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FOR THE TECHNOLOGY INSIDER | 10.20

A Special Report

The Next Pandemic

COVID-19 has galvanized tech communities. The tens of billions we're spending on vaccines, antivirals, tests, robots, and devices are transforming how we will respond to future outbreaks of infectious disease.

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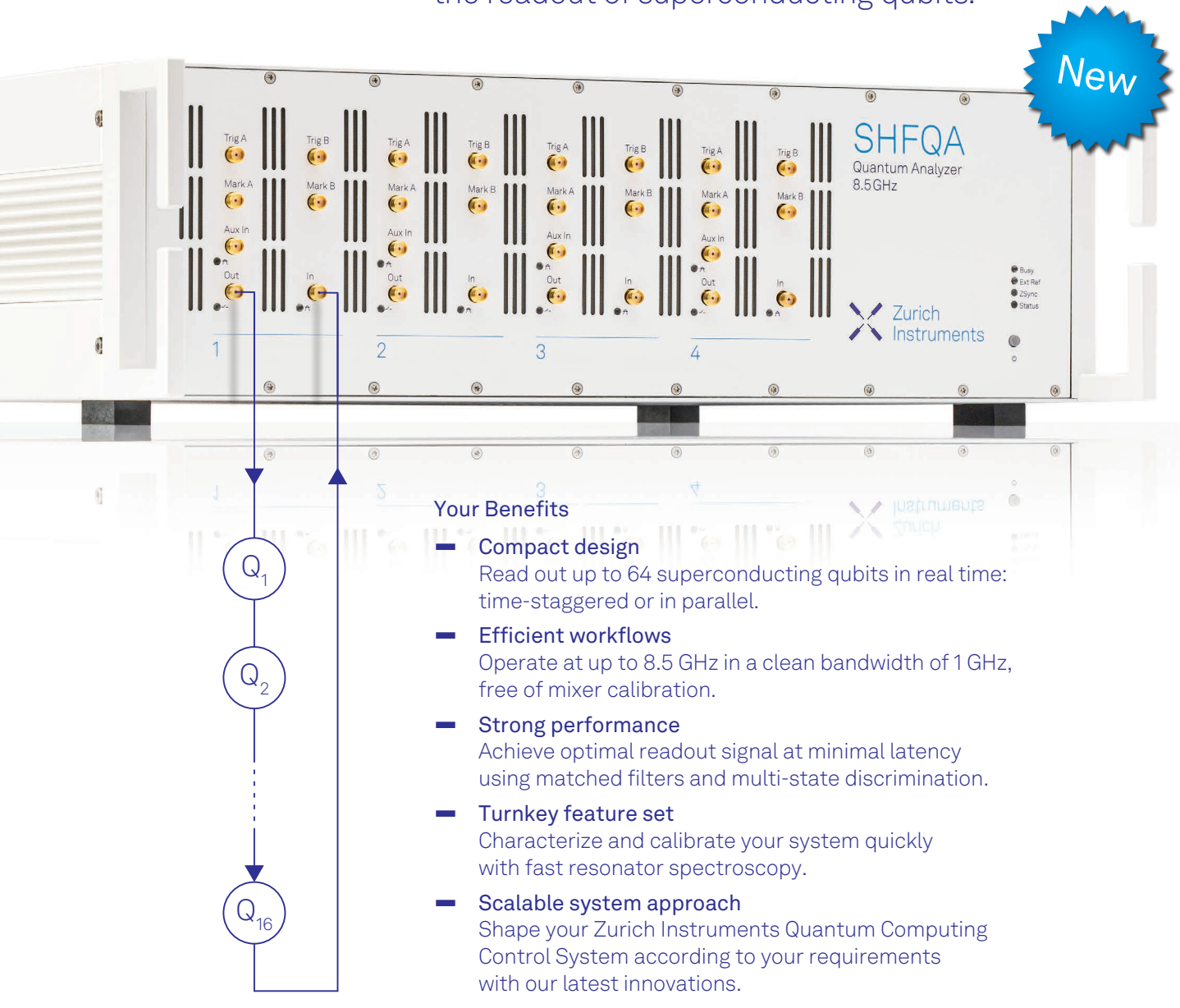

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A robot, developed by Asimov Robotics to spread awareness about the coronavirus, holds a tray with face masks and sanitizer. P. 36

SIVARAM V/REUTERS

THE NEXT PANDEMIC

COVID-19 HAS TAUGHT US THAT FORESIGHT AND TECH ARE A WINNING COMBINATION

BY ELIZA STRICKLAND & GLENN ZORPETTE PAGE 20

On the cover: Illustration for *IEEE Spectrum* by StoryTK

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IEEE

PURSUING THE PANDEMIC

TINY ROBOTS THAT MOVE THROUGH BLOOD VESSELS. Brain implants that translate thoughts into text. Artificial intelligence tools that diagnose disease. It takes a special kind of journalist to cover such topics, somebody who understands both cutting-edge technology and the messy biology of the human body. In 2016, when *IEEE Spectrum* launched its biomedical engineering blog, The Human OS, we took great pains to find two reporters who could handle it all. Megan Scudellari [left], based in Boston, and Emily Waltz, based in Nashville, have been mainstays of the blog since its inception.

And when the coronavirus pandemic became the biggest story in the world earlier this year, Scudellari and Waltz were ready. At the start, they gave *Spectrum* readers urgently needed reports on epidemiological tools used to track the virus's spread, new testing technologies, and efforts to use AI to identify drug treatments. As the pandemic has progressed, they've continued to follow the evolving story. In recent months, they've covered technologies that make it safer for people to venture out and for businesses to reopen, such as contact tracing apps and wearable biometric sensors.

For this special issue on the engineering world's response to COVID-19 and its preparations for the next pandemic, Waltz writes about AI tools used in vaccine design [p. 24], and Scudellari dives into the high-tech quest for antiviral treatments [p. 44].

Reporting during the pandemic hasn't been easy, the two writers say. "The No. 1 challenge was access," says Waltz. Previously accessible researchers suddenly became very hard to reach, she says, both because of their increased workloads and because other media outlets were competing for their time. "Suddenly *Vogue* was interested in science and trying to track down the same scientists," Waltz says.

Still, Scudellari says, the pandemic has underscored the need for strong science journalism. She takes it as her mission "to clearly share the most up-to-date, accurate information so people can make choices now and prepare for the future. I've never felt more that our job really matters," she says. ■

LEFT: RYAN SCUDELLARI; RIGHT: MICHAEL SHAPLAND

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Richard Brewster

Brewster is a former nuclear power engineer who served until recently as project engineer on the hospital ship *Global Mercy*. In this issue, he writes about a World War II handheld radio, the SCR-536 [p. 72], that prefigured today's walkie-talkies. Brewster has long had an interest in early radio, television, and electronics. For the June 2018 issue of *IEEE Spectrum*, he described how he re-created the first flip-flop, in celebration of that circuit's 100th anniversary.

Matthew Hutson

Hutson, a New York City-based freelance journalist, reports in this issue on the epidemiological models that forecast the coronavirus's spread ["The Mess Behind the Models," p. 30]. He learned that modelers had pulled every tool off their shelves. He gained new respect for agent-based models that use artificial intelligence to create virtual worlds and then let the pandemic unfold in simulation. "It's interesting trying to model something as complex as human civilization," Hutson says.

Jeremy Hsu

Hsu, a contributing editor at *Spectrum*, has been writing for the magazine and its website since 2009. When he first looked into digital contact tracing for this issue ["The Dilemma of Contact-Tracing Apps," p. 56], he thought the main problem with the apps involved gaining public trust. "What I didn't realize," Hsu says, "was that the Bluetooth-based apps being tried in the United States and many other countries still face major technical challenges."

Wudan Yan

Yan is a journalist based in Seattle. Her work has appeared in *The New York Times*, *The New Yorker*, and *Scientific American*, among other outlets. In this issue, she and *Spectrum* senior editor David Schneider explore advances in rapid testing for the COVID-19 virus [p. 60]. Yan says that after reading a lot about testing procedures for this story, "I developed a deeply irrational fear of getting a nasopharyngeal swab—envisioning someone poking at my brain."

Sam Zeloof

Zeloof is an electrical engineering undergraduate at Carnegie Mellon University. While still in high school, he fabricated integrated circuits in a home fab that he built in his parents' garage [see the January 2018 issue of *IEEE Spectrum*]. In this issue, he describes how he hooked up a Polaroid camera to a digital printer [p. 12]. "As with many electronics projects that initially seem simple, the conversion quickly revealed itself as being very involved!" Zeloof says.

Using Modeling to Understand How COVID-19 Preventive Measures Work

Washing hands, wearing masks: Does it help?

Wearing face coverings, practicing social distancing, washing hands, and shuttering schools and stores. These are some of the measures that have been implemented to protect people from catching the virus responsible for COVID-19. But just how effective have these interventions been? ● Engineers at Carnegie Mellon and Princeton believe they have developed a mathematical modeling approach that could tell us. Their project, called "Modeling and Control of COVID-19 Propagation for Assessing and Optimizing Intervention Policies," looks at various factors that can impact the spread of the SARS-CoV-2 virus, including virus mutations as well as preventive measures such as wearing masks. ● H. Vincent Poor, an IEEE Life Fellow, is the principal investigator of the team. Also on the team are IEEE Senior Member Osman Yağan, an associate research professor of electrical and computer engineering at Carnegie Mellon, and mathematical biologists from Princeton and the University of Pennsylvania who study viral spread. ● The model recently received a grant from the C3.ai Digital Transformation Institute, a new research consortium funding projects that could reduce the effects of pandemics. Related projects on viral spread by Osman and Poor are also being funded by the U.S. Army Research Office and the United States' National Science Foundation. ● The template for the new model was adapted from a mathematical theory the researchers developed in 2019 that investigated the process by which viruses and their mutations spread. In their paper, published in March in the *Proceedings of the National Academy of Sciences*, they compared how a virus spreads and mutates to how information changes as it's circulated by networks of people.

Current models tracking epidemics make predictions about how a disease advances among individuals, but they don't take into consideration how things change as it is passed along, such as how a virus mutates or what is being done to control its spread, Poor says. A common model being used for the coronavirus, known as SIR (susceptible, infected, and recovered), is a very basic one for viral spread. Poor says it doesn't take into account such factors as the underlying health conditions of patients or that some people spread more COVID-19 droplets than others.

In their 2019 paper, Poor and his colleagues noted that previous models for epidemics assumed that a pathogen or a piece of information is transferred across network nodes without going through any modification or evolutionary adaptations. "However, in real-life spreading processes," they added, "pathogens often evolve in response to changing environments and medical interventions, and the information is often modified by individuals before being forwarded."

The researchers will first model networks using data about the pandemic from a comprehensive data source, known as a data lake, maintained by C3.ai. The database includes the current number of COVID-19 cases, deaths, hospitalizations, and recoveries for countries, including by city, state, and province or county.

"It's quite extensive, and includes details about COVID-19 victims and spread from a variety of sources globally," Poor says.

The model can incorporate properties of the novel coronavirus's spread that public health and medical personnel have discovered over the past few months, Poor says. That includes the existence of "superspreaders," asymptomatic spreaders, and delays between when people become contagious and when they begin showing symptoms.

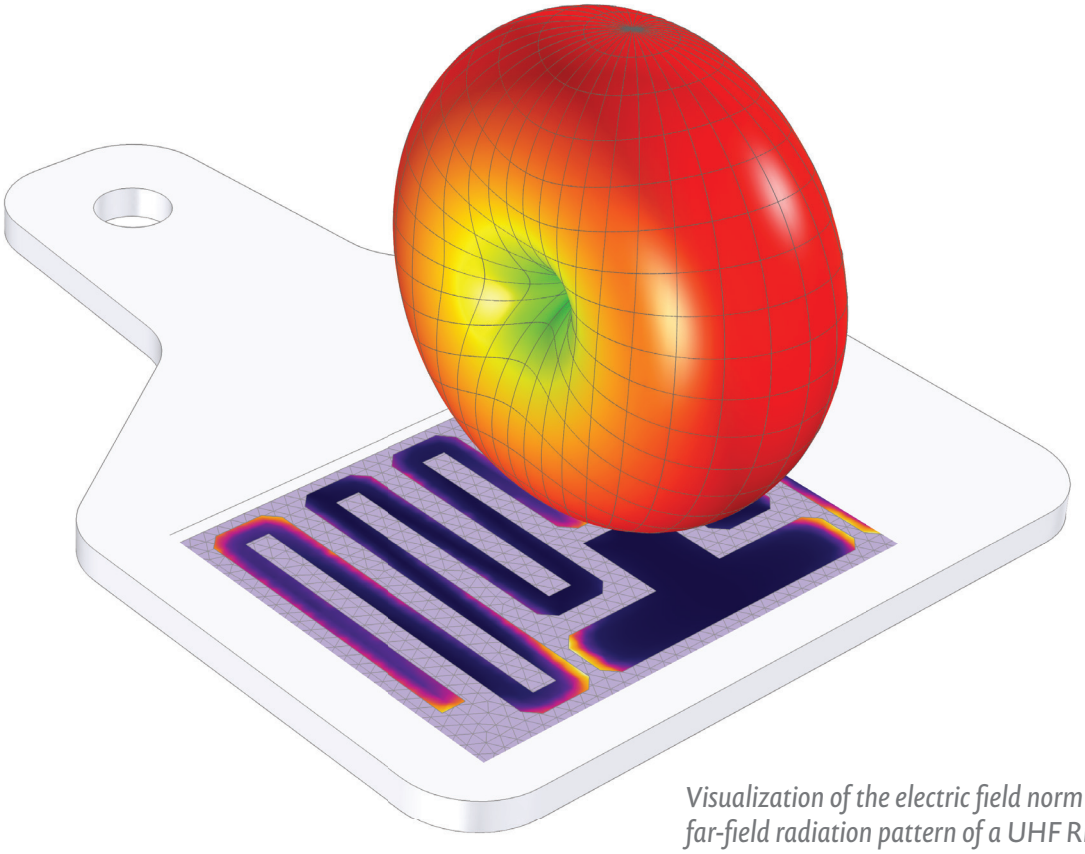
Poor says once the team has a model for how people are connected and how the spread of a virus occurs within that network, the researchers can then start looking at how various interventions or behaviors could have slowed the spread.

—KATHY PRETZ

An extended version of this article appears online in *The Institute*.

NOAM GALAI/GETTY IMAGES

Smartphones, smart homes, smart...healthcare?



Visualization of the electric field norm and far-field radiation pattern of a UHF RFID tag.

RFID tags are used across many industries, but when it comes to healthcare, there is a major design challenge: size. If wearable RFID tags are too big and bulky, they could cause patient discomfort. Or, if the tag is for a biomedical implant, it has to be smaller than a grain of rice! Design engineers can optimize the size of an RFID tag for its intended purpose using RF simulation.

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News

HEALING MIST: An antibody protein that keeps COVID-19 from infecting human cells could soon be available over the counter as a kind of breathable PPE.

NOAH BERGER

ENGINEERED ANTIBODY MIST BLOCKS CORONAVIRUS

Will the first breakthrough COVID-19 treatment be an inhaler or nasal spray?

Researchers have developed an inhalable artificial coronavirus antibody that they say "straitjackets" the SARS-CoV-2 virus and appears to impede its ability to infect human cells.

These early tests, though nonclinical to date, suggest the new therapy is potent and powerful enough to merit clinical trials, say the researchers. The team says this inhalable COVID-19 prophylaxis and treatment—which they envision as an over-the-counter home therapy—could ideally be ready for public release in "a matter of months."

The protein they've developed, called mNb6-tri (which they've dubbed AeroNabs), clamps efficiently and tenaciously atop the spike protein of the SARS-CoV-2 virus, hindering the coronavirus's ability to infect human cells. And, so far as the researchers have been able to determine, once mNb6-tri locks on to the spike protein (the pointy spines poking out of the coronavirus that make the virus particle look like an inflated blowfish), it doesn't readily come off. That appears to be great news for everyone but the coronavirus.

The paper describing the group's AeroNabs research was published this summer on the online preprint server bioRxiv.

As it turns out, the antibodies of some mammals (llamas and camels, for instance) consist of simpler proteins called nanobodies. And nanobodies can be both an order of magnitude lighter than COVID-19 and relatively easy to characterize. And they can potentially be engineered on an atom-by-atom basis.

So, if nanobodies were pressed into service in the COVID-19 war, one very potent target could be the invader's spike protein. That element is such a fundamental component of the coronavirus's infection mechanism that if it were somehow rendered ineffective, the coronavirus's progress through a human host might be stopped cold, or at least substantially hindered.

Aashish Manglik, assistant professor of pharmaceutical chemistry at the University of California, San Francisco, uses nanobodies extensively in his research and has spent much of this year investigating whether his specialty could help fight the COVID-19 pandemic. For this research, Manglik's lab began by performing an experiment in natural selection—that is, they produced a randomized sequence of more than 2 billion nanobodies. Having done that, the team went fishing, says coresearcher Peter Walter, professor of biochemistry and biophysics at UCSF.

Walter and his research group exposed a batch of nanobodies to a bunch of purified coronavirus spike proteins. And because they'd also added a magnetic particle to each spike, when they turned on a magnetic field, they were able to watch as the spike proteins were stripped out along with the nanobodies that bound most effectively to the spikes.

After a two- to three-week whittling process, according to Manglik, the researchers narrowed the pool of 2 billion candidates down to 20 semifinalist nanobodies that each appeared to bind quickly and tightly to the spike, remain robust in the presence of heat and other degrading real-world factors, and be as "human-like" as possible. (This last point was necessary to head off any potential complications such as an overzealous human immune system that counterproductively attacks the nanobody.)

Ultimately, they narrowed the nanobody field down to the best of the entire lot—and designated it Nb6. Using a new imaging technique called cryogenic electron microscopy, they studied Nb6 at the atomic scale as it clamped on to the COVID-19 spike protein. The team made adjustments, they say, that improved Nb6's binding affinity to the spike by another 500 times.

After further adjustments, "we found we got a 200,000-fold gain in the tightness of binding—such that once one of these [AeroNabs nanobodies] binds, it basically never comes off," says Manglik.

Walter anticipates that one dose of AeroNabs particles per day could be sufficient for testing its effectiveness for COVID-19 prevention or treatment. Walter calls AeroNabs—if its safety and effectiveness can be proved in clinical trials—essentially "molecular PPE."

For patients who already have SARS-CoV-2 in their lungs, Walter anticipates a nebulizer creating an AeroNabs mist, which the patient could inhale. "A few minutes once a day should be sufficient," he says.

And because a coronavirus infection often begins in the nasal airways, an AeroNabs nasal spray might also be tested as a preventive measure for frontline workers and other potentially exposed populations as well as people who are positive for the coronavirus but don't yet show symptoms.

On the question of AeroNabs's safety, Walter and Manglik point to the precedent of another nanobody therapy—caplacizumab for the blood disorder TTP (thrombotic thrombocytopenic purpura)—that was recently approved by the U.S. Food and Drug Administration.

Walter notes, too, that the name "nanobody" may be deceptive. AeroNabs, he points out, are not nanoparticles nor any such exotic creation of nanotechnology. Human airways and bloodstreams are awash in all kinds of proteins that are much like mNb6-tri. Except this particular protein has been engineered specifically to bind, as Manglik says, "absurdly tightly" to COVID's primary tool for breaking and entering human cells. —MARK ANDERSON

A version of this article appears in our Human OS blog.

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spectrum.ieee.org/mist-oct2020

JOURNAL WATCH

Motorized Backpack Lightens the Load

For backpackers, it's a treat to escape civilization and traverse the woods, enjoying the ruggedness of the great outdoors. But carrying that heavy backpack for days can undoubtedly be a drag.

One group of researchers in China has designed a new backpack that accounts for the inertial forces of the bag against a backpacker's body as the person walks, reducing the metabolic power demand on the user by an average of 11 percent. Their design is described in a study published 27 July in *IEEE Transactions on Neural Systems and Rehabilitation Engineering*.

Caihua Xiong, a professor at Huazhong University of Science and Technology, notes that his team designed the motorized backpack with two different modes. In its passive mode, two symmetrically arranged elastic ropes balance the weight of load within the backpack. When the user turns on the system's active mode, a rotary motor regulates the acceleration of load. The backpack, which weighs 5.3 kilograms, was designed to carry loads up to 30 kg.

In experiments with seven similarly sized men, the motorized backpack in active mode reduced the load acceleration by 98.5 percent on average. This resulted in that 11 percent dip in power demand on the user. The power savings in passive mode came in at 8 percent on average.

Xiong says he is interested in commercializing the product, but aims to first explore ways of improving the system for different walking speeds and terrains. **—MICHELLE HAMPSON**

A version of this article appears on our website in the Journal Watch section.

GOING CORDLESS: Momentum Dynamics tested inductive charging pads on buses in Washington state. The technology will soon be launched in Oslo for a fleet of Jaguar I-Pace taxis.

CURBSIDE CAB CHARGING

Wireless power tech keeps EVs on the go

Norway, already a world leader in EV adoption, will soon mark a world's first: an Oslo-based fleet of Jaguar I-Pace taxis that can charge wirelessly even as they queue up for passengers.

The inductive charging technology, developed by a former NASA consultant at Pennsylvania-based Momentum Dynamics, aims to solve perhaps the biggest disconnect in EVs: how to bring convenient charging to the urban masses—including apartment dwellers and drivers of taxis, buses, and delivery trucks—without clogging every inch of prime real estate with bulky, unsightly chargers. The conundrum becomes more pressing with the introduction of new electric models and each additional government mandate for fewer fossil-fueled cars and lower carbon emissions.

A great example of that action to combat climate change is Oslo, whose ambitious ElectriCity plan will require that all taxis produce zero tail-pipe emissions by 2024—effectively banning even gasoline-electric hybrid models. The result of punitive taxes on fossil-fueled cars and enticing incentives for electric models: Nearly 50 percent of Norway's new cars are now EVs, a higher percentage by far than in any other nation. Norway's government has decreed that all new cars must be zero-emissions by 2025.

That carrot-and-stick urgency led to a partnership between Jaguar, Momentum Dynamics, Nordic taxi operator Cabonline, and charging company Recharge Infra. The group aims to create the world's first wireless-charging taxi fleet. To that end, Jaguar is equipping 25 I-Pace SUVs with Momentum Dynamics' inductive charging pads. The pads, which are about 60 centimeters square, are rated at 50 to 75 kilowatts. As the cars work their way through taxi queues, the Jaguars will stop over a series of inductive coils embedded in the pavement. Using resonant magnetic coupling operating at 85 hertz, a charging pad will route enough energy to a taxi's batteries to add about 80 kilometers of range for every 15 minutes the car spends hovering over the inductive coils—with no physical plugs or human hookup required.

Rather than fill batteries to the brim, the idea is to replenish them in shorter bursts whenever the opportunity arises. "The concept is grazing, rather than guzzling," says Andrew Daga, chief executive of Momentum Dynamics. "You just keep adding energy back in as you need it."

Daga argues that current charging models—including the "one car, one plug" idea and the reliance on ever-more-potent DC chargers that can degrade battery life—are ultimately unworkable for congested cities, mobility fleets, and impatient drivers or riders.

"More frequent interactions with the grid are necessary," Daga says. "It's all about thinking differently about how fueling is going to be done in a world of electric vehicles."

The company's breakthrough was born from outer space and inner snow. Daga's cofounder, Bruce Long, who died in 2018, was an electrical engineering professor at Bucknell University, in Pennsylvania. During his Antarctic expeditions to measure glacial activity for Penn State's geophysics program, brutal elements inspired a wireless solution for recharging electronic equipment. Fine snow kept blowing into Long's sensitive instruments whenever their cases were cracked open to replace batteries. Daga, who had worked on the 35-meter-long solar power arrays of NASA's International Space Station, had already been envisioning ways to reduce their weighty aluminum cabling. That sparked the wireless energy transfer idea that's the basis for Momentum Dynamics' current project.

The company is also collaborating with China's EV giant Geely, which owns Volvo and Lotus. Momentum executives say they've struck a deal with an unnamed European manufacturer to produce a wireless-charging urban delivery truck.

This is just the latest turn in the road for Momentum Dynamics. In 2015, the company began proving its concept

MOMENTUM DYNAMICS

with electric bus trials in four U.S. cities. The transit trials featured a bus in Wenatchee, Wash., that slurped energy from a charging pad installed along its route at a rate of 200 kW. The bus was built by the Chinese company BYD at its facility in Lancaster, Calif. That's on par with some of the fastest DC chargers, enough to "keep the bus in 24/7 operation, without ever going back to the garage" to recharge, Daga says.

Daga points out that taxi or ride-hailing drivers are strongly inclined to avoid downtime—whether that means waiting in line for gasoline pumps or detouring for lengthy charges at depots. With an inductive system, "they won't lose a single minute of revenue time charging their vehicle."

The company claims its technology delivers 94 percent charging efficiency, which holds steady as scalable power climbs to 200 or even 350 kW. That's a winning contrast with DC fast chargers, whose efficiency drops sharply at higher power because of massive resistance and the resulting heat demands of liquid-cooled cables, which themselves create more energy losses.

"It's the perfect charging technology," said Morgan Lind, chief operating officer of Recharge Infra, owned by Infracapital and Fortum. Recharge Infra tabbed Momentum Dynamics after learning it could deliver 50 kW or more through a roughly 18-cm air gap between vehicle and pavement—a huge improvement over companies that promised no more than 11 kW.

Backers cite several additional benefits. With systems buried entirely underground, the plan eliminates chargers that compete for parking or sidewalk space; moving parts and vandalism or damage from the elements; and wired infrastructure, including unsightly towers for electric buses.

"It makes the experience of refueling invisible," Daga said. "We could get clean cities and clean streets at the same time."

Furthermore, says Daga, inductive systems will deliver a daisy chain of gains. With enough charging pads, they could keep vehicle batteries in a permanent "sweet spot" between 75 and 85 percent capacity, avoiding deep cycling, which kills batteries before their time. Largely freed from range concerns, EVs could carry smaller battery packs, trimming their daunting weight and cost, while further boosting energy efficiency.

For taxi fleets or passenger cars, Momentum Dynamics is developing software to track even the briefest charging events and bill customers automatically, similar to an automated tolling system. The company has also developed a Near Field Communication system, which would allow autonomous cars to align and connect with charging pads. Bidirectional charging could let cars contribute supplementary power to the grid.

Lind says the Jaguar taxis should start running their meters, and no-fuss chargers, by year's end. Lind called Norway—with only 5 million residents, but a determination to wean itself off of fossil-fueled vehicles—an ideal, if tiny, test bench.

"We are an extremely small country, but we see that we can be a guiding star to many other countries," says Lind. "The avalanche of EVs is coming, and there's no stopping it." —LAWRENCE ULRICH

A version of this article appears in our Cars That Think blog.

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spectrum.ieee.org/oslotaxi-oct2020

SAME OLD FIBERS, RECORD-BREAKING SPEEDS

Equipment in the lab can carry 100 million Zoom videos

A team at the Optical Networks Group at University College London (UCL) has sent 178 terabits per second through a commercial single-mode optical fiber that has been on the market since 2007. It's a record for the standard single-mode fiber widely used in today's networks, and twice the data rate of any system now in use. The key to their success was transmitting it across a spectral range of 16.8 terahertz, more than double the broadest range now in commercial use.

The goal is to expand the capacity of today's installed fiber network to serve the relentless demand for more bandwidth for Zoom meetings, streaming video, and cloud computing. Digging holes in the ground to lay new fiber-optic cables can cost over US $600,000 a kilometer in metropolitan areas, so upgrading transmission using fibers already in the ground in combination with new optical transmitters, amplifiers, and receivers could save serious money. But it will require a new generation of optoelectronic technology.

A new generation of fibers that has been in development for the past few years promises higher capacity by carrying signals on multiple paths through single fibers. Called spatial division multiplexing, the idea has been demonstrated in fibers with multiple cores, multiple modes through individual cores, or combining multiple modes

DOUBLE THE DATA: New transmitters, amplifiers, and receivers could dramatically increase the capacity of networks without digging up existing optical fibers.

in multiple fibers. But the technology is immature and would require the expensive laying of new fibers. Boosting capacity of fibers already in the ground would be faster and cheaper. Moreover, many installed fibers remain dark, carrying no traffic, or transmitting on only a few of the roughly 100 available wavelengths, making them a hot commodity for data networks.

"The fundamental issue is how much bandwidth we can get" through installed fibers, says Lidia Galdino, a UCL lecturer who leads a team including engineers from equipment maker Xtera and Japanese telecom firm KDDI. For a baseline, they tested Corning's SMF-28 ULL (ultra-low-loss) fiber, which has been on the market since 2007. With a pure silica core, its attenuation is specified at no more than 0.17 decibels per kilometer at the 1,550-nanometer minimum-loss wavelength—close to the theoretical limit. It can carry 100-gigabit-per-second signals more than a thousand kilometers through a series of amplifiers spaced every 125 km.

Generally, such long-haul fiber systems operate in the C band of wavelengths from 1,530 to 1,565 nm. A few also operate in the L band (1,565 to 1,625 nm), most notably the world's highest-capacity submarine cable, the 13,000-km Pacific Light Cable. That line has a nominal capacity of 24,000 Gb/s on each of six fiber pairs. For both bands, it uses well-developed erbium-doped fiber amplifiers, but that's about the limit of their spectral range.

To cover a broader spectral range, UCL added the largely unused 1,485- to 1,520-nm wavelengths in the S band. That required new amplifiers that use thulium to amplify those wavelengths. Because only two thulium amplifiers were available, they also added Raman-effect fiber amplifiers to balance gain across that band. In addition, they used inexpensive semiconductor optical amplifiers to boost signals reaching the receiver after passing through 40 km of fiber.

Another key to success is format. "We encoded the light in the best possible way," says Galdino: the geometric coding quadrature amplitude modulation (QAM) format, which takes advantage of differences in signal quality between bands. "Usually, commercial systems use 64 points, but we went to 1,024 [QAM levels]... an amazing achievement," for the best quality signals.

This experiment, reported in *IEEE Photonics Technology Letters*, is only the first in a planned series. The results are close to the Shannon limit on communication rates imposed by noise in the channel. The next step, says Galdino, will be buying more optical amplifiers so the group can extend transmission beyond 40 km.

Still, Galdino cautions, "This is fundamental research on the maximum capacity per channel." The goal of the UCL work is to find limits, rather than to design new equipment.

Industry will face the challenge of developing detectors, receivers, amplifiers, and high-quality lasers on new wavelengths, which it has already started. If it succeeds, a single-fiber pair will be able to carry enough video for all 50 million school-age children in the United States to be on two Zoom video channels at once. —JEFF HECHT

A version of this article appears in our Tech Talk blog.

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UNIVERSITY COLLEGE LONDON

A ROBOT THAT KEEPS IT SIMPLE

Hello Robot wants to reinvent how autonomous machines perform tasks at home

Ten years ago, a now-defunct Silicon Valley startup caused a sensation when it introduced the Personal Robot 2, or PR2. Researchers, in particular, loved the PR2 because it was versatile and easier to program than other robots. It allowed them to focus on their research rather than building a new system from scratch. The PR2 helped advance robotic sensing, navigation, and manipulation, but it wasn't perfect. It was big, heavy, and expensive: Each cost US $400,000.

Now, another robotics startup is generating excitement with a newly unveiled system. Hello Robot came out of stealth mode this past July to announce Stretch. Tall, slender, and equipped with a telescoping arm, Stretch features an unusual design that promises to be simultaneously lightweight, capable, and affordable. In its launch video, Stretch cleans a countertop, uses a vacuum, and removes laundry from a dryer. The demonstration required a human operator to control Stretch, but Hello Robot says its autonomous capabilities will improve. Another impressive feature is the price tag: The robot is selling for $17,950.

With offices in the San Francisco Bay Area and Atlanta, Hello Robot was founded by former Google robotics director Aaron Edsinger and Georgia Tech professor Charlie Kemp. Both once worked in the MIT lab of noted roboticist Rodney Brooks, and they combine decades of experience in industry and academia. Without venture capital funding, Hello Robot will initially offer Stretch as a research platform, hoping that future versions can be deployed commercially in homes and offices.

"The impact we want to have is through robots that are helpful to people in society," says Edsinger, the company's CEO. "We think primarily in the home context, but it could be in health care, or in other places. But we really want to have our robots be impactful, and useful."

Like the PR2, Stretch is a type of robot known as a mobile manipulator. While there are others on the market, like PAL Robotics' TIAGo and Fetch Robotics' Fetch, they are heavy and expensive. Hello Robot set out to reinvent the category by building a robot that has fewer sensors and lacks the strength of its competitors but beats them in size and cost. One of the key innovations is Stretch's stretchable arm. Made out of lightweight carbon fiber, it consists of five telescoping links that are driven by a single motor—a remarkably elegant design compared with traditional manipulators, which rely on powerful motors to support their own weight. This configuration gives Stretch a reach of over half a meter and the ability to lift up to 1.5 kilograms. The robot itself weighs only 23 kg, or one-tenth of a PR2.

For roboticists, size is a significant issue. "When I think about my long-term research vision, I want to deploy service robots in real homes," says Maya Cakmak, a robotics professor at the University of Washington, in Seattle. Robots like the PR2 are so large that moving them anywhere requires a truck and a lift. They're too big for use in many homes. "I felt immediately that Stretch is very different, and it makes a lot of sense," she says. "It's safe and lightweight, and you can probably put it in the back seat of a car."

And then there's the price tag. Cakmak says her lab acquired a refurbished PR2 for $180,000. "For that, with Stretch, I could have 10!"

As with any robot intended to be useful outside of a structured environment like a research lab, hardware is only part of the story. In order for Stretch to be able to operate without the supervision of a skilled roboticist, it has to be easy to control, autonomous, or ideally, both. For Kemp, Hello Robot's chief technical officer, Stretch is an attempt to get everything he's been teaching his robots at Georgia Tech's Healthcare Robotics Lab out into the world where it can actually be helpful to people.

"I have a personal bias, but we'd really like this technology to benefit older adults and caregivers," Kemp says.

—EVAN ACKERMAN & ERICO GUIZZO

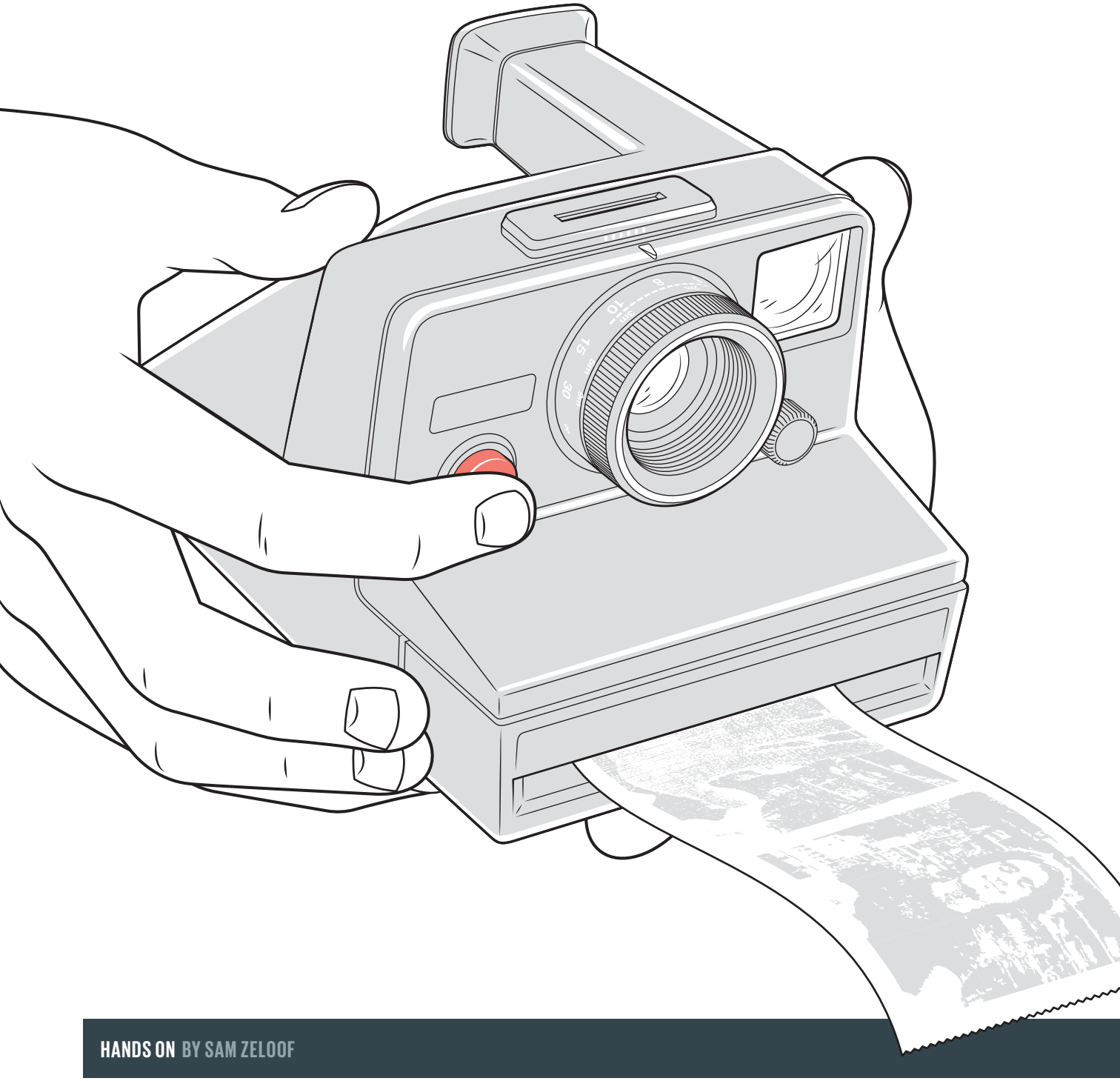
An extended version of this article appears in our Automaton blog.

POST YOUR COMMENTS AT
spectrum.ieee.org/hellorobot-oct2020

REACHING OUT: This mobile manipulator's telescoping arm gives it a long reach—without it reaching too deep into your pocket.

HELLO ROBOT

Hands On

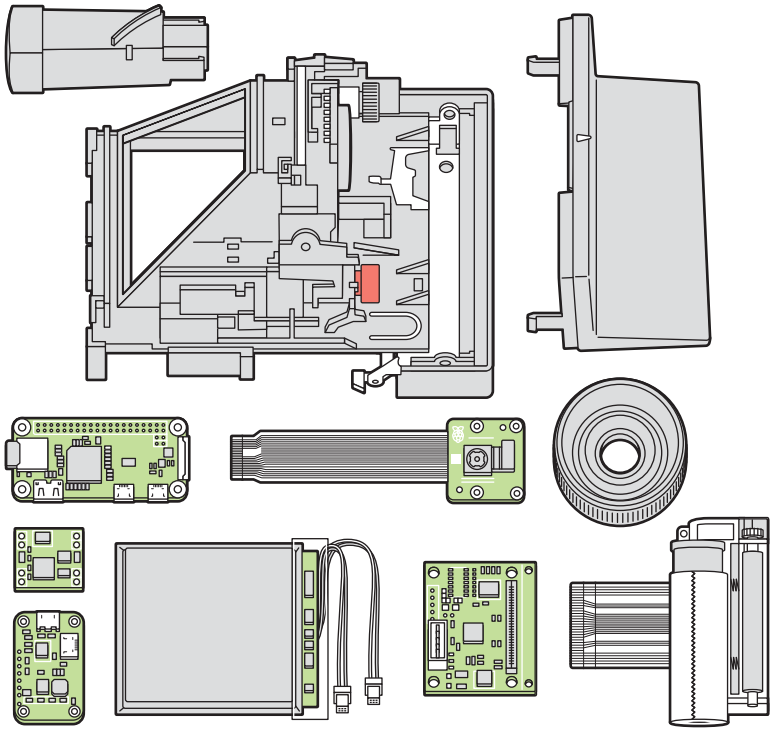


HANDS ON BY SAM ZELOOF

ILLUSTRATIONS BY James Provost

HACK A POLAROID WITH A THERMAL PRINTER

GO FROM FILM TO DIGITAL—AND ADD WI-FI



CRAM SESSION: Once the original innards of the Polaroid were removed, I was left with an awkwardly shaped volume. I carefully removed plastic supports until there was just enough room to hold the Raspberry Pi Zero W, camera module, printer, battery, and other supporting electronics. You operate the camera by looking through the viewfinder and pressing the shutter button, as usual.

I've been recently engaged with some fairly serious projects, building up my garage semiconductor fab. I wanted to take a break and build something entertaining I could share with other people without the complicated explanations that things like a laser interferometer often require. So I decided to make a digital camera that's purposely got a lower resolution than a smartphone cam but is a lot more fun.

I decided to convert a Polaroid instant camera—the sort that spits out self-developing paper photographs—into a digital camera. Initially, I was planning to stop there: If I wanted to print out any of the photos I would simply grab them via a wireless connection. But I felt that wasn't in the spirit of a Polaroid, so I began researching printers. Once I found out that Adafruit sold the guts of a thermal printer for US $40—just the print head and driver board from a thermal receipt machine—I immediately knew it was perfect for adding instant photographs.

Getting an old Polaroid was easy—they are a dime a dozen on eBay. But I took the time to find one where the case was in almost perfect condition (it cost me $15). I opened the case to begin working out how to take out the existing hardware, while still leaving enough internal structure to support my new electronics. And I must say,

ON A TEAR: The modified camera can hold enough paper for about 150 photographs. High-resolution color copies can be downloaded via Wi-Fi.

the original design is stunning. I recommend that anyone who has an old Polaroid lying around to take it apart. There's not a single screw in the camera—it's all fitted together with tabs. But I quickly realized that there was far less usable space inside the case than might be expected, because the shape is so strange and triangular and all the new circuit boards I intended to fit inside it are rectangular. About two-thirds of the project was just cutting out plastic with a Dremel tool and hoping that I didn't cut out too much.

For the controller, I used a Wi-Fi–enabled Raspberry Pi Zero W attached to a standard Pi-compatible camera module and the thermal printer driver board. I made a spool out of a brass rod to hold the printer paper. I turned the ends of the rod on a lathe so I could add a magnet to either end, and I glued corresponding magnets inside the camera. This lets me just snap the rod in place when replacing the paper. Each roll is long enough for about 150 photos.

My electronics are powered by two 3,000-milliampere-hour LiPo (lithium-polymer) batteries wired in series to provide the 7 to 8 volts needed by the printer driver. A step-down buck voltage converter provides the 5.1 V required by the Pi, and I get about 12 hours between charges with typical use.

I was able to cram in all the electronics and close up the case so that it all looked and felt like a untouched Polaroid: You can look through the viewfinder, and the shutter button is the same button, in the same place.

But my goal was to make a digital camera that didn't just look like the original but behaved like it, too: Press the shutter and snap!—a photo emerges. I discovered I was not the first to convert a Polaroid to print out images on thermal paper, but in similar projects I looked at there was a delay of several seconds between pressing the shutter button and actually taking the photograph.

The source of the delay is how the Raspberry Pi handles taking still images. This is typically done by calling a standard utility program each time you want to capture an image. When the utility launches following a shutter press, it starts adjusting the brightness and contrast from scratch, which is a slow process. But by looking at the utility's code I realized there was also a preview mode where, crucially, the brightness and contrast are continually adjusted, eliminating the delay. (Normally, this mode is used to stream whatever is in the camera module's view to a connected HDMI monitor.)

So as soon as my camera is turned on, I launch the utility as a background process and simply ignore its output most of the time. When the user presses the shutter, I send a signal to this process, which instantly captures the image. I then relaunch the utility in the background, ready for the next shot. A high-resolution color copy is saved, and a monochrome lower-resolution image is sent to the thermal printer.

I added two more flourishes to heighten the Polaroid experience: When an image is captured, I play a short shutter sound through a 2.5-centimeter speaker. And using a Python image-manipulation library, I add a yellow, seven-segment-style date stamp to the corner of the saved color image.

With a Wi-Fi connection, I can transfer the files wirelessly for later high-quality printing. Meanwhile, instant photos are printed, to share and enjoy in the moment. Normally with a DIY project, there's always some quirks—it's never quite as user friendly as an off-the-shelf thing. But with this conversion, I can bring it somewhere and hand it to someone. Without any explanation they instinctively treat it as a camera, and point and shoot. While we're currently in a time of social distancing in much of the world, I'm ready to capture and share some memories when better times come again.

—SAM ZELOOF

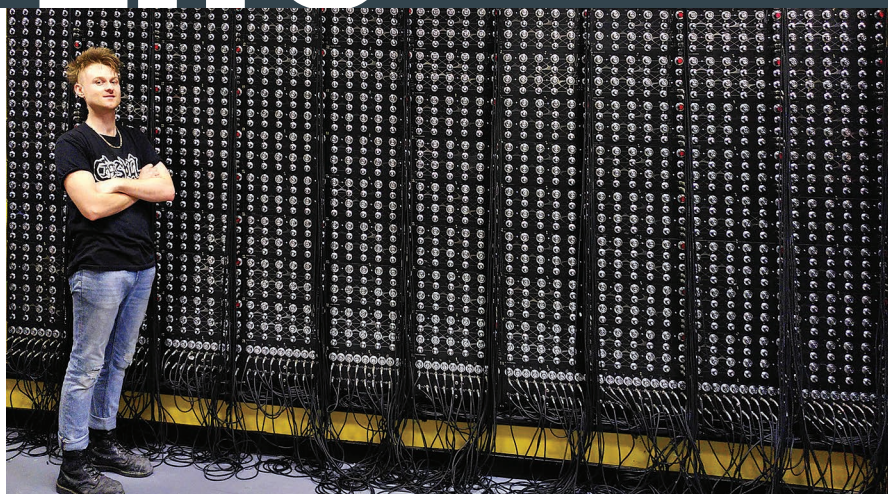
POST YOUR COMMENTS AT
spectrum.ieee.org/digitalcamera-oct2020

SAM ZELOOF

Geek Life

LET A THOUSAND ANALOG OSCILLATORS SING

SAM BATTLE, CHAMPION OF ANALOG ENGINEERING



DIAL-A-SONG: Sam Battle, aka Look Mum No Computer, with his KiloDrone, a musical instrument with 1,000 individually adjustable oscillators.

When the COVID-19 lockdown came to the United Kingdom, Sam Battle became a man on a mission. Battle has created many unusual electronic musical instruments under the sobriquet of Look Mum No Computer, including an organ made out of singing Furbys and a synthesizer-bicycle hybrid. As people isolated themselves, he embarked on his most ambitious project yet: the KiloDrone.

Many of Battle's projects involve analog synthesizers, in which a tone is generated by a circuit oscillating at audio frequencies. Multiple oscillators allow a synth to generate multiple tones simultaneously, creating richer sounds. Which raises the question: Can you ever have too many oscillators?

The KiloDrone was built to answer that question. It's a drone synth, which means it produces sustained sounds, rather than the characteristic attack and decay of, say, a piano. Typically, a drone synth has two to eight oscillators. The KiloDrone, as its name suggests, has 1,000.

The genesis of the KiloDrone came when Battle was "messing around with some transistors, and found a circuit that was lighting up an LED when it shouldn't be," he explains. Battle found that he'd rediscovered the reverse-avalanche oscillator, which requires just a capacitor, resistor, and transistor. He realized he could use it as an adjustable audio oscillator, and relied on one for a Red Bull sponsorship in which he built a light-controlled synthesizer out of a drink can in 2017. After that, while he was touring in Europe, a friend joked that he should build "a big box of them."

"Whenever something captures my imagination, it sort of stays there until it's done," says Battle. So he built the 100-oscillator MegaDrone. "And it didn't seem like that was enough," says Battle, who quickly settled on 1,000 oscillators as his next target. But "I kept on procrastinating. Then at the beginning of lockdown I was like, 'I've got a few months. I may as well pick up that project.'"

A 1,000-oscillator analog synth isn't exactly portable. The KiloDrone is wall mounted, 2.3 meters high, and 4 meters wide. Each oscillator is connected to an LED as well as a tuning knob and volume control. The oscillators are grouped in banks of 10, with each bank equipped with a master tuning and level control. (You can buy one of the printed circuit boards used to make the banks for US $53 and build your own smaller, standalone drone.)

Despite its size, the KiloDrone draws just 1.2 amperes at 12 volts. Consequently, it dissipates little heat, which keeps the oscillators' frequency stable. "A lot of people were very reserved about [the KiloDrone initially]," says Battle. "They were like, 'Oh, by the time you [adjust] the last oscillator it'll be out of tune.'"

So what does the KiloDrone sound like? Imagine the THX effect played before movies in cinemas—like that, only *more so*. You can listen to it in Look Mum No Computer's videos, but Battle says they don't fully capture the experience of hearing it live. He hopes that, when the pandemic ends, people can come to listen to it—and play it—in a planned Museum of Everything Else dedicated to DIY devices, especially analog instruments. "I like the tangibility of analog. I hate working on computers," says Battle. "I just can't stand looking at screens. I like standing up and moving around and making things in a physical world." **—STEPHEN CASS**

POST YOUR COMMENTS AT spectrum.ieee.org/kilodrone-oct2020

SAM BATTLE

DEPARTMENTS

CrossTalk

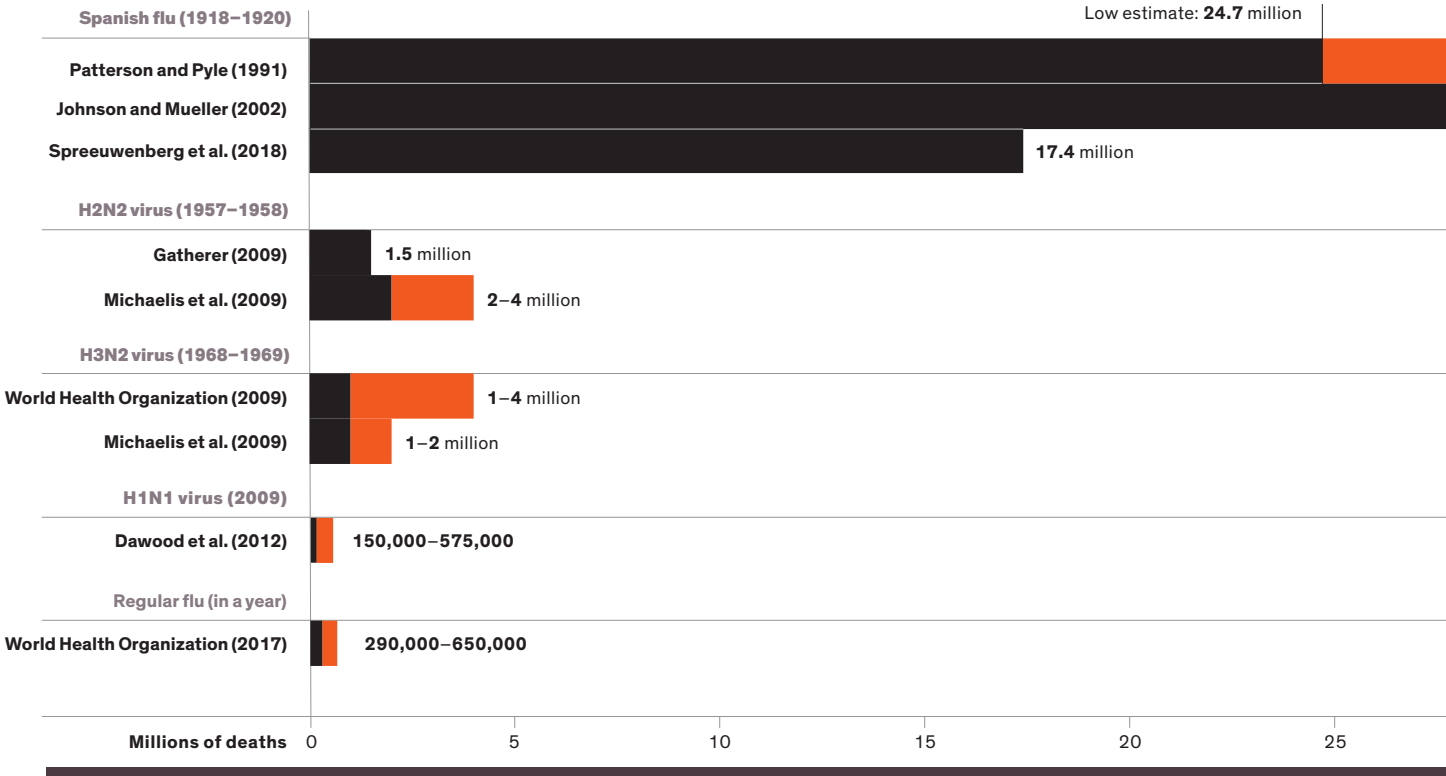
PANDEMIC MEMORIES AND MORTALITIES

WHEN SARS-COV-2, a new coronavirus, began to spread outside China in the early months of 2020, both the news media and scientific publications looked back to the most lethal pandemic in modern history. It was called the Spanish flu, though it had nothing whatever to do with Spain.

That pandemic began early in 1918, its third and final wave was spent only a year later, and we will never know the exact death toll. Published estimates range from about 17 million to 100 million, with 50 million being perhaps the most likely total. If we divide that number by the 1.8 billion people that were alive in the world, we get at a global mortality rate of about 2.8 percent.

What I find strange is that the unfolding COVID-19 event has prompted relatively few references to the three latest pandemics, for which we do have good numbers. The first event, caused by the H2N2 virus, began to spread from China in February 1957 and ended in April 1958. The second, also beginning in China, came in May 1968, when the H3N2 virus surfaced; the first wave peaked before the year's end, and in some countries the effects persisted until April 1970. Finally, there was the H1N1 virus, originating in

GLOBAL NUMBER OF DEATHS FOR INFLUENZA PANDEMICS (ESTIMATES)



NUMBERS DON'T LIE BY VACLAV SMIL

ILLUSTRATION BY Francesco Muzzi/StoryTK

Mexico and declared to be a pandemic by the World Health Organization on 11 June 2009; it stopped spreading before the end of the year.

The best reconstructions estimate that excess deaths—those presumably resulting from pandemics—ranged from 1.5 million to 4 million in the first of these three pandemics, from 1.1 million to 4 million in the second, and from 150,000 to 575,000 deaths in the third. The world's population grew throughout these years, and adjusting for that changing number yields excess death rates of about 52 per 100,000 from 1957 to 1958, 30 per 100,000 from 1968 to 1970, and 2.3 to 5.2 per 100,000 in 2009.

In comparison, the worldwide death toll attributable to SARS CoV-2 was about 865,000 by the end of August 2020. Given the global population of about 7.8 billion, this translates to an interim pandemic mortality of about 11 deaths per 100,000 people. Even if the total number of deaths were to triple, the mortality rate would be comparable to that of the 1968 pandemic, and it would be about two-thirds of the 1957 rate.

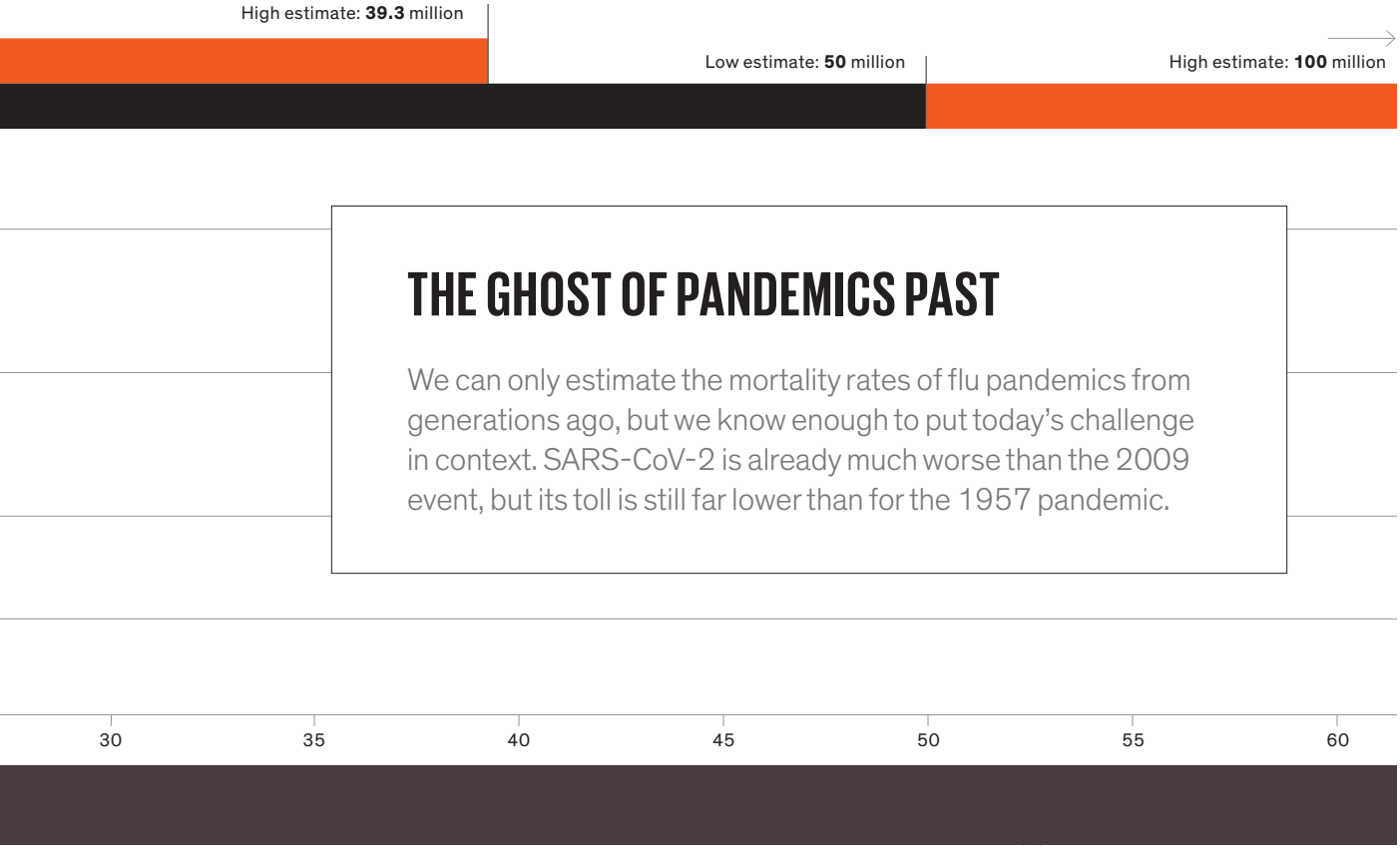
Yet it is remarkable that these more virulent pandemics had such evanescent economic consequences. The United Nations' World Economic and Social Surveys from the late 1950s contain no references to a pandemic or a virus. Nor did the pandemics leave any deep, traumatic traces in memories. Even if one very conservatively assumes that lasting memories start only at 10 years of age, then 350 million of the people who are alive today ought to remember the three previous pandemics, and a billion people ought to remember the last two.

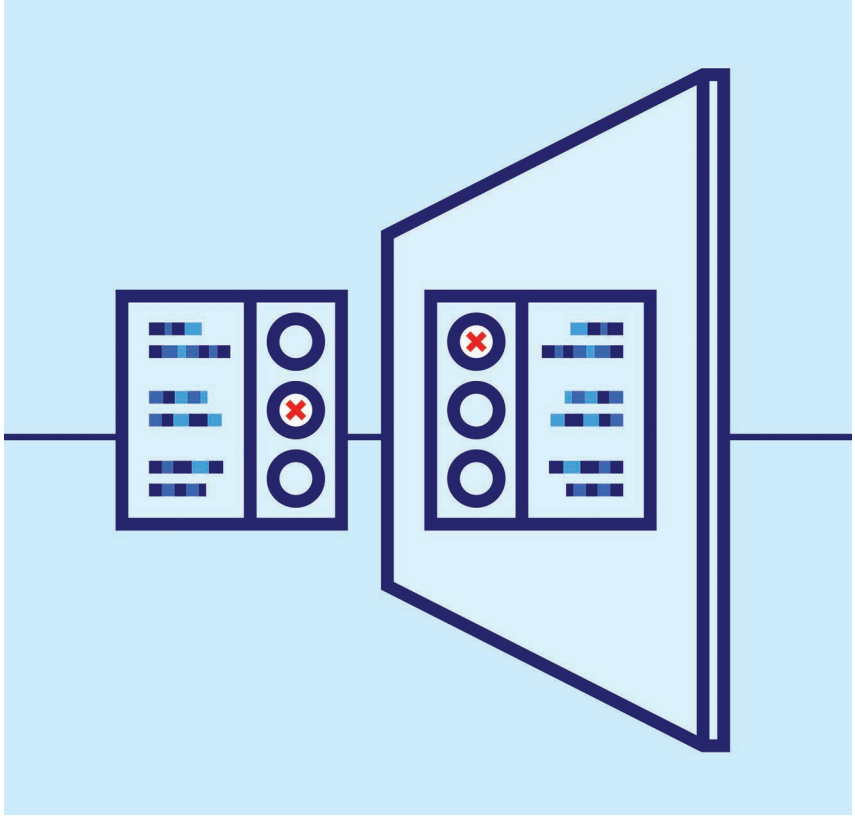
But I have yet to come across anybody who has vivid memories of the pandemics of 1957 or 1968. Countries did not resort to any mass-scale economic lockdowns, enforce any long-lasting school closures, ban sports events, or cut flight schedules deeply.

Today's pandemic has led to a deep (50 to 90 percent) reduction in flights, but during the earlier pandemics, aviation was marked by notable advances. On 17 October 1958, half a year after the end of the second pandemic wave in the West and about a year before the pandemic ended (in Chile, the last holdout), PanAm inaugurated its Boeing 707 jet service to Europe. And the Boeing 747, the first wide-body jetliner, entered scheduled service months before the last wave of the contemporary pandemic ended, in March 1970.

Why were things so different back then? Was it because we had no fear-reinforcing 24/7 cable news, no Twitter, and no incessant and instant case-and-death tickers on all our electronic screens? Or is it we ourselves who have changed, by valuing recurrent but infrequent risks differently? ■

POST YOUR COMMENTS AT spectrum.ieee.org/pandemics-oct2020





MAKING SURE VOTES COUNT

ELECTION EXPERTS were already concerned about the security and accuracy of the 2020 U.S. presidential election. Now, with the ongoing COVID-19 pandemic and the new risk it creates for in-person voting—not to mention the debate about whether mail-in ballots lead to voter fraud—the amount of anxiety around the 2020 election is unprecedented.

"Elections are massively complicated, and they are run by the most OCD individuals, who are process oriented and love color coding," says Monica Childers, a product manager with the nonprofit organization VotingWorks. "And in a massively complex system, the more you change things, especially at the last minute, the more you introduce the potential for chaos." But that's just what election officials are being forced to do.

Most of the conversation around election security focuses on the security of voting machines and preventing interference. But it's equally important to prove that ballots were correctly counted. If a party or candidate cries foul, states will have to audit their votes to prove there were no miscounts.

VotingWorks has built an open-source vote-auditing software tool called Arlo, and the organization has teamed up with the U.S. Cybersecurity and Infrastructure Security Agency to help states adopt the tool. Arlo helps election officials conduct a risk-limiting audit, which ensures that the reported results match the actual results. And because it's open source, all aspects of the software are available for inspection.

There are actually several ways to audit votes. You're probably most familiar with recounts, a process dictated by law that orders a complete recounting of ballots if an election is very close. But full recounts are rare. More often, election officials will audit the ballots tabulated by a single machine, or verify the ballots cast in a few precincts. However, those techniques don't give a representative sample of how an entire state may have voted.

This is where a risk-limiting audit excels. The audit takes a random sample of the ballots from across the area undergoing the audit and outlines precisely how the officials should proceed. This includes giving explicit instructions for choosing the ballots at random (pick the fourth box on shelf A and then select the 44th ballot down, for example). It also explains how to document a "chain of custody" for the selected ballots so that it's clear which auditors handled which ballots.

The random-number generator that Arlo uses to select the ballots is published online. Anyone can use the tool to select the same ballots to audit and compare their results. The software provides the data-entry system for the teams of auditors entering the ballot results. Arlo will also indicate how likely it is that the entire election was reported correctly.

The technology may not be fancy, but the documentation and attention to a replicable process is. And that's most important for validating the results of a contested election.

Arlo has been tested in elections in Michigan, Ohio, Pennsylvania, and a few other states. The software isn't the only way a state or election official can conduct a risk-limiting audit, but it does make the process easier. Childers says Colorado took almost 10 years to set up risk-limiting audits. VotingWorks has been using Arlo and its staff to help several states set up these processes, which has taken less than a year.

The upcoming U.S. election is dominated by partisanship, but risk-limiting audits have been embraced by both parties. So far, it seems everyone agrees that if your vote gets counted, the government needs to count it correctly. ■

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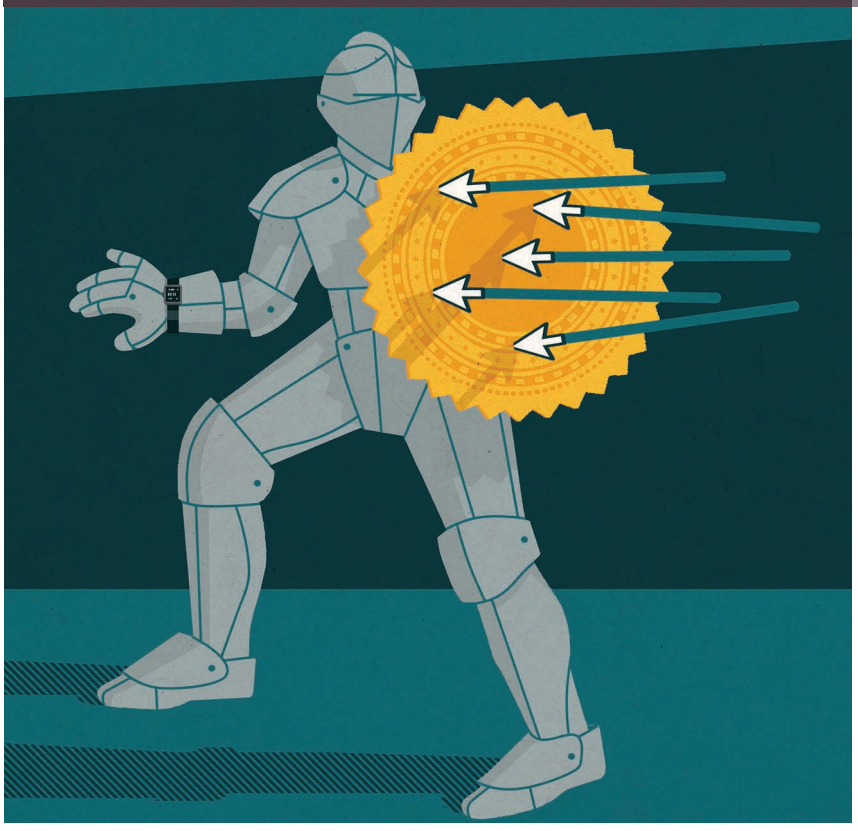
spectrum.ieee.org/countingvotes-oct2020

ILLUSTRATION BY Greg Mably



CERTIFIABLY SECURE IoT

AFTER UNBOXING a new gadget, few people stop to consider how things could go horribly wrong when it's plugged into the wall: A shorted wire could, for example, quickly produce a fire. We trust that our machines will not fail so catastrophically—a trust developed through more than a century of certification processes.

To display the coveted "approved" logo from a certification agency—for example, UL (from a U.S. organization formerly known as Underwriters Laboratories), CE (*Conformité Européenne*) in Europe, or Australia's Regulatory Compliance Mark—the maker of the device has to pull a production unit off the manufacturing line and send it to the testing laboratory to be poked and prodded. As someone who's been through that process, I can attest that it's slow, detailed, expensive—and entirely necessary. Many retailers won't sell uncertified devices to the public. And for good reason: They could be dangerous.

Sure, certification carries certain costs for both the manufacturer and consumer, but it prevents much larger expenses. It's now considered so essential that the biggest question these days isn't whether an electrical product is certified; it's whether the certification mark is authentic.

Certification assures us we can plug something in without worry that it will electrocute somebody or burn down the house. That's necessary but, in today's thoroughly connected era, insufficient. The consequences of plugging a compromised device into a home network are not as catastrophic as shock or fire, but they are still bad—and they've gone largely unappreciated.

We need to change our thinking. We need to become far more circumspect when we plug a new device into our networks, asking ourselves if its maker has given as much thought to cybersecurity as to basic electrical safety.

The answer to that question will almost invariably be no. A recent report detailing a security test of home Wi-Fi routers by Germany's Fraunhofer Institute FKIE showed *every unit tested* to have substantial security flaws, even when upgraded to the latest firmware.

Although security researchers plead with the public to keep the software on their connected devices up-to-date, it appears even that sort of digital hypervigilance isn't enough. Nor should this burden rest on the consumer's shoulders. After all, manufacturers don't expect consumers to do periodic maintenance on their blenders and electric toothbrushes to prevent them from catching fire or causing an electric shock.

The number of connected devices within our homes has grown by an order of magnitude over the last decade, enlarging the attack surfaces available to cyber-miscreants. At some point in the not-too-distant future, the risks will outweigh the benefits. Consumers will then lose their appetites for using such devices at all.

How could we prevent this impending security catastrophe? We can copy what worked once before, crafting a certification process for connected devices, one that tests and prods them and certifies only those that can resist—and stay ahead of—the black hats. A manufacturer does that by designing a device that can be easily and quickly updated—so easily that it can perform important updates unattended. Success here will mean that connected devices will cost more to design, and prices will rise for consumers. But security is never cheap. And the costs of poor security are so much higher. ■

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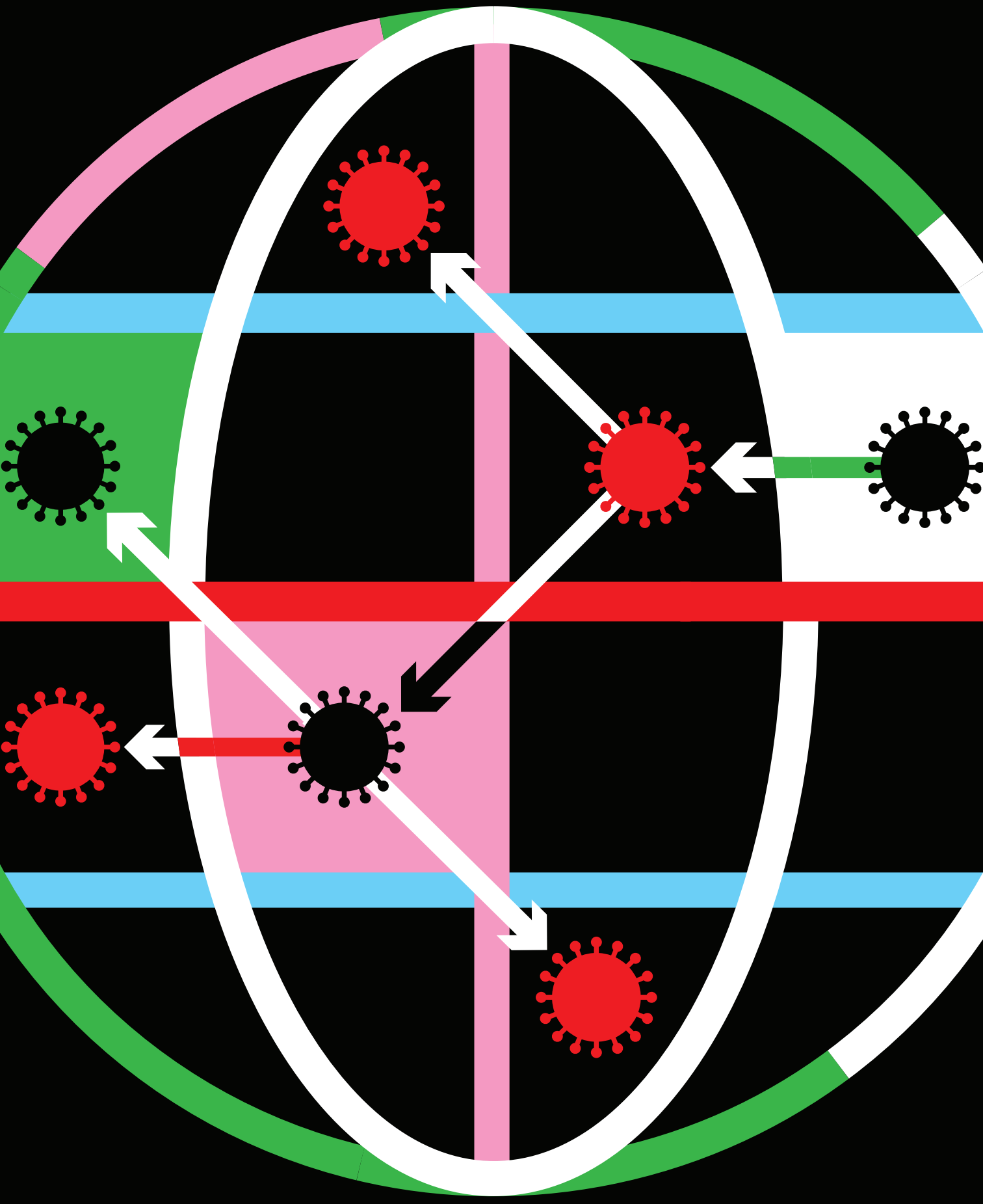
ILLUSTRATION BY Dan Page



COVID-19 HAS TAUGHT US THAT FORESIGHT AND TECH ARE A WINNING COMBINATION

PREPPING FOR THE NEXT BIG ONE

BY ELIZA STRICKLAND & GLENN ZORPETTE

ILLUSTRATIONS BY StoryTK

WHEN THE SPANISH FLU PANDEMIC swept across the globe in 1918, it ravaged a population with essentially no technological countermeasures. There were no diagnostic tests, no mechanical ventilators, and no antiviral or widely available anti-inflammatory medications other than aspirin. The first inactivated-virus vaccines would not become available until 1936. An estimated 50 million people died. • Today, a best-case scenario predicts 1.3 million fatalities from COVID-19 in 2020, according to projections by Imperial College London, and rapidly declining numbers after that. That in a world with 7.8 billion people—more than four times as many as in 1918. Many factors have lessened mortality this time, including better implementation of social-distancing measures. But technology is also a primary bulwark. • Since January of this year, roughly US $50 billion has been spent in the United States alone to ramp up testing, diagnosis, modeling, treatment, vaccine creation, and other tech-based responses,

according to the Committee for a Responsible Federal Budget. The massive efforts have energized medical, technical, and scientific establishments in a way that hardly anything else has in the past half century. And they will leave a legacy of protection that will far outlast COVID-19.

In the current crisis, though, it hasn't been technology that separated the winners and losers. Taking stock of the world's responses so far, two elements set apart the nations that have successfully battled the coronavirus: foresight and a painstakingly systematic approach. Countries in East Asia that grappled with a dangerous outbreak of the SARS virus in the early 2000s knew the ravages of an unchecked virulent pathogen, and acted quickly to mobilize teams and launch containment plans. Then, having contained the first wave, some governments minimized further outbreaks by carefully tracing every subsequent cluster of infections and working hard to isolate them. Tens of thousands of people, maybe hundreds of thousands, are alive in Asia now because of those measures.

In other countries, most notably the United States, officials initially downplayed the impending disaster, losing precious time. The U.S. government did not act quickly to muster supplies, nor did it promulgate a coherent plan of action. Instead states, municipalities, and hospitals found themselves skirmishing and scrounging for functional tests, for personal protective equipment, and for guidance on when and how to go into lockdown.

The best that can be said about this dismal episode is that it was a hard lesson about how tragic the consequences of incompetence can be. We can only hope that the lesson was learned well, because there will be another pandemic. There will always be another pandemic. There will always be pathogens that mutate ever so slightly, making them infectious to human hosts or rendering existing drug treatments ineffective. Acknowledging that fact is the first step in getting ready—and saving lives.

The cutting-edge technologies our societies have developed and deployed at lightning speed are not only helping to stem the horrendous waves of death. Some of these technologies will endure and—like a primed immune system—put us on a path toward an even more effective response to the next pandemic.

Consider modeling. In the early months of the crisis, the world became obsessed with the models that forecast the future spread of the disease. Officials relied on such models to make decisions that would have mortal consequences for people and multibillion-dollar ones for economies. Knowing how much was riding on the curves they produced, the modelers who create projections of case numbers and fatalities pulled out all the stops. As Matt Hutson recounts in "The Mess Behind the Models" [p. 30], they adapted their techniques on the fly, getting better at simulating both a virus that nobody yet understood and the maddening vagaries of human behavior.

In the development of both vaccines and antiviral drugs, researchers have committed to timelines that would have seemed like fantasies a year ago. In "AI Takes Its Best Shot" [p. 24], Emily Waltz describes how artificial intelligence is reshaping vaccine makers' efforts to find the viral fragments that trigger a protective immune response. The speed record for vaccine development and approval is four years, she writes, and that honor is held by the mumps vaccine; if a coronavirus vaccine is approved for the general public before the end of this year, it will blow that record away.

Antiviral researchers have it even tougher in some ways. As Megan Scudellari writes, hepatitis C was discovered in 1989—and yet the first antiviral effective against it didn't become available until *26 years* later, in 2015. "Automating Antivirals" [p. 44] describes the high-tech methods researchers are creating that could cut the current drug-development timeline from five or more years to six months. That, too, will mean countless lives saved: Even with a good vaccine, some people inevitably become sick. For some of them, effective antivirals will be the difference between life and death.

Beyond Big Pharma, engineers are throwing their energies into a host of new technologies that could make a dif-

ference in the war we're waging now and in those to come. For example, this pandemic is the first to be fought with robots alongside humans on the front lines. In hospitals, robots are checking on patients and delivering medical supplies; elsewhere, they're carting groceries and other goods to people in places where a trip to the store can be fraught with risk. They're even swabbing patients for COVID-19 tests, as Erico Guizzo and Randi Klett reveal in a photo essay of robots that became essential workers [p. 36].

Among the most successful of the COVID-fighting robots are those buzzing around hospital rooms and blasting floors, walls, and even the air with ultraviolet-C radiation. Transportation officials are also starting to deploy UV-C systems to sanitize the interiors of passenger aircraft and subway cars, and medical facilities are using them to sterilize personal protective equipment. The favored wavelength is around 254 nanometers, which destroys the virus by shredding its RNA. The problem is, such UV-C light can also damage human tissues and DNA. So, as Mark Anderson reports in "The Ultraviolet Offense" [p. 50], researchers are readying a new generation of so-called far-UV sterilizers that use light at 222 nm, which is supposedly less harmful to human beings.

When compared with successful responses in Korea, Singapore, and other Asian countries, two notable failures in the United States become clear: testing and contact tracing. For too long, testing was too scarce and too inaccurate in the United States. That was especially true early on, when it was most needed. And getting results sometimes took two weeks—a devastating delay, as the SARS-CoV-2 virus is notorious for being spread by people who don't even know they're sick and infectious. Researchers quickly realized that what was really needed was something "like a pregnancy test," as one told Wudan Yan [p. 60]: "Spit on a stick or into a collection tube and have a clear result 5 minutes later." Soon, we'll have such a test.

Digital contact tracing, too, could be an enormously powerful weapon, as Jeremy Hsu reports in "The Dilemma of Contact-Tracing Apps" [p. 56]. But it's a tricky one to deploy. During the pandemic, many municipalities have used some form of tracing. But much of it was low-key and low-tech—sometimes little more than a harried worker contacting people on a list. Automated contact tracing, using cloud-based smartphone apps that track people's movements, proved capable of rapidly suppressing the contagion in places like China and South Korea. But most Western countries balked at that level of intrusiveness. Technical solutions that trade off some surveillance stringency for privacy have been developed and tested. But they couldn't solve the most fundamental problem: a pervasive lack of trust in government among Americans and Europeans.

It has been 102 years since the Spanish flu taught us just how bad a global pandemic can be. But almost nobody expects that long of an interval until the next big one. Nearly all major infectious outbreaks today are caused by "zoonotic transfer," when a pathogen jumps from an animal to human beings. And a variety of unrelated factors, including the loss of natural habitats due to deforestation and the rapid growth of livestock farming to feed industrializing economies, is stressing animal populations and putting them into more frequent contact with people.

We're unlikely to halt or even measurably slow such global trends. What we can do is make sure we have suitable technology, good governance, and informed communities. That's how we'll mount a tougher response to the next pandemic. ■

TROUBLE BREWING: When forests are cut down to make way for agriculture and livestock is crowded together on farms, animal and human populations come into contact. Then pathogens that typically sicken animals have opportunities to mutate and take hold in human hosts. This "zoonotic transfer" is the cause of most outbreaks of new infectious diseases.

TOP: LEO CORREA/AP; BOTTOM: DAMIEN MEYER/AFP/GETTY IMAGES

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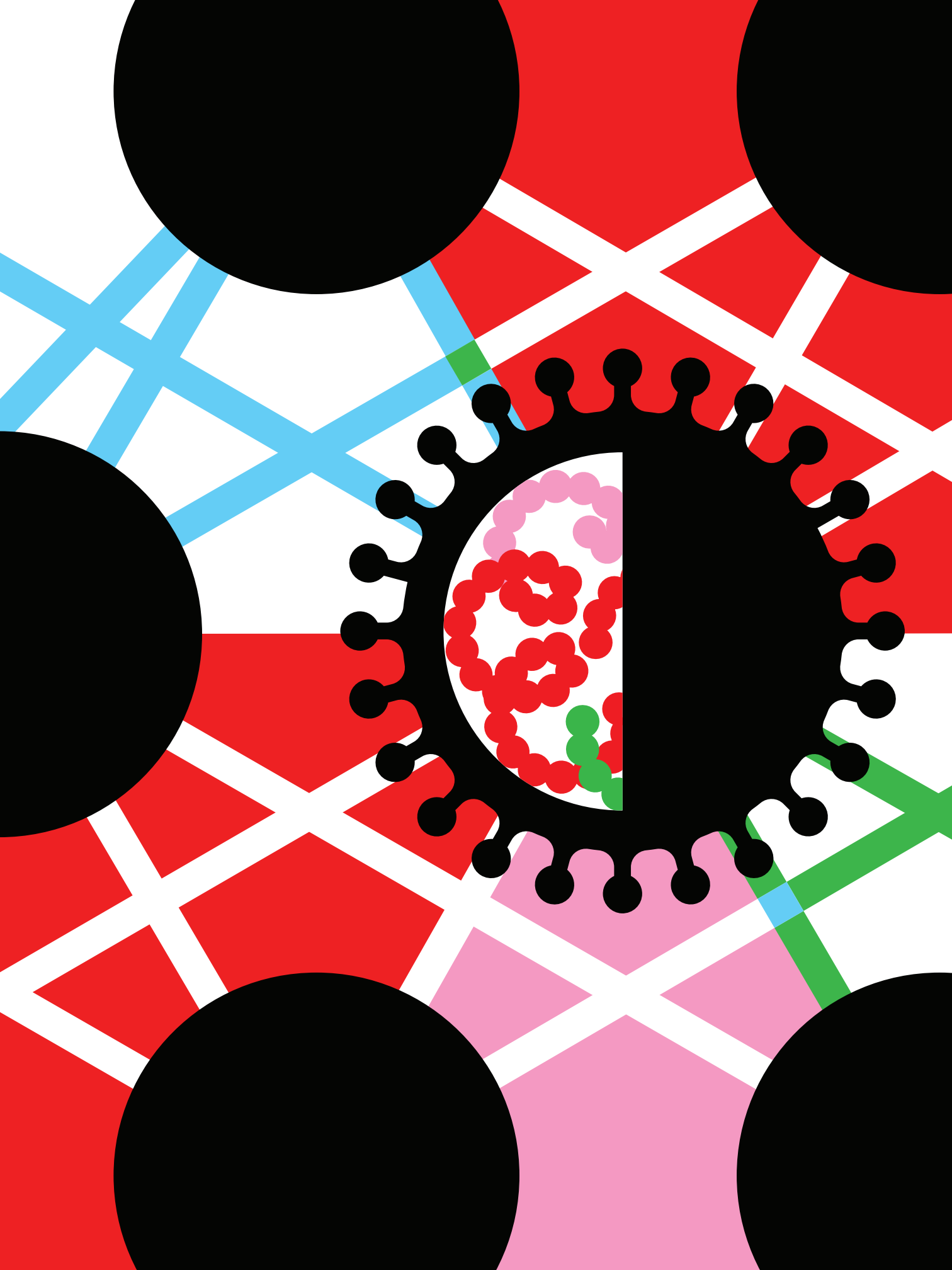


WHAT AI CAN—AND CAN'T—DO IN THE RACE FOR A CORONAVIRUS VACCINE

AI TAKES ITS BEST SHOT

BY EMILY WALTZ

IN AN ACHIEVEMENT that would have startled biomedical researchers merely a year ago, vaccines against COVID-19 were already being tested in humans this past March, less than three months after the initial outbreak was identified in China. Many of those vaccines owed their speedy start to the power of artificial intelligence (AI). • The feat is a promising and remarkable turn in the 200-year-plus history of immunization. The experience may revolutionize the way vaccines are created, potentially saving countless lives in epidemics yet to come. • As of early September, there were 34 vaccine candidates being tested in humans, according to the World Health Organization (WHO). Another 145 candidates were being tested in animals or in the lab, says WHO, which keeps a running worldwide list. Those are astonishing numbers, considering that less than a year ago no one had heard of the novel coronavirus, now known as SARS-CoV-2, which causes the respiratory disease COVID-19. It typically takes many years, or even decades, to develop a vaccine; until now, the speed record was

ILLUSTRATION BY StoryTK

held by the mumps vaccine, which went from a collected sample to a marketed product in about four years.

It's no wonder that research is sprinting ahead. Our societies and economies likely won't return to normal until a highly effective vaccine has been administered to a substantial portion of the planet's population. The search for a vaccine is now a vast undertaking, involving thousands of researchers at hundreds of laboratories around the world spending billions of dollars. It's like a moon shot in its magnitude, ambition, and intensity.

Laboratories are pursuing at least eight different types of vaccine. These include traditional ones based on inactivated viruses, as well as new, more experimental ones involving the use of genetic material—so-called DNA and RNA vaccines—as well as others based on special proteins or other biological agents.

At stake are not only human lives but also a piece of a global vaccine market that was estimated at US $35 billion even before COVID-19. Governments, philanthropies, and pharmaceutical companies have been spending accordingly. In July, the U.S. government agreed to pay pharmaceuticals giant Pfizer and German biotech firm BioNTech nearly $2 billion for 100 million doses of a vaccine, if and when it becomes available. Other major vaccine initiatives worldwide also have funding in the 10 figures.

Machine-learning systems and computational analyses have played an important role in the vaccine quest. These tools are helping researchers understand the virus and its structure, and predict which of its components will provoke an immune response—a key step in vaccine design. They can help scientists choose the elements of potential vaccines and make sense of experimental data. They also help scientists track the virus's genetic mutations over time, information that will determine any vaccine's value in the years to come.

"AI is a powerful catalyst," says Suchi Saria, a professor at the Johns Hopkins Whiting School of Engineering who directs the university's machine-learning and health care lab. AI enables scientists "to draw insights by combining data from multiple experimental and real-world sources," she explains. These data sets are often so messy and challenging that scientists historically haven't even attempted these sorts of analyses, she adds.

As AI tools become more powerful, researchers are anticipating a time when computational methods could help scientists solve our most vexing vaccine challenges—such as finding an effective HIV vaccine, or creating a flu vaccine that's good for more than a year.

The excitement surrounding new computational techniques comes with a caveat: AI cannot replace or speed up the most crucial, time-consuming aspect of vaccine development. Animal and human trials must happen via pure human effort, with thousands of scientists, health care workers, and participants logging their experience with a vaccine in real time. "Computation helps you optimize your chances of success, but ultimately you have to roll up your sleeves and do it in the lab," says Jacob Glanville, founding partner at Distributed Bio and its subsidiary, Centivax, which are developing vaccines for flu, HIV, and other pathogens using computational bioengineering.

Still, in the quest for a COVID vaccine, AI has done more than it ever has before. And it is just part of a larger suite of computational tools that are revolutionizing vaccine R&D. Few people may be thinking about the next pandemic, but researchers are already starting to understand how these tools will do quite a bit more the next time around.

MODERN VACCINE design is a hugely information-intensive endeavor, starting with the reams of data needed to understand both the virus and our immune system's reaction to it. There are more than 200 viruses known to infect human beings, and each of them is distinct in its mechanisms, behavior, and ultimately, its cures.

Though they vary in the details, viral attacks on the body mostly start off the same way. When a virus gets into the body—say, through the mouth or nose—it infiltrates healthy cells by binding to receptors on the cells' surfaces. The virus can then hijack the cells' machinery to make more copies of itself, and an infection ensues.

Putting a halt to all this is the job of the immune system, which hunts and destroys pathogens such as viruses and bacteria that cause disease. As a first step, the immune system sends a variety of basic weapons to the infection in what's called the innate immune response.

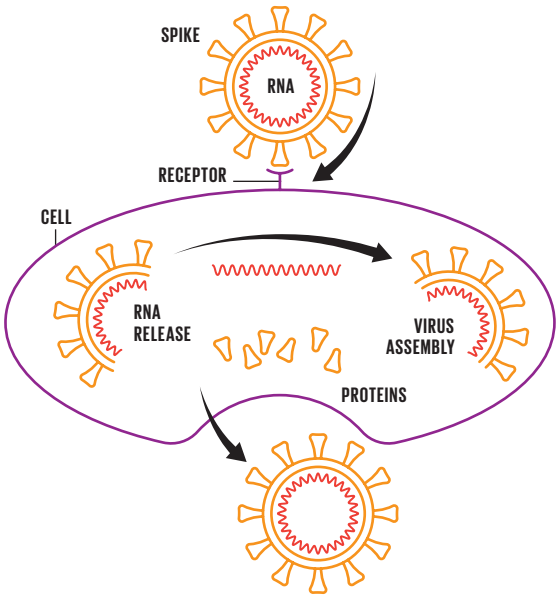
If that's not enough to control the infection—for example, if the pathogen is new to our bodies and the generalized weapons don't work—the immune system's adaptive immune response brings in the bigger guns. Adaptive immunity depends on two types of white blood cells, called B cells and T cells. B cells produce specialized proteins called antibodies, which bind to the pathogen and prevent it from entering healthy cells. T cells, meanwhile, can destroy cells that have been infected by the virus, to keep them from making more copies of it.

It takes days for the adaptive immune response to get revved up enough to begin wiping out a new virus. Our bodies have B cells and T cells tailored for nearly every pathogen the world can throw at us, but it takes time for the right immune cells to find the invader and multiply. In the meantime, we get sick.

The good news is that while this war is raging, the immune system also produces memory B and T cells, which make a record of the battles. If we get exposed to the same pathogen again, the immune system has an arsenal at the ready and responds much more rapidly. We may experience mild symptoms, or none at all.

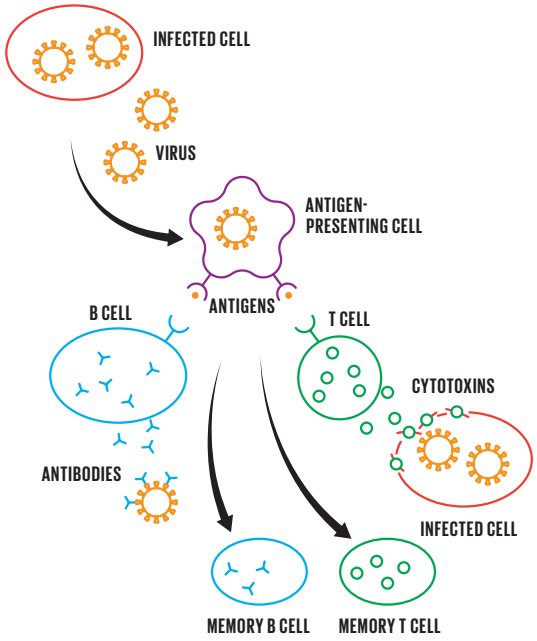
The goal of a vaccine, then, is to expose

VIRUS VS. IMMUNE SYSTEM



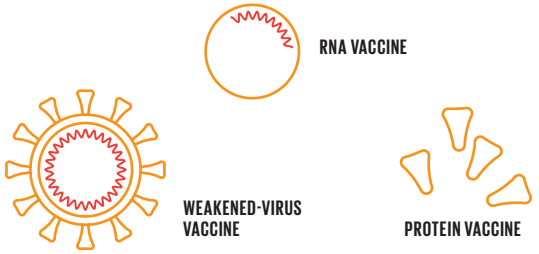
The Attack

The coronavirus has spikes that bind to receptors on the surface of certain human cells. The virus then fuses with the cellular membrane and releases its RNA genome into the cell. Next, the cell churns out copies of that RNA, as well as the structural proteins needed to assemble new viral particles—which are released into the body.



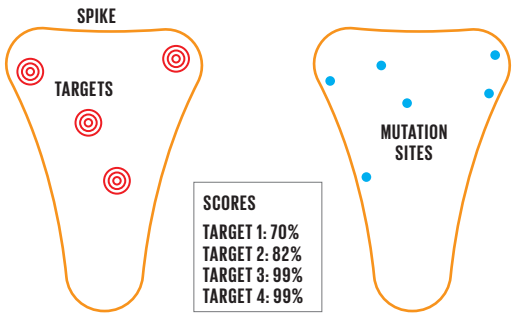
The Defense

In the body's adaptive immune response, specialized cells engulf the virus and present fragments of it, called antigens, to activate immune cells. B cells begin to make antibodies that bind to viral particles and prevent them from attaching to healthy cells, while T cells destroy cells that have already been infected. Meanwhile, memory B and T cells take note of the antigens, ensuring that the body will respond quickly if it encounters the coronavirus again.



Raising the Alarm

The task of vaccines is to present antigens that will trigger this immune response without making the person sick. Vaccines come in various forms, including weakened forms of the entire virus, specific fragments of the virus, and either DNA or RNA that causes a cell to make specific fragments of the virus.



AI Assistance

One role for AI in vaccine design is to study the proteins that make up the virus, which include the spike protein. By examining its complex structure, an AI system can sort through thousands of components to identify those that are most likely to trigger a robust immune response. What's more, viruses are always mutating. AI systems need to identify components that are unlikely to mutate, to ensure that a vaccine will remain effective over time.

ILLUSTRATION BY Chris Philpot

ALLIANCE	NATIONS	VACCINE TYPE	STATUS (Phase 1, 2, 3, or Approval)	FUNDING, US $	MAIN FUNDERS
University of Oxford, AstraZeneca	United Kingdom, United States	Viral-vector (adenovirus)	Phase 3	$1.25 billion	U.S. and British governments
Sinovac Biotech	China	Inactivated virus	Phase 3	$15 million	Advantec Capital, Vivo Capital
Wuhan Institute of Biological Products, Sinopharm	China	Inactivated virus	Phase 3	$142 million (with Beijing Institute of Biological Products)	Chinese government
Beijing Institute of Biological Products, Sinopharm	China	Inactivated virus	Phase 3	$142 million (with Wuhan Institute of Biological Products)	Chinese government
Moderna, National Institute of Allergy and Infectious Diseases	United States	RNA vaccine (mRNA)	Phase 3	$2.48 billion	U.S. government
Inovio Pharmaceuticals/ International Vaccine Institute	United States	DNA vaccine	Phase 1/2	$97 million	U.S. government (Department of Defense) and others
CureVac	Germany	RNA vaccine (mRNA)	Phase 2	$440 million	$355 million from German government plus $85 million loan from European Investment Bank
BioNTech, Fosun Pharmaceutical, Pfizer	United States, China, Germany	RNA vaccine (mRNA)	Phase 3	$1.95 billion	U.S. government
Gamaleya Research Institute of Epidemiology and Microbiology	Russia	Viral-vector (adenoviruses)	Approved for limited use	NA	Russian government
CanSino Biologics, Institute of Biotechnology at the Academy of Military Medical Sciences (China)	China	Viral-vector (adenovirus)	Approved for limited use	NA	Chinese government

SELECT COVID-19 VACCINE-DEVELOPMENT PROJECTS

SOURCES: WORLD HEALTH ORGANIZATION, UNIVERSITY OF MICHIGAN HEALTH LAB, THE LANCET, TRIALSITE NEWS, BARRON'S, REUTERS, COUNCIL ON FOREIGN RELATIONS, THE NEW YORK TIMES, PHARMAPHORUM, FIERCE PHARMA, THE WALL STREET JOURNAL, DIGITAL JOURNAL, GENETIC ENGINEERING & BIOTECHNOLOGY NEWS, INTELLIZENCE, INOVIO PHARMACEUTICALS

the body to a pathogen without making us sick so that the immune system is primed to fight it on any subsequent exposure. This can be done by exposing the body to specific pieces of a virus or weakened versions of it. Crucially, the vaccine must include key parts of the virus, called antigens, that are immunogenic, meaning that they're recognizable to B cells and T cells and will therefore trigger the desired adaptive immune response.

When faced with a new pathogen, the first question for vaccine designers is: Which parts of it are the most immunogenic? A typical virus consists of genetic material, either DNA or RNA, encapsulated by one or more layers of proteins. The outer membrane is often studded with so-called spike proteins, which enable the virus to bind to receptors on a host cell and inject its payload of genetic material. For this reason, spike proteins are a typical target for vaccines. If the immune system creates antibodies that disable the spike protein, the virus cannot break into cells.

However, for any given virus there are tens of thousands of different subcomponents of the outer proteins that the immune system can recognize, and therefore tens of thousands of different possibilities for vaccine targeting. This is a prime opportunity for AI. Machine-learning tools can predict, based on training data sets from known pathogens, which pieces of the virus the immune system is most likely to recognize.

Armed with this information, immunologists can design vaccines around a more manageable number of potential targets. The targets are then integrated into vaccine candidates and tested in animals to see if they provoke a good immune response. Machine learning "gives you a numerical score," says Tayab Waseem, a public policy fellow at the American Association of Immunologists and director of medical informatics and AI integration at Wagner Macula & Retina Center, based in Norfolk, Va. "Everything over a certain score—say, 99 percent—I'll be willing to go into the lab to test out."

In the early weeks of the pandemic, a team of computer scientists led by Russ

Altman and Binbin Chen, at the Stanford Institute for Human-Centered Artificial Intelligence (HAI), used machine learning to do just that. Using the neural-network algorithms NetMHCpan-4.0 and MARIA, and a linear-regression model called DiscoTope, the researchers came up with a list of targets on the novel coronavirus that were most likely to provoke an immune response. These targets, or epitopes, are components of the virus that B cells and T cells will likely recognize.

As expected, many of the system's top recommended targets were located on the virus's spike protein. Chen's team recommended, in a paper on the preprint server bioRxiv, that these epitopes be included in the design of COVID-19 vaccines. "We feel pretty confident that we'll get an immune response at the cellular level against what we predicted as targets," says Chen. "But there is a big gap between cellular response and clinical response," he adds.

Chen's machine-learning tools are among several dozen that have been built over the years to aid immunology work. In the past, machine learning has been a "minor sidekick" in vaccine development, according to Chen. But for COVID-19, "people in both academic and industry labs ran more computational studies," he says. "I suspect that all the pharma companies who developed a vaccine also ran a computational analysis."

Having identified a target on the virus's surface, researchers can then develop a vaccine. If the plan is to use an inactivated virus as a vaccine, for example, researchers will grow the live virus in the lab and kill it using heat, radiation, or a chemical method so that it can't replicate when injected into the body. Then researchers must make sure that the key immunogenic components weren't damaged when the virus was killed, as those parts must be intact in order to provoke an immune response. The next steps are to test the vaccine in the lab, then in small animals, and finally in humans.

TO TRAIN SOFTWARE to sift through target sites on a virus, it's important to first understand the three-dimensional structure of viral proteins. Viral proteins are made of linear chains of chemicals called amino acids, which spontaneously fold into compact, ribbonlike structures. Vaccine developers must choose targets on the virus's outer layer that face outward, so that they're physically accessible to immune-system weaponry.

When the pandemic hit, researchers at the University of Basel, in Switzerland, used a protein-modeling tool called Swiss-Model to predict the structures of the proteins on the outer surface of the SARS-CoV-2 virus. Their predictions were later shown to be consistent with the virus's actual protein structures. Similarly, the London-based AI company DeepMind applied its neural network, AlphaFold, to predict the three-dimensional shape of SARS-CoV-2 proteins based on the virus's genetic sequence.

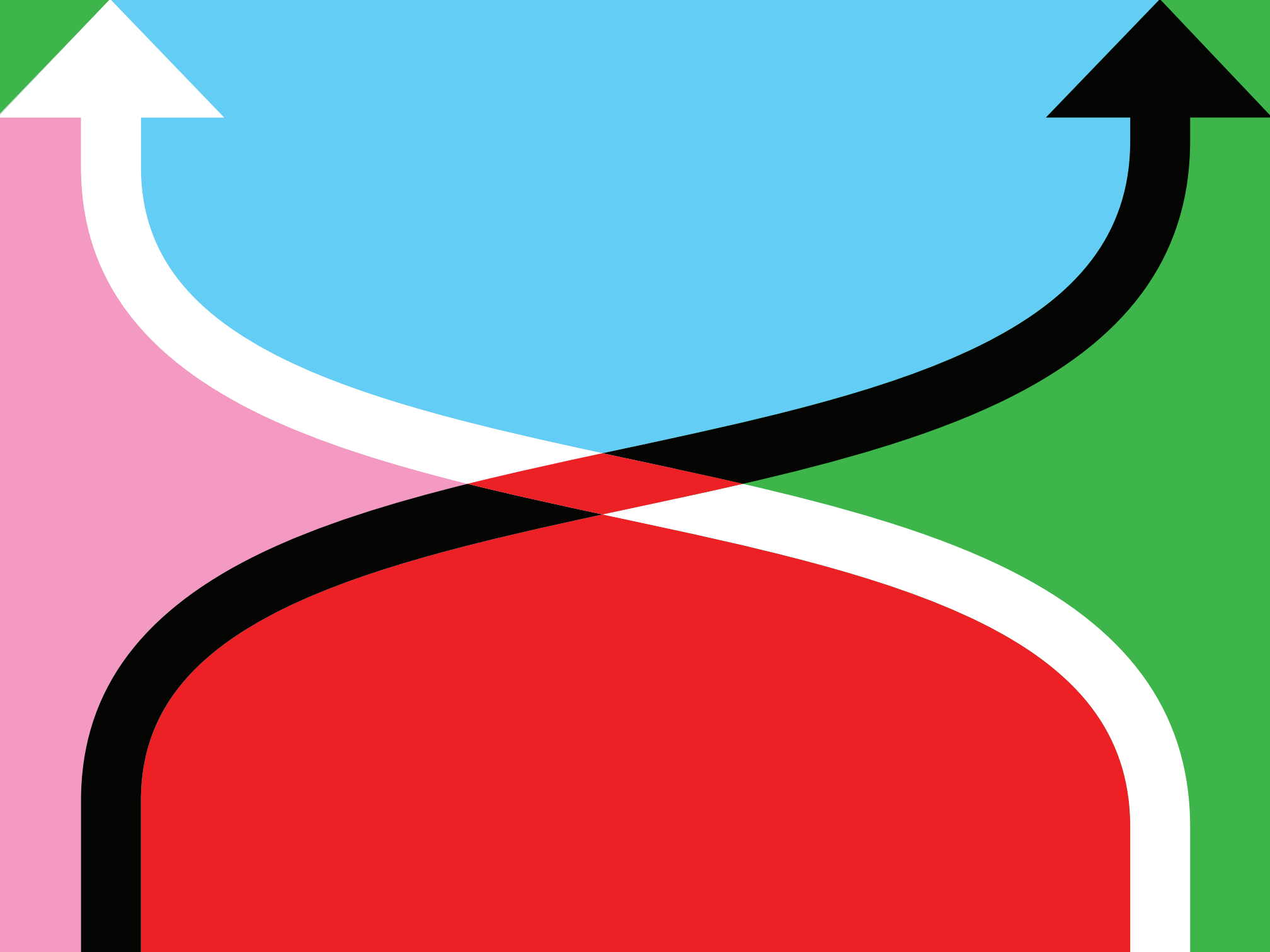
DEEPMIND APPLIED ITS NEURAL NETWORK, ALPHAFOLD, TO PREDICT THE THREE-DIMENSIONAL SHAPE OF SARS-COV-2 PROTEINS BASED ON THE VIRUS'S GENETIC SEQUENCE.

Despite these successes, not all researchers are enthusiastic about the promise of AI for this component of vaccine R&D. They note that, AI or no AI, the spike protein was an obvious target, based on knowledge of other coronaviruses and experimental work with SARS-CoV-2. "There are a lot of methods to identify immunogenic regions of pathogens that do not require artificial intelligence," says Glanville of Distributed Bio. Algorithms that predict such targets are nice to have, he says, but probably not necessary in the case of COVID-19. "AI still has the challenge of proving that it works better than simpler methods," such as serological screening, epitope mapping, and structural biology, he says.

But AI can do much more than zero in on the immunogenic sites on a virus. Many vaccine developers are already using computational tools to design and synthesize the genetic components of DNA-based vaccines. Inovio Pharmaceuticals in San Diego, one of the 34 groups with a COVID-19 vaccine in human trials, is one example.

"The team at Inovio waited enthusiastically for the genetic sequence of the virus to be posted online," says Kate Broderick, senior vice president of R&D at Inovio. "When it was uploaded by the Chinese authorities on January 10, our scientists immediately entered the sequence into our algorithm, and within 3 hours they had a fully designed and optimized DNA medicine vaccine," she says.

Inovio's DNA vaccines work by mimicking a part of the genetic sequence of the pathogen. These so-called nucleic-acid vaccines contain segments of genetic instructions, in the form of DNA or RNA, that code for a key immunogenic component of the virus. When the nucleic acid is inserted into | CONTINUED ON PAGE 66



TOO MANY OF THE COVID-19 MODELS LED POLICYMAKERS ASTRAY. HERE'S HOW TOMORROW'S MODELS WILL GET IT RIGHT

THE MESS BEHIND THE MODELS

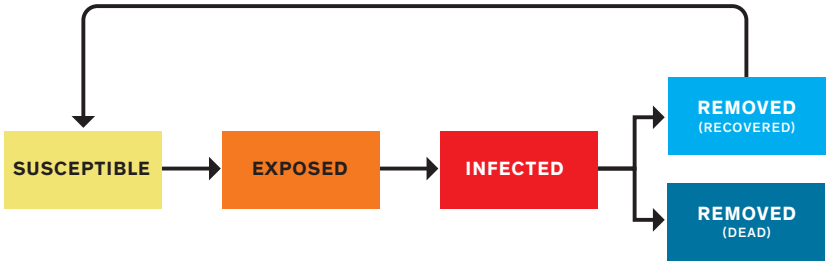
BY MATTHEW HUTSON

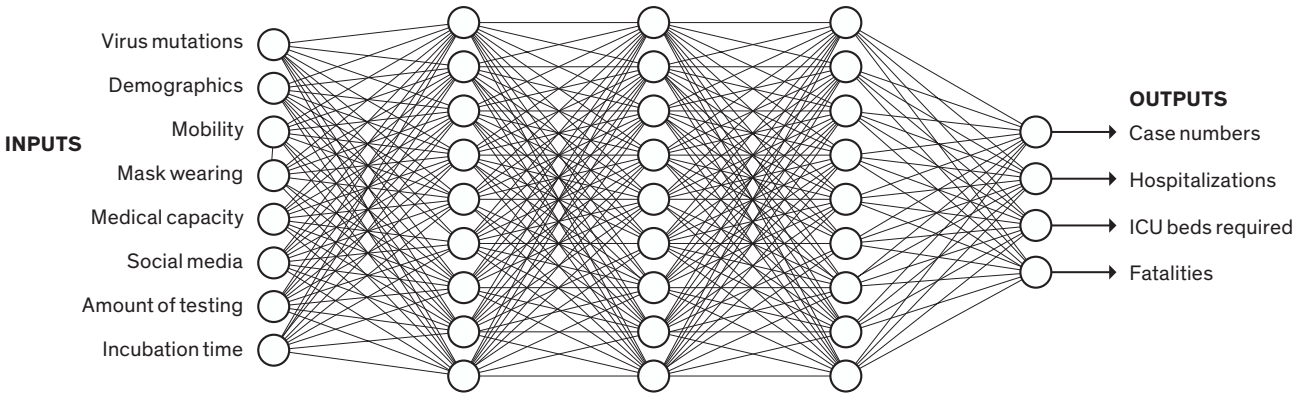
IF YOU WANTED TO "FLATTEN THE CURVE" IN 2019, you might have been changing students' grades or stamping down a rug ripple. Today, that phrase refers only to the vital task of reducing the peak number of people concurrently infected with the COVID-19 virus. Beginning in early 2020, graphs depicting the expected number of infections spread through social networks, much like the virus itself. We've all become consumers of epidemiological models, the mathematical entities that spit out these ominous trend lines. • Such models have existed for decades but have never received such widespread attention. They're informing public policy, financial planning, health care allocation, doomsday speculation, and Twitter hot takes. In the first quarter of 2020, government leaders were publicly parsing these computational speculations, making huge decisions about whether to shut down schools, businesses, and travel. Would an unchecked outbreak kill millions, or fizzle out? Which interventions would help the most? How sure could we be of any forecast? Models disagreed, and some people pointed to whichever curve best supported their predilections. It didn't help that the researchers building the models were still figuring out what the heck they were doing.

ILLUSTRATION BY StoryTK

THREE FLAVORS OF MODELS

A SEIRS MODEL puts people into categories: susceptible (S), exposed (E), infected (I), removed from the susceptible population (R), and potentially back to susceptible (S) again, depending on whether a recovered person has immunity from the disease. The modeler's job is to define the equations that determine how people move from one category to the next. Those equations depend on a wide variety of parameters drawn from biology, behavior, politics, the economy, the weather, and more.





DATA-DRIVEN MODELS don't sort people into categories; they just crunch numbers. Some data-driven models use neural networks. In this simplified example, a trained neural network infers complex relationships among a broad set of inputs to predict certain outputs. A neural network is a "black box," as the modeler can't know or understand the thousands of parameters being used in the prediction.

There's more than one way to model an epidemic. Some approaches are pure mathematical abstraction, just trying to get the lines right. Some re-create society in silicon, down to the person. Some combine several techniques. As modelers—a mix of computer scientists, epidemiologists, physicians, statisticians—fumble their way through the darkness of this pandemic, they pull tools off shelves, modify them, and create new ones, adapting as they learn what works and as new information emerges.

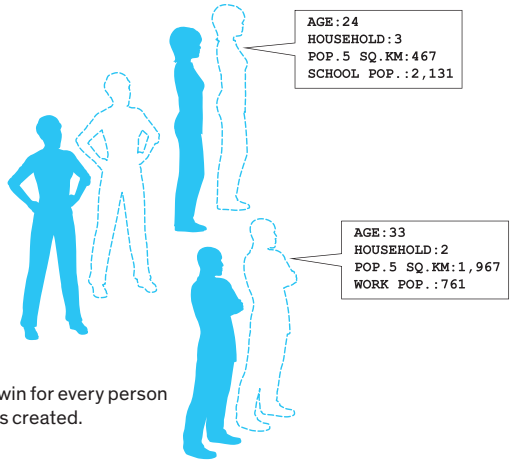
They hope, of course, to help quell the current outbreak. But their larger goal is to have tools in place to model any future disease, whether it's a seasonal flu or the next big bug. "In some ways, forecasting epidemics was still in its infancy when this pandemic started spreading," said biologist Lauren Ancel Meyers in June. Meyers, the head of the COVID-19 Modeling Consortium at the University of Texas at Austin, added, "And it has matured quite a bit over the last two or three months." So what has worked—and what hasn't?

THE MOST COMMON approach to modeling an epidemic is what's called a compartmental model. You divide the population into several categories and write mathematical rules that dictate how many people move from one category to another at each tick of the model's clock. First, everyone is susceptible. They're in the S compartment. Then some people become infected (I), and later they're removed (R) from the pathogen's path, through either recovery or death. These models are sometimes called SIR models. Variations include a group that's exposed (E) to the pathogen but not yet contagious—SEIR models. If postrecovery immunity is temporary, you might recycle recovered people back to S, making it an SIRS (or SEIRS) model. At its most basic, the model is a handful of numbers indicating how many people are in each compartment, plus differential equations governing the transitions between compartments. Each equation has adjustable parameters—the knobs that set the flow rates.

A graph over time of the removed (R) population usually resembles a sigmoid or elongated S-curve, as the numbers of dead or recovered rise slowly at first, then more steeply, then gradually plateau. The susceptible population (S) follows the same trend but downward, falling slowly, then quickly, then slowly. Around where the lines cross, at their steepest sections,

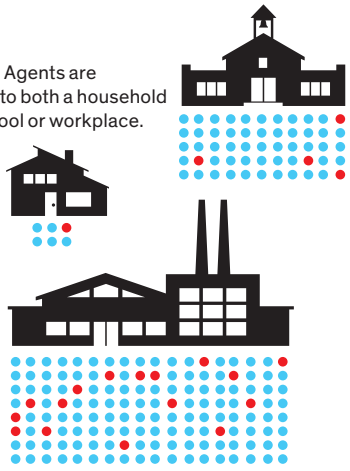
ILLUSTRATIONS BY Mark Montgomery

IN AGENT-BASED MODELS, a simulated world accounts for the actions of all the people in a given population. Researchers at the University of Sydney created a COVID-19 model with three layers: demographics, with a digital twin for every person counted by the census; mobility, with the agents moving among households and schools and offices; and the characteristics of the disease.

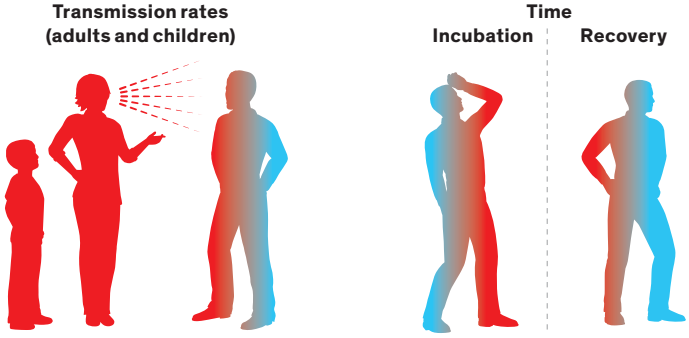


LAYER 1
Demographics: A digital twin for every person represented in the census is created.

LAYER 2
Mobility: Agents are assigned to both a household and a school or workplace.



LAYER 3
Disease: The virus spreads based on transmission rates and how the disease progresses in individuals.



the line for currently infected (I) forms a hump. This is the curve we want to flatten, lowering the hump's peak and stretching it out, to lighten the load on hospitals at any given time.

Forecasting the shapes of these lines requires getting the equations right. But their parameters—which can change over time—depend on such varied factors as biology, behavior, politics, the economy, and the weather. Compartmental models are the gold standard, says Sunetra Gupta, an epidemiologist at the University of Oxford, but "it's a question of what do you strap onto it."

A prominent group employing a compartmental model is the Institute for Health Metrics and Evaluation (IHME), at the University of Washington, in Seattle. The team actually started out early in the pandemic with a completely different approach called a curve-fitting model. Because the outbreak in the United States lagged behind those in some other countries, this model assumed that the U.S. curve would resemble those prior curves. According to Theo Vos, an epidemiologist at the University of Washington, the aim was to predict the peak in hospital use with curves for China, Italy, and Spain. In late March, with just a few thousand cumulative deaths in the United States, the IHME accurately predicted a rise to about 50,000 over the next four weeks. By April, policymakers and the media were lavishing the IHME model with attention. Dr. Deborah Birx, the White House's Coronavirus Response Coordinator, and her team talked with the IHME group almost daily.

But the U.S. curve didn't flatten as quickly as the IHME model anticipated. In mid-April, for example, it predicted that the death toll would reach 60,000 in mid-May, while the actual number turned out to be around 80,000. As the weeks went on, the model began to garner harsh criticism from some epidemiologists and biostatisticians for failing to account for all sources of uncertainty, and for being based on the unlikely assumption that social-distancing policies would be as extensive and effective in the United States as they were in other countries. (Vos notes, "If you read our documentation that we published on our website with model results at the time, you will see that this assumption was clearly stated.") By the end of April, IHME director Christopher Murray was admitting that his model was "orders of magnitude more optimistic" than others, while still defending its usefulness. In early May, the IHME team added an SEIR model as

ILLUSTRATIONS BY Chris Philpot

a central component of their continually evolving system.

Instead of manually defining the parameters in their SEIR equations, the team let computers do it, using Bayesian statistical methods, which estimate the likelihood of various causes for a given outcome. The group regularly receives statistics on COVID-19's course: how long it's taking people to show symptoms, how many people are reporting to hospitals, how many people are dying. They also collect data on factors such as mask wearing (from online surveys) and, as a proxy for social distancing, mobility (from anonymized phone location tracking).

"FORECASTING WAS IN ITS INFANCY WHEN THIS PANDEMIC STARTED."

—L.A. Meyers, University of Texas at Austin

To tune the SEIR model, the system tests different model parameters to see which ones result in predictions that best match the recent data. Once the best parameters are chosen, the SEIR model uses them, along with expected changes in the other inputs, to forecast infections and deaths over the next several months. Bayesian techniques incorporate uncertainty, so the model runs a thousand times with slightly different control-knob settings, creating a range of possible outcomes.

One of the most important knobs is reproduction number, or R (not the same as the R in SEIR). R is the number of people each infected person is expected to infect. Typically, if R is above 1.0, the early epidemic grows exponentially. Below 1.0, it fades away. "We learned how to tame an SEIR model," Vos says. "They're very reactive to small changes. The tendency is to go exponential." In a completely abstract model, slight differences in parameters such as R can cause wildly different outcomes, unbound by real-world social and environmental contingencies. Without using statistics to ground parameter setting in hard data, Vos says, "your cases go completely bonkers."

OTHERS HAVE ALSO COMBINED compartmental models with machine learning. One model called YYG has done well on a hub that feeds forecasts to the U.S. Centers for Disease Control and Prevention (CDC). The YYG model is run solely by an independent data scientist with a master's degree in computer science from MIT named Youyang Gu. His model is very simple: The only data it uses is daily deaths. From this statistic, it sets parameters—including reproduction number, infection mortality rate, and lockdown fatigue—using a grid search. For each parameter, it considers several options, and it tests every possible combination before choosing the set that best matches the data. It's like mixing and matching outfits—now let's try the red shirt with the green pants and yellow socks.

"I was frustrated at the quality of the models back in early April and late March," Gu says. "Back then, one of the most frequently cited models in the media"—the IHME curve-fitting model—"had deaths going to zero by June. When I looked at the data, I could not see how that was possible, so I just wanted to take my own shot." By 9 May, when the U.S. death toll almost exactly matched Gu's prediction of 80,000 by that date, the physician and public-health leader Eric Topol praised the YYG model as "the most accurate #COVID19 model."

"We've shown that a very simple model like ours can do a good job," Gu says. One benefit of simplicity is agility, he adds: He forecasts 50 states and 70 countries, all in under 30 minutes on his laptop. "Because it's so simple, it allows me to make changes quickly." In addition, simpler models with fewer parameters are more likely to generalize to new situations and can also be easier to understand.

One alternative to SEIR models is data-driven models. These churn through data without explicitly accounting for separate categories of people, explains B. Aditya Prakash, a computer scientist at Georgia Tech. His team uses a set of deep-learning models—large neural networks, with tens of thousands of parameters. These networks infer complex relations between input data (such as mobility, testing, and social media) and pandemic outcomes (such as hospitalizations and deaths).

Prakash points out that data-driven models can be good for predicting "composite signals, signals which don't have a clear epidemiological counterpart." For instance, if you're predicting medical visits, that's a "noisy" signal that depends on not only the number of infections but also all the social and economic factors that might make someone visit a doctor or stay at home. But he concedes that compartmental models are better than deep-learning models for exploring hypotheticals—if we could enact policies that reduced R (reproduction number) by 20 percent, would that change the curve much?—because the model's control knobs are more visible. And since SEIR models rely on epidemiological theory, they can make longer-term predictions. Deep learning is more tied to the data, so it can be more accurate in the short term, but it's a black box, with thousands of incomprehensible parameters that are determined by the learning process—so it's hard to know how well it will extrapolate to other situations or the distant future.

WHILE DATA-DRIVEN MODELS occupy the abstract number-crunching end of the modeling spectrum, the opposite, hyperrealistic end is marked by agent-based models. These are much like the video game *The Sims*. Each individual in a population is represented by their own bit of code, called an agent, which interacts with other agents as it moves around the world. One of the most successful agent-based models was designed at the Univer-

sity of Sydney. The model has three layers, beginning with a layer of demographics. "We're essentially creating a digital twin for every person represented in the census," said Mikhail Prokopenko, a computer scientist at the university. He and his colleagues built a virtual Australia comprising 24 million agents, whose distribution matches the real thing in terms of age, household size, neighborhood size, school size, and so on. The second layer is mobility, in which agents are assigned to both a household and a school or workplace. On top of demographics and mobility, they add the disease, including transmission rates within households, schools, and workplaces, and how the disease progresses in individuals. In 2018, the group published a similar model for the flu that used older census data. They were building an updated model for further flu studies when the COVID-19 epidemic broke out, so they pivoted to capture its distinctive characteristics in their disease-transmission layer.

When set in motion, the model ticks twice a day: People come in contact at school or work in the daytime, then at home at night. It's like throwing dice over and over. The model covers 180 days in a few hours. The team typically runs tens or hundreds of copies of the model in parallel on a computing cluster to generate a range of outcomes.

The biggest insight reported by the Sydney group was that social distancing helps very little if only 70 percent of people practice it, but successfully squashes COVID-19 incidence if 80 percent of people can manage it over a span of a few months. And 90 percent compliance achieved the same effect in a faster time frame. The model informed both a report to the federal government from the Group of Eight Australian universities, and two reports from the World Health Organization. "We're all pleased," Prokopenko says, "that an agent-based model—which we've been trying to advocate for so long—at the time of need did a good job."

Prokopenko says SEIR models have done a "rough job" in Australia, where some forecasts have been off by orders of magnitude. Further, they help you explore hypotheticals but don't tell you exactly how to intervene. Let's say the SEIR model tells you that reducing R by 20 percent will cut the speed of the pandemic's spread in half. But how do you reduce R by 20 percent in the real world? With agent-based models, you can make everyone stay home one day a week and see the predicted effects of that policy.

To date, agent-based models haven't been used extensively—possibly because they require massive computation power that hasn't been widely available until recently. Also, they're hard to calibrate. The Sydney model only started matching reality once the team made the ratio of ill people who were symptomatic much lower in children than in adults—one of COVID-19's stark differences from flu. "Now that we have the technology and expertise to deploy large-scale agent-based models," Prokopenko said, "it might make a real difference for the next pandemic."

RESEARCHERS SAY they've learned a lot of lessons modeling this pandemic, lessons that will carry over to the next.

The first set of lessons is all about data. Garbage in, garbage out, they say. Jarad Niemi, an associate professor of statistics at Iowa State University who helps run the forecast hub used by the CDC, says it's not clear what we should be predicting. Infections, deaths, and hospitalization numbers each have problems, which affect their usefulness not only as inputs for the model but also as outputs. It's hard to know the true number of infections when not everyone is tested. Deaths are easier to count, but they lag weeks behind infections. Hospitalization numbers have immense practical importance for planning, but not all hospitals release those figures. How useful is it to predict those numbers if you never have the true numbers for comparison? What we need, he said, is systematized random testing of the population, to provide clear statistics of both the number of people currently infected and the number of people who have antibodies against the virus, indicating recovery. Prakash, of Georgia Tech, says governments should collect and release data quickly in centralized locations. He also advocates for central repositories of policy decisions, so modelers can quickly see which areas are implementing which distancing measures.

Researchers also talked about the need for a diversity of models. At the most basic level, averaging an ensemble of forecasts improves reliability. More important, each type of model has its own uses—and pitfalls. An SEIR model is a relatively simple tool for making long-term forecasts, but the devil is in the details of its parameters: How do you set those to match real-world conditions now and into the future? Get them wrong and the model can head off into fantasyland. Data-driven models can make accurate short-term forecasts, and machine learning may be good for predicting complicated factors. But will the inscrutable computations of, for instance, a neural network remain reliable when conditions change? Agent-based models look ideal for simulating possible interventions to guide policy, but they're a lot of work to build and tricky to calibrate.

Finally, researchers emphasize the need for agility. Niemi of Iowa State says software packages have made it easier to build models quickly, and the code-sharing site GitHub lets people share and compare their models. COVID-19 is giving modelers a chance to try out all their newest tools, says Meyers, of the University of Texas. "The pace of innovation, the pace of development, is unlike ever before," she says. "There are new statistical methods, new kinds of data, new model structures."

"If we want to beat this virus," Prokopenko says, "we have to be as adaptive as it is." ■

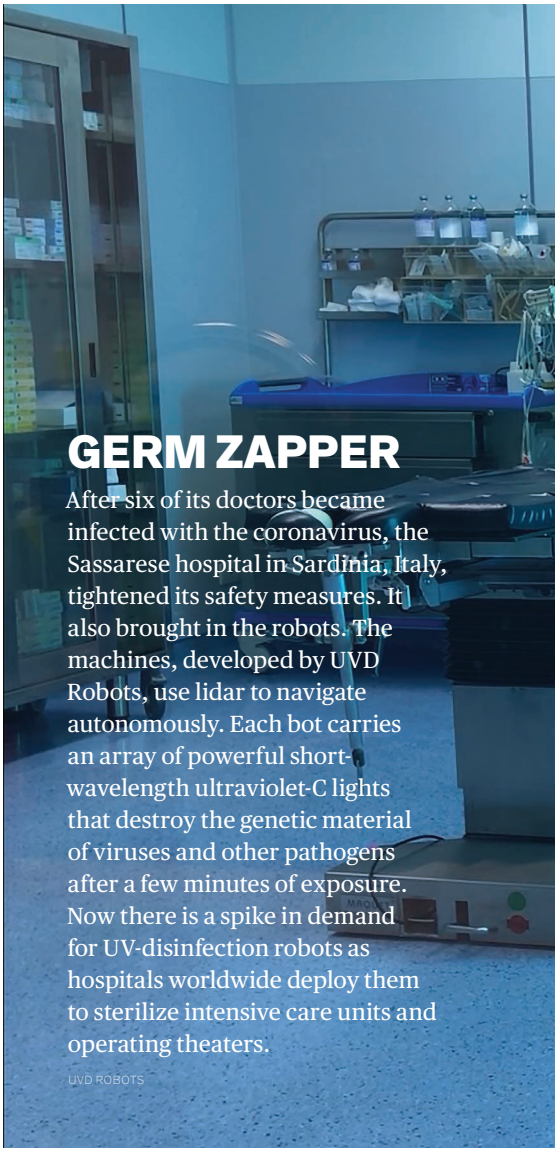
POST YOUR COMMENTS AT spectrum.ieee.org/modeling-oct2020

HOW ROBOTS BECAME ESSENTIAL WORKERS

They disinfected hospital rooms. They delivered medical supplies. They swabbed people's throats. Next time around, they'll be treating patients

AS THE CORONAVIRUS emergency exploded into a full-blown pandemic in early 2020, forcing countless businesses to shutter, robot-making companies found themselves in an unusual situation: Many saw a surge in orders. Robots don't need masks, can be easily disinfected, and, of course, they don't get sick.

An army of automatons has since been deployed all over the world to help with the crisis: They are monitoring patients, sanitizing hospitals, making deliveries, and helping frontline medical workers reduce their exposure to the virus. Not all robots operate autonomously—many, in fact, require direct human supervision, and most are limited to simple, repetitive tasks. But robot makers say the experience they've gained during this trial-by-fire deployment will make their future machines smarter and more capable. These pages illustrate how robots are helping us fight this pandemic—and how they might be able to assist with the next one. —ERICO GUIZZO & RANDI KLETT



GERM ZAPPER

After six of its doctors became infected with the coronavirus, the Sassarese hospital in Sardinia, Italy, tightened its safety measures. It also brought in the robots. The machines, developed by UVD Robots, use lidar to navigate autonomously. Each bot carries an array of powerful short-wavelength ultraviolet-C lights that destroy the genetic material of viruses and other pathogens after a few minutes of exposure. Now there is a spike in demand for UV-disinfection robots as hospitals worldwide deploy them to sterilize intensive care units and operating theaters.

UVD ROBOTS

RUNNING ERRANDS

In medical facilities, an ideal role for robots is taking over repetitive chores so that nurses and physicians can spend their time doing more important tasks. At Shenzhen Third People's Hospital, in China, a robot called Aimbot drives down the hallways, enforcing face-mask and social-distancing rules and spraying disinfectant [left]. At a hospital near Austin, Texas, a humanoid robot developed by Diligent Robotics [far left] fetches supplies and brings them to patients' rooms. It repeats this task day and night, tirelessly, allowing the hospital staff to spend more time interacting with patients.

LEFT: UBTECH ROBOTICS;
FAR LEFT: DILIGENT ROBOTICS

DROID TEAM

A squad of robots serves as the first line of defense against person-to-person transmission at a medical center in Kigali, Rwanda. Patients walking into the facility get their temperature checked by the machines, which are equipped with thermal cameras atop their heads. Developed by UBTech Robotics, in China, the robots also use their distinctive appearance—they resemble characters out of a Star Wars movie—to get people's attention and remind them to wash their hands and wear masks.

CLEMENT UWIRINGIYIMANA/REUTERS (2)

SAY "AAH"

To speed up COVID-19 testing, a team of Danish doctors and engineers at the University of Southern Denmark and at Lifeline Robotics is developing a fully automated swab robot. It uses computer vision and machine learning to identify the perfect target spot inside the person's throat; then a robotic arm with a long swab reaches in to collect the sample—all done with a swiftness and consistency that humans can't match. In this photo, one of the creators, Esben Østergaard, puts his neck on the line to demonstrate that the robot is safe.

UNIVERSITY OF SOUTHERN DENMARK

THE DOCTOR IS IN

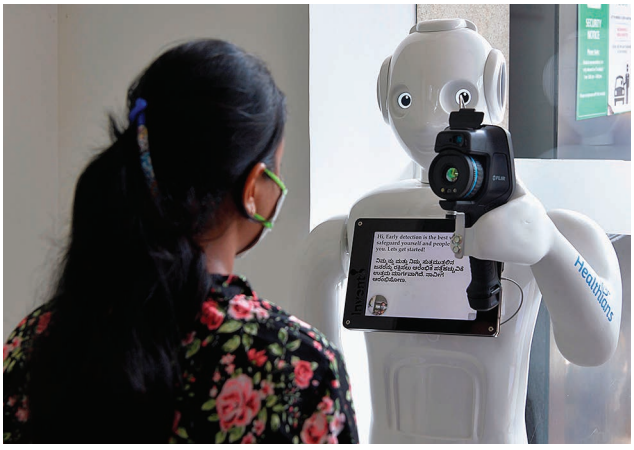
Nurses and doctors at Circolo Hospital in Varese, in northern Italy—the country's hardest-hit region—use robots as their avatars, enabling them to check on their patients around the clock while minimizing exposure and conserving protective equipment. The robots, developed by Chinese firm Sanbot, are equipped with cameras and microphones and can also access patient data like blood oxygen levels. Telepresence robots, originally designed for offices, are becoming an invaluable tool for medical workers treating highly infectious diseases like COVID-19, reducing the risk that they'll contract the pathogen they're fighting against.

MIGUEL MEDINA/AFP/GETTY IMAGES

SENTRY ROBOTS

Offices, stores, and medical centers are adopting robots as enforcers of a new coronavirus code. At Fortis Hospital in Bangalore, India, a robot called Mitra uses a thermal camera to perform a preliminary screening of patients [near right]. In Tunisia, the police use a tanklike robot to patrol the streets of its capital city, Tunis, verifying that citizens have permission to go out during curfew hours [far right]. And in Singapore, the Bishan-Ang Moh Kio Park unleashed a Spot robot dog [below], developed by Boston Dynamics, to search for social-distancing violators. Spot won't bark at them but will rather play a recorded message reminding park-goers to keep their distance.

CLOCKWISE FROM TOP LEFT: MANJUNATH KIRAN/AFP/GETTY IMAGES; KHALED NASRAOUI/PICTURE ALLIANCE/GETTY IMAGES; ROSLAN RAHMAN/AFP/GETTY IMAGES



HELP FROM ABOVE

Authorities in several countries attempted to use drones to enforce lockdowns and social-distancing rules, but the effectiveness of such measures remains unclear. A better use of drones was for making deliveries. In the United States, startup Zipline deployed its fixed-wing autonomous aircraft to connect two medical facilities 17 kilometers apart. For the staff at the Huntersville Medical Center, in North Carolina, masks, gowns, and gloves literally fell from the skies. The hope is that drones like Zipline's will one day be able to deliver other kinds of critical materials, transport test samples, and distribute drugs and vaccines.

ZIPLINE (3)

LIFE THROUGH ROBOTS

Robots can't replace real human interaction, of course, but they can help people feel more connected at a time when meetings and other social activities are mostly on hold. In Ostend, Belgium, ZoraBots brought one of its waist-high robots, equipped with cameras, microphones, and a screen, to a nursing home, allowing residents like Jozef Gouwy to virtually communicate with loved ones despite a ban on in-person visits [top]. In Manila, nearly 200 high school students took turns "teleporting" into a tall wheeled robot, developed by the school's robotics club, to walk on stage during their graduation ceremony [center]. And while Japan's Chiba Zoological Park was temporarily closed due to the pandemic, the zoo used an autonomous robotic vehicle called RakuRo, equipped with 360-degree cameras, to offer virtual tours to children quarantined at home [bottom].

FROM TOP: YVES HERMAN/REUTERS; EZRA ACAYAN/GETTY IMAGES; TOMOHIRO OHSUMI/GETTY IMAGES

SPECIAL DELIVERY

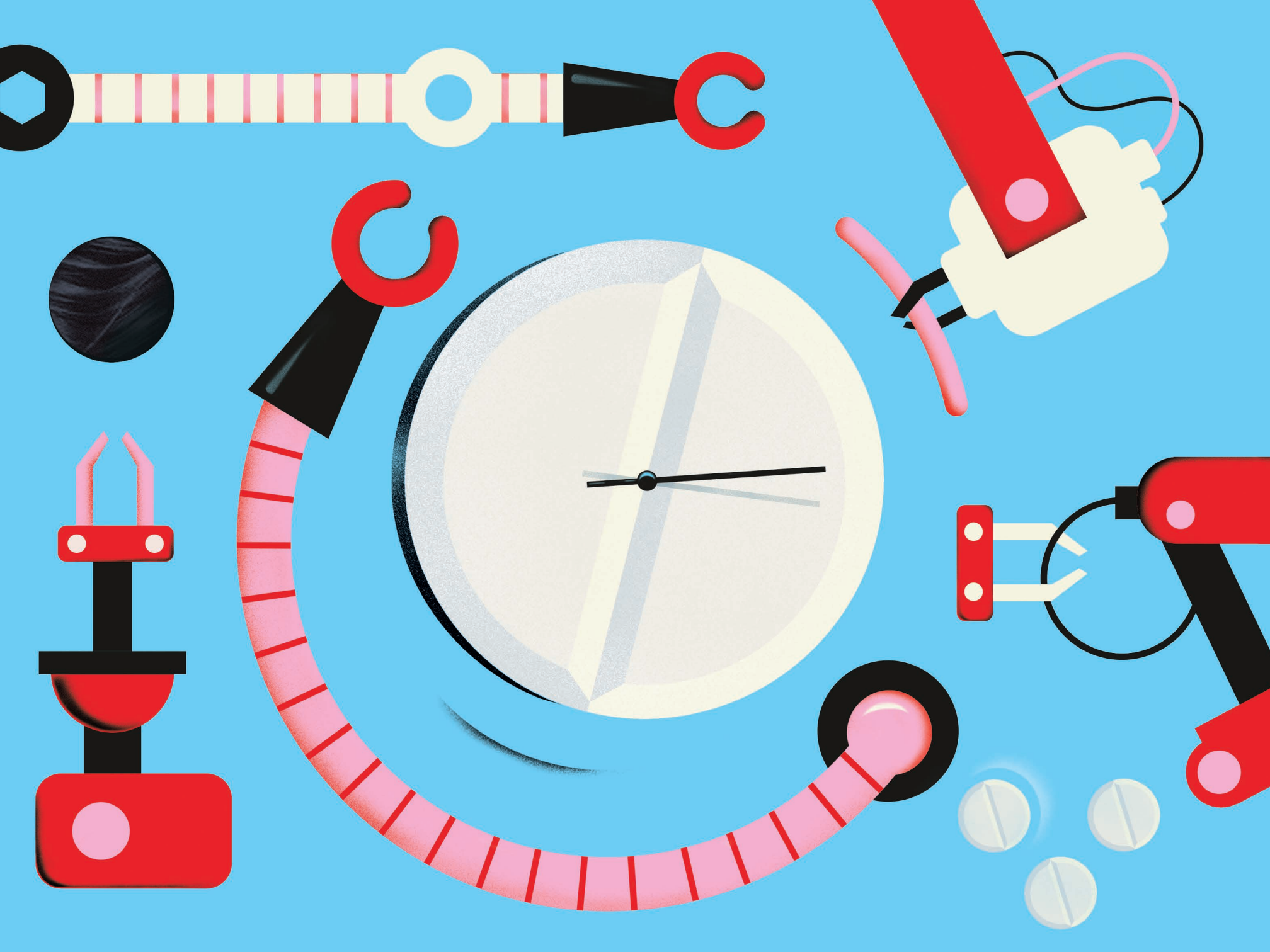
It's not quite a robot takeover, but the streets and sidewalks of dozens of cities around the world have seen a proliferation of hurrying wheeled machines. Delivery robots are now in high demand as online orders continue to skyrocket. In Hamburg, the six-wheeled robots developed by Starship Technologies navigate using cameras, GPS, and radar to bring groceries to customers [right]. In Medellín, Colombia, a startup called Rappi deployed a fleet of robots, built by Kiwibot, to deliver takeout to people in lockdown [top left]. China's JD.com, one of the country's largest e-commerce companies, is using 20 robots to transport goods in Changsha, Hunan province; each vehicle has 22 separate compartments, which customers unlock using face authentication [top center and right].

CLOCKWISE FROM BOTTOM: CHRISTIAN CHARISIUS/PICTURE ALLIANCE/GETTY IMAGES; JOAQUIN SARMIENTO/AFP/GETTY IMAGES; TPG/GETTY IMAGES (2)


JD 2022


JD 2022


Hungrig Hamburg?
Hol dir die App
starshipdeliveries.com
RANKWERK
maister
MAIS KOHLE



RESEARCHERS ARE BETTING THAT AI AND AUTOMATION CAN CUT DRUG DISCOVERY FROM FIVE YEARS TO SIX MONTHS

BY MEGAN SCUDELLARI

AUTOMATING ANTIVIRALS

WITHIN MOMENTS OF MEETING EACH OTHER at a conference last year, Nathan Collins and Yann Gaston-Mathé began devising a plan to work together. Gaston-Mathé runs a startup that applies automated software to the design of new drug candidates. Collins leads a team that uses an automated chemistry platform to synthesize new drug candidates. ● "There was an obvious synergy between their technology and ours," recalls Gaston-Mathé, CEO and cofounder of Paris-based Iktos. ● In late 2019, the pair launched a project to create a brand-new antiviral drug that would block a specific protein exploited by influenza viruses. Then the COVID-19 pandemic erupted across the world stage, and Gaston-Mathé and Collins learned that the viral culprit, SARS-CoV-2, relied on a protein that was 97 percent similar to their influenza protein. The partners pivoted. ● Their companies are just two of hundreds of biotech firms eager to overhaul the drug-discovery process, often with the aid of artificial intelligence (AI) tools. The first set of antiviral drugs to treat COVID-19 will likely come from sifting

ILLUSTRATION BY Marysia Machulska

through existing drugs. Remdesivir, for example, was originally developed to treat Ebola, and it has been shown to speed the recovery of hospitalized COVID-19 patients. But a drug made for one condition often has side effects and limited potency when applied to another. If researchers can produce an antiviral that specifically targets SARS-CoV-2, the drug would likely be safer and more effective than a repurposed drug.

There's one big problem: Traditional drug discovery is far too slow to react to a pandemic. Designing a drug from scratch typically takes three to five years—and that's *before* human clinical trials. "Our goal, with the combination of AI and automation, is to reduce that down to six months or less," says Collins, who is chief strategy officer at SRI Biosciences, a division of the Silicon Valley research nonprofit SRI International. "We want to get this to be very, very fast."

That sentiment is shared by small biotech firms and big pharmaceutical companies alike, many of which are now ramping up automated technologies backed by supercomputing power to predict, design, and test new antivirals—for this pandemic as well as the next—with unprecedented speed and scope.

"The entire industry is embracing these tools," says Kara Carter, president of the International Society for Antiviral Research and executive vice president of infectious disease at Evotec, a drug-discovery company in Hamburg. "Not only do we need [new antivirals] to treat the SARS-CoV-2 infection in the population, which is probably here to stay, but we'll also need them to treat future agents that arrive."

THERE ARE CURRENTLY about 200 known viruses that infect humans. Although viruses represent less than 14 percent of all known human pathogens, they make up two-thirds of all new human pathogens discovered since 1980.

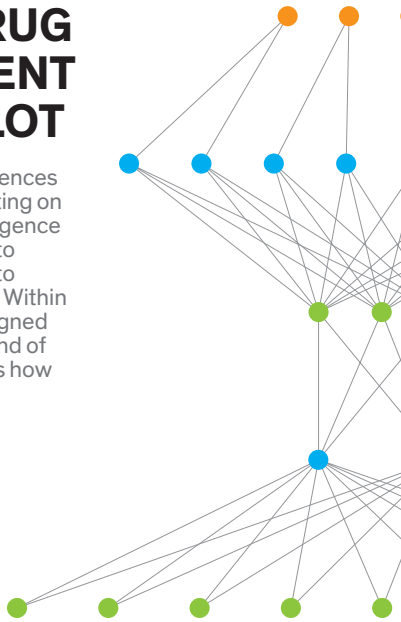
Antiviral drugs are fundamentally different from vaccines, which teach a person's immune system to mount a defense against a viral invader, and antibody treatments, which enhance the body's immune response. By contrast, antivirals are chemical compounds that directly block a virus after a person has become infected. They do this by binding to specific proteins and preventing them from functioning, so that the virus cannot copy itself or enter or exit a cell.

The SARS-CoV-2 virus has an estimated 25 to 29 proteins, but not all of them are suitable drug targets. Researchers are investigating, among other targets, the virus's exterior spike protein, which binds to a receptor on a human cell; two scissorlike enzymes, called proteases, that cut up long strings of viral proteins into functional pieces inside the cell; and a polymerase complex that makes the cell churn out copies of the virus's genetic material, in the form of single-stranded RNA.

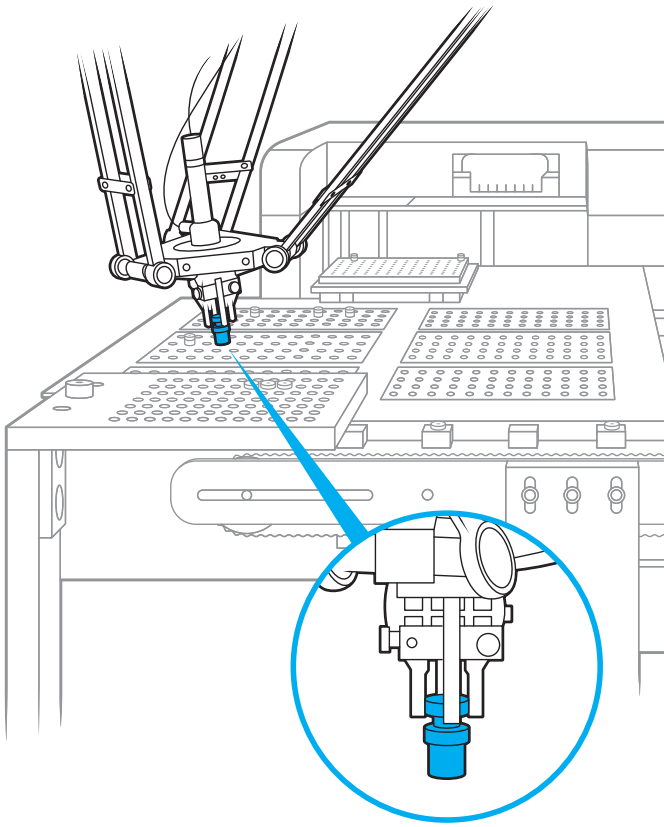
But it's not enough for a drug candidate to simply attach to a target protein. Chemists also consider how tightly the com-

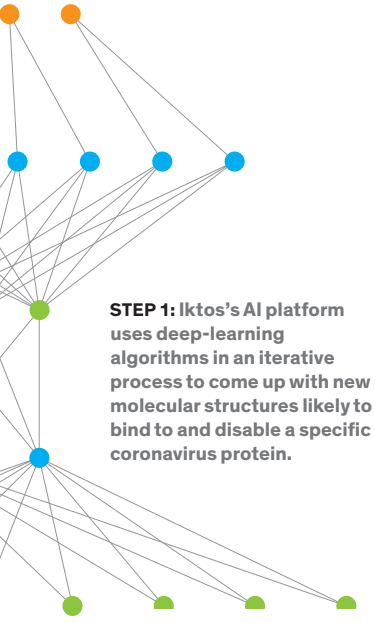
PUTTING DRUG DEVELOPMENT ON AUTOPILOT

Earlier this year, SRI Biosciences and Iktos began collaborating on a way to use artificial intelligence and automated chemistry to rapidly identify new drugs to target the COVID-19 virus. Within four months, they had designed and synthesized a first round of antiviral candidates. Here's how they're doing it.

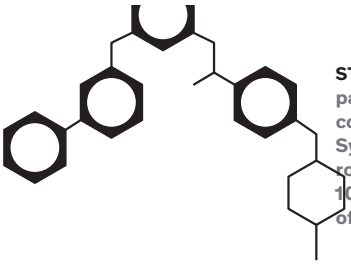


STEP 3: SynJet, an automated inkjet printer platform, tests the routes by printing out tiny quantities of chemical ingredients to see how they react. If the right compound is produced, the platform tests it.

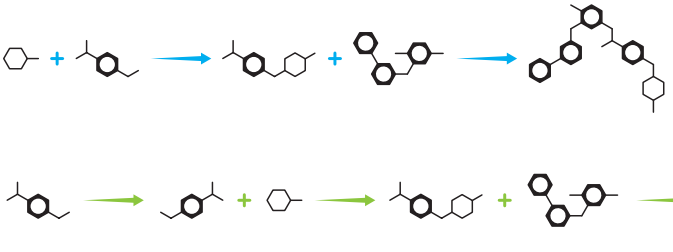


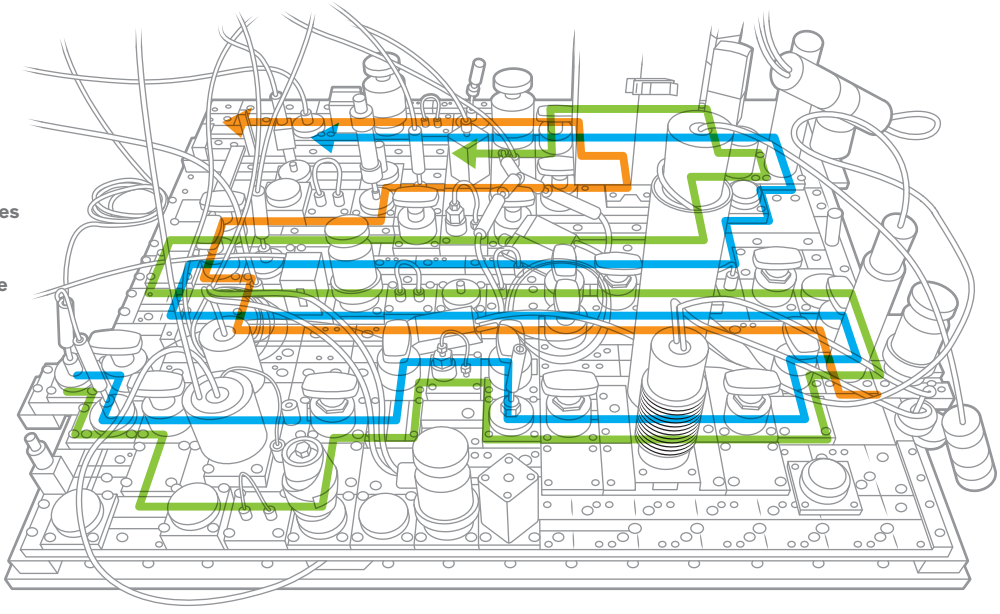


STEP 1: Iktos's AI platform uses deep-learning algorithms in an iterative process to come up with new molecular structures likely to bind to and disable a specific coronavirus protein.

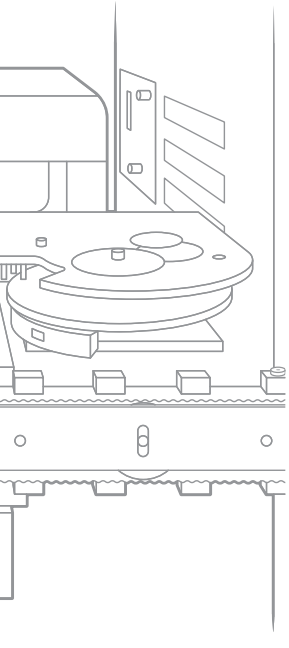


STEP 2: SRI Biosciences's SynFini system is a three-part automated chemistry suite for producing new compounds. Starting with a target compound from Iktos, SynRoute uses machine learning to analyze and optimize routes for creating that compound, with results in about 10 seconds. It prioritizes routes based on cost, likelihood of success, and ease of implementation.





STEP 4: AutoSyn, an automated tabletop chemical plant, synthesizes milligrams to grams of the desired compound for further testing. Computer-selected "maps" dictate paths through the plant's modular components.



STEP 5: The most promising compounds are tested against live virus samples.

ILLUSTRATION BY Chris Philpot

pound binds to its target, whether it binds to other things as well, how quickly it metabolizes in the body, and so on. A drug candidate may have 10 to 20 such objectives. "Very often those objectives can appear to be anticorrelated or contradictory with each other," says Gaston-Mathé.

Compared with antibiotics, antiviral drug discovery has proceeded at a snail's pace. Scientists advanced from isolating the first antibacterial molecules in 1910 to developing an arsenal of powerful antibiotics by 1944. By contrast, it took until 1951 for researchers to be able to routinely grow large amounts of virus particles in cells in a dish, a breakthrough that earned the inventors a Nobel Prize in Medicine in 1954.

And the lag between the discovery of a virus and the creation of a treatment can be heartbreaking. According to the World Health Organization, 71 million people worldwide have chronic hepatitis C, a major cause of liver cancer. The virus that causes the infection was discovered in 1989, but effective antiviral drugs didn't hit the market until 2014.

While many antibiotics work on a range of microbes, most antivirals are highly specific to a single virus—what those in the business call "one bug, one drug." It takes a detailed understanding of a virus to develop an antiviral against it, says Che Colpitts, a virologist at Queen's University, in Canada, who works on antivirals against RNA viruses. "When a new virus emerges, like SARS-CoV-2, we're at a big disadvantage."

Making drugs to stop viruses is hard for three main reasons. First, viruses are the Spartans of the pathogen world: They're frugal, brutal, and expert at evading the human immune system. About 20 to 250 nanometers in diameter, viruses rely on just a few parts to operate, hijacking host cells to reproduce and often destroying those cells upon departure. They employ tricks to camouflage their presence from the host's immune system, including preventing infected cells from sending out molecular distress beacons. "Viruses are really small, so they only have a few components, so there's not that many drug targets available to start with," says Colpitts.

Second, viruses replicate quickly, typically doubling in number in hours or days. This constant copying of their genetic material enables viruses to evolve quickly, producing mutations able to sidestep drug effects. The virus that causes AIDS soon develops resistance when exposed to a single drug. That's why a cocktail of antiviral drugs is used to treat HIV infection.

Finally, unlike bacteria, which can exist independently outside human cells, viruses invade human cells to propagate, so any drug designed to eliminate a virus needs to spare the host cell. A drug that fails to distinguish between a virus and a cell can cause serious side effects. "Discriminating between the two is really quite difficult," says Evotec's Carter, who has worked in antiviral drug discovery for over three decades.

And then there's the money barrier. Developing antivirals is rarely profitable. Health-policy researchers at the London School of Economics recently estimated that the average cost of developing a new drug is US $1 billion, and up to $2.8 billion for cancer and other specialty drugs. Because antivirals are usually taken for only short periods of time or during short outbreaks of disease, companies rarely recoup what they spent developing the drug, much less turn a profit, says Carter.

To change the status quo, drug discovery needs fresh approaches that leverage new technologies, rather than incremental improvements, says Christian Tidona, managing director of BioMed X, an independent research institute in Heidelberg, Germany. "We need breakthroughs."

IKTOS'S AI PLATFORM was created by a medicinal chemist and an AI expert. To tackle SARS-CoV-2, the company used generative models—deep-learning algorithms that generate new data—to "imagine" molecular structures with a good chance of disabling a key coronavirus protein.

For a new drug target, the software proposes and evaluates roughly 1 million compounds, says Gaston-Mathé. It's an iterative process: At each step, the system generates 100 virtual compounds, which are tested in silico with predictive models to see how closely they meet the objectives. The test results are then used to design the next batch of compounds. "It's like we have a very, very fast chemist who is designing compounds, testing compounds, getting back the data, then designing another batch of compounds," he says.

The computer isn't as smart as a human chemist, Gaston-Mathé notes, but it's much faster, so it can explore far more of what people in the field call "chemical space"—the set of all possible organic compounds. Unexplored chemical space is huge: Biochemists estimate that there are at least 10^{63} possible druglike molecules, and that 99.9 percent of all possible small molecules or compounds have never been synthesized.

Still, designing a chemical compound isn't the hardest part of creating a new drug. After a drug candidate is designed, it must be synthesized, and the highly manual process for synthesizing a new chemical hasn't changed much in 200 years. It can take days to plan a synthesis process and then months to years to optimize it for manufacture.

That's why Gaston-Mathé was eager to send Iktos's AI-generated designs to Collins's team at SRI Biosciences. With $13.8 million from the Defense Advanced Research Projects Agency, SRI Biosciences spent the last four years automating the synthesis process. The company's automated suite of three technologies, called SynFini, can produce new chemical compounds in just hours or days, says Collins.

First, machine-learning software devises possible routes for making a desired molecule. Next, an inkjet printer platform tests the routes by printing out and mixing tiny quanti-

OUT OF 10^{63} POSSIBLE DRUGLIKE MOLECULES, 99.9 PERCENT HAVE NEVER BEEN SYNTHESIZED.

ties of chemical ingredients to see how they react with one another; if the right compound is produced, the platform runs tests on it. Finally, a tabletop chemical plant synthesizes milligrams to grams of the desired compound.

Less than four months after Iktos and SRI Biosciences announced their collaboration, they had designed and synthesized a first round of antiviral candidates for SARS-CoV-2. Now they're testing how well the compounds work on actual samples of the virus.

THEIRS ISN'T THE ONLY collaboration applying new tools to drug discovery. In late March, Alex Zhavoronkov, CEO of Hong Kong-based Insilico Medicine, came across a YouTube video showing three virtual-reality avatars positioning colorful, sticklike fragments in the side of a bulbous blue protein. The three researchers were using VR to explore how compounds might bind to a SARS-CoV-2 enzyme. Zhavoronkov contacted the startup that created the simulation—Nanome, in San Diego—and invited it to examine Insilico's AI-generated molecules in virtual reality.

Insilico runs an AI platform that uses biological data to train deep-learning algorithms, then uses those algorithms to identify molecules with druglike features that will likely bind to a protein target. A four-day training sprint in late January yielded 100 molecules that appear to bind to an important SARS-CoV-2 protease. The company recently began synthesizing some of those molecules for laboratory testing.

Nanome's VR software, meanwhile, allows researchers to import a molecular structure, then view and manipulate it on the scale of individual atoms. Like human chess players who use computer programs to explore potential moves, chemists can use VR to predict how to make molecules more druglike, says Nanome CEO Steve McCloskey. "The tighter the interface between the human and the computer, the more information goes both ways," he says.

Zhavoronkov sent data about several of Insilico's compounds to Nanome, which re-created them in VR. Nanome's chemist demonstrated chemical tweaks to potentially improve each compound. "It was a very good experience," says Zhavoronkov.

Meanwhile, in March, Takeda Pharmaceutical Co., of Japan, invited Schrödinger, a New York-based company that develops chemical-simulation software, to join an alliance working on antivirals. Schrödinger's AI focuses on the physics of how proteins interact with small molecules and one another.

The software sifts through billions of molecules per week to predict a compound's properties, and it optimizes for multiple desired properties simultaneously, says Karen Akinsanya, chief biomedical scientist and head of discovery R&D at Schrödinger. "There's a huge sense of urgency here to come up with a potent molecule, but also to come up with molecules that are going to be well tolerated" by the body, she says. Drug developers are seeking compounds that can be broadly used and easily administered, such as an oral drug rather than an intravenous drug, she adds.

Schrödinger evaluated four protein targets and performed virtual screens for two of them, a computing-intensive process. In June, Google Cloud donated the equivalent of 16 million hours of Nvidia GPU time for the company's calculations. Next, the alliance's drug companies will synthesize and test the most promising compounds identified by the virtual screens.

Other companies, including Amazon Web Services, IBM, and Intel, as well as several U.S. national labs are also donating time and resources to the Covid-19 High Performance Computing Consortium. The consortium is supporting 85 projects, which now have access to 6.8 million CPU cores, 50,000 GPUs, and 600 petaflops of computational resources.

WHILE ADVANCED TECHNOLOGIES could transform early drug discovery, any new drug candidate still has a long road after that. It must be tested in animals, manufactured in large batches for clinical trials, then tested in a series of trials that, for antivirals, lasts an average of seven years.

In May, the BioMed X Institute in Germany launched a five-year project to build a Rapid Antiviral Response Platform, which would speed drug discovery all the way through manufacturing for clinical trials. The €40 million ($47 million) project, backed by drug companies, will identify outside-the-box proposals from young scientists, then provide space and funding to develop their ideas.

"We'll focus on technologies that allow us to go from identification of a new virus to 10,000 doses of a novel potential therapeutic ready for trials in less than six months," says BioMed X's Tidona, who leads the project.

While a vaccine will likely arrive long before a bespoke antiviral does, experts expect COVID-19 to be with us for a long time, so the effort to develop a direct-acting, potent antiviral continues. Plus, having new antivirals—and tools to rapidly create more—can only help us prepare for the next pandemic, whether it comes next month or in another 102 years.

"We've got to start thinking differently about how to be more responsive to these kinds of threats," says Collins. "It's pushing us out of our comfort zones." ■

POST YOUR COMMENTS AT spectrum.ieee.org/antiviral-oct2020

FLY SAFE: The UV Cabin System from Dimer UVC and Honeywell is designed to disinfect an entire airplane in a few minutes.

GERMICIDAL UV LAMPS DESTROY VICIOUS VIRUSES. NEW TECH MIGHT PUT THEM MANY MORE PLACES WITHOUT HARMING HUMANS

BY MARK ANDERSON

THE ULTRA-VIOLET OFFENSE

WALK INTO THE CAMBRIDGE, ONT., OFFICE of health-care equipment company PrescientX and you probably wouldn't suspect you're entering one of the most sanitary places in North America. • In this otherwise-ordinary Toronto-area office suite, you can disinfect your keys, phone, and other portables at the reception area's ultraviolet-sterilization stand. In cooler months, the air you breathe is cleansed of mold and bacteria in UV-sterilized heating units as well as blasted by UV fixtures in the office air ducts to eliminate viruses. In-room UV fixtures pointing at the ceiling disinfect the air, while other UV lights that turn on only when no one's in the room zap pathogens on desks, keyboards, and high-touch surfaces in bathrooms and work spaces. • The office, says PrescientX founder and CEO Barry Hunt, represents a possible future in which pandemics like COVID-19 are more commonplace—but in which germicidal ultraviolet light is one of the most potent weapons we have to face them down.

PHOTOS BY Honeywell Aerospace

For nearly a century and a half, scientists have been investigating ultraviolet light's deadly effect on germs. In recent times, UV was deployed as a disinfectant against deadly coronavirus particles during the SARS outbreak in 2003. And as soon as the new coronavirus began spreading in earnest in China late last year, UV returned as a potentially powerful weapon to fight this new scourge. While antiviral drugs and vaccines concentrate on minimizing and repelling infections in the body, the ultraviolet systems being deployed focus on killing the virus in the environment, before it has a chance to infect anyone.

Germicidal UV technology is now being used to sterilize air, surfaces, and personal protective equipment like N95 masks. Meanwhile, experts in the field are devoting much of their time to educating the public about the technology's effectiveness against the coronavirus—and outbreaks and pandemics yet to come. The main hurdle for germicidal UV, says Dean Saputa, vice president and cofounder of UV Resources, a Santa Clarita, Calif.-based UV technology company, "is overcoming the lack of…understanding about this technology."

For starters, experts point out, not all ultraviolet rays are created equal. Ultraviolet light lies in a region of the electromagnetic spectrum beyond indigo and violet. Anyone who's read the label on a bottle of sunscreen knows the UV wavelengths that give you a suntan or a sunburn are called UV-A (with wavelengths between 400 and 315 nanometers) and UV-B (315 to 280 nm). Germicidal UV tech focuses on shorter, more energetic UV wavelengths, known as UV-C, which lie between 280 and 100 nm. The Earth's ozone layer prevents virtually all UV-C light from reaching us. So microbes and viruses (and everything else, really) evolved for millions and billions of years without ever being exposed to these wavelengths.

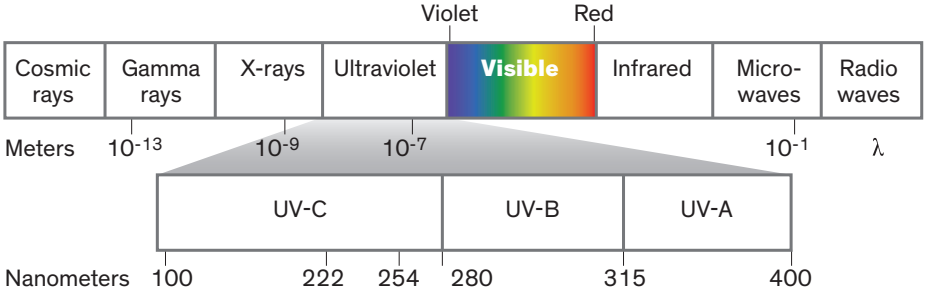
That changed in 1901, with the invention of the mercury-vapor lamp. It produces a potent wavelength of UV-C light—254 nm—that has proved devastating for nearly any genetic material in its path, including that of a coronavirus or a human.

Much of the trick to wielding germicidal UV light against the spread of disease lies in finding a way to keep people safe from that light. Those involved have already built up a lot of expertise in that area, but new technology could make the job of using UV-C in occupied spaces easier.

WHILE UV-C LIGHT has been used successfully against germs for more than a century, it's only recently that researchers have understood why it's so successful. In DNA's four-letter alphabet of nucleotides, thymine (T) and cytosine (C) are particularly susceptible to UV. The UV knocks an electron loose and causes two T molecules or two C molecules to bond together, introducing an error into a string of DNA. Humans have genetic self-repair mechanisms, including a molecule called p53. This protein (sometimes referred to as the "guardian of the genome") patrols DNA strands and looks for just this kind of nucleotide damage. But p53 can do only so much. Too much damage overwhelms it and can lead to cancer.

SARS-CoV-2, the virus that causes COVID-19, lacks such sophisticated self-repair mechanisms, and its genetic material is made up of RNA rather than DNA. RNA contains uracil instead of thymine, but the effect of UV-C is essentially the same: Genetic damage accumulates and the virus is destroyed.

The main hitch with UV-C light in the 254-nm range is that it penetrates human



DEATH RAYS: UV-C is at the far end of the ultraviolet portion of the spectrum. Most UV-C products use mercury-vapor lamps, which shine at 254 nanometers. Scientists are exploring another wavelength, 222 nm, because it may be safer for use around humans.

SOURCE: UV RESOURCES

THE AIR UP THERE: AeroMed Infinity germicidal UV-C fixtures installed near the ceilings at Kings County Hospital Center, in New York City, help keep aerosolized coronavirus particles from spreading where patients wait.

AEROMED (2)

skin and eyes, leading to skin cancer and cataracts. So UV-C's DNA-smashing effect means that any disinfecting device that uses it has to be designed to operate either when no one is in the room or in a self-contained space where humans can't go.

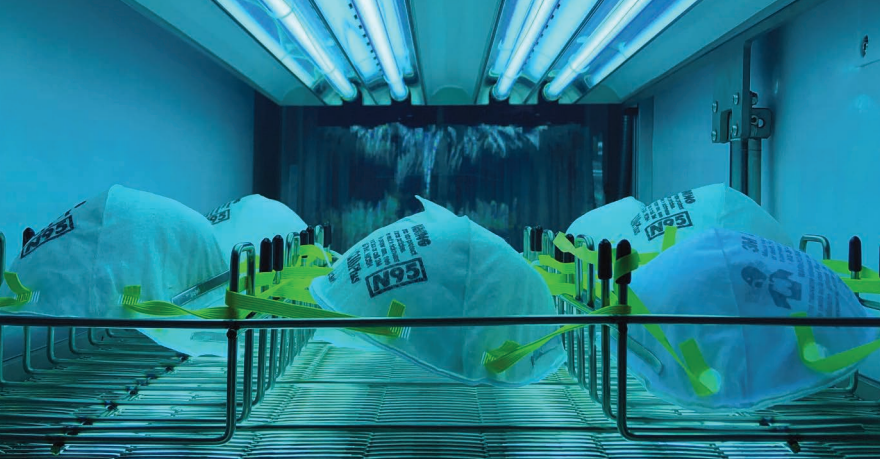
Researchers have been trying to balance the benefits and dangers of UV-C for decades. In the late 1930s and early 1940s, the U.S. epidemiologist William F. Wells installed UV-C-emitting mercury-vapor lamps in Philadelphia schools to combat an outbreak of measles, as a follow-up to his groundbreaking work that showed airborne bacteria and viruses could cause infection. The fixtures were designed to irradiate the air only in the upper portion of the room, to protect students and staff from exposure to the rays. And they worked. Schools that had the air-sanitizing equipment experienced a 13.3 percent infection rate compared with 53.6 percent for the population at large.

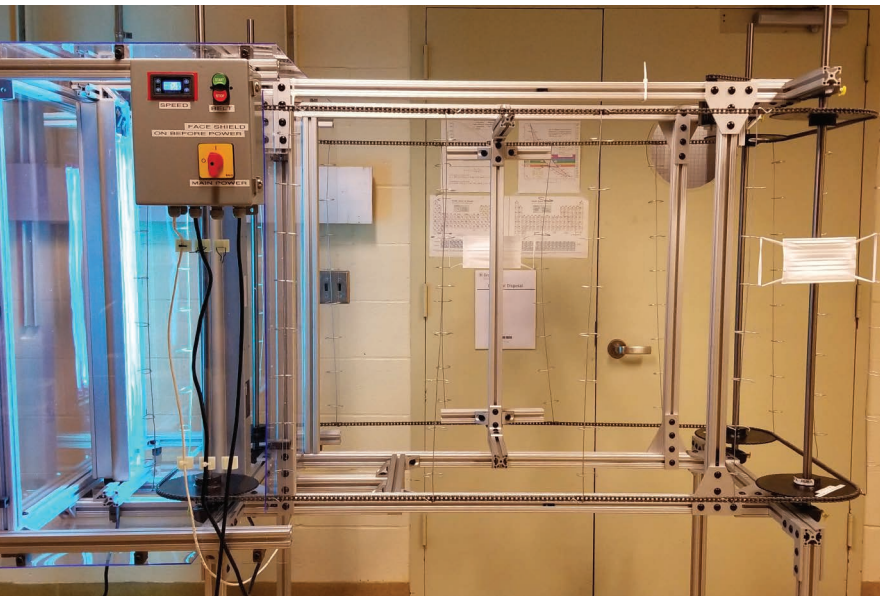
Germicidal UV in most commercial and industrial settings today still comes from mercury-vapor lamps, says PrescientX's Hunt. These devices have a spectral peak at 254 nm. That emission is the result of an arc of electricity that ionizes (typically) argon gas and vaporizes liquid mercury. Glass would block the radiation, so these lamps are made of quartz instead.

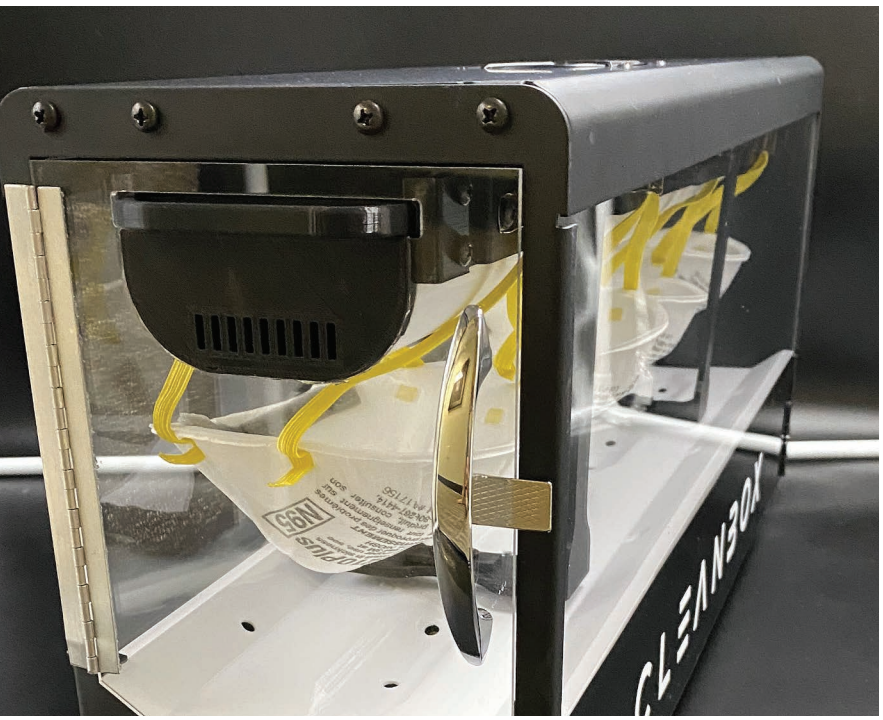
UV-C-emitting LEDs, made from alloys of aluminum nitride, are much newer and have a number of potential advantages over mercury lamps—no toxic mercury, greater durability, faster startup, and emission at a diversity of wavelengths, which may aid in their germicidal role. Most important, though, is UV-C LEDs' theoretical potential for higher efficiency. That potential is as yet unrealized, however. Jae-hak Jeong, technical research fellow and vice president at Seoul Semiconductor, told *IEEE Spectrum* that today's mercury lamps have a higher wall-plug efficiency—electrical power in versus optical power out—than the UV-C LEDs on the market now. But mercury lamps' advantage is not expected to last, because researchers predict UV-C LEDs to improve in much the same way that blue LEDs did to reach their dominant position in lighting. For now though, UV-C LEDs aren't powerful enough to sterilize more than small volumes of air or nearby surfaces.

Recent experience with UV-C light confirms what Wells found in the 1930s: Air disinfection with 254-nm UV light is "very effective," Hunt says. Direct illumination of the air in the upper part of a room produces better throughput than irradiating the air inside HVAC units, he adds. According to the Illuminating Engineering Society, 17 milliwatts of 254-nm-lamp radiation per cubic meter of upper-air space is the evidence-based dose developed to control tuberculosis. However, some bacteria, viruses, and other microorganisms are more resistant to UV-C light than others.

At that dose, upper-air fixtures can destroy germs in the lamps' direct line of sight "in a matter of seconds," says Saputa







USE, STERILIZE, REPEAT: UV light irradiates the surfaces of N95 protective masks in Prescient X's system [top], so the masks can be reused. Rensselaer Polytechnic Institute's sterilizer [middle] bathes both sides of a mask at once in UV. Cleanbox Technology's system [bottom] was adapted from one that sanitized VR gear.

of UV Resources. To keep humans safe, the fixtures, which typically cost a few thousand dollars each, are placed at heights above 2 meters, and nonreflective baffles direct the ultraviolet energy upward and outward. (UV-C reflects poorly off of most surfaces, so there's little danger of exposure from rays bouncing off ceilings and other fixtures; nonetheless, installers must make sure by using UV-C meters.) Such installations can be used in a variety of settings, including patient rooms, waiting rooms, lobbies, stairwells, and emergency-room entrances and corridors.

AIR ISN'T THE ONLY thing that needs disinfecting. During the pandemic, UV-wielding robots in hospitals and UV germ zappers in airplanes and subway cars have joined a host of technologies being rolled out to disinfect surfaces.

The main difference between these systems and UV air sterilizers is that the former can't operate when people are present, so they're not continuously keeping areas virus-free. "Design engineers must keep in mind disinfection only lasts until people are placed into that hospital bed or sit in that airplane seat," says Saputa.

But sporadic disinfection is preferable to none at all. Before this year, Carlsbad, Calif.–based Cleanbox Technology had been developing a UV-C LED box to sterilize virtual-reality and augmented-reality headsets. The company's system was readily adaptable to sterilizing N95 masks, says Cleanbox's chief technology officer and cofounder David Georgeson.

The result, the CleanDefense N95 sanitizing light box, can hold four masks at a time. The box is portable and powered from the wall or a battery bank, enabling use in mobile environments like ambulances and airplanes as well as in health care settings, restaurants, and shopping centers.

The challenge with this technology and any other type of UV disinfection is

FROM TOP: PRESCIENTX; ROBERT KARLICEK/RPI; CLEANBOX TECHNOLOGY

that "the radiation has to actually strike the virus to break the [RNA] and inactivate it," says Robert Karlicek, director of Rensselaer Polytechnic Institute's Center for Lighting Enabled Systems & Applications, in Troy, N.Y. "If those virus particles are sitting behind dirt or covered by another fiber, you'd have to scatter a lot of light before you got a good kill rate."

The problem is illustrated by what's called the "canyon wall" effect. To bacteria and viruses, textural features on common surfaces can be like 100-meter-deep canyons would be to us. In experiments with surfaces having submillimeter texture, UV-C's kill rate against the bacteria *Staphylococcus aureus* varied as much as 500-fold depending on the angle at which the mercury lamp's light fell.

That dependence on angle is why it typically takes three UV systems to disinfect a hospital room, according to Marc Verhougstraete, assistant professor of public health at the University of Arizona. Even then, there are still unexposed areas. So for that application, UV-C surface sanitizers should be part of a system that includes routine surface disinfection, hand hygiene, and air treatment, he says.

Getting a thorough dosage from more than one angle is key to sanitizing N95 masks for reuse. Karlicek and his team developed a mercury-lamp N95-mask sterilizer that was tested at Mount Sinai Hospital in New York City. It uses two sets of UV lamps to irradiate the front and back of the masks at the same time. PrescientX is also getting into the N95-mask-sterilization business with a UV-C light box called Terminator CoV. And there are other systems in various states of development and commercialization as well.

The precise UV-C dose needed to inactivate a SARS-CoV-2 virus particle is yet to be determined, says PrescientX CEO Hunt. But, he adds, a number of peer-reviewed studies have looked at UV-C doses for the H5N1 and H1N1 strains of influenza and for previous coronavirus outbreaks, including MERS and SARS. Experts think it's reasonable to assume that a similar amount of energy will inactivate the coronavirus that causes COVID-19.

Those studies all found that irradiating masks with 1 to 2 joules of UV-C energy per square centimeter was sufficient to inactivate between 99.9 and 99.99 percent of the virus particles on the mask. That said, eliminating coronavirus particles is not just a numbers game. If the sterilization unit casts any shadows on the mask, that mask will not be fully disinfected. That's why these systems are designed with fasteners and hooks that stretch the mask and minimize shadows.

"You need intensity and geometry to get rid of the virus," Hunt says.

GIVEN THE HARMFUL effects of 254-nm UV-C, scientists are exploring the higher-energy wavelength of 222 nm, in the far-UV region. This wavelength has been found to kill viruses and bacteria, and initial studies show that it's substantially safer than photons in the 254-nm range. In fact, far-UV may be able to safely bathe an entire room in sterilizing light, even with people present.

Far-UV light at 222 nm "hardly penetrates the outer layer of skin," says David Sliney, retired manager of the U.S. Army's Laser and Optical Radiation Program at the Army Public Health Center, near Baltimore. "It's heavily absorbed by protein. But there is some evidence that it may even be more effective against airborne viruses" than other UV light. The wavelength appears to be safe for the eyes as well because it penetrates no deeper than the layer of tears that coat the eye. A 2019 study of albino rats in Japan found prolonged far-UV exposure induced no skin or eye damage.

At present, far-UV is generated by krypton-chlorine excimer lamps. ("Excimer" is a portmanteau of "excited" and "dimer," meaning an excited state of a two-part molecule.) Inside the sealed quartz-glass chamber of such a lamp, krypton and chlorine are heated by electric discharge whose energy is sufficient to momentarily create a KrCl excimer, which spits out a 222-nm spectral line before dissociating again.

However, these light sources don't just give off far-UV light. "Excimer lamps produce a peak at 222 nm, but they also produce [longer]-wavelength light," explains David Brenner, director of Columbia University's Center for Radiological Research, in New York City. "And that is damaging, because it doesn't have the protective properties of 222 nm. It can penetrate [skin] and damage DNA."

Filters can eliminate the extraneous wavelengths, but Brenner says a better solution would be a far-UV LED lamp with a narrow spectral profile right at 222 nm. Such an LED does not yet exist. "LEDs have been coming down in wavelength for a long time," he says. "Once you go down below 250, 240, 230 [nm], the efficiency falls off dramatically. It's like a cliff."

So in the near term, excimer lamps are the best hope. Brenner expects such lamps to be on the market by the end of this year or early 2021.

DESPITE THIS arsenal of ultraviolet technologies—UV-C LEDs, mercury vapor lamps, and KrCl excimer lamps—the current pandemic may yet come and go before the world has rolled out germicidal UV broadly enough to make a big impact. And so experts are already planning for the next dangerous pathogen, and when it comes, they hope to greet it with a phalanx of UV air purifiers and surface sterilizers in hospitals, airports, public transit, offices, schools, nursing homes, stores, restaurants, elevators, and elsewhere. The ubiquity of UV technology should make it much harder for an outbreak to spread, perhaps preventing a lethal contagion from ever becoming a pandemic. ■

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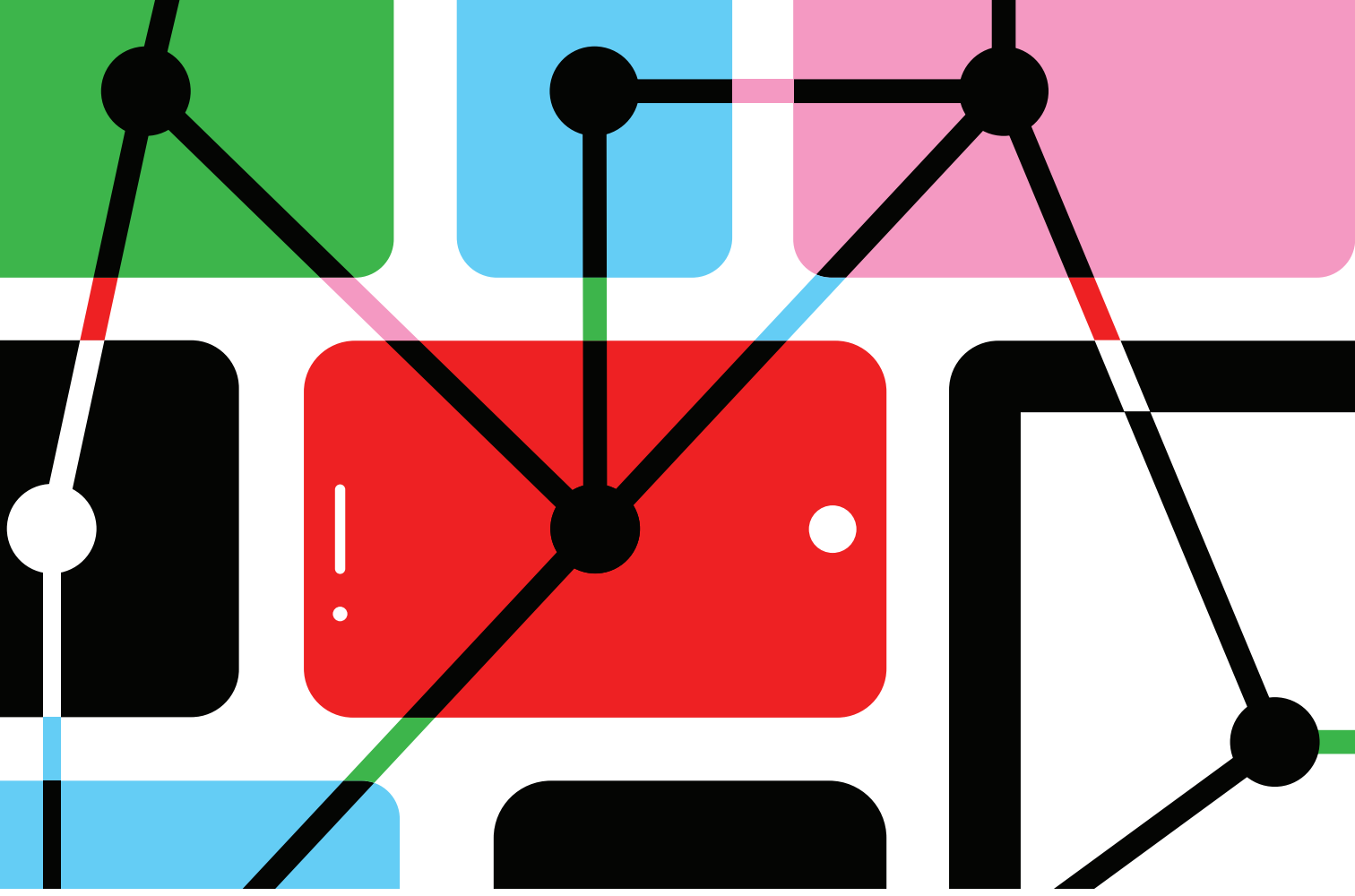


THE DILEMMA OF CONTACT-TRACING APPS

CAN THIS CRUCIAL TECHNOLOGY BE BOTH EFFECTIVE AND PRIVATE?

BY JEREMY HSU

IN JUNE, as the coronavirus swept across the United States, Paloma Beamer spent hours each day helping her university plan for a September reopening. Beamer, an associate professor of public health at the University of Arizona, was helping to test a mobile app that would notify users if they crossed paths with confirmed COVID-19 patients. • A number of such "contact tracing" apps have recently had their trials by fire, and many of the developers readily admit that the technology has not yet proven that it can slow the spread of the virus. But that caveat has not stopped national governments and local communities from using the apps. • "Right now, in Arizona, we're in the full-blown pandemic phase," Beamer said, speaking in June, well before the new-case count had peaked. "And even manual contact tracing is very limited here—we need whatever tool we can get right now to curb our epidemic." • Traditionally, tracers would ask newly diagnosed patients to list the people they'd spent time with recently,

ILLUSTRATION BY StoryTK

then ask those people to provide contacts of their own. Such legwork has helped to control other infectious-disease outbreaks, such as syphilis in the United States and Ebola in West Africa. However, while these methods can extinguish the first spark or the last embers of an epidemic, they're no good in the wildfire stage, when the caseload expands exponentially.

That's the reason to automate the job. Digital contact tracing may also jog fuzzy memories by dredging up relevant information on where a patient has been, and with whom. Some technologies can go further by automatically alerting people who have been in close proximity to a patient and thus may need to get tested or go into isolation. Speedy notification is particularly important during the COVID-19 pandemic, given that asymptomatic people seem capable of transmitting the virus.

Automatic alerts may sound great, but there are "limited real-world use cases" and "limited evidence for their effectiveness," says Joseph Ali, associate director for global programs at the Johns Hopkins Berman Institute of Bioethics and coauthor of the book *Digital Contact Tracing for Pandemic Response*, published in May. Rushed deployment of unproven technologies runs the risk of misidentifying moments of exposure that in fact never happened—false positives—and missing moments that did happen, or false negatives.

Some governments have embraced these apps; others have struggled with the decision. The United Kingdom, for example, initially spent millions developing an app that would collect data and send it to a centralized data storage system run by the National Health Service. But privacy advocates raised concern about the system, and in June the government announced that it would abandon that effort and switch to a less-centralized alternative built on technology from the tech giants Apple and Google.

The U.K.'s indecision shows how the choice of strategy revolves around privacy trade-offs. Some countries have staked everything on effectiveness and nothing on privacy.

Wuhan, the Chinese city at the heart of the pandemic, squashed the virus, eased the lockdown, then saw a small resurgence of the contagion in May. Public-health authorities went all out: They tested the entire population of 11 million and instituted the tracking of each person's movements. Would-be customers could enter a shop only by having their temperature taken and exchanging personal bar codes, displayed on their phones, with the shop's own identifying barcode. They then had to repeat the exchange upon leaving. That way, if anyone in the shop ended up testing positive, the authorities would be able to find whoever was in the same place at the same time, test those people, and, if necessary, quarantine them.

It worked. As of mid-July, Wuhan was reporting that no new cases of the virus had been recorded for 50 consecutive days. But such a gargantuan effort is not always an option. In many parts of the world, most people will willingly participate only if they trust in the system.

This may prove especially challenging in the United States, where early apps rolled out by states such as Utah and North Dakota failed to catch on. Making matters even more awkward, an independent security analysis found that the North Dakota app violated its own privacy policy by sharing location data with the company Foursquare.

In an online survey of Americans conducted by Avira, a security software company, 71 percent of respondents said they don't plan to use a COVID contact-tracing app. Respondents cited privacy as their main concern. In a telling contrast, 32 percent said they would trust apps from Google and Apple to keep their data secure and private—but just 14 percent said they would trust apps from the government.

ONE SHINING EXAMPLE of effective digital contact tracing is South Korea, which built a centralized system that scrutinized patients' movements, identified people who had been in contact with patients, and used apps to monitor people under quarantine. To date, South Korea has successfully contained its COVID-19 outbreaks without closing national borders or imposing local lockdowns.

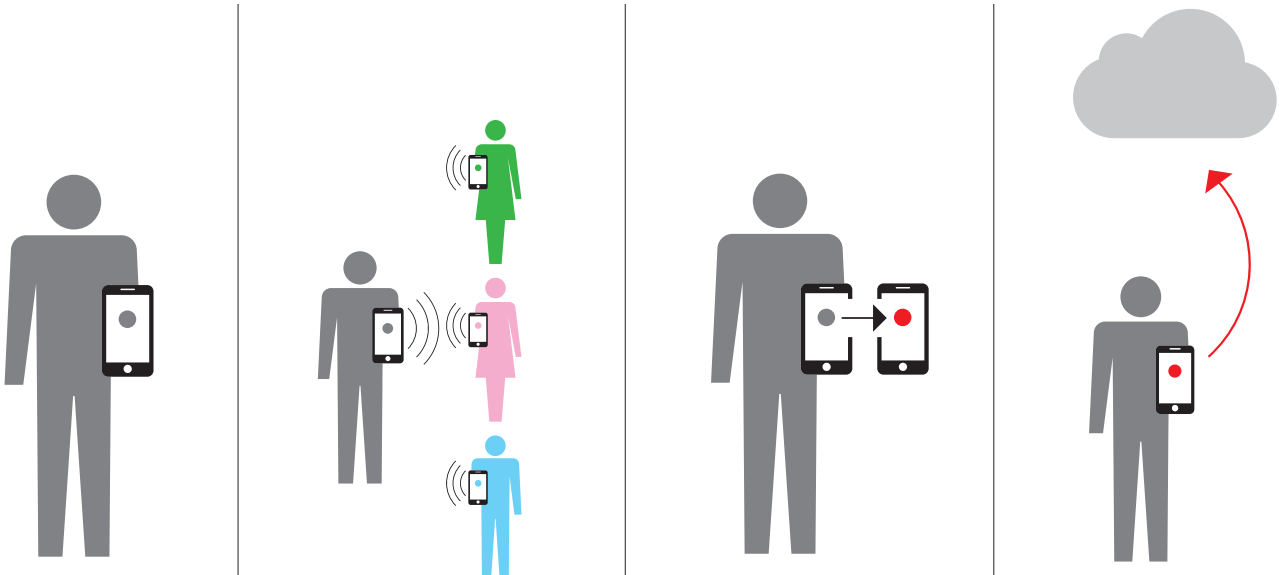
The South Korean government's system gave contact tracers access to multiple information sources, including footage from security cameras, GPS data from mobile phones, and credit card transaction data, says Uichin Lee, an associate professor of industrial and systems engineering at the Korea Advanced Institute of Science and Technology (KAIST), in Daejeon. "This system helps them to quickly identify hot spots and close contacts," Lee says.

But South Korea's system also publicly shares patients' contact-trace data—including pseudonymized information on demographics, infection information, and travel logs. This approach raises serious privacy concerns, as Lee and his colleagues outlined in the journal *Frontiers in Public Health*. The travel logs alone could enable observers to infer where a patient lives and works.

By comparison, public-health authorities in Europe and the United States have shied away from publicly sharing such patient data. There's also a middle way: A person's phone may store data identifying people or location, and it may be left to the owner of the phone whether to share that information with public-health officials.

And then there's the radical idea of not storing such data at all. That's the approach taken by the Google/Apple Exposure Notification (GAEN) system. As these tech giants own, respectively, the Android and iOS smartphone standards, the GAEN system enables inde-

TELL IT TO THE CLOUD



1 Person A commutes to work, bringing a Bluetooth-enabled phone with a digital key, which is used to communicate with other phones.

2 Person A comes in contact with persons B, C, and D; all their phones exchange key codes.

3 Person A later learns he's infected and enters his new status in the app.

4 By agreeing to share his status with the database, A instructs the app to send the data to the cloud.

pendent developers to build apps that can run on either standard. The system records Bluetooth transmissions between phones in close proximity to one another, and stores that data as anonymized beacons on each phone for a limited time. If one phone user tests positive for COVID-19 and enters that positive status in a mobile app built upon GAEN, the system will alert other phone users who have been in close proximity within the potentially infectious time period.

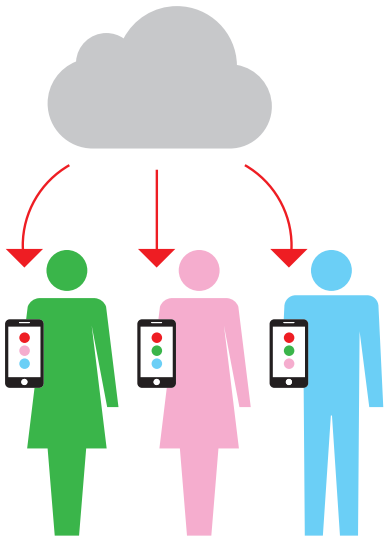
To protect user privacy, the system does all these things without ever recording the exact location of such encounters. It also limits the reported exposure time for each encounter to 5-minute increments, with a maximum possible total of 30 minutes. That constraint makes it more difficult for users to guess the source of their exposure.

The GAEN system also appeals to those wary of increased surveillance in the name of public health. Germany, Italy, and Switzerland have already deployed exposure-notification apps based on GAEN, and other countries will likely follow. In the United States, Virginia was the first to introduce one.

"If you collect identifying information along with Bluetooth data, it could potentially lead to new forms of surveillance," says Tina White, founder and executive director of the nonprofit COVID Watch and a Ph.D. candidate at the Stanford Institute for Human-Centered Artificial Intelligence. "And that's exactly what we don't want to see." COVID Watch is working with the University of Arizona on a privacy-centric app based on the GAEN system. Preliminary testing involving two phones placed at different indoor locations has ramped up to more real-life campus scenarios inside classrooms, dining halls, and the Cat Tran student shuttle, followed by a campuswide rollout in mid-August.

THERE'S ONE BIG hitch: Repurposing Bluetooth from its original communication function poses serious technical difficulties. At Trinity College Dublin, researchers found that Bluetooth can perform poorly on the crucial task of proximity detection when a phone is in the presence of reflective metal surfaces. In one experiment on a commuter bus, a Swiss COVID-19 app built on the GAEN system failed to trigger exposure notifications

ILLUSTRATION BY Anders Wenngren



5 Meanwhile, B's, C's, and D's phones are regularly checking the cloud database to check the status of their users' contacts. When B, C, and D discover that A has reported himself infected, they all know they should get tested for the virus.

even though the phones were within 2 meters (a little over 6 feet) of each other for 15 minutes.

"Public transport, which seems kind of mundane, is actually one of the core use cases for contact-tracing apps, but it's also a terrible radio environment," says Douglas Leith, a professor of computer science and statistics at Trinity College. "All our measurements suggest that it probably won't work on buses and trains."

Another problem is the variation in antenna configuration over the thousands of Android phone models. Engineers must calibrate the software to make up for any loss in signal strength, Leith explains. And although Bluetooth-signal "chirps" require minimal power, simply listening for such chirps requires that the main phone processors be turned on, which can quickly drain battery power unless the apps are restricted to short listening periods.

Beyond the technical challenges faced by Bluetooth-based apps, all contact-tracing apps suffer from the same general problem: Unless a certain percentage of the population installs an app, it can't do its work. People won't opt in unless they believe in the public-health strategy behind an app and in the personal advantages they can hope to gain from it. Making that sale has been tough. In Germany, which has had some of the best results of any country in containing the virus, only 41 percent of the population has said it was willing to download what is known as the Corona-Warn-App.

Some researchers point to a University of Oxford study that modeled the coronavirus's spread through a simulated city of 1 million people; it found that 60 percent adoption is needed to stop the pandemic and keep countries out of lockdown (although the study suggested that lower rates of adoption could still prove helpful).

The tech giants are making widespread adoption easier by deploying an app-less Exposure Notifications Express function for iOS and Android devices. If a phone user opts in, the phone begins listening for nearby Bluetooth beacons from other phones. And later, if a stored Bluetooth beacon proves to be a match for someone confirmed to be positive for COVID-19, the system will prompt the user to download an exposure-notification app for more information.

BLUETOOTH IS NOT the only way forward. The COVID Safe Paths project led by the nonprofit PathCheck Foundation, an MIT spin-off, has been developing and fielding a mobile app that uses GPS location data instead. The GPS approach provides more location data than Bluetooth does, in exchange for less user privacy. But Safe Paths also aims to build a Bluetooth-based version with the GAEN system. "We have been mostly agnostic to the technology we want to use," says Abhishek Singh, a Ph.D. candidate in machine learning at the MIT Media Lab and a member of Safe Paths.

"It matters less what's actually happening in the back end, and more about communication and perception," says Kyle Towle, a member of the technology team at Safe Paths and former senior director of cloud technology at PayPal. The crucial component, he says, is the "appeal to our community members to gain that trust in the first place."

The best path to success may come from ample preparation. South Korea's experience with an outbreak of Middle East respiratory syndrome (MERS) in 2015 prompted the government to update national laws and lay the bureaucratic and technological foundations for an efficient contact-tracing system. The resulting public-private partnership enables human contact tracers to pull together digital data on a suspected or confirmed case's travel history within 10 minutes.

"A country like South Korea, maybe because they went through this before with other viruses five years ago, really got a head start, and they didn't mess around," says Marc Zissman, associate head of the cybersecurity and information sciences division at MIT Lincoln Laboratory. The lab is among those in the PACT (Private Automated Contact Tracing) project, which is testing GAEN's Bluetooth-based app performance.

Zissman says that developing digital contact tracing during a pandemic is like building a plane and flying it at the same time while also measuring how well everything works. "In a perfect world, something like this would have taken a couple years to implement," he says. "There just isn't the time, so instead what's happening is people are doing the best they can, and making the best engineering judgments they can, with the data they have and the time that they have." ■

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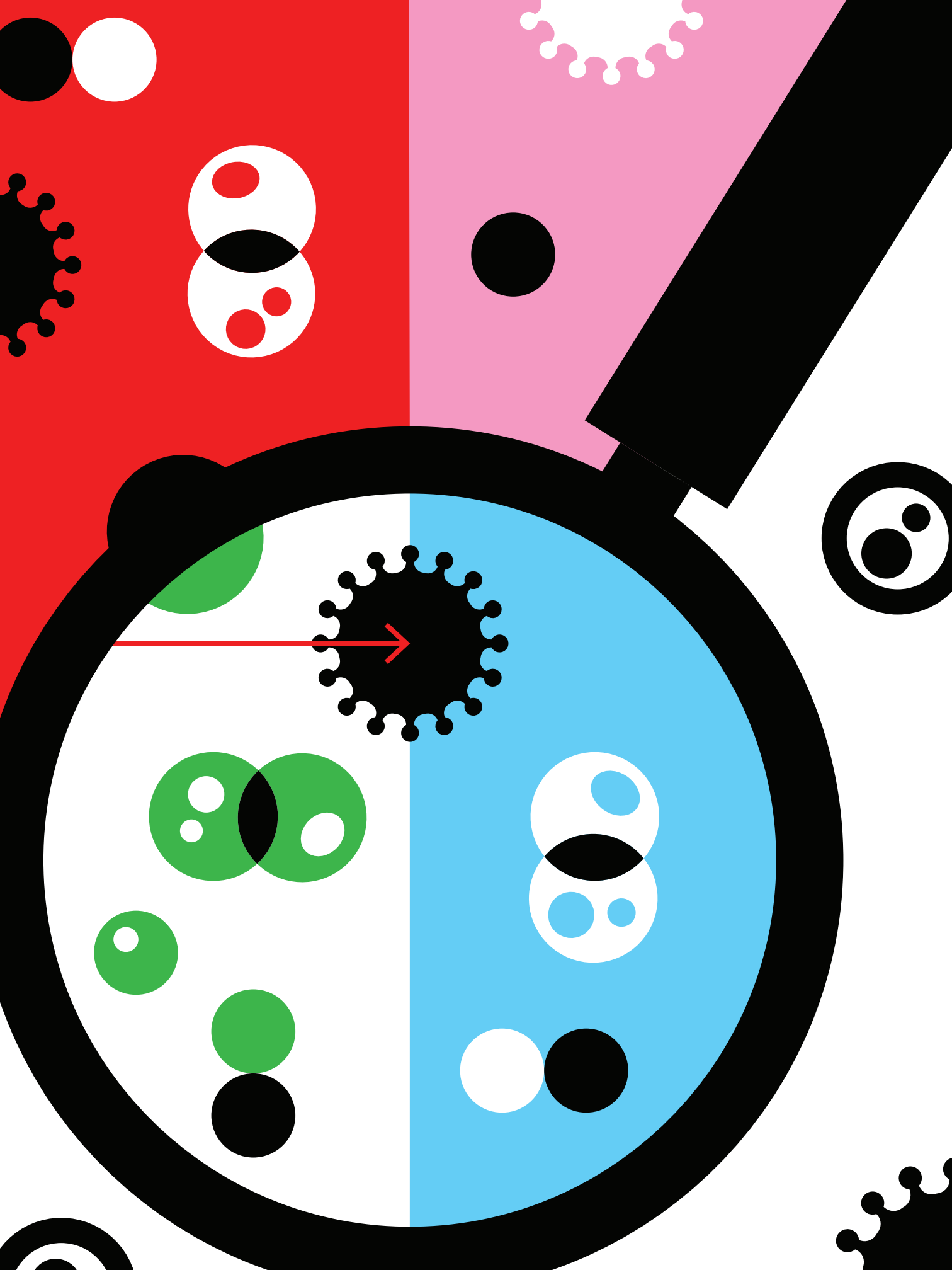


FAST, HIGH-TECH, USE-ANYWHERE DIAGNOSTIC TESTS ARE KEY TO BATTLING PANDEMICS

THE RACE FOR A HERE-AND-NOW COVID-19 TEST

BY WUDAN YAN & DAVID SCHNEIDER

DIAGNOSTIC TESTING FOR COVID-19 infections is one of the linchpins of the global effort to combat the deadly pandemic. But the strategy normally used for that has a few downsides. For one, the nasopharyngeal swabbing required demands the services of a health care worker, who is then put at risk of contracting the disease. Also, the sample-taking procedure, which involves sticking a very long flexible swab through a nostril and into the nasopharynx at the back of the nose and throat, is so unpleasant that some people resist being tested. And because the samples must normally be sent to a distant lab for processing, it often takes hours to days for results to become available. • What the world desperately needs is a way to diagnose infections with the virus more quickly and easily. Breakthroughs here would allow for truly widespread testing and the identification of people with asymptomatic infections, who often inadvertently spread the disease. • Researchers across the world have been racing to develop better COVID-19 tests, and biochemists and molecular biologists have made significant progress in just a

ILLUSTRATION BY StoryTK

handful of months. But engineers, too, have been working on technologies that might provide what everyone so dearly wants: inexpensive tests that don't require swabbing and that can be rapidly performed by anyone, anywhere—if not for this pandemic, then perhaps in time for the next one.

IN THE USUAL method for diagnosing COVID-19 infections, the nasopharyngeal swab sample is sent to a lab. There, technicians use a procedure called reverse-transcription polymerase chain reaction (RT-PCR) to check for the presence of the SARS-CoV-2 virus, which causes COVID-19. The processing requires first converting a characteristic segment of viral RNA into DNA and then "amplifying" that DNA through a sequence of biochemical tricks and heating and cooling cycles. The presence or absence of large quantities of amplified DNA reveals whether the virus was present in the original sample.

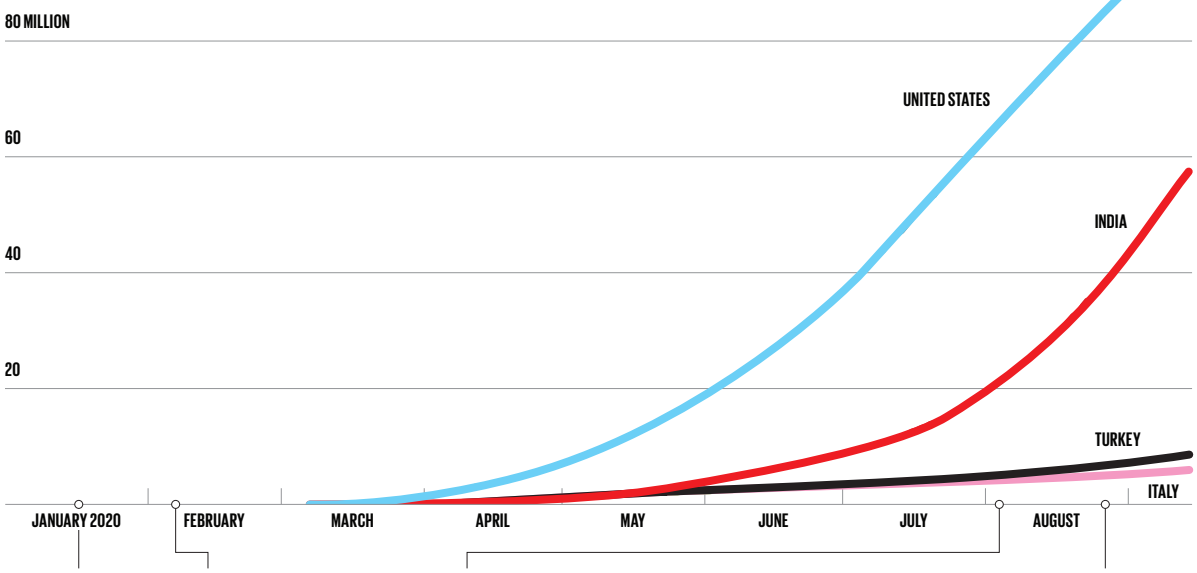
But there are faster ways to test for infections. Perhaps the best-known example of a rapid test for this coronavirus, at least in the United States, is one being used at the White House: a COVID-19 testing system from Abbott Laboratories, which received emergency-use authorization from the U.S. Food and Drug Administration in March. It uses a toaster-size instrument called ID NOW, which Abbott introduced in 2014 to detect influenza, strep A, and respiratory syncytial virus. The device employs a biochemical strategy to amplify viral RNA without the need for heating and cooling, which allows it to produce results from a swab sample in 13 minutes or less; that's much faster than RT-PCR-based tests, which take an hour or more to run through the necessary series of thermal cycles.

The speedy results you can get with Abbott's ID NOW COVID-19 test make it immensely attractive, but there has been considerable controversy about the reliability of those results. A study posted to a preprint server in May found that the ID NOW test missed a third of positive samples, although Abbott has stated that it misses only a few percent of positives in real-world situations.

Other companies have developed similarly compact systems that can detect the presence of genetic material specific to the SARS-CoV-2 virus on-site. In August, the U.K. government announced that it would be rolling out equipment devised by two such companies, DnaNudge and Oxford Nanopore Technologies, to labs, hospitals, and nursing homes. Both machines can be operated by someone who's not a trained health professional, and both companies' tests take under 90 minutes to produce results.

A RISING TIDE

The United States, India, Turkey, and Italy lead the world in the number of tests for COVID-19 that have been performed.



16 JAN German researchers first develop a test for the COVID-19 virus.

6 FEB The U.S. Centers for Disease Control starts shipping its own test kits for the COVID-19 virus.

3 AUG The U.K. government announces that it will do a large-scale rollout of two new desktop COVID-19 testing systems, one from DnaNudge and one from Oxford Nanopore.

26 AUG Abbott Laboratories receives emergency-use authorization from the U.S. Food and Drug Administration for its rapid BinaxNOW Ag Card test for the COVID-19 virus.

SOURCE: OURWORLDINDATA.ORG/CORONAVIRUS

IN THE CARDS: Abbott Laboratories' new antigen-based test is performed on a card that's about the size of a credit card [left]. A nasal swab is inserted into the card, a reagent is added, and 15 minutes later, a technician reads the result and uses a smartphone app to provide the person tested with a time-stamped verification of their results [right].

In another key development, the FDA has granted emergency-use authorization for several testing protocols that do away with the nasopharyngeal swab and rely instead on saliva. These include one called SalivaDirect from the Yale School of Public Health and another developed at Rutgers University that allows people to collect the sample at home. Such advances make it more likely that spit sampling will one day become the norm for tests based on RT-PCR.

It may prove impossible, though, to create a system that amplifies genetic material of the virus rapidly, with inexpensive portable equipment, and with sufficient sensitivity to detect the virus in saliva. Fortunately, there is a fundamentally different strategy that might check all these boxes: antigen-based tests.

ANTIGEN-BASED tests don't look for genetic material specific to the virus. Instead, they use antibodies—large molecules that have just the right shape to bind with protein molecules specific to the virus, such as the now-famous spike protein that decorates the surface of SARS-CoV-2. The molecular targets of such antibodies are called antigens.

When people are infected, one part of their immune response is to manufacture antibodies to the virus. These molecules can also be mass produced and incorporated into test kits to be mixed with a sample of mucus or saliva. The tricky part is determining whether the antibodies in the test solution have indeed attached to the virus, which is what signals that the person being tested has an active infection.

Biochemists have experience with this challenge and have developed various antigen-based point-of-care tests for other viral diseases. At the time of this writing, the FDA has granted emergency-use authorization to four companies for such antigen-based tests for the COVID-19 virus. One of these, developed by Becton, Dickenson and Co., takes advantage of the company's already-deployed Veritor handheld instruments and provides results in just 15 minutes.

But the world could still benefit from the ability to test people for this virus using simpler, cheaper equipment and by testing saliva, instead of requiring a swab. "The best situation would be like a pregnancy test," says Angela Rasmussen, a virologist at Columbia University. "Spit on a stick or into a collection tube and have a clear result 5 minutes later."

On 26 August, Abbott Laboratories obtained emergency-use authorization from the FDA for a test that is approaching that ideal, which it calls the BinaxNOW Ag Card. Unlike this company's earlier rapid-testing system, this one requires no desktop analyzer. The antigen-based test is performed on a card that's about the size of a credit card: A nasal swab is inserted into the card, a reagent is added, and 15 minutes later the technician reads the result. The only relevant device here is a smartphone.

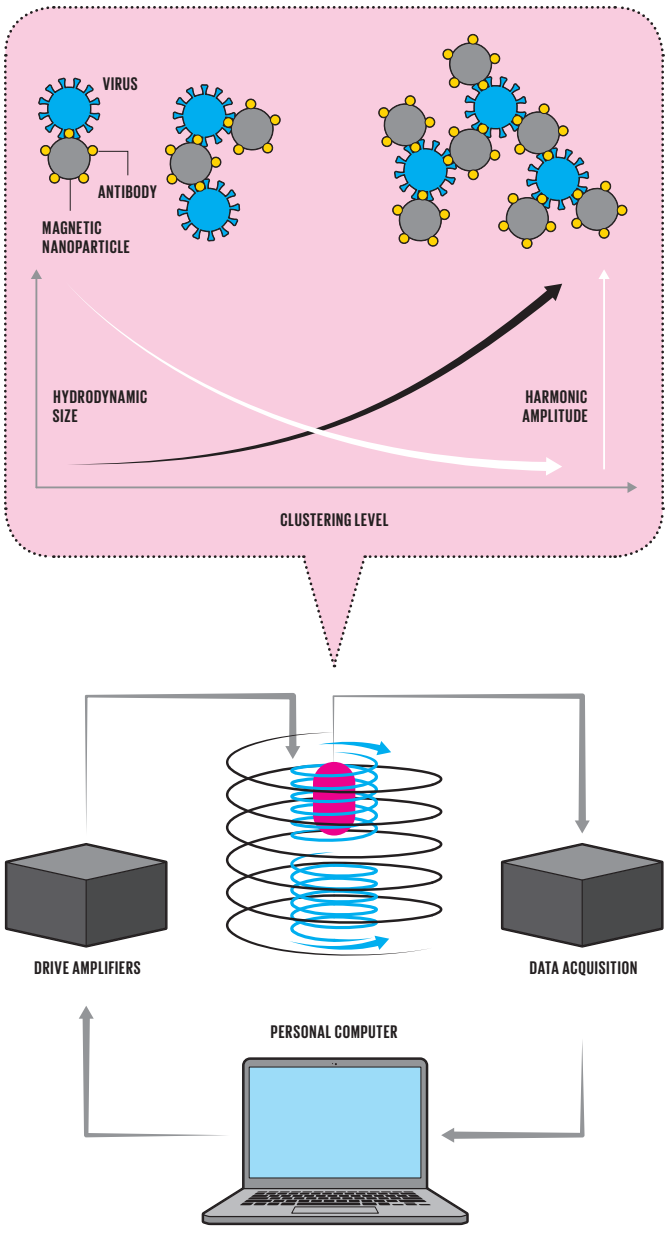
That's because Abbott has also developed a companion phone app, which it called Navica. People who install the app can present their phones to the technician, who will then enter the results of their tests through the Navica app on his or her own phone. Those who test negative will soon have time-stamped QR codes on their phones that attest to that result, enabling schools and workplaces to check people's statuses using the app's verification feature.

The availability of Abbott's BinaxNOW Ag Card, which the company expects to ship soon in large quantities (tens of millions each month) for a cost of only US $5 per test, portends a new phase of the pandemic, one in which it becomes much more straightforward to identify people infected with the COVID-19 virus. Going forward, we still require a test that is equally fast and inexpensive but that could work with saliva, so that anyone, anywhere could determine whether they've been infected. Here's where some new technologies might be able to make a special contribution in the quest for such a test.

AT THE UNIVERSITY of Minnesota, materials-science engineer Jian-Ping Wang had been working on a novel technique called magnetic-particle spectroscopy for detecting influenza, but at the end of March he made a big pivot, modifying his device to aid in the battle against COVID-19. Wang's approach mixes the sample with magnetic nanoparticles coated with antibodies that target the SARS-CoV-2 virus. The challenge, as with any antigen-based technique, is figuring out whether the virus has indeed attached to them.

ABBOTT (2)

LASSOING A VIRUS



THE APPROACH TO TESTING that Jian-Ping Wang at the University of Minnesota is taking relies on magnetic particles that are a few tens of nanometers in diameter [top, gray circles]. These particles are coated with antibodies [yellow] that can attach to certain structures on the surface of the SARS-CoV-2 virus [blue]. When mixed with a sample that contains the virus, the antibody-coated magnetic particles tend to clump together. These clumps, having a larger hydrodynamic size than individual particles, are slower to rotate into alignment with a changing magnetic field, applied using coils of wire that surround the sample, which for clarity is shown here as a single spiral [bottom, black]. This difference in agility can be detected using two counterwound sense coils [blue], which nullify the effects of the applied field while picking up signals from the changing magnetization of the sample [pink]. Low harmonic amplitude in the sensed signal indicates the magnetic particles have clumped, revealing the presence of the virus.

The clever scheme that Wang has worked out relies on the behavior of his magnetic nanoparticles when they're subjected to an external magnetic field. Electrical engineers are well aware that the magnetization of iron-containing materials can change direction when a magnetic field is applied to them. For the 30-nanometer-diameter magnetic particles that Wang works with, that change in magnetization comes about by the physical rotation of the particle in solution. These particles are small and nimble enough to act like tiny compass needles, rotating into alignment with the applied magnetic field. If you subject them to a slowly oscillating magnetic field—say, one created inside a coil of wire—their orientations will flip back and forth in sync with the changes in the polarity of the applied field.

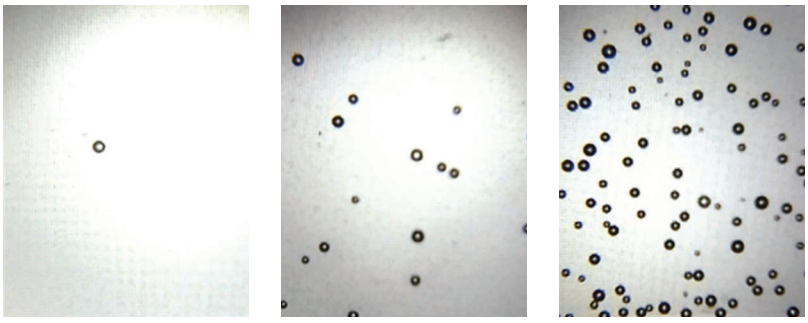
The surface of each magnetic particle holds more than one antibody, and the surface of each viral particle contains more than one antigenic protein. So when many of these two kinds of particles are present together in solution, they tend to link up into extended networks, with the virus acting as a sort of glue holding clusters of magnetic particles together.

Those clumps, being much larger than single magnetic particles, cannot rotate as quickly in solution, so they behave differently in an oscillating magnetic field. As the frequency of the applied field grows into the kilohertz range, the rotation of the particle clusters increasingly lags behind the applied field. You'd see something analogous if you placed a compass inside a coil and applied a current that oscillated in polarity faster than the needle could physically respond to the rapid changes in the magnetic field.

It's difficult to measure directly how much the rotating magnetic particles lag the applied field. But for complicated reasons, when the lag is small, the oscillatory motions of the magnetic particles include frequencies that were not present in the applied field. Conversely, when the lag is substantial, those additional frequency components are much diminished. So the frequency content provides a simple measure of whether or not clusters formed. If they did form, it indicates that the target virus was present.

The detection of those changes in the frequency content is not difficult, requiring only a suitable pickup coil, an amplifier, and a computer to do some straightforward digital signal processing.

ILLUSTRATION BY Chris Philpot



INCREASING CONCENTRATION

SEEING IS BELIEVING: Researchers at the University of Pennsylvania explored the intrinsic sensitivity of their microbubbling assay by taking smartphone images of their chip after exposing it to different concentrations of platinum nanoparticles. The number of bubbles produced grows with the increasing concentration of those particles. The researchers also showed that the number of bubbles grows with the increasing concentration of the targeted protein in the sample.

Wang is using a benchtop system connected to a laptop now, but he envisions all this being done by a handheld device. After the test sample mixes with the magnetic nanoparticles for about 10 minutes, it would be placed in that device, which in a few seconds would provide a readout of whether the virus was present. "We're screening different technologies to figure out the best way to create a low-cost and convenient [device] for the customer to use," says Wang.

We can certainly hope that Wang will be able to lower the costs enough for his device to become a consumer product and that it will have sufficient sensitivity to detect the COVID-19 virus in saliva. But his isn't the only possible solution on the table.

AT THE UNIVERSITY of Pennsylvania's Penn Center for Research on Coronavirus and Other Emerging Pathogens, Ping Wang (no relation to Jian-Ping Wang at the University of Minnesota) is working on yet another new way to detect tiny quantities of the SARS-CoV-2 virus. Wang calls the technique her group has pioneered a "microbubbling digital assay." It also uses magnetic particles to which SARS-CoV-2-specific antibodies are attached. But these magnetic particles are much larger than those used in the other Wang's magnetic-particle spectroscopy: Rather than being tens of nanometers in diameter, these are a few micrometers across. Her approach also employs nanometer-size particles of platinum that are attached to the same antibodies.

When both of these kinds of engineered particles are added to a solution containing SARS-CoV-2, the virus hooks up to both, sometimes linking a platinum nanoparticle on one side to a much larger magnetic particle on the other. The challenge is to figure out whether such a virus sandwich has formed. The tool Wang devised to determine that is a novel microchip. Being made of various polymers, it's very different from the silicon chips found in electronic gadgets. But like electronic chips, it's fabricated using lithography and physical vapor deposition.

Wang's chip is about 3 millimeters on a side. It contains an array of tiny square depressions, each 14 micrometers wide and 7 micrometers deep, which is just large enough to hold one of those virus sandwiches. A magnet is placed beneath the chip, and hydrogen peroxide is added to the sample solution on top. The magnet draws the magnetic particles downward, and some land in the tiny depressions.

This chip can reveal the presence of a virus because platinum catalyzes the decomposition of hydrogen peroxide into water and oxygen. Any virus sandwich caught in a well will generate oxygen there. Virus sandwiches that land between wells don't form bubbles for reasons that are currently unclear. But over time, the oxygen created inside a well forms a bubble, which is big enough to be seen with a smartphone camera using just a small amount of magnification. If there is no virus present in the sample, the platinum nanoparticles won't be linked up with the magnetic particles, and no bubbles will be generated inside the wells.

To automate the task of bubble identification and counting during her work on this technique last year, Wang trained a neural network using hundreds of images. That allowed her to develop a smartphone app that is able to tally the number of bubbles on a chip in seconds.

Currently, Wang's team is trying to miniaturize the equipment needed for this microbubbling assay, so that it could be carried out using a device attached to a smartphone. She's now testing this approach using samples from COVID-19 patients and planning to apply for emergency-use authorization from the FDA if the system proves accurate enough.

IT'S TOO SOON to know whether either of these two new antigen-detection technologies will indeed provide a way to detect the COVID-19 virus with inexpensive equipment, in near real time, and with sufficient sensitivity to do so using a person's saliva. With luck, one of them will meet that high bar. With even more luck both will, which would help enormously when it comes time to scale up production of the requisite devices to meet demand. One thing is for sure, though: If scientists and engineers are able to solve this technical challenge in the not-too-distant future, many people around the world will rapidly incorporate such tests into their daily lives. ■

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UNIVERSITY OF PENNSYLVANIA/WILEY (3)

CONTINUED FROM PAGE 29

human cells, the cells produce the antigen, which triggers an immune response. Inovio researchers knew, based on previous research on other coronaviruses, that the spike protein of SARS-CoV-2 would likely elicit an immune response. So that region of the virus's genome became their starting point for a vaccine.

There are many different ways to write out a DNA sequence that codes for the production of the same protein. To find the one that will work best as a vaccine, that bit of code has to be enhanced with other genetic and molecular elements. Inovio's proprietary gene-optimization algorithm showed researchers how to do this in such a way that the vaccine would provoke the large-scale production of an immunogenic spike protein.

Inovio's COVID-19 vaccine went from bench to bedside in just 83 days, Broderick says. The vaccine performed well in animals—as shown by a study that she and her colleagues published in May in *Nature Communications*. In late June, the company announced that the vaccine proved safe and appeared to provoke immune responses in 40 healthy people in a trial in the United States. The vaccine also provided protection for four months in monkeys that were vaccinated and then exposed to the virus, according to a report from Inovio in late July.

Keeping up with a virus's genetic changes also presents a challenge well-suited for computational analysis. Viruses are constantly mutating in small ways, so a vaccine must be designed around a relatively stable region of the virus's genome—a region of its genetic code that doesn't tend to mutate. "There are certain parts of the surface proteins on the virus that have a very high turnover, which you only find out as you sequence it and get changes in structure as it mutates," says Waseem of the Wagner Macula & Retina Center.

Over the last 10 months, tens of thousands of COVID-19 virus samples taken from patients around the world have been genetically sequenced and uploaded into an online repository hosted by the Global Initiative on Sharing All Influenza Data (GISAID), in Germany. Algorithms that compare those sequences can reveal which segments of the virus's genome frequently change, and which segments don't. As the virus continues to conquer new territories, researchers will keep tabs on their ever-changing foe.

ALL OF THIS WORK takes a lot of computing power. In March, the White House announced that it would collaborate with public and private groups to provide researchers worldwide with access to the most powerful supercomputers in an effort to "rapidly advance scientific research for treatments and a vaccine."

Called the COVID-19 High Performance Computing Consortium, the program includes resources from the U.S. Department of Energy National Laboratories and several universities and private companies, such as IBM and Hewlett-Packard Enterprise. The consortium boasts nearly

80 active projects, which have access to over 400 petaflops of computing power.

Mahmoud Moradi, a computational chemist at the University of Arkansas, in Fayetteville, led one of those projects. He used supercomputers at the Texas Advanced Computing Center to create enhanced 3D simulations of coronavirus spike proteins. The simulations revealed that the spike proteins become active and infect human cells much faster than those of a previous infectious coronavirus, SARS-CoV-1, which caused an outbreak in Asia in 2003.

Broderick at Inovio says that this kind of research is vital to vaccine-development teams. "Scientists can learn a huge amount of relevant information to assist with vaccine design," she says, "as well as understanding the mechanisms behind the pathogenesis of this virus."

Once a vaccine candidate is designed, the bulk of the work then shifts to testing. Vaccines are first tested in the lab on cells and on animals, and then on increasing numbers of people in clinical tests. Tens of thousands of trial volunteers will have received a vaccine before it's approved by U.S. regulators.

Unfortunately, AI tools can't replace those time-consuming steps. They might be able to predict which antigens the immune system will see, but what the immune system will actually do, in a live human, is beyond the capabilities of today's computers. "The human body is so complex that our models cannot necessarily predict with reliability what this molecule or this vaccine will do for the body," says Oren Etzioni, CEO at the Allen Institute for Artificial Intelligence. "That's why we have these slow and painful trials—our predictive models aren't good enough to give you reliable data."

Although AI can't predict the success of human trials, it can make sense of the mountains of data from these experiments by looking at all the parameters and finding patterns that a human brain might not spot. As vaccine candidates advance to second and third phases of clinical testing, thousands of patients will be involved, and AI systems will be key in rapidly analyzing the clinical and immunological data.

And as more researchers add their studies to the ever-increasing body of literature on the novel coronavirus, scientists will need help sorting through those papers. The Allen Institute developed a resource called CORD-19 that provides more than 130,000 scholarly articles on COVID-19 in machine-readable format. The Kaggle community, among other groups, leveraged the data set to create multiple AI systems to help researchers keep up with literature and answer high-priority research questions.

"I believe that within a decade AI will be an indispensable part of any medical researcher's tool kit both for scouring the literature and for analyzing experimental data," says Etzioni. And when the next pandemic comes—because there will always be a next pandemic—researchers will be poised to unlock the secrets of the deadly pathogen, design many potential vaccines to protect us, and rapidly identify the ones that can prevent a disaster like COVID-19 from befalling humanity again. ■

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ROBOTIC END-EFFECTORS

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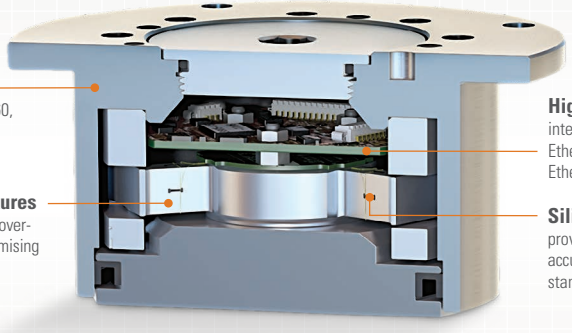

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EPFL

Faculty Position in Low-Power Analog Electronics

at the Ecole polytechnique fédérale de Lausanne (EPFL)

The Institute of Electrical Engineering in the School of Engineering is soliciting applications for a faculty position at the level of a tenure track Assistant Professor in **Low-Power Analog and RF Electronics**.

We seek top-level applicants with research interests in the broad area of analog and RF circuit design. Topics of interest include, but are not limited to: (i) the design of analog circuits and RF transceivers for IoT and 5G/6G devices, (ii) the design of low-noise and low-power sensor interfaces including imagers, (iii) time-of-flight (ToF) sensors and radar transceivers, (iv) ultra-low-power time and frequency references. The candidate is also expected to explore the design of low-power circuits using new devices in emerging technologies.

Applicants should have demonstrated a record of excellence in their chosen scientific area. Candidates with strong academic background, but with few years of experience in industry are also welcome.

This new position is aimed at reinforcing the collaboration between academia and the Swiss industry in the field of ultra-low-power electronics and RF integrated circuits. Applicants should demonstrate a potential for direct interactions with industrial partners to pursue specific technological advances.

As a faculty member of the School of Engineering, the successful candidate will be expected to initiate and develop an independent and creative research program, as well as to participate in undergraduate and graduate teaching. Internationally competitive salaries, start-up resources, and benefits are offered.

Applications should include a cover letter with a statement of motivation, curriculum vitae, list of publications and patents, and concise statements of research and teaching interests. Applicants should also provide the names and addresses of 3 to 5 referees. Applications must be uploaded in PDF format to the recruitment web site:

https://facultyrecruiting.epfl.ch/position/23691275

Formal evaluation of candidates will begin on **December 1, 2020**.

Enquires may be addressed to:
Prof. Jean-Philippe Thiran
Search Committee Chair
e-mail: iel-search@epfl.ch

For additional information on EPFL, please consult the websites: www.epfl.ch, sti.epfl.ch, iel.epfl.ch

EPFL is an equal opportunity employer and family friendly university. It is committed to increasing the diversity of its faculty. It strongly encourages women to apply.

COLLEGE OF ENGINEERING
ELECTRICAL & COMPUTER ENGINEERING
UNIVERSITY OF MICHIGAN

THE ELECTRICAL AND COMPUTER ENGINEERING (ECE) Division of the Electrical Engineering and Computer Science Department at the University of Michigan, Ann Arbor invites applications for junior or senior faculty positions, especially from women and under-represented minorities.

Successful candidates will have a relevant doctorate and a record of outstanding research in academia, in industry, or at national laboratories. They should have a strong commitment to teaching at undergraduate and graduate levels, providing service to the university and profession, and broadening the ECE Division's intellectual diversity.

We invite candidates across all research areas to apply. The highly ranked ECE Division (**www.ece.umich.edu**) prides itself on the mentoring of junior faculty toward successful careers. Ann Arbor is highly rated as a family friendly best-place-to-live.

Please see application instructions at:
https://ece.engin.umich.edu/people/ faculty-positions/

Applications will be reviewed as they are received; the site will remain open until **February 2021**

We seek faculty members who commit to excellence in graduate and undergraduate education, will develop impactful, productive and novel research programs, and will contribute to the department's goal of eliminating systemic racism and sexism by embracing our culture of Diversity, Equity and Inclusion (DEI).

The University of Michigan is an Affirmative Action, Equal Opportunity Employer with an Active Dual-Career Assistance Program. The College of Engineering is especially interested in candidates who contribute, through their research, teaching, and/or service, to the diversity and excellence of the academic community.

MIT EECS ELECTRICAL ENGINEERING AND COMPUTER SCIENCE

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Cambridge, MA

FACULTY POSITIONS

The Massachusetts Institute of Technology (MIT) Department of Electrical Engineering and Computer Science (EECS) seeks candidates for faculty positions starting in July 1, 2021, or on a mutually agreed date thereafter. Appointment will be at the assistant or untenured associate professor level. In special cases, a senior faculty appointment may be possible. Faculty duties include teaching at the undergraduate and graduate levels, research, and supervision of student research. Candidates should hold a Ph.D. in electrical engineering and computer science or a related field by the start of employment. We will consider candidates with research and teaching interests in any area of electrical engineering and computer science.

Candidates must register with the EECS search website at **https://school-of-engineering-faculty-search.mit.edu/eecs/**, and must submit application materials electronically to this website. Applications must include a cover letter, curriculum vitae, 2–3 page statement of research and teaching interests and goals.In addition, candidates should provide a statement regarding their views on diversity, inclusion, and belonging, including past and current contributions as well as their vision and plans for the future in these areas. Each application should include the names and addresses of three or more individuals who will provide letters of recommendation. Letter writers should submit their letters directly to MIT, preferably on the website or by mailing to the address below. Complete applications should be received by **December 1, 2020**. Applications will be considered complete only when both the applicant materials and at least three letters of recommendation are received.

*It is the responsibility of the candidate to arrange reference letters to be uploaded at **https://school-of-engineering-faculty-search.mit.edu/eecs/ by December 1, 2020**.*

Send all materials not submitted on the website to:
Professor Asu Ozdaglar
Department Head, Electrical Engineering and Computer Science
Massachusetts Institute of Technology
Room 38-403
77 Massachusetts Avenue
Cambridge, MA 02139

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UC DAVIS

University of California, Davis

Department of Electrical and Computer Engineering
Assistant, Associate or Full Professor Position
Position JPF03707

As part of UC Davis' commitment to hire leading research faculty with a strong commitment to teaching, research and service that will promote the success of historically underrepresented and marginalized student communities and address the needs of our increasingly diverse state and student population, the Department of Electrical and Computer Engineering at the University of California, Davis invites applications for an open rank faculty position to commences in July 2021.

The search focus shall include candidates with a depth of expertise in the following areas (not in order of importance): computer system and architecture, hardware security, high performance and parallel computing, domain specific hardware, Internet of things and networking, hardware and systems for machine learning and artificial intelligence, and cyber physical systems. Candidates whose research extends beyond these categories, and are in other emerging fields of computer engineering with the potential for high impact will also be considered.

We are searching for innovative and collaborative researchers who would seek interdisciplinary collaborations within the department and the campus. Candidates must have a Ph.D., a research record of high distinction, a demonstrated commitment to educate both undergraduate and graduate students, a track record or potential for attracting significant extramural research support, and aspire to help advance UC Davis' strategic goal of improving access and building an inclusive community for all marginalized populations. We seek candidates dedicated to educating a student body rich in diversity with respect to gender, ethnicity, first generation status, socioeconomic status, and academic inclusiveness, as well as to help advance UC Davis' strategic goal of improving access and building an inclusive community for marginalized populations.

Candidates must complete their application by no later than 11:59pm PST on **12/31/2020** to **ensure full consideration**. Applications will continue to be accepted until **3/31/2021**, but applications received **after** the initial review date will **only be considered if the position has not yet been filled**.

*Additional information and application instructions can be found at **http://www.ece.ucdavis.edu/**. Please review the full position description, which provides guidance on application requirements and recommendations to strengthen your application: **https://recruit.ucdavis.edu/JPF03707** Department of Electrical and Computer Engineering*

Department of Electrical and Computer Engineering
and Institute of Transportation Studies
Assistant, Associate or Full Professor Position
Position JPF03708

As part of UC Davis' commitment to hire leading research faculty with a strong commitment to teaching, research and service that will promote the success of historically underrepresented and marginalized student communities and address the needs of our increasingly diverse state and student population, the Department of Electrical and Computer Engineering at the University of California, Davis invites applications for an open rank faculty position to commences in July 2021.

This search focusses on computer vision, machine learning, data science, robotics and autonomous systems in complex and uncertain environments, and cyber-physical systems. Of interest are individuals working on system-level research that addresses multiple technical aspects of autonomous vehicles, ranging from sensing/perception, mixed autonomy traffic, human-machine interaction, to decision-making and control by leveraging advancement in sensor and information technology, machine learning and artificial intelligence (AI) techniques. Cybersecurity and privacy of connected and automated vehicles (CAVs) is also an area of interest. Expertise and interest in large scale simulations is a plus.

We are searching for innovative and collaborative researchers who will contribute to a plurality of our department's strong research areas as well as to the broader research initiatives of the UC Davis Institute of Transportation Studies (ITS-Davis). The candidate is expected to contribute towards the research and teaching mission of ITS-Davis, including creating a sustainable transportation future with electric vehicles and autonomous driving technology and participating in or leading center-planning activities. Preferences will be given to those who have a solid plan and track record of working across disciplines and leading teams. Candidates must have a Ph.D., a research record of high distinction, a demonstrated commitment to teaching both undergraduate and graduate students, and a track record or potential for attracting significant extramural research support. We are also actively seeking faculty who aspire to educate a student body rich in diversity with respect to gender, ethnicity, first-generation students, socioeconomic status, and academic interests, as well as to help advance UC Davis' strategic goal of improving access and building an inclusive community for marginalized populations.

Candidates must complete their application by no later than 11:59pm PST on **12/31/2020** to **ensure full consideration**. Applications will continue to be accepted until 3/31/2021, but applications received **after** the initial review date will **only be considered if the position has not yet been filled**.

*Additional information and application instructions can be found at **http://www.ece.ucdavis. edu/**. Please review the full position description, which provides guidance on application requirements and recommendations to strengthen your application: **https://recruit.ucdavis.edu/JPF03708***

*UC Davis is ranked 5th nationally by the **Wall Street Journal/Times Higher Education** and 11th nationally by **US News and World Report** among U.S. public universities overall and for research funding. The university is ranked third in the world for campus sustainability practices by the **2019 UI GreenMetric World University Rankings**. The campus is located in a beautiful natural setting near Silicon Valley and the San Francisco Bay area which offers abundant opportunities for corporate and academic collaborations. Please read our full job description to learn more about UC Davis.*

Massachusetts Institute of Technology

The Department of Brain & Cognitive Sciences (http://bcs.mit.edu), in collaboration with **the McGovern Institute for Brain Research, the Picower Institute for Learning and Memory, and the Schwarzman College of Computing** at MIT, is looking to hire a tenure-track faculty member at the assistant professor level or higher. The Department of Brain and Cognitive Sciences offers supportive mentorship to new faculty, an exceptional environment for scientific inquiry, and a strong commitment to an inclusive, welcoming culture. Applications from under-represented minorities will be given our highest consideration.

We encourage applications from candidates who aim to understand natural intelligence by building artificially intelligent systems. We seek candidates with a diverse range of computational tools and methods, including (but not limited to) machine learning, computer vision, robotics, probabilistic modeling, dynamical systems, planning, programming languages, and natural language processing. Candidates from computer science, engineering or related backgrounds that seek to develop collaborations with neuroscientists and cognitive scientists are particularly encouraged to apply. This position will have an affiliation with the new MIT Schwarzman College of Computing and the MIT EECS department.

Successful applicants are expected to develop and lead independent, internationally competitive research programs and to share in our commitment to excellence in undergraduate and graduate education by teaching courses and mentoring graduate and undergraduate students. PhD must be completed by start day of employment and some postdoctoral training is preferred.

Please submit application materials – cover letter, CV, statement of research and teaching interests and representative reprints – online at **https://academicjobsonline.org/ajo/jobs/16758**. In addition, candidates should provide a statement regarding their views on diversity, inclusion, and belonging, including past and current contributions as well as their vision and plans for the future in these areas.

To help direct the application, applicants should select "computational approaches to understanding intelligence" from the drop-down list on the application web page. In addition, please arrange to have three letters of recommendation submitted online. All application materials are due by midnight (EST) on **December 1, 2020**.

MIT is an equal opportunity, affirmative action employer. All qualified applicants will receive consideration for employment regardless of race, color, religion, sex, sexual orientation, gender identity, national origin, veteran status, or disability. We will take affirmative action to ensure that individuals historically discriminated against by race or gender are represented in our workforce and promoted within our institution.

United States Naval Academy
Annapolis, MD, USA

The Electrical and Computer Engineering Department at the United States Naval Academy invites applications for a tenure-track faculty appointment starting as early as Fall 2021 at the rank of Assistant Professor in all fields of electrical engineering and related interdisciplinary topics. USNA is a four-year undergraduate institution with a mission to prepare midshipmen morally, mentally, and physically for commissioning as officers in the naval services. For more information about this position and how to apply please visit the USNA position announcement at: **https://www.usna.edu/HRO/jobinfo/Tenure-track-ECE-AY21.php**

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ZJU-UIUC INSTITUTE

Zhejiang University-University of Illinois at Urbana-Champaign Institute

Zhejiang University-University of Illinois at Urbana-Champaign Institute
Tenure-Track Faculty Positions in Electrical Engineering and Computer Science

Zhejiang University/University of Illinois at Urbana-Champaign Institute (the ZJU-UIUC Institute) is an engineering college of Zhejiang University (ZJU), China. The institute invites highly qualified candidates for multiple tenure-track faculty positions at all levels from Assistant Professor to Full Professorship, and in areas of electrical, electronic and computer science that matches its multidisciplinary mission. Candidates should have exceptional academic record or demonstrate strong potential in the cutting-edge research areas of engineering and science multidisciplinary technologies.

Duties: Established as a world-class research institute, it conducts undergraduate and postgraduate teaching and research, and conducts classes and student activities in English.

Applications are particularly encouraged from candidates whose interests address interdisciplinary topics exemplified by computer and digital engineering, artificial intelligence, network and communications, electromagnetic and microwave, electronic engineering, power engineering, control, microelectronics and photonics.

Successful candidates will initiate and lead collaborative research and perform academic and professional service duties associated with the ZJU-UIUC Institute. They will be leaders for teaching and research innovation, giving students a meaningful and interactive engineering education.

Faculty at the institute will serve as Adjunct faculty in University of Illinois at Urbana-Champaign (UIUC).

Compensation and benefits: Salary and research initiation support will be commensurate with qualifications and competitive with international norms, including housing benefits.

Application materials should include a cover letter with current contact information including email address, as well as complete curriculum vitae, statements of research and teaching goals, and the names of three or more references. Please submit applications at **https://my.zjui.illinois.edu/submit/** or at **zjuihr@zju.edu.cn**. For more information, please visit job opportunities on **http://zjui.zju.edu.cn**.

JOINT INSTITUTE
交大密西根学院

The University of Michigan-Shanghai Jiao Tong University (UM-SJTU) Joint Institute invites applications for tenure-track or tenured positions at all levels (Assistant, Associate, and Full) in Electrical and Computer Engineering. Candidates should hold a Ph.D. in electrical and computer engineering, computer science, or a closely related field. The Joint Institute particularly seek candidates in the areas of micro-electronics, communication theory and networking, signal and image processing, robotics, computer architecture, data science, artificial intelligence, and database. The candidates are expected to establish vigorous research programs and contribute to undergraduate and graduate education. Salaries are highly competitive and commensurate with qualifications and experience.

The UM-SJTU Joint Institute receives strong support from both partner universities and the Chinese government. It offers B.S., M.S., and Ph.D. degrees in Electrical and Computer Engineering and related fields. Its ECE program is the first ABET accredited ECE program in the mainland of China, and its students are among China's best. The Joint Institute models itself after the world class U.S. research universities, in terms of its tenure review and promotion system, academic environment, research program, and undergraduate curriculum. Its official language is English.

For full consideration, please send a CV, statement of research interests and teaching goals, copies of three key publications, and the names and contact information of five references, as a single PDF file, to the Search Committee of the Joint Institute at ***ji-ece-facultysearch@sjtu.edu.cn****. More information is available at* ***http://ji.sjtu.edu.cn/****.*

EPFL

Professor in Photonics

at the Ecole polytechnique fédérale de Lausanne (EPFL)

and

PAUL SCHERRER INSTITUT
PSI

Head of Nanophotonics Laboratory

Paul Scherrer Institute (PSI)

The School of Engineering (STI) of EPFL and the Paul Scherrer Institute (PSI) invite applications for a tenured full or associate professor at EPFL who will also be Head of the Nanophotonics Laboratory of PSI. The holder of this joint EPFL/PSI position will lead the exploitation of nanotechnology for the use of short wavelength (UV to hard X-ray) light and the exploitation of short wavelength light for nanotechnology.

Applications are encouraged from leaders in photonics with particular achievements in nano- and micro-fabricated optical devices for the shaping, direction and detection of photon beams, and strong interest in providing such devices for the world-class accelerator-based short wavelength photon sources SwissFEL and SLS at PSI. As a faculty member of the EPFL School of Engineering and head at the PSI Micro- and Nano-technology Laboratory (LMN), the successful candidate will be expected to initiate an independent and creative research program with laboratories located at PSI and doctoral students from EPFL as well as participate in undergraduate and graduate teaching. The successful candidate will also be responsible for the management of LMN with 60-80 people and substantial nano- and microfabrication facilities dedicated to the creation of photonics components. She/he will play a key role in strengthening collaboration between PSI and EPFL and also with established industries and startups.

EPFL with its main campus located in Lausanne, and PSI located near Zürich, are dynamic and well-funded institutions of the Swiss ETH Domain that foster excellence and diversity. The successful candidate's main research activities will be undertaken at PSI while teaching and other academic activities will be performed at EPFL. The pairing of a technical university covering essentially the entire palette of engineering and science and a national laboratory with unique large-scale facilities for provision of brilliant photon beams offers a fertile environment for high-impact experiments and cooperation between different disciplines. EPFL and PSI are multi-lingual and multi-cultural institutions, with English often serving as a common interface.

Applications should include a cover letter with a statement of motivation, curriculum vitae, list of publications and patents, and concise statements of research and teaching interests. Applicants should also provide the names and addresses of at least five referees. Applications must be uploaded in PDF format to the recruitment web site:

https://facultyrecruiting.epfl.ch/position/23691272

Formal evaluation of candidates will begin on **15 November 2020** and continue until the position is filled.

Enquiries may be addressed to:
Prof. Demetri Psaltis
Search Committee Chair
E-mail: photonics-search@epfl.ch

For additional information on EPFL and PSI, please consult the web sites: epfl.ch, sti.epfl.ch, psi.ch and psi.ch/syn

EPFL and PSI are equal opportunity employers and family friendly institutions. They are committed to increasing the diversity of their faculty and staff. They strongly encourage women to apply.

BUILT FOR BATTLE

The SCR-536 Handie-Talkie was "designed for operation under battle conditions," according to its technical manual. An ad for the World War II handheld radio set, a direct ancestor of modern-day walkie-talkies, featured a soldier's endorsement: "Just like having a house telephone at your fingertips. We're never alone. We feel safer, stronger, because we're always in touch with our command post!" Years later, though, a retired Army officer who used the radio during the Allied invasion of North Africa in November 1942 offered a less enthusiastic review: "In our amphibious landing in North Africa…it leaked water—and salt water ruined the sliding switch contacts." Users could be hard on the 536, he added: "One set came into our shop…with all the tubes dead. Some infantryman had used it to pound in tent pegs!" ■

↗ **For more on battlefield radios, see spectrum.ieee.org/pastforward-oct2020**

AUSTRALIAN WAR MEMORIAL

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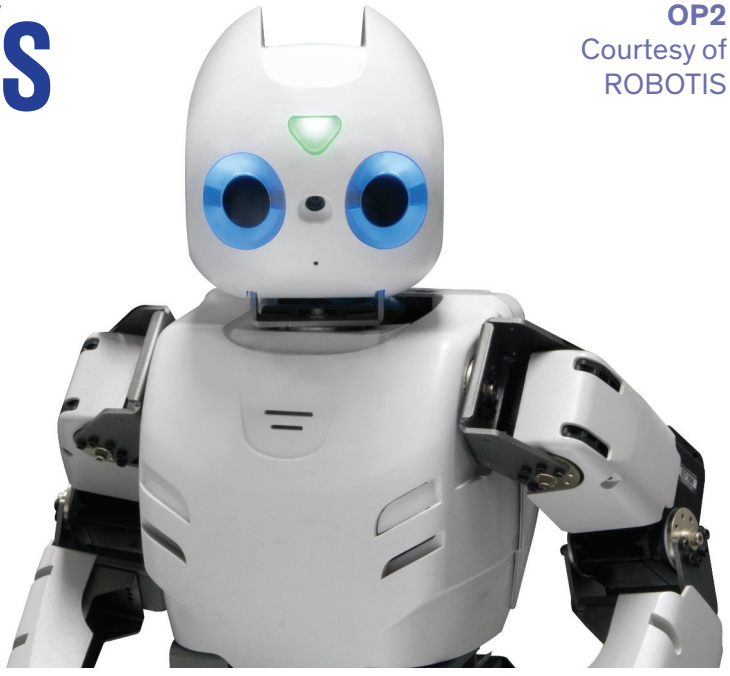

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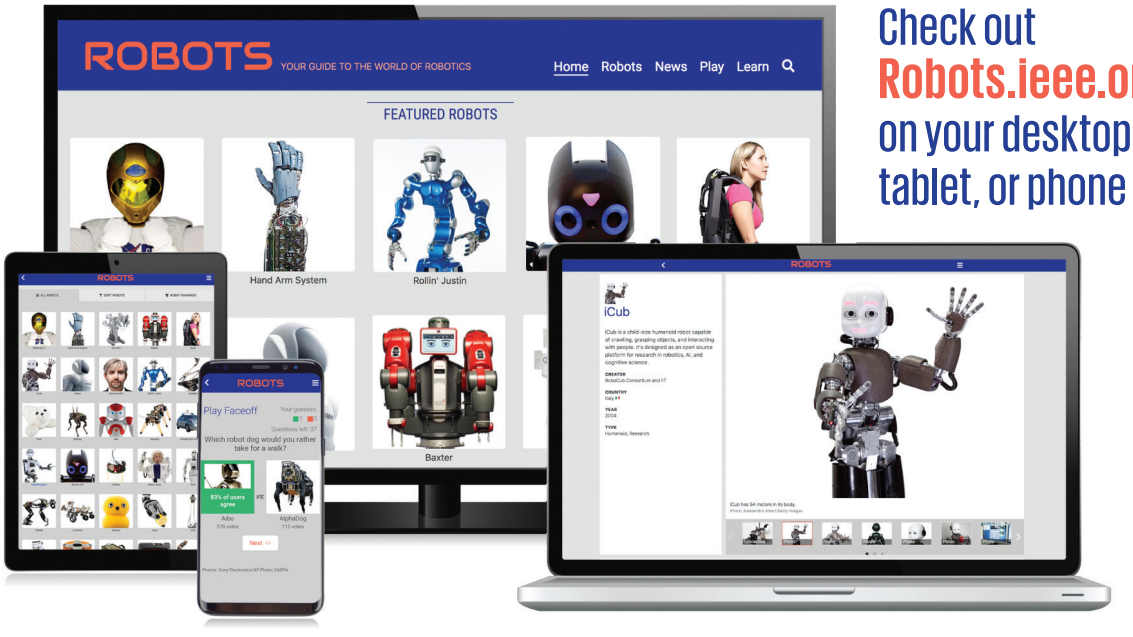

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