," Rezek says. "You really need good preservation at the site and to excavate in the right area."

Radiocarbon dating put the bones between 43,650 and 45,820 years old, during the Middle to Upper Paleolithic period when Neanderthals still endured in Europe—though these remains undoubtedly came from *H. sapiens*.

Questions remain about the genetic, cultural, and ecological inheritances that shaped the early groups of our species biologically and behaviorally, Rezek says. "Our emergence and dispersal is a very complex story."

***TOP, BOTTOM:** Personal ornaments and bone tools from Bacho Kiro Cave in Bulgaria, artifacts that are attributed to* Homo sapiens *and date to approximately 45,000 years ago.*

***MIDDLE:** An excavator records artifacts, each marked with a colored pin. The bags with barcodes will hold individual artifacts once all positions have been recorded. (Pre-pandemic photo)*

Combating Misinformation and Disinformation About Public Health

SOCIAL SCIENCE

When SARS-CoV-2 emerged in the United States in January 2020, people faced a familiar quandary: Which sources and guidance should they trust and how could they parse fact from fiction?

In March 2020, Kathleen Hall Jamieson, an Annenberg School for Communication professor of communication and director of the Annenberg Public Policy Center (APPC), conducted a national phone survey about the seasonal flu, the novel coronavirus, and media preferences. In the *Harvard Kennedy School (HKS) Misinformation Review,* she and co-author Dolores Albarracín of the University of Illinois published what they learned from the 1,008 participants.

Early in the COVID-19 outbreak, people relying on mainstream media—NBC News or *The New York Times*, for example—more accurately understood the disease's lethality and protective measures to prevent infection. Conversely, those who turned to social media or conservative outlets like Fox News were more likely to believe virus conspiracy theories and misinformation.

> *"We've always had this kind of misinformation, but its capacity to act on the electorate is new."*

"We've always had this kind of misinformation, but its capacity to act on the electorate is new," Jamieson says. Now, "you can identify vulnerabilities and all but ensure that people hear the information they are most disposed to believe."

The reach of misinformation and beyond that, disinformation—created with the intent to deceive—extends outside the pandemic, to areas like the presidential election and anti-vaccination claims.

To study the latter, Jamieson and two APPC postdoctoral fellows surveyed nearly 2,500 Americans during the 2019 measles outbreak. In another *HKS Misinformation Review* paper, they showed that those reading and watching traditional media were better informed about vaccines than those who relied on social media.

"Holding misbeliefs in the context of vaccinations is problematic," Jamieson says. "The mother of all misbeliefs is that the MMR vaccine causes autism. There's not just a preponderance of evidence against it, but all available, respectable, well-gotten evidence finds no association."

Misbeliefs about a COVID vaccine are equally consequential, Jamieson adds, especially if people think CDC leaders are exaggerating the risks of COVID and delayed promising vaccine announcements to undermine former President Donald Trump. "The threat of COVID is real," she says. "It takes time to determine whether a vaccine is safe and effective."

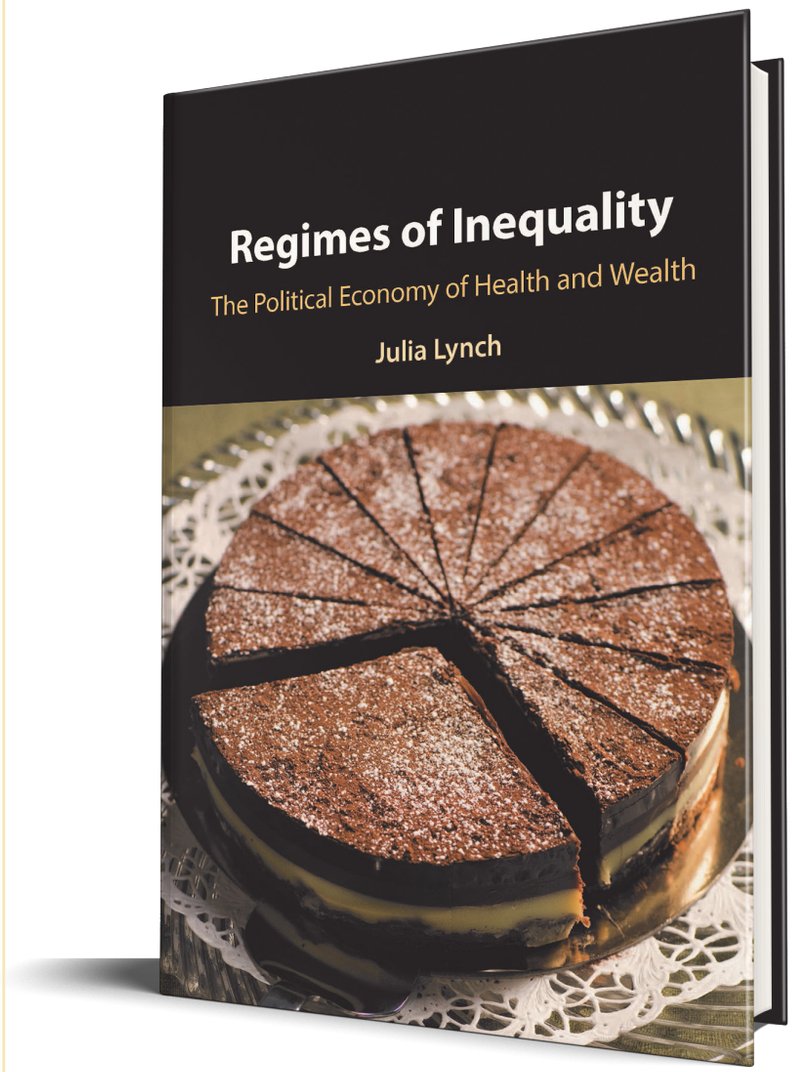
Combating inaccuracies around subjects like the coronavirus and vaccines, the research concludes, requires knowing what needs debunking, proactive communication, and widespread access to reputable news sources.

THE POLITICS OF HEALTH INEQUALITY

Julia Lynch, an associate professor of political science in the School of Arts & Sciences, is not new to the study of health inequalities. But, finally, people are starting to listen.

"On the one hand, there's part of me that wants to say, 'I told you so,' but I take no pleasure in having been right," she says.

Since the early 2000s, Lynch has been examining socioeconomic inequality. Often, she says, U.S. policymakers at the time recognized the problem, but expressed there was not much they could do about it. So, she thought, she could reframe the conversation in a way that related socioeconomic inequality to health inequality.



"Surely," she remembers thinking, "if people understood this as a matter of life and death—that people are dying because they're poor—people will have a less relaxed attitude about socioeconomic inequality."

Unfortunately, that didn't happen, as documented in her 2020 book, "Regimes of Inequality: The Political Economy of Health and Wealth," published by Cambridge University Press.

After mapping out public opinion research, which was the beginning of her investigation for the book, she found that framing the political conversation of socioeconomic inequality as health inequality had no effect on actual action.

"Which is to say," she clarifies, "that if you didn't care much about the public's socioeconomic inequality, thought it was non-problematic, that it led to a more efficient economy, etc., you weren't going to care about health inequality either."

Her next mission was to pinpoint why policymakers thought this way, which, she suggests, can be understood by how the U.S. discusses this in terms of racial equity compared to Europe's focus on economic inequity. Her ultimate finding was that when policymakers framed inequality as a problem of health, it made health and socio-economic inequalities *harder* to solve.

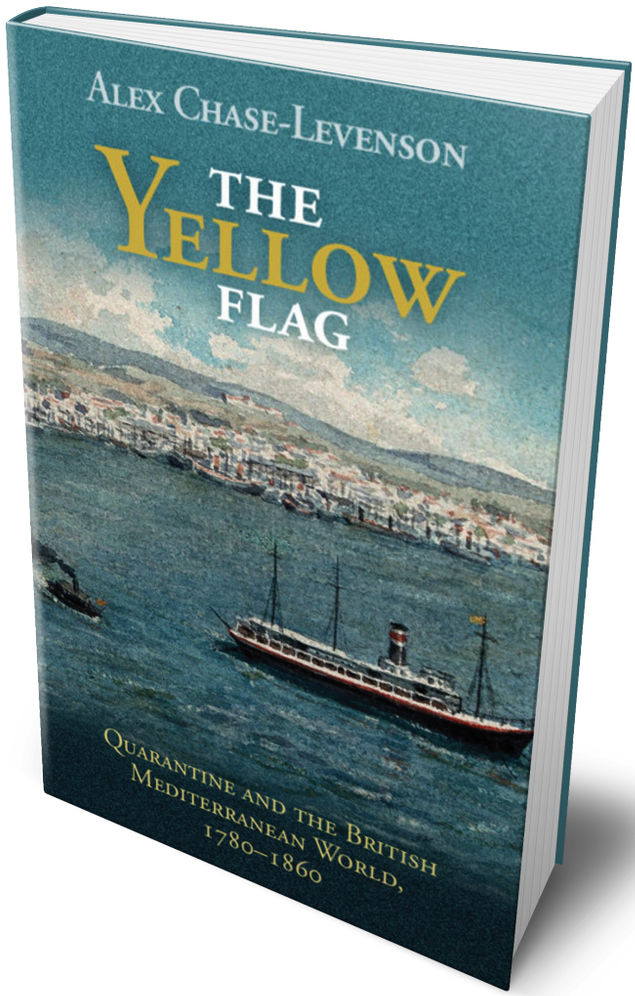
"That was the key insight of the book," she explains. "You can't solve this problem by changing how you talk about inequality. If you want to change it, you have to just do it. Engage the policy levers you have at your disposal—mainly, taxation, social benefits, and macroeconomic policy."

The problem, she says, is that public opinion will always lag rather than lead policy. The global coronavirus pandemic and ensuing financial crisis, she says, have only made the need to address socioeconomic inequalities more apparent.

Lynch will next prepare a book on health inequalities during the pandemic, written from a comparative perspective alongside co-authors in the United Kingdom. That book will discuss the politics of how we measure death.

The Vast and Complex Quarantine System of Early 19th-Century Europe

Until the 1850s, every person, ship, or thing traveling by ship from North Africa and the Middle East to Western Europe had to submit to a period of quarantine lasting between 10 and 40 days, depending on their port of arrival and their ship's bill of health. Quarantine laws were enacted by all major Western European countries to protect their territory from the bubonic plague, which was still present in parts of the Ottoman Empire. But quarantine applied at all times—even when there was no report of epidemic disease.



Quarantine laws were enacted by all major Western European countries to protect their territory from the bubonic plague.

In his book, "The Yellow Flag: Quarantine and the British Mediterranean World, 1780–1860," Alex Chase-Levenson, an assistant professor of history in the School of Arts & Sciences, shows how the transnational, complex, Mediterranean quarantine system reshaped British public health policy, how the British coordinated with the rest of Europe to create a union of shared sanitary procedures, and how the system created a lasting line of demarcation between "West" and "East" that influenced European culture, politics, and diplomacy for decades.

Chase-Levenson became interested in the topic while researching the history of travel in the Mediterranean, particularly British travelers to Egypt in the early 19th century.

"I was reading one of the first modern guidebooks to Egypt, published around 1840, and I realized how very much of it was devoted to explaining the intense, onerous, and invasive procedures of quarantine that every single traveler had to go through on their way back to Western Europe," he says.

As soon as a traveler arrived in a European port city, he or she was placed in a fortress called a lazaretto and confined to a room or suite for a set period. Even chance contact with a traveler who arrived later could mean one's own quarantine was extended, and a complex set of divisions between what was "safe" and what was suspicious meant every person in a lazaretto had to practice social distancing at all times.

For his research, Chase-Levenson worked in archives in Britain, France, Italy, Austria, and Malta, examining travel narratives, medical treatises, and the administrative records of boards of health across the Mediterranean.

The quarantine system came to an end gradually. In 1847, the British stopped quarantining ships with clean bills of health. As the plague became less frequent in the Ottoman Empire, this amounted to almost all ships being made exempt. An international sanitary conference was held in 1851, where all major European powers agreed on the same reform. Yet, Chase-Levenson points out, it was after this point, when "universal" quarantine ended and medical suspicion began to fall on specific groups of people rather than ports of origin, that quarantine practice became much more discriminatory.

HUMANITIES / ROMANCE LANGUAGES

Archiving the Social History of Cuban Punk

Carmen Torre Pérez, a fifth-year graduate student in the Department of Romance Languages in the School of Arts & Sciences, has assembled the online archive punkcubano.net to shed light on a subculture that offers an underground perspective of Cuban social history. This is the first digital archive dedicated to Cuban punk, Torre Pérez says, and includes music recordings and video interviews. These tracks were often collected by Torre Pérez through music transfers conducted during her research.

Originating in Britain in the 1970s in response to a major economic crisis, punk did not arrive in Cuba until the early 1990s. This coincided with the beginning of el Período Especial (the Special Period) after the fall of the Soviet Union.

"Punk emerges in times of great crisis as an alternative way of life, embraced by a generation that feels hopeless about their future and stuck in a present where they don't belong," Torre Pérez says. "This was the case in England and the U.S. in the 1970s with the collapse of the Fordist capitalist system, and in Cuba with the start of the Special Period in the early 1990s. Although these crises were in response to different economic, social, and political systems, both had a similar impact in their population, especially the younger generations."

This project collects testimonies and songs from punk groups and uses them to build the critical history of this counterculture from the 1990s to the present. During this time, Cuba saw the dissolution of the Soviet bloc and the death of Fidel Castro, says Odette Casamayor-Cisneros, an associate professor of Latin American and Caribbean literatures and cultures and Torre Pérez's Ph.D. advisor.

"The most remarkable aspect of her research is not only that she's documenting the history of Cuban punk, but she's dissecting the sociopolitical realities," says Casamayor-Cisneros. "Through her research, we have been able to follow how nonconformist Cubans can interact and counteract."

The subculture has evolved together with the country's sociopolitical and economic circumstances, and there are still issues with racism, sexism, and homophobia within Cuban punk that, in a way, reflect pervasive problems within Cuban society. Although it is a rebellious and anti-establishment culture, Torre Pérez says, it is important to realize that punk also acts as a microcosm of the society in which it exists.

HUMANITIES / MUSIC

THE SHAPING OF JAPANESE PERCEPTIONS OF BLACKNESS

For Keisuke Yamada, a recent Ph.D. graduate in ethnomusicology, what began as a conversation in 2015 during a Penn Music Department seminar about Africana studies evolved into a years-long effort to examine the Japanese perception of Blackness.

His primary interest was the connection between Africa and East Asia, particularly in Japan, a country that keeps such discussions on the margins. So, he wrote a seminar paper on the early historical connection between Africa and Japan, drawing influence from Afro-Asian scholarship and scholars like Marvin D. Sterling and John G. Russell.

In the years since, that work has been fleshed out and culminated in a peer-reviewed paper published in *Japanese Studies* in 2019, where Yamada delivers a detailed look at the journey of how Japanese people came to see Black people as at first "Unknowns," and then "Others."

His research differs from contemporaries by taking a genealogical approach, examining a modern observation and tracing it back to its roots.

"People in the popular music industry [in Japan] often appear, first, in blackface, and there are many apologists for blackface

Bankoku sōzu *(A Chart of the Myriad Lands)* comprising a world map (sekaizu)*(right)* and a chart of the persons in the world (sekai jinbutsuzu) *(left), from the early 17th century. Preserved by the Kobe City Museum, Kobe.*

performance," Yamada explains. "They say that because Japan has no history of Black discrimination or slavery, they just paid a respect to their performance."

However, he says, because geographical and anthropological knowledge was brought by Europeans as early as the 17th century—who categorized people based on the concept of race—what came was a sort of imitation of European thinking.

"My work is to show the history to the Japanese people, to realize what they did," he says, emphasizing the genealogical perspective of his analysis, which he says reveals the current geographical understanding of the world.

"And so, I think my work is a little different from historical work," Yamada says. "That is the making of the past, and my approach is how to use history to make the present."

The Health and Economic Effects of Partially Reopening During the Pandemic

In response to the coronavirus pandemic, the Penn Wharton Budget Model (PWBM) is analyzing the health and economic effects when states partially reopen—lifting emergency declarations, stay-at-home orders, and school closures—as well as fully reopen all of the above, businesses, and restaurants.

"The stay-at-home orders and business restrictions have taken an economic toll, to be sure," says Wharton professor Kent Smetters, faculty director of the PWBM. "But those social distancing policies are designed to reduce coronavirus cases and deaths. Faster reopening will stem the job loss, but at the price of more deaths."

The PWBM's Coronavirus Policy Response Simulator, which is updated weekly, shows health and economic projections for each state. These projections include employment change based on different state reopening scenarios, and projections of cumulative reported cases and coronavirus-related deaths.

The PWBM combines modern advances in economic modeling, big data science, cloud computing, and visualization tools to provide a "sandbox" that allows policymakers and the public to test their policy ideas before legislation is drafted. Tools are transparent and accessible to all, without policy advocacy. Interactive simulation tools provide instant visual feedback.

The PWBM's simulator is unique in its ability to project the impact of different levels of policy for each state based on data at the county and even ZIP code level. The model includes population density, public transit, and labor force and industry characteristics, as well as cell phone, business opening, web search, payroll, and even weather data. Sources include Johns Hopkins, the American Community Survey, and others at the state and local levels. Rather than running two economic and epidemiological models separately in parallel, the PWBM is fully integrated, which is key for determining the impact of policy changes on economic and health variables.

The model incorporates the rich details of the existing economy before a policy change, as well as the behavioral changes needed to analyze a new economy after a policy change.

The PWBM combines both "reduced-form" and "structural" types of models, Smetters explains, thereby allowing for real-world detail while incorporating the ability to analyze new policy changes.

BUSINESS ECONOMICS

BUSINESS

Why Don't Women Promote Themselves?

New research from the Wharton School and Harvard University has found that when it comes to self-promotion, women systematically rate themselves lower than men do, even when their work is objectively better.

The findings are outlined in a National Bureau of Economic Research working paper by Judd Kessler, a professor of business economics and public policy at the Wharton School, and Christine Exley of Harvard Business School.

In their study, "The Gender Gap in Self-Promotion," the researchers conducted a series of experiments to measure self-promotion.

They measured the participants' self-promotion by asking them four subjective questions that might be on a performance review. On a question asking about prior performance on a test, men gave themselves an average score of 61, and women rated themselves at 46, even though their scores were the same on average. Similar patterns arose for the other three questions.

Kessler and Exley say the findings are worrisome because they indicate an inherent unfairness in how women may be perceived in the labor market. They find the tendency for women to undervalue themselves—whether in a formal performance review, a job interview, a staff meeting, or a casual question about last week's project—makes it more difficult to achieve parity and close the gender gap in the workplace.

"Our research suggests that hiring managers and employers should think twice before relying on subjective self-assessments to determine the performance of applicants or employees," Kessler says.

In their study, Kessler and Exley note that they're concerned about the self-promotion gender gap because it is pervasive in a wide variety of settings, from academia, to the factory floor, to corporate offices.

"We are eager to see whether there are interventions or policies that can close the gender gap in self-promotion," Kessler says. "We would also love to better understand the underlying causes of the gap. If we have a better sense of what causes the gap, that may help us design solutions to mitigate it or, ideally, close it."

BUSINESS ANALYTICS

Evaluating and Employing AI in Business

Research from Wharton School professors Peter Cappelli and Prasanna Tambe challenges the use of artificial intelligence in human resources. In their paper, "Artificial Intelligence in Human Resources Management: Challenges and a Path Forward," the researchers show how limited data, the complexity of HR tasks, fairness, and accountability pose problems for digital HR.

"The language of human resources, which is coded in law, has an awful lot to do with fairness questions, and fairness and optimization don't often go together very nicely," Cappelli says.

The study also looks at how to remedy those problems.

The Wharton School has established Wharton AI for Business (Artificial Intelligence for Business), led by professor Kartik Hosanagar. The center will inspire cutting-edge teaching and research in artificial intelligence, while joining with global business leaders to set a course for better understanding of the discipline.

Operating within Analytics at Wharton, Hosanagar says the research will explore AI's applications and impact across industries.

"Our students and professors are energized by the idea that AI is influencing nearly every aspect of humanity, and our efforts to understand it can make a difference for years to come," he says.

WHY SOME COUNTRIES RESPOND TO PANDEMICS BETTER THAN OTHERS

Research by Mauro Guillén, a professor of management at the Wharton School, has shown that the capacity of a state and the degree of economic inequality among its residents will determine how successful it is in coping effectively with a pandemic like COVID-19.

In his working paper, "The Politics of Pandemics: Democracy, State Capacity, and Economic Inequality," Guillén tracks epidemic outbreaks in 146 countries since 1995. His research has found that whether a country is a democracy or dictatorship matters relatively little.

"In democracies, greater transparency, accountability, and public trust are theoretically expected to reduce the frequency and lethality of epidemics, shorten response time, and enhance people's compliance with public heath measures," Guillén writes in his paper. However, "democracy has no effects on the likelihood and lethality of epidemics."

Guillén says democracies and dictatorships may face different challenges with the COVID-19 pandemic "in terms of the sacrifices that it demands from the population in order to contain it." He says dictatorships can respond "more swiftly and resolutely" in imposing quarantines and enforcing other steps that infringe on individual liberties.

Guillén's research suggests inequality increases the frequency and scale of an epidemic, and it undermines people's compliance with epidemic containment policies, such as social distancing and sheltering in place, because people at the low end of the socioeconomic scale must go to work and cannot afford to stay at home. But strong state and government structures could help offset most of the shortcomings.

"State capacity is a bulwark against the occurrence and ill effects of crises and emergencies, while economic inequality exacerbates them," Guillén says.

Guillén identified "three big debates" around the pandemic. One is about whether democracies do a better or worse job than dictatorships—non-democracies of various types—in managing health crises.

The second is about whether the governments are prepared with the requisite capacity to deal with health emergencies.

And the third is about how economic inequality makes a country vulnerable to relatively harsher consequences than others that are better off on that score.

Guillén's research is the first-of-its-kind study to explore the effects of democracy, state capacity, and income inequality on epidemic dynamics.

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