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Top 10 Emerging Technologies of 2021

The Threat of Solar Superflares

Software That Spies on Your Emotions

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THE FATE OF OUR GALAXY

New research on cosmic collisions is revealing the Milky Way's future

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SCIENTIFIC AMERICAN



ASTRONOMY

32 Cosmic Crashes

New revelations about how galaxies collide offer a preview of the Milky Way's future. *By Aaron S. Evans and Lee Armus*

TECHNOLOGY

40 Spying on Your Emotions

Tech companies now use AI to analyze your feelings in job interviews and public spaces. But the software is prone to racial, cultural and gender bias. *By John McQuaid*

SPECIAL REPORT

48 Top 10 Emerging Technologies for 2021

Innovations to help tackle societal challenges—especially climate change. A collaboration between *Scientific American* and the World Economic Forum.

SPACE WEATHER

60 The Threat of Solar Superflares Geomagnetic storms may occur more often than scientists thought, with ominous implications for a wired global society. *By Jonathan O'Callaghan*

SPECIAL REPORT

- S1 Innovations in Cancer Early Detection
- S3 The Equity Equation By Melba Newsome
- **S7** The COVID Cancer Effect By Usha Lee McFarling
- S10 Graphic: Cancer Diagnoses before and during COVID in the U.S.
- **S12** The Colon Cancer Conundrum By Cassandra Willyard
- S14 Graphic: Concerning Trends in Colorectal Cancer Incidence in the U.S.

ON THE COVER

In billions of years the Milky Way and its nearest spiral neighbor, Andromeda, will crash together, eventually combining to form a single galaxy. Astronomers are studying galaxy mergers across the universe to foretell our own future and understand how these events have shaped cosmic history. **Illustration by Ron Miller**



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4 From the Editor

Letters 6

Science Agenda 10

The pandemic revealed-and exacerbated-the need for stronger systems of mental health care. By the Editors

12 Forum

COVID's lessons could help stop AIDS. By Emily Rymland

14 Advances

What new spy tech can learn from a blank wall. A satellite programmable from afar. Bacteria-produced proteins that snag nuclear waste. An ultra rare tiger fur mutation.

28 Meter

The binary code of snow in verse. By Glenn R. McLaughlin

30 The Science of Health

Black children have worse outcomes in common surgeries than do white kids. By Claudia Wallis

70 Recommended

Rachel Carson's poetic observations of the sea. Tracing humans' relationship with elephants. A novel that braids technology and mysticism. Celebrating a forgotten botanist. By Amy Brady

72 Observatory

Women were once shunned by Antarctic science but now are doing crucial research. By Naomi Oreskes

74 50, 100 & 150 Years Ago By Mark Fischetti

76 Graphic Science

An ancient tusk reveals the extensive travels of a mammoth. By Tess Joosse, Beth Zaiken and Jen Christiansen

Scientific American (ISSN 0036-8733), Volume 325, Number 6, December 2021, published monthly by Scientific American, a division of Springer Nature America, Inc., 1 New York Plaza, Suite 4600, New York, N.Y. 10004-1562. Periodicals postage paid at New York, N.Y., and at additional mailing offices. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 40012504. Canadian BN No. 127387652RT; TVQ1218059275 TQ0001. Publication Mail Agreement #40012504. Return undeliverable mail to Scientific American, P.O. Box 819, Stn Main, Markham, ON L3P 8A2, Individual Subscription rates: 1 year \$49,99 (USD), Canada \$59,99 (USD), International \$69,99 (USD). Institutional Subscription rates: Schools and Public Libraries: 1 year \$84 (USD), Canada \$89 (USD), International \$96 (USD), Businesses and Colleges/Universities: 1 year \$399 (USD), Canada \$405 (USD), International \$411 (USD). Postmaster: Send address changes to Scientific American, Box 3187, Harlan, Iowa 51537. Reprints inquiries: RandP@sciam.com. To request single copies or back issues, call (800) 333-1199. Subscription inquiries: U.S. and Canada (800) 333-1199; other (515) 248-7684. Send e-mail to scacustserv@cdsfulfillment.com. Printed in U.S.A. Copyright © 2021 by Scientific American, a division of Springer Nature America, Inc. All rights reserved



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Introducing ATEM Mini Pro The compact television studio that lets you create presentation videos and live streams!

Blackmagic Design is a leader in video for the television industry, and now you can create your own streaming videos with ATEM Mini. Simply connect HDMI cameras, computers or even microphones. Then push the buttons on the panel to switch video sources just like a professional broadcaster! You can even add titles, picture in picture overlays and mix audio! Then live stream to Zoom, Skype or YouTube!

Create Training and Educational Videos

ATEM Mini's includes everything you need. All the buttons are positioned on the front panel so it's very easy to learn. There are 4 HDMI video inputs for connecting cameras and computers, plus a USB output that looks like a webcam so you can connect to Zoom or Skype. ATEM Software Control for Mac and PC is also included, which allows access to more advanced "broadcast" features!

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Monitor all Video Inputs!

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FROM THE EDITOR

Long-Range Forecast

What does the future hold? Ultimately that's determined by gravity. Our Milky Way galaxy is destined to collide with our closest large neighbor, the Andromeda galaxy, in about five billion years. There's no stopping it, but we can predict what's going to happen, and thanks to powerful new telescopes, we can even watch previews by studying other galaxy mergers. In our cover story this month (page 32), astronomers Aaron S. Evans of the University of Virginia and Lee Armus of the California Institute of Technology foretell how our two galaxies will become one, creating energetic new star-forming regions and smashing their central black holes together in a burst of gravitational waves. We won't be around to watch, but we will get a great view of other galaxies' collisions (including a triple merger!) if the James Webb Space Telescope (JWST, which some astronomers call the Just Wonderful Space Telescope to focus on the space rather than the former NASA administrator) launches successfully in the next weeks or months.

Our sun will be a red giant by the time we merge with Andromeda, engulfing Mercury and Venus and then Earth as it grows to a diameter as large as Earth's current orbit. But the sun can cause a lot of trouble for us well before that time, as space journalist Jonathan O'Callaghan explains on page 60. You may have heard of the Carrington Event, a massive geomagnetic storm in 1859 that fried telegraph lines. It and a similar solar eruption in 1921 were mostly curiosities in their times, but now they are recognized as warnings that a blast from the sun could cause catastrophic fires and meltdowns in our electrical infrastructure and satellite networks. That would be bad, but it could be worse: In 2012 scientists discovered a solar flare from the year



Laura Helmuth is editor in chief of *Scientific American*. Follow her on Twitter @laurahelmuth

775 that was 10 or 100 times more energetic. Now researchers looking for odd isotopes in ice cores have found evidence for two more superflares, from 5259 and 7176 before the current era. Someday it'll happen again, and we are not yet prepared.

If you're reading about these ominous events within view of a surveillance camera, it might—well, so boosters claim—be able to pick up on any distress, engagement or amusement on your face. The field of "emotion AI" is moving quickly, and its applications are moving even faster, with marketers using the technology to gauge customer behavior and some companies using it to screen job applicants. But as with any artificial intelligence trained on human data sets, emotion and facial-recognition AI reinforce biases, as author John McQuaid writes on page 40. The research has brought new attention to the nature of emotion and whether human facial expressions are truly universal.

If you've been meaning to catch up on your health checkups (that's on my to-do list), please read our Innovations In package about cancer screening to understand how and why this would be a good time to schedule an appointment (*page S1*). Colon cancer rates are going up in people younger than 50, and there are life-threatening racial and other disparities in access to all kinds of cancer screening. The COVID pandemic delayed regular tests for many people, and we'll be seeing the consequences of those missed screenings for years to come.

This year marks our 10th collection of the Top 10 Emerging Technologies of the year, a collaboration run by *Scientific American* emerita editor in chief Mariette DiChristina with the World Economic Forum and a group of experts from around the world (*page 48*). It's an inspiring collection, full of actionable ideas to fight climate change, improve food systems, treat diseases, and more. We're looking forward to covering the successes of some of these technologies in the future.

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August 2021

BROWN DWARFS

In "<u>Not Quite Stars</u>," by Katelyn Allers, the diagram "A Guide to Brown Dwarfs" states that these objects are "at least" 13 Jupiter masses. Yet it shows one brown dwarf that is eight Jupiter masses and another that is between three and 10. Meanwhile the main text refers to "planetary-mass brown dwarfs" that are less than 13 Jupiter masses.

I thought the definition of brown dwarfs precluded Jupiter masses below about 13—and that the process of their formation would not produce objects below a certain mass. So what, exactly, is the lower limit? Do we know?

ROBERT WALTY Stephens City, Va.

ALLERS REPLIES: Astronomers haven't settled on an accepted name for objects with planetary masses lower than 13 times that of Jupiter that don't orbit a host star, and there's still some good-spirited debate about the dividing line between exoplanets and brown dwarfs. Ideally, we would define extrasolar planets as objects that formed from the disk of a host star and brown dwarfs as objects that formed like scaled-down stars. Unfortunately, we can't easily observe how an individual object formed. I personally prefer the term "planetary-mass brown dwarf," but that can be a bit of a mouthful.

We use the same techniques to discover and characterize free-floating objects whether they have masses above or below 13 times

"Alzheimer's disease victims and families are desperate for real cures."

MICHAEL J. DEWEERT KANEOHE, HAWAII

that of Jupiter. So for most purposes, lumping them together as brown dwarfs makes sense. In the end, I'm much more interested in what we can learn about and from these objects than what name we label them with.

PLAY AND IDENTITY

I noticed an unexpected connection between "Why Animals Play," by Caitlin O'Connell, and the gem that was "The World's First Trans Clinic," by Brandy Schillace. O'Connell stated that animals, from pachyderms to primates, engage in play as practice for hunting, fighting, fleeing or mating. Growing up, I learned an additional function of play: identity formation. I viscerally cringed when I heard my female name, so I reinvented myself as a dog or dinosaur to whom names meant nothing. It should be noted that sexual differences in those species are far more subtle than in humans. For the hours in which I was fantasizing, I could escape the body that abraded me, as well as any roles of "daughter" and "girl."

Now, four years after realizing my identity as a gay transgender man, I gaze down at the black-and-white image of a costume party in the early 20th century at the Institute for Sexual Research in Germany that opens Schillace's article. If I had lacked the privilege to live in a time and location where social and medical transition is safe, you can bet I would be attending all sorts of "costume parties." Sometimes the guise of mere play is what we need to align ourselves with instinctual ipseity. Thank you for giving visibility to transgender and other LGBTQ+ people.

STEPHEN HUITING Grass Valley, Calif.

POPULOUS POULTRY

"<u>Counting Birds</u>," by Clara Moskowitz and Jen Christiansen [Graphic Science], claims that no single avian species has an estimated population of more than 1.6 billion individuals, according to an analysis of 92 percent of extant bird species. This is a remarkable number for two reasons. First, it implies that humans outnumber every single bird species, despite weighing far more than common birds. Second, it ignores domesticated avian species. In 2019 there were 25.9 billion farmed chickens worldwide, making them by far the most common avian species on Earth.

The article questions what effect humanity has on avian populations. Any such inquiry would be incomplete without considering farmed species.

David Leppik via e-mail

MOSKOWITZ REPLIES: It's sobering and true that the most numerous avian species on Earth is the domesticated chicken rather than any of the species in the wild examined by the researchers. This fact is all the more alarming when we remember that humans are also the reason that so many of the populations of birds in nature are decreasing, just as our consumption of farmed chickens rises every year.

WEAPONS OF PEACE

In the concluding paragraph of "<u>Overhyped</u>," David Wright and Cameron Tracy note that there are shrinking resources for impartial research on the abilities and impacts of novel weapons. Although this is far from my own research area of music history, and as a Quaker, I am a pacifist, I recognize the importance of that work: it was my father's.

In the 1950s and early 1960s Laurence B. Dean, Jr., was a member of the Weapons Systems Evaluation Group and its successor, the Institute for Defense Analyses. Among his colleagues (and indeed his closest friend) was the late political scientist George W. Rathjens, who wrote for *Scientific American* on national-security matters in April 1969, January 1970 and February 1993.

Although the work they were doing was focused on weaponry, they construed it as directed toward peace. I see the work of Wright and Tracy and their colleagues in a similar light, and I fervently hope it can be sustained at a level strong enough to inform policy- and decision-making in an area that affects the peace and security of us all.

JEFFREY J. DEAN Royal Birmingham Conservatoire, Birmingham City University, England FISHER INVESTMENTS[®]

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LIVING WITH STUTTERING

Thank you for "<u>The Stuttering Mind</u>," by Lydia Denworth. Now pushing 80, I have stuttered since early childhood. I endured countless trips to "therapists," one of whom squirted me in the face with a water pistol when I stuttered. My father was convinced that I just didn't try hard enough to use the various "techniques" that were the standard of the day. I was never able to convince him that trying harder often made things worse.

Even at my age, learning from Denworth's article that my brain is apparently wired differently brought a tremendous sense of relief—and tears to my eyes. We now have scientific evidence that this is not a personal failing or a character weakness. Despite my stuttering, I enjoyed a 30-year career as a college professor. Now retired, I still recall the pride and sense of accomplishment I experienced when marching into the auditorium at commencement with my faculty colleagues.

GERRY MYERS via e-mail

ALZHEIMER'S UNKNOWNS

As the primary caregiver for an elderly Alzheimer's patient, I eagerly read "<u>A New Understanding of Alzheimer's</u>," by Jason Ulrich and David M. Holtzman. Unfortunately, I ultimately found it disappointing. The insight that microglia can modulate the course of the disease is interesting, and immune system seasonality might explain some phenomena, such as the <u>seasonal de-</u> pendenceof Alzheimer's symptoms, which I have observed in my own patient.

But the research does nothing to elucidate the underlying *causes* of the disease. Based on the article, my impression is that therapies aimed at microglia might ease symptoms but not be curative.

Alzheimer's disease victims and families are desperate for real cures. Sadly, we still have a long way to go. I'll keep looking for breakthroughs in the science, although it is likely already too late to help my own loved one.

MICHAEL J. DEWEERT Kaneohe, Hawaii

ERRATUM

"<u>Not Quite Stars</u>," by Katelyn Allers, should have said that astronomers Rafael Rebolo López, María Rosa Zapatero-Osorio and Eduardo L. Martín observed elements in Teide 1's atmosphere, not molecules.

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Expand Mental Health Care

The pandemic showed why it is a medical necessity

By the Editors

It is a classic refrain in psychological research: people are more resilient than they realize. The acute upheaval of the early pandemic era led to a spike in depression and anxiety. A year or so later those numbers appeared, in many studies, to return to prepandemic levels, reflecting the science that says most of us tend to bounce back from traumatic events. But the longer-term disruptions, losses and volatile shifts from hope to fear to languishing are harder to parse. COVID has already killed or disabled millions, deepened economic insecurity and racial inequality, and forced radical adaptations to daily life; its serious effects on mental health and well-being very likely will continue and in ways still unknown.

In 2020 the U.S. Congress responded to the mental health crisis by providing temporary funding for services and forcing the expansion of insurance coverage. These emergency measures must be permanently extended to meet emerging needs—and expanded to tackle long-standing and systemic inadequacies in care. In September the American Psychological Association called on Congress to do just that, along with mandating increases in the number of mental health providers. The *Lancet* COVID-19 Commission Task Force on Mental Health, meanwhile, wrote that the pandemic "offers a critical opportunity to invest in and strengthen mental health care systems to achieve a 'parity of esteem,' meaning that someone who is mentally ill should have equal access to evidencebased treatment as someone who is physically ill."

The idea that mental health is less legitimate than physical health has led to paltry insurance coverage, a scarcity of counseling professionals, and regulatory hurdles that make finding care especially difficult in rural and other underserved locations. Yet research has continued to reveal that the separation between mind and body is a false one: chronic emotional distress can significantly increase the chances of developing serious physical disease.

Talk therapy is especially well-suited to telemedicine, which has grown rapidly as an emergency measure and can be adopted as a true alternative to clinical settings. Video-based sessions work as well as, if not better than, in-person sessions, perhaps because it is easier for people to show up consistently. Insurance companies must continue to cover virtual appointments. Equally important are systemic policy changes to bolster socioeconomic support: it is harder to cope with emotional distress when also worrying about financial security.

Young people, in particular, have been hurt by pandemic disruptions. Many are struggling to see a hopeful future for themselves—a key to resilience. Researchers agree that preempting behavioral problems and mental illness makes more sense than be-



ginning treatment after a crisis. One way to proactively reach more young people is to teach cognitive-behavioral therapy and mindfulness in schools. Using standard textbooks and trainings, students could learn to self-soothe, regulate emotions and form healthy coping mechanisms for stress. Such institutional programs would be especially helpful for the more than two million children worldwide who have lost a caregiver to COVID.

Two other groups of people need dedicated focus: those who were infected with COVID and those who treat them. In a recent global review, more than half of people who tested positive report symptoms of so-called long COVID, including brain fog, lethargy and depression. Approximately one in three survivors has been diagnosed with a generalized anxiety disorder and one in eight with post-traumatic stress disorder. Clinicians must prepare for a surge of patients who need psychiatric treatment. Nurses, doctors and other health-care workers, too, need more institutional support; many still avoid speaking up about psychological distress, fearing (often rightly) that it could jeopardize their jobs. Ending the stigma of seeking care would help acknowledge the traumas of COVID, as well as the burnout that was already endemic in the profession.

The "end" of the pandemic must not signal a return to the status quo, if only because it is not the only global force threatening emotional resilience. Severe wildfire seasons, rapidly intensifying hurricanes and deluges of rain—all consequences of climate change—mean that more and more people are experiencing terrifying disasters and loss. Such upheavals will keep overlapping rather than dissipating. It is long past time to prioritize mental health as essential to overall health. Fostering resilience in a world of accelerating uncertainty depends on it.

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Lessons from COVID Could End AIDS

Taking testing and prevention from the clinic to where people live is a good start

By Emily Rymland

The COVID pandemic has taught America's health-care system a lot about fighting a highly contagious, deadly virus. There have been victories and failures, and we hope both will make us better prepared for the next infectious disease threat. But other medical providers and I working in HIV prevention say we should not wait to put those lessons to work. We need to apply some of the urgency and innovation we are using to fight the raging inferno of the COVID pandemic to extinguish the smoldering embers of the still deadly HIV/AIDS epidemic.

The HIV/AIDS community has racked up heroic, lifesaving victories with medications that make HIV a survivable chronic condition. When taken properly, these treatments may render the infection nontransmissible. And when preexposure prophylaxis (PrEP) is taken as prescribed by HIV-negative people, it confers nearly perfect protection against contracting the virus through sex. Both HIV infections and AIDS deaths have dropped steadily, and this outcome is worthy of celebration. Nevertheless, there are new infections every day in the U.S. and around the world. In spite of treatments and PrEP, there are still too many people lacking access to good HIV care and education about prevention. Here at <u>Nurx</u>, a telemedicine company where we order home HIV tests and prescribe PrEP, we have to inform a newly infected patient of their status at least twice a week, or about 100 times a year. It is never an easy call to make.

We often hear people ask whether HIV even still exists, which makes my colleagues and me angry—not at the person asking the question but at public health authorities' inertia and the media's silence around the virus. In the U.S., approximately 1.2 million people are living with HIV, and 14 percent of them do not know they have it. Persistent stigma and a lack of testing keep this population in the shadows.

In 2019 the approximately 34,800 new infections in the U.S. were mostly in Southern states and were not evenly distributed across their populations. This is because testing, prevention and treatment are not reaching those who need it most: men who have sex with men, Black and Latino Americans, and transgender people. That being said, education must be shared with all groups. Statistics do not matter when you are the one affected.

For instance, we fail women when we leave them out of the discussion. Whenever we tell a cisgender woman that she is HIV-positive, she is completely shocked, and often she says she nev-

er thought it was even a possibility. Our patients have included a divorced grandmother in her 60s who contracted HIV from a single sexual encounter at her college reunion and a student attending a privileged, prestigious university. The student was very sick and had full-blown AIDS by the time she was diagnosed, but none of the many doctors she had consulted about her illness had thought to test her for HIV.

After what we have witnessed this past year, it is hard not to see HIV's persistence in the U.S. as a failure of will. COVID showed that our health-care system can rapidly reorganize to provide things such as drive-through testing centers in sports stadiums; a warp-speed vaccine effort; and public education efforts that had everyone talking about antibodies, antigens and viral load as easily as they had once chatted about the weather. We can certainly exert the much less disruptive effort required to end HIV. Here's how:

• **Test, test, test.** With COVID we saw that frequent testing, including that of asymptomatic people and especially of those working or living in high-risk environments, was essential to containing the virus until a vaccine came along. Medical providers should recommend that sexually active patients be tested for HIV unless they are certain these people are at particularly low risk. Often they do not offer HIV testing to patients who they assume have little risk, and patients do not know to ask. Going forward, we should act more like the <u>University of Chicago</u> <u>Medical Center</u>, which set up a combination HIV-COVID testing site for the public during the pandemic.

• Destigmatize. Health-care providers should not judge or shame people for COVID infection-whether they caught it working at an essential job or attending a highrisk social gathering out of a human need for interpersonal connection. Similarly, we should destigmatize HIV and the ways people contract it. Health-care providers can be uncomfortable talking about sex, and when their schedules allow for only 15 minutes per patient, they may feel there is no time for what are actually crucial conversations about a patient's sex life. The combination of these two things may leave patients without the care they should get because they are being treated within a system that does not normalize and prioritize sexual health as a crucial component of comprehensive care. All people should be asked about their sexual health so they can get tested for HIV at the frequency that is right for them and be prescribed PrEP if their sex life puts them at risk for contracting HIV.

• Meet people where they are. During COVID we have brought tests and vaccines to stadiums, schools, supermarkets, and more—so let's make HIV prevention and treatment that easy by moving testing and prevention outside the clinic to where people live and work. Patients who need HIV testing and prevention have to jump



Emily Rymland is director of clinical operations at Nurx and is certified by the American Academy of HIV Medicine as an HIV specialist. She also runs the Buseesa Community Development Center, a small bush clinic in western Uganda.



through too many hoops to get care. The first hoop is finding a provider that they can trust. Imagine living in a small town where everyone knows you and your family or where the lab technician or pharmacist is also a member of your church community. The shame and fear associated with disclosing one's sexual behavior prevent many from seeking care face-to-face.

One way to bring informed, nonjudgmental HIV prevention to people is through telehealth, which allows them to reach out to a medical provider any time, day or night, from their smartphones to request an HIV test or a prescription for PrEP—no looking for a clinic, waiting for an appointment, taking time off from work, or letting shame or stigma lead them to cancel their appointment. At-home tests and PrEP medication then can be sent to the patient's door in discreet packaging, and communications with medical providers can happen in the comfort and convenience of the person's home.

But to fulfill the potential of telehealth, we need policy changes. A step is to change laws that prohibit providers from offering care across state lines. Acknowledging that medical professionals can effectively give preventive care to patients across states or time zones will improve access to the best HIV care (often concentrated in cities) for those who need it most (those in poor, rural areas). During the pandemic, those in-state requirements were waived, dramatically reducing the burden on clinics and keeping patients at home when that was the safest place to be.

Another way to make this lifesaving and cost-saving care more accessible is to improve telehealth reimbursements. State laws requiring that care begin in person or that a patient have a prior relationship with a medical provider before telehealth can be used or reimbursed create an often insurmountable barrier to access for populations that need it most, face stigma and in many cases are at greater risk of contracting HIV.

The city of San Francisco has had low rates of COVID compared with other dense cities. Its success has been attributed to a public health infrastructure that learned hard lessons from the AIDS epidemic and was prepared to sound the alarm early, test people and trace contacts of infected individuals. Now let's take those lessons, alongside what the health system as a whole has learned from COVID, and apply them to ending HIV in all communities around the country.

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ADVANCES



DISPATCHES FROM THE FRONTIERS OF SCIENCE, TECHNOLOGY AND MEDICINE



INSIDE

- Elephants combine simple trunk movements into complex motions
- Trees tap deep bedrock to quench thirst
- Bacteria build lengthy muscle proteins for synthetic fibers
- Eye contact plays an unexpected role in one-on-one discussions

TECH

Watching You

A new surveillance technique is the latest to glean surprising info from unassuming sources

Stare at a blank wall in any room, and you are unlikely to learn much more than the paint color. But a <u>new technology</u> can inconspicuously scan the same surface for shadows and reflections imperceptible to the human eye, then analyze them to determine details including how many people are in the room—and what they are doing. This tool could extrapolate information from a partial view of a space, perhaps spying on activity from around a corner or monitoring someone who avoids a camera's line of sight.

As people move around a room, their bodies block a portion of any available light to create subtle and indistinct "soft shadows" on walls. Brightly colored clothing can even cast a dim, reflected glow. But these faint signals are usually drowned out by the main source of ambient light. "If we could do something like subtracting this ambient term from whatever we are observing, then you would just be left with camera noise—and signal," says Prafull Sharma, a graduate student at the Massachusetts Institute of Technology. Sharma and other M.I.T. researchers isolated that ambient term by filming a wall in a room as its occupants moved around and averaging the frames over time. This eliminated the humans' shifting shadows, leaving only the light from the main source plus shadows from furniture or other stationary objects. Then the researchers removed these features from the video in real time, revealing moving shadows on the wall.

Next, Sharma's team recorded blank walls in several rooms in which the researchers enacted various scenarios and activities. People moved around, alone or in pairs, outside the camera's view. Others crouched, jumped or waved their arms. Then the team fed the videos into a machine-learning model to teach it which soft shadow patterns indicated which behavior. The resulting system can automatically analyze footage of a blank wall in any room in real time, determining the number of people and their actions. The work was presented at the 2021 International Conference on Computer Vision in October.

Although this system can function without calibration in any room, it performs poorly in dim lighting or in the presence of a flickering light source such as a television. It can register only group sizes and activities for which it has been trained, and it requires a high-resolution camera; a standard digital camera created too much background noise, and smartphone camera results were even worse.

Despite its limitations, the method highlights how imaging and machine learning can transform imperceptible indicators into surveillance. "It's a very cool scientific finding that such a low-intensity signal can be used to predict information," Sharma says. "And of course, as we established, the naked eye cannot do this at all."

A blank wall is far from the first innocentlooking item to reveal secrets about its surroundings. "In general, these are called sidechannel attacks, or side-channel surveillance," says Bennett Cyphers, staff technologist at the nonprofit Electronic Frontier Foundation, which promotes digital rights. "It's when you use sources of information that aren't directly what you're looking for—that might be outside the box of normal ways of gathering information—to learn things that it doesn't seem like you'd be able to."

Side-channel attacks can take advantage of some extremely unassuming inputs. In 2020 researchers used reflections from various shiny objects—including a bag of chips to reconstruct an image of a surrounding room. Sound and other vibrations can also yield a lot of indirect information. For example, audio of a person typing at a computer can reveal the words being written. And a computer itself can act as a microphone: in a 2019 study, researchers developed software that detected and analyzed how ambient sound waves jiggled a hard drive's read head over its magnetic disk—and could thus effectively record conversations taking place near the machine.

Scientists have also developed floorbased sensors capable of <u>detecting footstep</u> vibrations, discerning individuals' identities and even diagnosing them with certain illnesses. Most of these techniques rely on machine learning to detect patterns that human intelligence cannot. With high-resolution audiovisual recording and computational power becoming more widely available, researchers can train systems with many different inputs to glean information from often overlooked clues.

So far at least, the surveillance potential does not seem to be keeping many privacy advocates awake at night. "This blank-wall attack, and other sophisticated side-channel attacks like it, simply should not be a worry for the average person," says Riana Pfefferkorn, a research scholar at the Stanford Internet Observatory. "They are cool tricks by academic researchers that are a long way off from being operationalized by law enforcement." Routine use is "way off in the future, if ever-and even then, the police still couldn't just trespass on your property and stick a camera up against your window." Cyphers agrees. "Everyone carries a smartphone, tons of people have smart speakers in their houses, and their cars are connected to the Internet," he notes. "Companies and governments don't usually have to turn to things like footage of a blank wall to gather the kind of information that they want."

Although side-channel methods are unlikely to target an average person for now, they could eventually find their way into realworld applications. "The military and intelligence agencies have always had specific uses for any kind of surveillance they can get their hands on," Cyphers says. Sharma agrees that such uses are possible, but he also suggests some more innocuous ones: for example, vehicles could scan blank walls as part of an autonomous pedestrian-detection system for areas with poor lines of sight, such as parking garages. And some researchers who explore side-channel techniques suggest they could be used to monitor the elderly and detect falls or other problems.

Sharma says his own system would be capable of fall detection—if he had gathered the examples to train it. But, he quips, "I refuse to fall down in 20 different rooms to collect data." —Sophie Bushwick

CONSERVATION

Smartphone Patrol

Community-based monitoring could reduce Amazon deforestation

Efforts to preserve the Amazon rain forest, which supports immense biodiversity and locks away about 123 billion metric tons of climatethreatening carbon, are growing ever more urgent as the ecosystem's destruction accelerates. Indigenous peoples have been trying to protect the region by patrolling their territorial boundaries for illegal activities, blocking dam construction, and more. But rapid deforestation continues.

A recent study shows that combining on-the-ground monitoring with satellite data and smartphone technology could help put the brakes on Amazon deforestation and potentially that of forests elsewhere. The results were detailed in the Proceedings of the National Academy of Sciences USA.

Illegal logging, agriculture and coca cultivation particularly threaten the Amazon in the Peruvian Indigenous communities the study examined—and outsiders are often the culprits. The research team wondered if providing training for local people to use satellite-based "early deforestation alerts" could help.

The scientists collaborated with 76 Indigenous communities, 36 of which participated in using these alerts to watch over the forest. Three people from each of the latter communities received training to use an early-alert system on a smartphone app and to patrol forests and document damage.

Over the next two years these trained participants were paid to work as forest monitors and received monthly alerts via the app when satellite data indicated local forest losses. Monitors investigated alerts and patrolled for deforestation in other areas. They reported confirmed losses back to their communities, which



decided whether to deal with the culprits on their own or inform state authorities.

The researchers analyzed the same forest-loss satellite data from the given time period in all 76 communities. They found the early-alert program reduced forest loss by 8.4 hectares in the first year—a 52 percent reduction compared with the average loss in the control communities, says study co-author Tara Slough, a political economist at New York University. "This reduction in deforestation was concentrated in communities facing the largest threat" of forest loss, she adds. "If one were to continue the program, targeting it to the communities facing the biggest threats should avert the most tree-cover loss."

Results for the monitoring program were less striking in its second year, when forest loss was reduced by only 3.3 hectares compared with that in control communities. The researchers suggest a Peruvian government campaign against coca cultivation that year may have discouraged deforestation in both experimental and control communities' territories, shrinking differences between the two groups in the pilot program.

FG Trade Getty

Experts say this approach to tackling Amazonian deforestation—community monitoring combined with smartphone early alerts—looks promising. "Would this work in all communities that have high risk of deforestation? Given the results, it's worth a try," says Catherine Tucker, a forest governance researcher at the University of Florida, who was not involved in the study. But some communities may not have access to the resources needed for such a program, or their territories may hold valuable minerals or petroleum that would increase the risk of deforestation by outsiders despite monitoring efforts, Tucker notes.

Indigenous groups may continue the work they started in the pilot program. "We want to replicate this in other communities. In doing so, we are making a contribution to the world," wrote Francisco Hernandez Cayetano, a community member involved in the research and president of the Federation of the Ticuna and Yaguas Communities of the Lower Amazon, in a translated statement to *Scientific American*. "We as Indigenous peoples ask the world for support." —Annie Sneed

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ANIMAL BEHAVIOR

Trunk Tricks

Elephants build simple actions into complex motions, intriguing roboticists

Elephants move their powerful trunks with precision and complexity, delicately picking up a single leaf as easily as they heft a log. But researchers have struggled to explain how, exactly, the trunks manage to do so. New research published in *Current Biology* reveals part of the answer, thanks to motion-capture technology typically used to make movies.

"Elephants have evolved these amazing organs with an infinite number of degrees of freedom," says lead author and University of Geneva biologist Michel Milinkovitch. His team traveled to a South African elephant reserve to study how the animals specifically <u>use that freedom</u>. The researchers taped retroreflective markers to two bull elephants' trunks and put various items in front of them. As the elephants moved the objects around, the researchers filmed them with a semicircle of infrared cameras, capturing how the markers moved in threedimensional space—similar to the process used for mapping movie actors' movements to computer-generated characters.

An elephant's proboscis, like a human tongue, is a type of muscular hydrostat: it has no bones, so it can move in myriad ways. The new study shows that the bulls combine simple actions—such as curling, twisting and elongating parts of their trunks—to achieve complex movements. The animals also form pseudo-joints, or rigid sections of trunk, that they can shift from point to point.

"It's the first time that we've gotten a hint of what these more simplified commands might be in elephants," says William Kier, a biologist at the University of North Carolina at Chapel Hill, who studies trunk, tongue and tentacle movement and was not a part of the study. "I think it is a pretty important advance."

This investigation into how an elephant's 40,000 trunk muscles work together will be invaluable for developing new, versatile robots, says Cecilia Laschi, a roboticist at the National University of Singapore, who was not involved in the new study: "For roboticists, this is sort of a dream." A team of engineers in Pisa using the study data expects to have a trunklike robot prototype in 18 months. —Susan Cosier



TELECOMMUNICATIONS

On the Fly

A reprogrammable satellite creates new possibilities

Companies, governments and other customers will soon be able to directly access instruments on a satellite and assign them new missions on the fly. According to program manager Frédéric Piro, the Eutelsat Quantum, which blasted into space from Kourou in French Guiana this summer, is the world's first commercial satellite that can be fully reprogrammed in orbit. Adjustable antennas, reconfigurable transmission beams and customized electronics let the satellite run a wide range of applications—and switch between them in minutes—at 36,000 kilometers above Earth.

Governments can use the satellite for such tasks as disaster safety operations and border monitoring, and private operators might facilitate telecommunications for air and sea, the company says. According to Therese Jones, senior director of policy at Washington, D.C.-based Satellite Industry Association, Eutelsat Quantum "excels in mobility applications by reallocating com-



munication channels to, for example, airplanes, ships or vehicles on the ground, based on demand in real time." Its eight radio-frequency beams can help it maintain communications with moving sources, "which is much harder to manage for traditional satellites with one wide beam," says Jones, who is not involved with the project.

The satellite can also detect and deal with rogue transmissions that might interfere with signals, automatically changing beams' frequencies or power to prevent disruption. This is important because jamming a satellite's signals by blasting "noise" on the same frequency it uses has become very easy, Jones says. "All one needs is a jammer, some of which are available for less than \$100. Whereas earlier it used to be purely state actors that were jamming satellite signals, there are now even small organizations that do it," she adds. "Sometimes it's intentional, while in other cases it's the unintended interference from some other radio device."

Piro says strong encryption will protect the satellite software itself against hacking. Jones notes that satellites in general tend to be very secure because they also handle military services; most problems arise from user errors, such as bad choice of passwords.

To design a mission, customers can use a dedicated software application to choose an assignment's coverage area and capacity. "The software will then compute these parameters and direct them to the spacecraft," Piro says. "All this will be done autonomously without the operator's involvement. Moreover, customers can predesign more than one application and switch between the two at the press of a button."

The satellite was developed in a privatepublic partnership with the European Space Agency and other organizations. "With Eutelsat Quantum," Piro says, "we have managed to make the technology affordable and accessible for commercial use."

-Dhananjay Khadilkar

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Radioactive Recycling

A ubiquitous bacterium might help manage nuclear waste

Fission in nuclear reactors forges radioactive metal by-products so toxic that they must be stored deep underground, at great cost and effort, for millennia. But a protein made by a common microbe could help ease this hazardous burden, researchers report in the Journal of the American Chemical Society.

Two of nuclear waste's most problematic ingredients are metals called americium and curium; each has particularly longlived forms that decay much more slowly than uranium. They need to be monitored for thousands of years—and because they radiate so much heat, waste packages containing them must be buried far apart. Isolating them properly is critical to avoid radiation harm to people or the environment, according to Pennsylvania State biochemist Joseph Cotruvo, Jr. "It's a really big problem if these elements are around even in very small quantities," he says.

In 2018 Cotruvo and a team of researchers first reported that *Methylorubrum extorquens* (an innocuous bacterium commonly found in soil and on plants) produces a protein called lanmodulin. The microbe uses this protein to grab naturally occurring metals, typically from a group called the lanthanides, to drive its metabolism.

More recently, Cotruvo and his colleagues found in the lab that lanmodulin binds tightly and readily to americium and curium—and prefers them to many of its regular dance partners. Plus, the bond was thousands of times stabler than that of the nextstrongest naturally occurring molecular suitor. They are not sure if lanmodulin produced by the ubiquitous *M. extorquens* naturally captures or disperses americium and curium ions already in the environment, such as those released by nuclear weapons tests and waste leaks—a possible future study focus.

The researchers propose integrating the protein into radiation detectors and filters to extract these long-lived radioactive metals from contained nuclear waste. They could then be sequestered separately, decreasing the volume of material that needs extended monitoring and spacing. Alternatively, Cotruvo suggests, captured americium and curium could be recycled back into nuclear fuel. It is serendipitous that a bac-

terium-created molecule might help build tools to scavenge hazardous humanmade contaminants, says Gemma Reguera, a microbiologist at Michigan State University who was not involved in the study. "It's like a toy," she says. "There are so many possibilities." —*Nikk Ogasa*

ADVANCES

ECOLOGY

Water Beds

Tree roots routinely drill into bedrock for precious moisture

Naturalists have long noted isolated examples of tree roots boring far down through loose soil and into the unforgiving bedrock below—rare incursions that were deemed a mere curiosity. But in 2013 hydrologist Daniella Rempe probed deep into a northern California hillside and found tree roots extracting substantial amounts of moisture from pores and crannies in the rock, where groundwater had seeped in and become trapped. "We wanted to assess how big of a phenomenon this was," says Erica McCormick, an ecohydrologist in Rempe's laboratory at the University of Texas at Austin. So the team decided to map plants' bedrock water use across the continental U.S.

The researchers combined reams of geologic data from 2003 to 2017 to determine where U.S. forests and shrublands overlie bedrock that roots could feasibly reach. They then used known rates of precipitation, evaporation and soil moisture capacity to calculate how much circulating water was

MICROBIOLOGY

Muscle Makers

Microbe-produced muscle proteins could build resilient fibers

Bacteria may soon be muscling in on new kinds of manufacturing. Researchers have developed a technique that uses the common bacterium *Escherichia coli* to synthetically produce a muscle protein called titin, which could someday build tough and pliable fibers. Uses could range from medical sutures to impact-resistant or biodegradable fabrics. The titin is dozens of times larger than most molecules that have been produced in a laboratory, the researchers say.

Because *E. coli* is easy to control and replicates quickly, scientists use it to <u>pro-</u> <u>duce many kinds of substances</u>, including biodiesels and pharmaceuticals. Until recently, however, synthesizing bigger proteins such as titin—which is about 50 times the size of the proteins *E. coli* naturally makes has been out of reach.



unaccounted for—and thus likely came from stores deep inside the rock. This analysis, published in *Nature*, revealed that bedrock water is far from a last resort for many plants. At least 24 percent of the country's trees and shrubs regularly tap water from this layer to satiate their thirst, even in years with normal rainfall. And in the <u>hot, dry states</u> of California and Texas, more than 50 percent of the water used by trees comes from bedrock.

Bedrock water may help some trees withstand dry conditions wrought by climate change. But current efforts to predict how forests will fare in a warming future do not typically include this moisture in their projections, says Texas State University ecologist Susan Schwinning, who was not involved with the new study. "The authors here show that this is not just a local, spe-

In a new study detailed in Nature Communications, the researchers spurred E. coli to manufacture titin by introducing a circular strand of engineered DNA instructions called a plasmid. But building such a large protein drains cellular resources, says study co-author and Washington University in St. Louis biochemist Cameron Sargent. If a plasmid instructs E. coli to build the whole protein at once, the bacterium will avoid the production burden by removing or truncating the plasmid. So the team instead engineered a plasmid that makes E. coli construct shorter protein fragments that are structured to spontaneously link together inside the bacterium.

Once scientists extracted titin from the bacteria, they dissolved the proteins at high concentration in an organic solvent. Next, they squirted the solution through a syringe into a water bath, letting the proteins assemble along an emerging fiber as it was spun an extrusion process inspired by how spiders build silk draglines. The engineered strands' strength and toughness exceeded that of natural titin as measured in muscle fibers. cialized phenomenon but should be looked at broadly," she adds. The study researchers are now focusing on how plants are using bedrock water at their field sites as California faces severe droughts, Rempe says.

But how do relatively soft roots manage to burrow into rock in the first place? Bedrock and soil layers are somewhat diffuse, Schwinning says. Percolating rainfall weathers the deep bedrock over time, she explains, creating delicate fractures that fingerlike root offshoots can grow into to soak up pooled water when needed. Microbes and fungi latch onto the roots, helping to increase their surface area and pull moisture from the tiniest cracks. "They find this beautiful home in the pores," Rempe says. "There's a whole world down there." —Tess Joosse

Sargent likens titin molecules' size and arrangement within the fibers to a pot of congealed spaghetti. "It's a lot harder to pull long spaghetti apart compared with short spaghetti because the longer the spaghetti is, the more interactions there are between each strand," Sargent says. The researchers found that the way these interactions react to stress is key to titin's toughness: when the fibers are pulled on, bonds within the molecules break first, absorbing much of the applied force's energy before the bonds between strands eventually snap.

Inha University chemical engineer Yun Jung Yang, who was not involved in the study, says she finds it "remarkable that the researchers were able to replicate the actual mechanical properties of natural titin in an engineered protein."

Researchers can now apply this manufacturing technique to other large proteins, making it feasible to explore additional candidate biomaterials—such as resilin, an elastic polymer that powers a flea's jump, or the tough mother-of-pearl that lines abalone shells—for practical use.—*Connie Chang*

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HUMAN BEHAVIOR

Losing Contact

Gaze patterns reveal an intriguing subtlety in human communication

Conversation goes far beyond talking. It also involves, as Swedish author Annika Thor has written, "eyes, smiles, the silences between the words." When those elements hum along together, conversational partners feel most deeply engaged and connected.

Like good conversationalists, Dartmouth College neuroscientists have taken that idea and carried it to new places. They report some surprising findings on the interplay between eye contact and how two people synchronize neural activity while talking. The researchers suggest, in a paper published in the Proceedings of the National Academy of Sciences USA, that being in tune with a conversational partner is good—but that occasionally falling out of sync might be even better.

Maintaining eye contact has long been thought to act as the glue that connects two people in conversation. Its absence can signal social dysfunction. Similarly, the

Ryan McVay Getty Images

growing study of neural synchrony has largely focused on the way alignment in individuals' brain activity benefits the social connection between them.

Earlier research by the Dartmouth lab had showed that synchronized pupil dilation serves as a reliable indicator of shared attention, which in turn marks greater neural synchrony. In the new study, which measured pupil dilation during unstructured 10-minute conversations, the researchers found that the initial moment of eye contact-rather than a sustained period of locked gazes-marks a peak in shared attention. Synchrony, in fact, drops sharply just after you look into your interlocutor's eyes and begins to recover only when you and that person look away from each other. "Eye contact is not eliciting synchrony; it's disrupting it," says Thalia Wheatley, the paper's senior author.

Why would this happen? Wheatley and lead study author Sophie Wohltjen contend that making and breaking eye contact ultimately propels the conversation forward. "Perhaps what this is doing is allowing us to break synchrony and move back into our own heads so that we can bring forth new and individual contributions to keep the conversation going," Wohltjen says. "It's a fantastic study," says psychiatrist and social neuroscientist Leonhard Schilbach of the Max Planck Institute of Psychiatry in Munich, who studies social interaction but was not involved in the new research. He applauds how the experiment was designed to replicate natural encounters and focus on free-form conversation. The results suggest, he says, that "interpersonal synchrony is an important aspect of social interactions but may not always be desirable."

Thinking further about eye contact's function, the researchers examined past studies on creativity—which pointed to the constraints of too much synchrony. "If people are trying to innovate in some way, you don't want people in lockstep with each other," Wheatley says. "You want people to [say], 'What if we did this? What if we did that?' You need people to be providing their independent insights."

Connections between gaze and synchrony might be relevant to research in autism and other psychiatric conditions that involve atypical interaction. The findings also help explain frustrations over video-conferencing platforms, on which real eye contact is nearly impossible to make—or break—because of the positioning of cameras and windows on screens. —Lydia Denworth

ADVANCES



Science in Images By Leslie Nemo

The "hair" sprouting off this branch resembles a downy feather duster or fluffy tuft of cotton—maybe even fragments of a bad white wig. But each strand is in fact made of hard, cold ice.

For these manes of silky-smooth ice crystals (aptly termed "hair ice") to appear, a particular fungus called *Exidiopsis effusa* has to colonize rotting wood from a broadleaf tree, and temperatures must hover just below freezing in a sufficiently humid environment. Such a specific convergence of conditions might seem rare, but it happens often enough that scientists had been puzzling over this bizarre ice formation's cause for more than a century including Alfred Wegener, the scientist who proposed in 1912 that Earth's continents were once a single mass—before researchers pinpointed the role of *E. effusa* in 2015.

By observing hair ice in the wild (and growing some in a home garden), investigators have learned a few things about its formation. Under the right temperature and humidity conditions, ice forms on a branch surface while water stays liquid inside the wood's pores. The temperature difference between the two states of water creates a suction that draws liquid water to the freezing front—gradually extending the reach of the growing "hair."

Studies suggest that as the fungus digests part of the wood, it provides fragments of larger molecules that serve as a scaffold on which the ice can grow. This process can churn out hairs stretching to a length of 20 centimeters (almost eight inches). Each strand can be as thin as 0.02 millimeter in diameter, and some curl or wave. They might last for days, even as temperatures fluctuate near the freezing point. Some researchers hypothesize that the thin crystals are able to endure such changing conditions because something within the plant material acts like an antifreeze, which can keep ice crystals from changing shape even as the temperature varies. When it gets cold outside every year, scientists continue to document this icy mystery.

For more, visit www.ScientificAmerican.com/ science-in-images

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IN THE NEWS Quick Hits By Nikk Ogasa

PANAMA

While monitoring vampire bats in Panama, researchers discovered that the bloodthirsty fliers help one another find food by screeching after locating a juicy meal, despite departing their roosts alone.

FRENCH POLYNESIA

Scientists reconstructed historic Polynesian settlement routes by tracking rare gene variants in DNA from hundreds of islanders. Findings suggest that the shared tradition of carving massive statues, such as the Moai at Rapa Nui (Easter Island), may have originated at the Tuamotu Islands in French Polynesia.

SAUDI ARABIA

A massive collection of gnawed human and animal

bones found in the Umm Jirsan lava tube was

the site served as an underground den for the

animals from around 4,500 to 150 years ago.

mostly left there by striped hyenas, researchers

report. Fossilized feces and other markers suggest

For more details, visit www.ScientificAmerican.com/dec2021/advances

Tiger Fashionistas

A subpopulation of big cats with rare coloring shows evolution in action

Tigers can indeed change their stripes—and in the Similipal Tiger Reserve in India, many have done just that. So-called black tigers, genetic mutants that sport unusually wide and merged stripes, were extremely rare even when tigers were plentiful centuries ago. But in Similipal today, one in three are black. A new study in the Proceedings of the National Academy of Sciences USA pinpoints the peculiar pattern's genetic cause and reveals evolution at work among these endangered cats.

After sequencing the genomes of three zoo-born black tigers and their typical-coated parents, researchers at India's National Center for Biological Sciences and their colleagues tracked the

UZBEKISTAN

Paleontologists unearthed a 90-million-year-old dinosaur jawbone belonging to new species called *Ulughbegsaurus uzbekistanensis*. The 1,000-kilogram dinosaur had serrated teeth and was likely an apex predator, and its existence may have delayed the rise of large tyrannosaurs.

AUSTRALIA

Smoke from Australia's 2019– 2020 bushfire season littered the Southern Ocean with iron, nourishing an unprecedented algal bloom more expansive than Australia itself. Although blooms consume carbon dioxide from the air, they can also suffocate or poison marine life.

BRAZIL

Three decades of Amazon satellite data reveal that illegal mining incursions have quintupled on Indigenous lands in the past 10 years. These operations contribute to the Amazon's deforestation, which causes 8 percent of global carbon emissions.

> Altered *taqpep* genes were already known to cause blotched tabby patterns in cats, as well as king cheetahs' unusually large spots and stripes. But such patterns are so rare because they occur only when genes from both parents have matching mutations. The new study found that 10 out of the 12 Similipal tigers sampled had at least one copy of this particular *taqpep* change—and four were black tigers, with two copies each. But remarkably, not one of the 395 tigers surveyed outside the reserve had even one copy of the mutation. This suggests that the Similipal tigers are so isolated that they never breed with tigers outside that range and that the group has begun to maintain genetic changes over generations. "It was an astonishing finding," remarks molecular ecologist and lead author Vinay Sagar.

> For senior author Uma Ramakrishnan, a molecular ecologist who has studied Indian tigers' diminishing genetic diversity for more than a decade, this finding is "the most exciting discovery" of her career stark observable evidence of tigers' fragmentation across the region. The extensive data collected for this research "provide the much

> needed baseline for further studies on the genetics of endangered

pattern to a tiny change in a gene called *taqpep*. They then spent months hiking about 1,500 kilometers of jungles across India, collecting tiger droppings, fur, blood and drool. Analyzing these samples helped them determine the prevalence of this genetic change—and its virtual absence in tigers outside Similipal.



tigers," says University of Rochester evolutionary biologist Nancy Chen, who was not involved in the study. Although it is unknown if the unusual stripes help or harm the Similipal tigers, the markings underscore the fact that these animals are breeding exclusively among themselves—perhaps to their own peril. —Spoorthy Raman

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Fortune Business Insights. ⁴ Typical passenger vehicle emits around 4.6 metric tons of CO₂ per year. Source: EPA





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IEA (2017), The Future of Trucks, IEA, Paris IEA (2020) CO₂ emissions from heavy-duty vehicles in the Sustainable Development Scenario, 2000–2030 One young tree absorbs 5.9kg CO₂ per year. Source: Urban Forestry Network.

Glenn R. McLaughlin is the 2013 Poet Laureate of Montgomery County, Pennsylvania. He worked in the chemical industry for 30 years before becoming a teacher of high school chemistry and physics. His four self-published collections of poems and essays include *Forms of Lectio*,* which was a finalist for the Eric Hoffer Award in Poetry in 2009.



The Scalar Nature of Snow

elusive if not rare.

there are always vectors and other values

if not measured at least felt or experienced

at the boundary of ground: imbalance and, therefore, movement.

the creation comes, then with the condition of height and time:

eight stories up suspended in a moment

binary values of ones and zeroes-

just snow or not snow—

no vectors of momentum or spin

no description of unique shape or crystalline order

just points to move between floating to observe

as picking through pond lilies or stars in the winter sky

there or not there in this moment

the scalar nature of snow

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THE SCIENCE OF HEALTH



Unequal Surgery

Black children suffer more complications after operations than white kids

By Claudia Wallis

A pandemic is a stress test for society, revealing not only hidden cracks in health systems but also broader social failings. A deep fissure further exposed by COVID is the long-standing inequity in the health and medical care of racial and ethnic minorities. The outbreak has shown that Black, brown and Indigenous adults in the U.S. are more medically vulnerable than other people because of factors such as a heavier burden of chronic diseases, limited access to care and the cumulative effects of racism. The care gap is so bad even minority children who are relatively healthy and have not experienced decades of discrimination fare worse than their white peers during common, straightforward operations. The questions for all of us are: Why—and what can be done about it?

First the facts. An abundance of studies has shown that Black children do worse than white children in surgery. More complications and higher death rates have been documented in abdominal, cardiac, oncological and other types of procedures in Black children, and it isn't just because they routinely start off sicker. A 2020 study in the journal *Pediatrics* by researchers at Nation-wide Children's Hospital in Columbus, Ohio, looked at the rate of surgical complications and deaths in the 30 days after inpatient procedures for 172,549 Black and white children who were judged—by a standard medical rating system—to be in general good health. Problems were rare overall, but Black children were



Claudia Wallis is an award-winning science journalist whose work has appeared in the New York Times, Time, Fortune and the New Republic. She was science editor at Time and managing editor of Scientific American Mind.

18 percent more likely than white children to have complications and more than three times as likely to die.

"We were surprised," says Christian Mpody, a pediatric epidemiologist and co-author of the paper. "We know that the sicker you are at presentation, the more likely you are to have complications. When we see a relatively healthy population, we should not see the disparity."

To investigate further, Mpody and his colleagues zoomed in on one of the most common surgeries for children: appendectomy. They compared the rates of complications between Black and white children, examining the records of 100,639 procedures between 2001 and 2018. In a paper published this October, they reported that the overall rate of complications declined through the years, but the race gap scarcely narrowed. Black children always were more likely to have complications, and the disparity held true whether kids had an intact appendix or a burst one—a likely indicator that the child was delayed in reaching the hospital or receiving care. The difference remained when researchers adjusted for factors such as socioeconomic status and insurance coverage.

The two studies suggest that "there are some within-hospital factors that play a role," Mpody says. Earlier studies hint that facilities may not be treating all children equally. A <u>2020 analysis</u> of emergency department records found that Black children with appendicitis were less likely to be promptly diagnosed and to get timely diagnostic imaging than white children. A <u>2015</u> <u>study</u> showed they were also less likely to receive any medication for their abdominal pain. Such inequities may reflect implicit and explicit racial bias on the part of staff, as well as structural racism embedded in practices at the facilities, says Monika Goyal, lead author of both studies and an emergency medicine specialist at Children's National Hospital in Washington, D.C.

Mpody's appendicitis study did more than size up racial inequality; it put a price on it. The study found that hospitals incurred higher costs from dealing with complications in Black patients—a median of \$629 more per child than for white kids. That means hospitals could potentially save money by improving health care for minorities. "While the cost argument feels sort of icky, we operate in a health-care system built on capitalism, so it matters," says Rachel Hardeman of the University of Minnesota School of Public Health, who studies racial equity and reproductive health. She points out that hospitals routinely engage in "continuous quality improvement" efforts, but they don't often prioritize health inequities as part of them. Hardeman says the economic argument made by studies such as Mpody's could begin to change that.

Hardeman's own work suggests that training doctors and staff to reduce unconscious bias could help close the race gap in outcomes. Increasing the racial diversity of the medical workforce could also help. <u>Her research</u>—and that of others—shows the outcome gap narrows dramatically when Black doctors care for Black patients. Black people make up 13 percent of the U.S. population but only <u>5 percent of doctors</u>, a number that has barely budged despite diversity recruitment programs at medical schools. By hiring more diverse staff, among other efforts, hospitals could become places where all children have equal rights to get well.





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ASTRONOMY

New revelations about how galaxies collide offer a preview of the Milky Way's future By Aaron S. Evans and Lee Armus

Illustration by Ron Miller

FORECASTED FUTURE: An illustration shows a possible view of the merging Milky Way-Andromeda system as seen from Pluto, which may get tossed to the galaxy's outskirts, along with the solar system.

Aaron S. Evans is a professor of astronomy at the University of Virginia and an astronomer at the National Radio Astronomy Observatory and the North American ALMA Science Center.

Lee Armus is a senior scientist at the Infrared Processing and Analysis Center and a member of the professional staff at the California Institute of Technology.

ff

N APPROXIMATELY FIVE BILLION YEARS, AS THE SUN EXPANDS INTO A RED GIANT STAR ROUGHLY THE diameter of Earth's orbit around it, our galaxy will collide with its nearest large neighbor, Andromeda. As gravity draws the pair toward each other for a close encounter, stars will be ripped from their orbits to make spectacular tails, and gas and dust will be squeezed toward the approaching nuclei, destroying the stately, grand spirals that have existed for almost three quarters of the age of the universe.

Eventually the centers of the galaxies will merge, and the gas pouring toward the center

will ignite an explosion of star formation, producing stars more than 100 times faster than either galaxy does today. It will also feed the now quiet supermassive black holes that lurk at the centers of both galaxies. The black holes will grow while releasing a storm of energetic particles and radiation that will easily outshine the light from all the stars in both galaxies combined. After another 100 million years or so, the two supermassive black holes will spiral toward each other and merge into a single black hole in a cataclysm that will send strong gravitational waves reverberating throughout space. Despite the fireworks, this process—which is happening around us today and was even more common in the early universe—is not really a "collision" in the strictest sense of the word. Galaxies are mostly empty space. The roughly 300 billion stars in a galaxy like the Milky Way are, on average, separated by nearly five light-years. The density of air at sea level on Earth is about 100 million billion times greater than the average density of gas in interstellar space. In other words, although a merger is transformative in the life of a galaxy and a source of immense


power, most stars just pass right by one another during the event.

Nevertheless, galaxy pileups are fascinating and important. By studying the mergers of other galaxies, we can see the future of our own. Studying galaxy mergers also helps us understand the history of the universe because when the cosmos was younger and denser, galactic collisions were much more common. Simulations suggest that over the past 10 billion years the Milky Way has undergone as many as five major mergers on its way to becoming the grand spiral it is today.

It is an exciting time to be doing this work. Until recently, astronomers lacked the tools to carefully measure and model colliding galaxies. Most of the action is obscured behind thick clouds of dust that are difficult to penetrate at visual wavelengths, even with the largest telescopes. With new instruments on current and planned telescopes, we will begin to answer some big questions about galaxy mergers, such as how stars are born during the chaos of a galactic collision and how radiation released by growing and eventually merging central black holes affects the new galaxy taking shape around them.

GALACTIC PILEUPS

IT HAS BEEN almost a century since Edwin Hubble first discovered that many of the glowing blobs in the sky—known at the time as "nebulae"—are not objects within the Milky Way but are instead independent "island universes." He classified these "extragalactic nebulae" into three categories: those with spherical or elliptical shapes (the elliptical galaxies), those with flattened and sometimes barred disks with a central bulge (the spiral galaxies, like our own), and misshapen oddities (the irregular galaxies).

A small fraction of the irregular galaxies were in fact highly distorted pairs or small groups of galaxies. In the years after Hub-

ble's discovery, such pioneers as Boris Vorontsov-Velyaminov of Moscow University, Fritz Zwicky of the California Institute of Technology, and Halton Arp of the Mount Wilson and Palomar Observatories studied this class of "interconnected galaxies" in detail. Long-exposure images made from photographic plates, published in Arp's 1966 Atlas of Peculiar Galaxies, clearly show the distorted shapes that we now recognize as the signatures of merging galaxies. In the 1970s the brothers Juri and Alar Toomre used computers to model interactions of simple disk galaxies on bound, parabolic orbits, re-creating the shapes of several peculiar galaxies-in particular the long, sweeping tails of stars launched to great distances during the merger. These and other early simulations showed that the unusual, sometimes spectacular features highlighted by Arp and others could be explained solely by gravitational interactions. Using modern computers and state-of-the-art simulations, teams led by Joshua E. Barnes of the University of Hawaii, Lars Hernquist of Harvard University and Philip Fajardo Hopkins of Caltech have further mapped the diversity of galaxy interactions and the importance of mergers in the life cycle of galaxies.

In 1983 the Infrared Astronomical Satellite, or IRAS, was launched. This satellite produced the first far-infrared map of the entire sky—a huge boon to the study of the hidden universe and, in particular, galactic mergers. At the wavelengths it captured, the satellite was sensitive to thermal emission from warm and cool dust. Interstellar dust in galaxies almost always signals a nursery for stellar birth. In normal galaxies, stars are born in clouds of (mostly) molecular hydrogen gas and dust. As stars evolve and die, they shed heavy, dust-forming elements such as carbon and oxygen, which were produced in their interiors through nuclear fusion, thus further enriching the surrounding



clouds with dust. (The dust already in the clouds was formed in prior episodes of star formation.) In colliding galaxies, this process is in overdrive—the merger concentrates gas and dust into compact regions, igniting waves of star formation called starbursts that in turn produce more heavy elements and more dust. Therefore, although young and massive stars release most of their energy at short ultraviolet wavelengths, very little of this light actually makes it to Earth. The surrounding dust grains absorb the ultraviolet light and reemit it in the infrared. Telescopes equipped with sensitive infrared detectors can measure this light, allowing us to peer through the veil of dust and study the earliest stages of stellar birth and the growth of supermassive black holes.

IRAS detected many such stellar nurseries in the Milky Way and in thousands of other galaxies, greatly improving our understanding of galaxy mergers in two important ways. First, IRAS provided accurate measures of the energy generated within these objects and showed that merging galaxies are among the most intrinsically luminous objects in the universe. Second, IRAS detected colliding galaxies, solely on the basis of their infrared emission, over vast distances, giving us our first accurate census of galaxy mergers over cosmic time. Some of these collisions were so far from Earth that the light we see was emitted when the universe was just one fifth of its current age. In some merging galaxies, more than 90 percent of the total power output occurs at farinfrared wavelengths—their true natures are completely hidden from optical telescopes.

But IRAS showed us that a large infrared "excess" is an excellent way to find interacting and merging galaxies. In particular, it discovered a class of galaxies called luminous infrared galaxies, or LIRGs for short. These objects, with far-infrared luminosities above 100 billion times the brightness of the sun (about three times more than the total energetic output of all the stars in the Milky Way), are often merging galaxies. Even rarer and more spectacular are ultraluminous infrared galaxies, or ULIRGs. These galaxies, which have a far-infrared luminosity of more than a trillion times the sun's brightness, are almost always violent galactic collisions.

Scientists took a step toward explaining what happens at the cores of merged galaxies in the late 1980s, when they made a connection between mergers and another class of celestial bodies called quasars, which are powered by active supermassive black holes. These are the most energetic objects in the universe, with a brightness more than a trillion times that of the sun. David Sanders, who was then a postdoctoral fellow at Caltech working with Tom Soifer and the late Gerry Neugebauer, postulated that ULIRGs are an early, dust-enshrouded phase between galaxy mergers and quasars. This evolutionary link between ULIRGs and quasars built on previous studies by Alan Stockton of the University of Hawaii, John MacKenty of the Space Telescope Science Institute in Baltimore and Timothy Heckman of Johns Hopkins University, who showed that galaxies hosting active central black holes often looked distorted, consistent with their being galaxy mergers.

The proposed connection between powerful infrared galaxies and quasars, two types of celestial objects that are seemingly very different, provided a testable model that spurred research on the relation between these apparently disparate classes. By providing a framework to connect luminous infrared galaxies, powerful starbursts, and active galaxies and quasars, it helped renew interest in how galactic mergers influence galaxy evolution over cosmic time. Because more than half the light ever generated by stars in the history of the universe gets reprocessed into infrared light by dust, the role of mergers may be critical.



AMBITIOUS GOALS

IN 2004 the two of us and our collaborators initiated the Great Observatories All-Sky LIRG Survey (GOALS) to collect images and spectroscopy of colliding galaxies using three of NASA's Great Observatories: the Spitzer Space Telescope, the Hubble Space Telescope and the Chandra X-ray Observatory. These instruments provide a multiwavelength view of the merger life cycle. The GOALS sample consists of all the brightest infrared luminous galaxies in the local universe. This collection of more than 200 objects, all within 1.3 billion light-years, enabled the most detailed studies of infrared luminous galaxies to date.

Our team also uses ground-based telescopes such as the Very Large Array (VLA) in New Mexico, the Hale 200-inch telescope at Mount Palomar in California, the twin Keck 10-meter telescopes in Hawaii, and the Atacama Large Millimeter/submillimeter Array (ALMA) in Chile. The team has also collected data with Europe's far-infrared Herschel Space Telescope and NASA'S NuSTAR x-ray telescope; the latter studies very high-energy hard x-rays.

GOALS has already significantly increased our knowledge of colliding galaxies. A long-standing question, for instance, has been whether young stars or active black holes contribute more to the light coming from merging galaxies. One way we can separate out their respective contributions at different times in the merger life cycle is by looking at the different energy profiles (the amount of energy released as a function of wavelength) of the two types of objects. Stars are simple thermal sources of radiation—they emit most of their energy at a peak wavelength that depends on their temperature, and their energy output declines very rapidly at shorter and longer wavelengths. In contrast, the accretion disk around a feeding black hole is viscous and hot, and its temperature increases from its exterior toward the event horizon of the black hole. An accretion disk has a much broader energy profile and produces a much larger fraction of high-energy radiation than a star, and it can heat and ionize (strip electrons from) a wide range of elements in the surrounding gas. Finding strong emission from highly ionized elements in a galaxy's spectrum is a dead giveaway that an accreting supermassive black hole lies at its center.

GOALS found that over the entire population of LIRGs, starbursts appear to be more important energy sources than black holes. About one fifth of all the luminous infrared galaxies in GOALS seem to host active supermassive black holes, but even in these galaxies stars contribute a significant amount of energy. But we may be missing active black holes that are so buried by dust that even infrared diagnostics cannot identify them-a phenomenon that is currently being studied in detail by two members of the GOALS team, George Privon of the National Radio Astronomy Observatory and Claudio Ricci of the Diego Portales University in Chile, and by a team at Chalmers University of Technology in Sweden led by Susanne Aalto. Also, we tend to identify active black holes during the latter stages of a merger life cycle, which suggests that much of the supermassive black hole growth may lag behind star formation, giving starbursts more time to contribute to the total energy. Alternatively, some black holes may also grow early, as has been suggested by observations of some LIRGs at the highest resolution in the infrared by GOALS team member Anne Medling of the University of Toledo. The precise timescales over which the stars and the central supermassive black holes grow inside galaxies is the subject of a great deal of current research attempting to understand one of the deepest mysteries of the past two decades: why the mass of the central black hole and the stars in the bulges of present-day spiral and elliptical galaxies have a nearly constant mass ratio of roughly one to 1,000 in galaxies today.



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NEW INSIGHTS

OTHER RECENT PROJECTS have revealed new clues about LIRGs and how stars form in colliding galaxies. For instance, by mapping the gas heated by the most massive stars inside these objects, researchers, including GOALS members Kirsten Larson of the Space Telescope Science Institute, Tanio Díaz-Santos of the Foundation for Research and Technology–Hellas in Crete, and Loreto Barcos-Muñoz and Yiqing Song of the University of Virginia, have found that most of the star formation in LIRGs happens in extremely compact and energetic starburst regions. These areas have starformation rates and gas densities a factor of 10 or more higher than we find in normal galaxies. Early in the merger process, the most active star-forming regions tend to reside in areas outside the nuclei of LIRGs. As the merger evolves, however, the primary starbursts are compact clumps in and around the merging nuclei, as gas originally in the spiral arms falls toward the center.

Interestingly, the densities of the central concentrations of molecular gas in the most energetic late-stage mergers are so high that they begin to resemble giant molecular clouds. A prime example of this phenomenon is the nearest ultraluminous infrared galaxy, Arp 220, which is located 250 million light-years away. Kazushi Sakamoto of Taiwan's Academia Sinica and Nick Scoville of Caltech have mapped the molecular gas at the center of this object in exquisite detail with the ALMA array, showing it contains several Milky Way's worth of molecular gas concentrated in a region not larger than 3,000 light-years across—a factor of 20 smaller than the extent of the Milky Way's gaseous disk.

Although mergers are powerful stellar factories, star clusters formed in the collision may actually live surprisingly short lives. Using data from the Hubble Space Telescope, Angela Adamo of Stockholm University and GOALS member Sean Linden of the University of Massachusetts Amherst have seen a dramatic dropoff in the number of clusters as a function of cluster age, suggesting that significant numbers of star clusters are destroyed in merging galaxies shortly after they are born. The collision triggers enhanced star formation, but gravitational tidal forces and winds from supernovae within the clusters may easily tear them apart.

Just as the gas in clusters can be swept clear as stars evolve, so, too, can the merger fall victim to feedback from supernovae and the central black holes, with profound effects on further galactic evolution. Large flows of ionized gas streaming away from mergers were first studied in the early 1990s by Heckman and his collaborators, who found evidence for powerful winds-dubbed superwinds-in some low-redshift LIRGs and ULIRGs. Subsequent studies targeting this hot atomic gas have found not only that winds are common in LIRGs and ULIRGs but that the fastest of these can break free from the galaxy and eject gas into intergalactic space, as has been shown by David Rupke of Rhodes College and others. On the finest scales, jets and bubbles of hot, shocked gas mark the regions where the nuclei pour energy into the galaxy and drive the outflows, as has been mapped by GOALS team members Medling and Vivian U of the University of California, Irvine, using the twin Keck telescopes.

Galactic superwinds are multiphase, meaning they can contain hot and cold atomic and molecular gas. A number of astronomers, including Sakamoto, Barcos-Muñoz, Miguel Pereira-Santaella of Spain's Center of Astrobiology and Eduardo González Alfonso of the University of Alcalá in Spain, have studied the dense, molecular gas in superwinds, often finding large amounts of cold gas flowing outward from merging galaxies. These outflows can easily cover 10,000 light-years and sometimes carry more gas than is being made into stars in the nuclei, effectively robbing the gal-



axy of fuel for ongoing star formation. Just as important, these winds can send heavy elements (metals) and dust into intergalactic space. In nearly all cases, the outflows seem to originate near the nucleus of the merger, driven by the combined effects of supernovae, radiation pressure and jets (fast columns of gas) from the central black hole. These outflows may be important in the life cycle of galaxies, as detailed simulations by Chris Hayward of the Flatiron Institute suggest that stellar feedback can simultaneously regulate star formation and drive outflows.

THE BIGGEST EYES ON THE SKY

THE SOON-TO-LAUNCH James Webb Space Telescope is poised to greatly expand our understanding of galaxy mergers across cosmic time. This 6.5-meter-diameter infrared telescope is due to lift off at the end of 2021. Webb is the scientific successor to IRAS, the Infrared Space Observatory (which flew in the 1990s) and Spitzer (which was decommissioned in 2020), but Webb will be at least 50 times more sensitive and have nearly 10 times the spatial resolution of Spitzer, delivering sharp images of galaxies in the near- and mid-infrared part of the spectrum. It will also carry imaging spectrometers that can generate hundreds of spectra in a single pointing. This capability will allow it to map star-forming regions and the regions around actively accreting supermassive black holes in nearby mergers in exquisite detail.

The GOALS collaboration will observe four nearby luminous infrared galaxies as part of a Webb Director's Discretionary Early Release Science program. Other researchers will use the observatory to target nearby, bright active galaxies, distant quasars and deep, blank fields in search of the earliest galaxies. The GOALS early-release targets include galaxies with powerful starbursts and active central black holes. They are all caught in the throes of a galactic merger and are all experiencing galactic outflows. These galaxies will be valuable local laboratories for understanding how these processes unfold in the early universe. Beyond the early-release programs, several projects have been selected in the first General Observer Cycle for Webb, which will examine feedback from young clusters and active black holes, the fraction of star formation hidden from us at optical wavelengths and the nature of obscured nuclei in LIRGs.

The next-generation Very Large Array is the planned replacement for the 27-dish Very Large Array. This 263-dish radio- and millimeter-wave interferometer will observe star-forming regions, active black holes and light associated with exploding stars with 10 times the sensitivity and resolution of the VLA.

Overall, these new telescopes will unveil the astrophysics occurring in nearby and early-universe galaxy mergers. High-resolution simulations, coupled with these detailed new observations, will be the key to understanding how physical feedback processes help to regulate star formation and black hole growth in merging galaxies. Future planned and proposed observatories will be able to detect the gravitational-wave signatures of colliding supermassive black holes and the dusty cores of forming galaxies over the vast majority of cosmic time. As we discover more exotic objects at the farthest reaches of the universe, we will continue to use these new tools to better understand how galaxies are born and live out their lives.

FROM OUR ARCHIVES

Colliding Galaxies. Rudolph Minkowski; September 1956.

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TECHNOLOGY

SPYING ON YOUR EMOTIONS

Tech companies now use AI to analyze your feelings in job interviews and public spaces. But the software is prone to racial, cultural and gender bias

By John McQuaid

021 Scientific American



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N LIVERPOOL, ENGLAND, AT A FEBRUARY 2020 CONFERENCE ON THE RATHER UNGLAMOROUS TOPIC of government purchasing, attendees circulated through exhibitor and vendor displays, lingering at some, bypassing others. They were being closely watched. Around the floor, 24 discreetly positioned cameras tracked each person's movements and cataloged subtle contractions in individuals' facial muscles at five to 10 frames per second as they reacted to different displays. The images were fed to a computer network, where artificial-intelligence algorithms assessed each person's gender and age group and analyzed their expressions for signs of "happiness" and "engagement."

About a year after the Liverpool event, Panos Moutafis, CEO of Austin, Tex.-based Zenus, the company behind the technology, was still excited about the results. "I haven't seen lots of commercial systems getting this level of accuracy," he said to me during a video call, showing me a photograph of the crowd, the faces outlined with boxes. Zenus engineers had trained the system to recognize emotions by having it examine a huge data set of facial expressions with labels describing relevant feelings. The company validated the program's performance in various ways, including live tests when people reported how they felt when an image was taken. The system, Moutafis said, "works indoors, it works with masks, with no lighting, it works outdoors when people wear hats and sunglasses."

The Zenus setup is one example of a new technology—called emotion AI or affective computing—that combines cameras and other devices with artificial-intelligence programs to capture facial expressions, body language, vocal intonation, and other cues. The goal is to go beyond facial recognition and identification to reveal something previously invisible to technology: the inner feelings, motivations and attitudes of the people in the images. "Cameras have been dumb," says A.C.L.U. senior policy analyst Jay Stanley, author of the 2019 report <u>*The Dawn of Robot Surveillance*</u>. "Now they're getting smart. They are waking up. They are gaining the ability not just to dumbly record what we do but to make judgments about it."

Emotion AI has become a popular market research tool—at another trade show, Zenus told Hilton Hotels that a puppies-and-icecream event the company staged was more engaging than the event's open bar—but its reach extends into areas where the stakes are much higher. Systems that read cues of feeling, character and intent are being used or tested to detect threats at border checkpoints, evaluate job candidates, monitor classrooms for boredom or disruption, and recognize signs of aggressive driving. Major automakers are putting the technology into coming generations of vehicles, and Amazon, Microsoft, Google and other tech companies offer cloud-based emotion-AI services, often bundled with facial recognition. Dozens of start-ups are rolling out applications to help companies make hiring decisions. The practice has become so common in South Korea, for instance, that job coaches often make their clients practice going through AI interviews.

AI systems use various kinds of data to generate insights into emotion and behavior. In addition to facial expressions, vocal intonation, body language and gait, they can analyze the content of spoken or written speech for affect and attitude. Some applications use the data they collect to probe not for emotions but for related insights, such as what kind of personality a person has and whether he or she is paying attention or poses a potential threat.

But critics warn that emotion AI's reach exceeds its grasp in potentially hazardous ways. AI algorithms can be trained on data sets with embedded racial, ethnic and gender biases, which in turn can prejudice their evaluations—against, for example, nonwhite job applicants. "There's this idea that we can off-load some of our cognitive processes on these systems," says Lauren Rhue, an information systems scientist at the University of Maryland, who has studied racial bias in emotion AI. "That we can say, 'Oh, this person has a demeanor that's threatening' based on them. That's where we're getting into a dangerous area."

The underlying science is also in dispute. Many emotion-AI apps trace their origins to research conducted half a century ago by psychologists Paul Ekman and Wallace Friesen, who theorized that a handful of facial expressions correspond to basic emotions (anger, disgust, fear, happiness, sadness and surprise; Ekman later added contempt to the list) and that these expressions form a universally understood emotional language. But these ideas are now hotly debated. Scientists have found evidence of significant



cultural and individual variations in facial expressions. Many researchers say algorithms cannot—yet, anyway—consistently read the subtleties of human expressions in different individuals, which may not match up with stereotypical internal feelings. Ekman himself, who worked to develop early forms of emotion-recognition technology, now argues it poses a serious threat to privacy and should be heavily regulated.

Emotion AI is not intrinsically bad. If ma-

chines can be trained to reliably interpret emotions and behavior, the potential for robotics, health care, automobiles, and other fields is enormous, experts say. But right now the field is practically a free-for-all, and a largely unproven technology could become ubiquitous before societies have time to consider the potential costs.

IN 2018 MARK GRAY, then vice president for people and business operations at <u>Airtame</u>, which makes a device for screen-sharing presentations and displays, was looking for ways to improve the company's hiring process. Efficiency was part of it. Airtame is small, with about 100 employees spread among offices in Copenhagen, New York City, Los Angeles and Budapest, but the company can receive hundreds of applications for its jobs in marketing or design. Another factor was the capricious nature of hiring decisions. "A lot of times I feel it's coming from a fake voice in the back of someone's head that 'oh, I like this person personally,' not 'this person would be more competent,'" says Gray, who is now at Proper, a Danish property management tech company. "In the world of recruitment and HR, which is filled with the intangible, I kind of wanted to figure out how can I add a tangible aspect to hiring."

Airtame contracted with <u>Retorio</u>, a Munich-based company that uses AI in video interviews. The process is quick: job candidates record 60-second answers to just two or three questions. An algorithm then analyzes the facial expressions and voice of the interviewees and the text of their responses. It then generates a profile

INSIDE OUT: Some emotion-AI systems rely on work by psychologist Paul Ekman. He argues universal facial expressions reveal feelings that include (*from left*) sadness, happiness, anger, fear and surprise. based on five basic personality traits, a common model in psychology shorthanded as OCEAN: openness to experience, conscientiousness, extraversion, agreeableness and neuroticism. Recruiters receive a ranked list of candidates based on how well each profile fits the job.

Such software is starting to change how business decisions are made and how organizations interact with people. It has reshaped the hiring process at Airtame, instantly elevating some can-

didates over others. Gray says that is because the profiling works. He shared a chart showing that the job performance of several recent hires in sales tracked their personality scores, with employees who had scored higher in conscientiousness, agreeableness and openness doing the best.

Machines that can understand emotions have long been the subject of science fiction. But in computer science and engineering, human affect remained an alien concept for a long time. As recently as the 1990s, "it was a taboo topic, something undesirable," says Rosalind Picard of the Massachusetts Institute of Technology, who coined the term "affective computing" in a 1995 technical report. "People thought I was crazy, nuts, stupid, embarrassing. One respected signal- and speech-processing person came up to me, looked at my feet the whole time, and said, 'You're wasting your time—emotion is just noise.'"

Picard and other researchers began developing tools that could automatically read and respond to biometric information, from facial expressions to blood flow, that indicated emotional states. But the current proliferation of applications dates to the widening deployment starting in the early 2010s of deep learning, a powerful form of machine learning that employs neural networks, which are roughly modeled on biological brains. Deep learning improved the power and accuracy of AI algorithms to automate a few tasks that previously only people could do reliably: driving, facial recognition, and analyzing certain medical scans.



Yet such systems are still far from perfect, and emotion AI tackles a particularly formidable task. Algorithms are supposed to reflect a "ground truth" about the world: they should identify an apple as an apple, not as a peach. The "learning" in machine learning consists of repeatedly comparing raw data—often from images but also from video, audio, and other sources—to training data labeled with the desired feature. This is how the system learns to extract the underlying commonalities, such as the "appleness" from images of apples. Once the training is finished, an algorithm can identify apples in any image.

But when the task is identifying hard-to-define qualities such as personality or emotion, ground truth becomes more elusive. What does "happiness" or "neuroticism" look like? Emotion-AI algorithms cannot directly intuit emotions, personality or intentions. Instead they are trained, through a kind of computational crowdsourcing, to mimic the judgments humans make about other humans. Critics say that process introduces too many subjective variables. "There is a profound slippage between what these things show us and what might be going on in somebody's mind or emotional space," says Kate Crawford of the University of Southern California Annenberg School for Communication and Journalism, who studies the social consequences of artificial intelligence. "That is the profound and dangerous leap that some of these technologies are making."

The process that generates those judgments is complicated, and each stage has potential pitfalls. Deep learning, for example, is notoriously data-hungry. For emotion AI, it requires huge data sets that combine thousands or sometimes billions of human judg-



CONTEXT COUNTS: A woman looks upset in a cropped photo from 1964 (*left*). But the complete image shows she is part of a joyous crowd (*above*). These are ecstatic Beatles fans outside the band's hotel in New York City.

ments—images of people labeled as "happy" or "smiling" by data workers, for instance. But algorithms can inadvertently "learn" the collective, systematic biases of the people who assembled the data. That bias may come from skewed demographics in training sets, unconscious attitudes of the labelers, or other sources.

Even identifying a smile is far from a straightforward task. A 2020 <u>study</u> by Carsten Schwemmer of the GESIS–Leibniz Institute for the Social Sciences in Cologne, Germany, and his coleagues ran pictures of members of Congress through cloud-based emotion-recognition apps by Amazon, Microsoft and Google. The scientists' own review found 86 percent of men and 91 percent of women were smiling—but the apps were much more likely to find women smiling. Google Cloud Vision, for instance, applied the "smile" label to more than 90 percent of the women but to less than 25 percent of the men. The authors suggested gender bias might be present in the training data. They also wrote that in their own review of the images, ambiguity—ignored by the machines—was common: "Many facial expressions seemed border-line. Was that really a smile? Do smirks count? What if teeth are showing, but they do not seem happy?"

Facial-recognition systems, most also based on deep learning, have been widely <u>criticized for bias</u>. Researchers at the M.I.T. Media Lab, for instance, found these systems were less accurate when matching the identities of nonwhite, nonmale faces. Typically these errors arise from using training data sets that skew white and male. Identifying emotional expressions adds additional layers of complexity: these expressions are dynamic, and faces in posed photos can have subtle differences from those in spontaneous snapshots.

Rhue, the University of Maryland researcher, used a public data set of pictures of professional basketball players to test two emotion-recognition services, one from Microsoft and one from Face++, a facial-recognition company based in China. Both consistently ascribed more negative emotions to Black players than to white players, although each did it differently: Face++ saw Black players as angry twice as often as white players; Microsoft viewed Black players as showing contempt three times as often as white players when the expression was ambiguous. The problem can likely be traced back to bias in the labeled images in training data sets, she says. Microsoft and Face++ did not respond to requests for comment.

Many companies now emphasize that they are aware of and addressing such issues. Retorio's algorithm was trained on a data set, compiled over a period of years using paid volunteers, of short interview videos labeled with personality traits, co-founder Christoph Hohenberger says. The company has taken steps to filter out various demographic and cultural biases that would tend to favor one group over another in the personality assessments, he says.

But because there is currently no regulation or oversight of the industry, in most cases we have to take a company's word for it—the robustness and equity of proprietary data sets are hard to verify. HireVue, a company that does video interviews with algorithmic analysis of the text and vocal tone, brought on an outside auditor to check for bias, but that is rare.

"This idea that there exists one standard for humans to be and that everyone can meet it equally" is fundamentally flawed, says Ifeoma Ajunwa, an associate professor at the University of North Carolina School of Law, who studies AI deci-

sion-making. The assumption, she says, means that "everyone who doesn't meet that standard is disadvantaged."

N ADDITION TO CONCERNS about bias, the idea that outside appearances match a decipherable inner emotion for everyone has also started to generate strong scientific opposition. That is a change from when the concept got its start more than 50 years ago. At that time Ekman and Friesen were conducting fieldwork with the Fore, an Indigenous group in the highlands of southeast Papua New Guinea, to see if they recognized and understood facial expressions the same way as people from radically different backgrounds did-a stevedore from Brooklyn, say, or a nurse in Senegal. Volunteers were shown sets of photos of people making expressions for what the scientists called the six basic emotions. To provide context, a translator provided brief descriptors ("He/ she is looking at something which smells bad" for disgust, for instance). The Fore responses were virtually identical to those of people surveyed in countries such as Japan or Brazil or the U.S., so the researchers contended that facial expressions are a universally intelligible emotional language.

The notion of a shared group of expressions that represented basic emotional states quickly became popular in psychology and other fields. Ekman and Friesen developed an atlas of thousands of facial movements to interpret these expressions, called the Facial Action Coding System (FACS). Both the atlas and the theory became cornerstones of emotion AI. The work has been incorporated into many AI applications, such those developed by the company Affectiva, which include in-car systems and market research.

But scientists have argued that there are holes in Ekman's theories. A 2012 study published in the *Proceedings of the National Academy of Sciences USA*, for instance, presented data showing that facial expressions varied considerably by culture. And in 2019 Lisa Feldman Barrett, a psychologist at Northeastern University, along with several colleagues, published a <u>study</u> that examined more than 1,000 scientific papers on facial expressions. The notion that faces revealed outward signs of common emotions had spread to fields ranging from technology to law, they found—but there was little hard evidence that it was true.

The basic emotions are broad stereotypical categories, Barrett says. Moment to moment, facial expressions reflect complicated internal states—a smile might cover up pain, or it might convey sympathy. And today, she contends, it is almost impossible for an AI system to consistently, reliably categorize those internal states if it has been trained on data sets that are essentially collections of

"There is a profound slippage between what these things show us and what might be going on in somebody's mind." —Kate Crawford

University of Southern California

labeled stereotypes. "It's measuring something and then inferring what it means psychologically," Barrett says. "But those are two separate things. I can't say this about every company obviously, because I don't know everything that everybody is doing. But the emotion-recognition technology that's been advertised is routinely confounding these two things."

One reason for this problem, Crawford says, is that the world of tech start-ups is not aware of scientific debates in other fields, and those start-ups are attracted to the elegant simplicity of systems such as FACS. "Why has the machine-learning field been drawn to Ekman?" Crawford asks. "It fits nicely with a machine-learning capacity. If you say there is a limited set of expressions and strictly limited numbers of potential emotions, then people will adopt that view primarily because the theory fits what the tools can do." In addition to Ekman's work and the personality-trait model of OCEAN, emotion-AI companies have adopted other systems. One is a "wheel of emotions" devised by the late psychologist Robert Plutchik, which is used by Adoreboard, a U.K.-based company that analyzes emotion in text. All these approaches offer to translate the complexity of human affect into straightforward formulas. They may suffer from similar flaws, too. One study found that OCEAN produces inconsistent results across different cultures.

Nevertheless, researchers say emotion apps can work—if their limitations are understood. Roboticist Ayanna Howard, dean of the College of Engineering at the Ohio State University, uses a modified version of Microsoft's facial-expression-recognition software in robots to teach social behavior to children with autism. If a robot detects an "angry" expression from its interlocutor, for example, its movements will adapt in ways that calm the situation. The stereotypical facial expressions may not always mean exactly the same thing, Howard says, but they are useful. "Yeah, we're unique but we're not that different from the person next door," she says. "And so when you're talking about emotion in general, you can get









GENDER BIAS: In a study using politicians' faces, researchers found that an emotion-AI program determined that only a few men were smiling. The scientists' own review, however, indicated the vast majority of men had a smile. In contrast to men, the program, Google Cloud Vision, applied the "smile" label to many women. Percentages on labels of attributes in two images (*below*) indicate the confidence the AI had in the label accuracy. The woman got a smile label at 64 percent confidence—along with labels focused on her hair—whereas the man did not get that label at all.























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speech: 66%

suit: 74%

official: 88%

businessperson: 80%

public speaking: 56%

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business: 56%

spokesperson: 82%

speaker: 72%







it right maybe not all the time but more than random right."

In general, algorithms that scan and aggregate the reactions of many people—such as those Zenus uses to read crowds—will be more accurate, Barrett says, because "better than random" becomes statistically meaningful with a large group. But assessing individuals is more treacherous because anything short of 100 percent accuracy ends up discriminating against certain people.

Many computer vision specialists are now embracing a more agnostic view of facial expressions. (And more companies have begun stating they do not directly map emotions or internal states.) "As the field has developed, there's increasing understanding that many expressions have nothing to do with emotion," says Jonathan Gratch, a computer science professor at the University of Southern California, who specializes in affective computing. "They're kind of tools we use to influence each other, or they're almost like words in a conversation, and so there's meaning in those words. But it is not direct access to what I'm feeling in the moment."

ET AS ATTEMPTS TO MAP and monetize emotional expressions, personality traits and behaviors grow, they are expanding the parts of our lives that can fall under surveillance. After 20 years of tech companies mining personal data from online behavior, a new, more intimate domain—faces and bodies and the signals they send—is poised for similar treatment. "If you're a Coca-Cola, and you're driving a campaign, and your principal methodology for messaging is the Internet, you know everything about what audience you reached," says Jay Hutton, CEO of Vancouver-based company <u>VSBLTY</u>, which markets smart cameras and software that scan crowds, analyzing demographics and reactions to products for retailers. "But what if we could take computer vision and turn bricks and mortar into that same level of analytics?"

In December 2020 VSBLTY announced a partnership with Mexican brewer Grupo Modelo to create in-store networks of cameras to capture data in the beverage company's 50,000 Modelorama convenience stores and neighborhood bodegas in Mexico and other Latin American countries by 2027. Demand will exist wherever there are screens and advertising, Hutton says. The technology "will be used in transit hubs, or in an airport, or a stadium," he says. "Advertisers are paying millions of dollars to be a sponsor, and their ads appear on screens throughout the stadium, [and] they are looking for validation of that spin."

This trend raises a basic legal and social question: Do the data from your face and body belong to you? In most places around the world, the answer is no—as long as your personal identity is kept separate from that data. "If you would like to know, and somebody's in public, there seems to be no limit in scanning them for their emotions," says Jennifer Bard, a professor at the University of Cincinnati College of Law, who has <u>studied the issue</u>.

Most emotion-AI companies that capture data in public say the information is anonymized, and thus its collection should not provoke concern. VSBLTY does not store facial images or other data that can be linked to identities, Hutton says. Zenus's Moutafis notes that his company's app does not upload the actual facial images that its cameras capture—only the relevant metadata on mood and position—and that it puts up signs and notices on meeting screens that the monitoring is occurring. "Explicit consent is not needed," he says. "We always tell people deploying it that is a very good practice; when you have a surveillance sensitivity, you have to put up a sign that these areas are being monitored." Typically, Moutafis says, people do not mind and forget about the cameras. But the diversity of applications means there are no common standards. It is also far from clear whether people and politicians will embrace such routine surveillance once it becomes a political and policy issue.

Ekman, who earlier worked with the company Emotient and with Apple on emotion AI, now warns it poses a threat to privacy and says companies should be legally obligated to obtain consent from each person they scan. "Unfortunately, it is a technology that can be used without people's knowledge, and it's being used on them, and it's not being used on them to make them happier," he says. "It's being used on them to get them to buy products they might not otherwise buy. And that's probably the most benign of the nonbenign uses of it."

Emotion AI has entered personal spaces, too, where the potential hoard of behavioral data is even richer. Amazon's Alexa analyzes users' vocal intonation for signs of frustration to improve its algorithms, according to a spokesperson. By 2023 some automakers will be debuting AI-enabled in-cabin systems that will generate huge amounts of data on driver and passenger behavior. Automakers will want those data, also likely anonymized, for purposes such as refining system responses and in-car design and for measuring aggregated behavior such as driver performance. (Tesla already collects data from multiple sources in its vehicles.) Customers would likely have the option of activating various levels of these systems, according to Modar Alaoui, CEO of emotion-AI company Eyeris, so if occupants do not use certain functions, data would not be collected on those. The in-cabin systems designed by Affectiva (recently acquired by Swedish firm Smart Eye) do not record video but would make metadata available, says chief marketing officer Gabi Zijderveld.

ALEIX MARTINEZ, a computer vision scientist at Ohio State and Amazon and a co-author with Barrett of the 2019 paper criticizing the face-emotion connection, has a <u>photo</u> he is fond of showing people. It is of a man's face that appears to be twisted in a mixture of anger and fear. Then he shows the full image: it is a soccer player exultant after scoring a goal. Facial expressions, gestures, and other signals are not only a product of the body and brain, he notes, but of context, of what is happening around a person. So far that has proved the biggest challenge for emotion AI: interpreting ambiguous context. "Unless I know what soccer is, I'm never going to be able to understand what happened there," Martinez says. "So that knowledge is fundamental, and we don't have any AI system right now that can do a good job at that at all."

The technology becomes more effective, Martinez says, if the task is narrow, the surroundings are simple, and the biometric information collected is diverse—voice, gestures, pulse, blood flow under the skin, and so on. Coming generations of emotion AI may combine exactly this kind of information. But that, in turn, will only create more powerful and intrusive technologies that societies may not be prepared for.

FROM OUR ARCHIVES

scientificamerican.com/magazine/sa

What's in a Face? Susana Martinez-Conde and Stephen L. Macknik; Scientific American Mind, January/February 2012.

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TOP 10 EMERGING TECHNOLOGIES FOR 2021

Innovations to help tackle societal challenges—especially climate change

Illustrations by Vanessa Branchi





Think of our planet's grand challenges: Managing climate change. Reducing energy use. Sustaining food production. Improving global health. Many of these efforts involve overlapping problems—and the potential for interlinked solutions. It's no wonder the United Nations names "Partnerships" as its 17th Sustainable Development Goal.

In this 10th edition of the "Top 10 Emerging Technologies," created by *Scientific American* and the World Economic Forum, that interlinking is front and center. With the acceleration of government and industry commitments for decarbonization, we will see an array of novel approaches in low-emission transportation, residential and commercial infrastructure, and industrial processes. Two such technologies—the production of "green" ammonia and engineered crops that make their own fertilizer—will improve agricultural sustainability. In remote areas, 3-D printing with local soils will erect stronger houses with less energy.

Because health is on everyone's mind, this year's Top 10 salutes the rise of breath sensors that can detect COVID-19 and other diseases, as well as wireless biomarker monitors that make it easier to diagnose and manage chronic illnesses. New results from the field of genomics could allow us to engineer longer "healthspans," and on-demand drug manufacturing will result in tailored medicines while helping to solve today's supply challenges with largescale production.

To keep track of it all, the number of devices that make up the Internet of Things is rapidly growing. They will become more globally connected through the use of orbiting nanosatellites and be powered by energy harvested from wireless signals. The future has never looked so interconnected.

> -Mariette DiChristina and Bernard S. Meyerson



CLIMATE CHANGE

DECARBONIZATION RISES

Sweeping commitments to address climate change will birth new technologies By Bernard S. Meyerson

More than a century after the first scientist argued that carbon dioxide could trap heat in the atmosphere and decades after "climate change" entered the vernacular, countries and industries have been making new commitments to cut their carbon footprints. In 2021 the U.S., the second-largest source of national carbon emissions, committed to halve its output relative to 2005 levels by 2030. The U.K. announced its own aggressive goal of a 68 percent reduction compared with 1990 levels by that date. The European Union Parliament recently passed a law requiring carbon-emissions reductions by at least 55 percent by 2030 compared with 1990 levels. Although industries such as oil and aviation are more resistant to change, the rate at which companies are joining the Science-Based Targets initiative, which helps them reduce their emissions to stay in line with the Paris agreement, has doubled since 2015. General Motors, Volkswagen and other major auto manufacturers have set ambitious targets for decarbonization in the past year.

This acceleration of commitments—along with its associated challenges—is a clear indicator of decarbonization's emergence worldwide. It will force a diverse suite of technologies to "emerge"—that is, to demonstrate the ability to operate at scale in the next three to five years. To make this a reality, solutions that have already been identified must mature and scale at greater speed. Existing technology gaps will require sustained innovation. We expect several broad areas to see significant focus and growth.

Today 2 percent or less of global private and commercial roadway transportation fleets produce zero emissions, despite Tesla's highly visible initial success in driving consumer interest. Meanwhile bulk shipping, both rail and seaborne, has devised low-carbon solutions. Yet many of them, such as the Coradia iLint, a passenger train powered by hydrogen fuel cells and manufactured by Alstom, have yet to be applied at scale. The barriers are not just technological but also political, given that such transformational programs require significant capital investment.

In the U.S., an estimated 13 percent of total carbon emissions come from fuel used for heating and cooking in residential and commercial buildings. Reducing that number in America and elsewhere will demand net-zero-emission HVAC (heating, ventilation and air-conditioning), and



passive solar environmental systems must become commonplace. It will also be important to switch to natural and novel building materials such as renewable timbers and low-carbon-footprint cement.

As renewable energy sources become abundant, we will need to employ them to decarbonize pervasive sources of greenhouse gases. One example is "green" hydrogen. When produced without using carbon-based fuels, hydrogen can become a nonpolluting fuel while also serving the chemical industry as a basic ingredient with no carbon footprint. Similarly, if data centers, which often require megawatts of electricity, are co-located with the same renewable energy sources, their carbon footprint is dramatically reduced.

Meeting the power-generation goals set by nations and industries requires a radical expansion of photovoltaic, wind, hydroelectric, tidal, nuclear and other zero-emission tech. Some critical hurdles remain: Reliable, efficient and affordable energy storage at the industrial scale is nascent. Carbonfree, fission-based nuclear energy (including disposal of its waste products) that is both safe and affordable is also still aspirational. To lessen the pollution from existing fossil-fuel power generation, we will also need to bring on far more technologies that capture, reuse and sequester carbon.

In the agriculture sector, protein substitutes such as the Impossible Burger and Beyond Meat will need to take over a much greater share of the market to mitigate the massive levels of carbon and methane produced in raising livestock. Data from sensors connected via the Internet of Things will increasingly enable intelligent land and crop management as well as fertilizer and water use, aiding in further carbon reductions.

In addition to the myriad technological challenges to rapid decarbonization, nations must develop global governance methods to ensure energy equality. Emergent economies cannot face identical carbon-reduction targets that would stifle development. Nations will also need to thoughtfully allocate land to expand infrastructure for renewables. And to ensure compliance with global accords, governments will need global environmental monitoring infrastructure, similar to the protocols of the International Atomic Energy Agency.

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AGRICULTURE



CROPS THAT SELF-FERTILIZE

Root-grown instead of sown By Wilfried Weber and Carlo Ratti

Providing food for the world's growing population relies heavily on the use of nitrogen-containing industrial fertilizers. Some 110 million tons of nitrogen are required to sustain global crop production annually, according to the U.N.'s Food and Agriculture Organization. Nitrogen fertilizer is typically produced by converting nitrogen from the air into ammonia, a form of nitrogen that can be utilized by plants. This conversion sustains approximately 50 percent of global food production and accounts for an estimated 1 percent of the world's primary energy needs, but it is also an energyintensive process: it accounts for 1 to 2 percent of global carbon dioxide emissions. Furthermore, industrial fertilizers are too expensive for smallholder farmers in many countries, leading to strongly decreased yields and increased pressure on natural lands.

To develop a solution, researchers are taking cues from nature's own approach to making nitrogen fertilizer. Whereas staple food crops such as corn and other cereals rely on inorganic nitrogen from the soil, legume plants such as soy and beans have maintained a clever way to produce their own. The roots of legumes interact with soil bacteria, leading to bacterial colonization of the root and formation of symbiotic organs called nodules. Within these structures, the plant provides sugars to sustain the bacteria and profits from the bacteria's ability to fix nitrogen—that is, to convert atmospheric nitrogen into ammonia. Thus, through an evolutionarily ancient symbiosis with soil bacteria, legumes are independent of modern nitrogen fertilizers.

Researchers have shown that the formation of the nodules—the natural fertilizer factories—involves intimate molecular communication between soil bacteria and legume roots. This knowledge has inspired exciting new approaches to engineering nitrogen fixation into nonlegume plants. For example, scientists are coaxing the roots of cereals to engage in symbiotic interaction with nitrogen-fixing bacteria. The researchers emulate the molecular communication between legumes and bacteria and steer the process by which the bacteria can colonize plant roots. In an alternative approach, soil bacteria that naturally colonize the roots of cereals but cannot fix nitrogen are taught to produce nitrogenase, the key enzyme that converts nitrogen from the air into plant-compatible ammonia.

With governments and private foundations recently providing strong support for research and development in the area of engineering nitrogen fixation, crops that harness the power of natural symbiosis might soon become a key element of a more sustainable food production.





BIOCHEMISTRY



BREATH SENSORS DIAGNOSE DISEASES

Puffing is far faster than drawing blood By Rona Chandrawati and Daniel E. Hurtado

When police officers suspect a motorist is intoxicated, they can use a Breathalyzer: a handheld device that measures the level of alcohol in the blood. Can the same be done for disease diagnosis?

The short answer is yes. Human breath contains more than 800 compounds, and recent discoveries have shown a strong correlation between certain concentrations of compounds and different disease states. For example, breath with a significantly elevated acetone concentration is a strong indication of diabetes mellitus; a higher concentration of exhaled nitric oxide is correlated with inflamed cells and therefore can be used as a biomarker for respiratory diseases; greater amounts of aldehydes are closely related to lung cancer.

When a person puffs into a sampler, that breath is fed into a sensor that generally makes detections based on changes in the electrical resistance of metal oxide semiconductors. Within minutes, a software analysis by an external computer generates a profile of the compounds present.

Beyond delivering results far faster than a blood draw, breath sensors could streamline medical diagnostics by providing a noninvasive way to collect critical health data. In low-income countries with limited medical resources, their ease of use, portability and costeffectiveness provide new opportunities for health care. These devices could also help mitigate community spread of a virus in a manner similar to how temperature checks screen individuals before they enter shared indoor spaces such as supermarkets or restaurants.

In March 2020 Hossam Haick and his co-workers at Technion-Israel Institute of Technology concluded an exploratory clinical study in Wuhan, China, for COVID detection in exhaled breath. The sensors achieved a remarkable 95 percent accuracy and 100 percent sensitivity in differentiating people who were positive or negative for the disease. In 2021 the U.S. Department of Health and Human Services provided \$3.8 million to repurpose NASA's E-Nose—a monitor that uses nanosensor array technologies to autonomously scan the air on the International Space Station for potentially dangerous chemicals—to detect COVID.

Critical challenges need to be met before breathsensor technology becomes widespread. First, detection accuracy must be improved for some diseases, particularly for tuberculosis and cancer. Second, various compounds in a breath sample can confound test results, creating false positives. The algorithms that analyze sensor data will also need to be improved to reach greater accuracy. Finally, bigger investments in clinical trials are needed to help validate this technology in large populations.

ENGINEERING



ON-DEMAND DRUG MANUFACTURING

Making pharmaceuticals where and when they are needed By Elizabeth O'Day and Mine Orlu

What if the next time you went to your local pharmacy, rather than the pharmacist looking through aisles of premade drugs to fill your prescription, he or she made it to the exact dose and formulation tailored for you? Recent advances in microfluidics and on-demand drug manufacturing are poised to make this idea a reality.

Traditionally drug products are made in large batches through a multistep process with different parts dispersed among many locations across the globe. Hundreds of tons of material support such mass production, creating challenges in ensuring the consistency required for both quality and reliable supply. It can take several months to complete drugs and deliver them to stores.

In contrast, on-demand drug manufacturing, also known as continuous-flow pharmaceutical manufacturing, makes drugs all in one go. It works by flowing ingredients via tubes into a series of small reaction chambers. Producing drugs as needed at a single site means that drugs can be made in remote locations or in field hospitals. It also means fewer resources are needed to store and transport drugs and that doses can be tailored to individual patients.

In 2016 researchers at the Massachusetts Institute of Technology working with DARPA (Defense Advanced Research Projects Agency) first demonstrated it was possible to make on-demand drugs. They created a refrigerator-size machine that used continuous flow to make four common drugs: diphenhydramine hydrochloride, which is used to relieve symptoms of allergy; diazepam, which is used to treat anxiety and muscle spasms; the antidepressant fluoxetine hydrochloride; and the local anesthetic lidocaine hydrochloride. They made 1,000 doses of each drug within 24 hours.

On Demand Pharmaceuticals is now commercializing the original M.I.T. work, with several platforms available or in development, including American Made Precursors on Demand (AMPoD), which enables full drug-product manufacturing from precursor to final formulation; Bio-Mod, which enables the manufacture of biologics; and IV Medicines on Demand, which produces sterile injectables. A number of pharma manufacturers, among them Eli Lilly, Johnson & Johnson, Novartis, Pfizer and Vertex Pharmaceuticals, are also making use of continuous-manufacturing technology at least for parts of their manufacturing processes.

Currently portable machines for on-demand drug manufacturing cost millions of dollars, preventing widespread rollout. New methods of quality assurance and quality control also will be needed to regulate both the personalization of formulas and single-person drug batches. As cost goes down and regulatory frameworks evolve, on-demand manufacturing may revolutionize where, when and how drugs are made.





COMPUTING



ENERGY FROM WIRELESS SIGNALS

5G will help power the Internet of Things *By Joseph Costantine*

The wireless devices that make up the Internet of Things (IoT) constitute the backbone of an ever more networked world. They are deployed as gadgets in homes, as wearable devices for biomedical uses, and as sensors in hazardous and hard-to-reach areas. As the IoT grows, it is enabling agricultural practices that use less water and pesticide; more energy-efficient smart grids; sensors that monitor flaws that can weaken bridges or concrete infrastructure; and early-warning sensors for disasters such as mudslides and earthquakes.

With an estimated 40 billion IoT devices coming online by 2025, providing convenient, on-demand power to those devices is a fast-growing challenge. One solution that is already in the works leverages the wireless signals emanating from Wi-Fi routers and access points. The emerging fifth generation of cellular technology, or 5G, will elevate wireless-energy harvesting to a new level. With 5G, the Federal Communications Commission is allowing cell signals to move into the higher (but still safe for humans) millimeter range of the electromagnetic spectrum for the first time. Along with higher information rates, 5G wireless signals transmit a greater amount of radiated energy than 4G. This capability points to a future where many low-power wireless devices never need to plug in to charge.

How can devices grab power from wireless signals? Wi-Fi and 5G are electromagnetic waves that propagate at frequencies within the broad spectrum between FM radio, microwaves and millimeter waves. The first step of the process involves a receiving antenna that captures energy carried with the wireless signal. The antenna routes that energy into an electronic rectifier circuit, which in turn uses semiconductors to convert it into a direct-current (DC) voltage that can charge or power a device. This combination of antenna and rectifier (or converter) is called a rectenna. A power-management circuit follows the rectenna, amplifying the voltage while itself consuming negligible power.

Many start-up companies are now offering wireless charging products that currently rely on dedicated wireless transmitters; research suggests it is likely, however, that such devices will be able to harvest Wi-Fi and 5G signals in the near future. Just as cell phones free us from landlines and have transformed our communication ability, this emerging technology will free us even further.



GENOMICS



ENGINEERING BETTER AGING

A focus on increasing "healthspan," not just lifespan

By Wilfried Weber and P. Murali Doraiswamy

According to the World Health Organization, between 2015 and 2050 the proportion of the global population older than 60 will nearly double from 12 to 22 percent, posing enormous challenges to health and social systems. Aging is related to chronic diseases such as dementia, cancer, type 2 diabetes and atherosclerosis. The desire to reverse aging or to find a "fountain of youth" is likely as old as humankind. We are beginning to understand the molecular mechanisms of aging that could help us lead lives that are not just longer but healthier.

Through the advent and refinement of so-called omics technologies (which simultaneously quantify, for example, the activity of all genes or the concentration of all proteins and metabolites in a cell), combined with insights from epigenetics, those key mechanisms are becoming clearer. One exciting example involves combinations of specific epigenetic marks (modifications that change gene activity because of behavior and environment) or metabolic compounds that can serve as identifiers of an organism's biological age. Such marks also are strong predictors of diseases in the elderly and the accompanying risk of death. Advances in sequencing the genetic information of single cells in an organism have demonstrated that the number of mutations increases during aging; the body's repair of such mutations may leave aging-related traces on the DNA—another type of marker. DNA damage is also associated with driving cells into senescence (meaning they can no longer reproduce) or exhausting the stem cells that are key for cell and tissue renewal.

This recent and continuously growing understanding of aging mechanisms is enabling the development of targeted therapies. For example, one recent initial clinical study suggested that a one-year-long administration of a pharmaceutical cocktail, including human growth hormone, could turn back the "biological clock" 1.5 years. Similarly, researchers successfully demonstrated in a rodent model that gene therapy targeting three longevity-linked genes could improve or reverse four common age-related conditions. Scientists have also identified proteins in the blood of young humans that, when infused into older mice, improved markers of age-related brain dysfunction. The result suggests therapeutic potential to reverse human age-related cognitive decline.

Inspired by new insights into the aging process at the molecular level and encouraged by the first promising results from clinical trials, more than 100 companies are actively developing pharmaceutical or geneengineering approaches to analyze and engineer "healthspan" and lifespan. Most of these companies are at preclinical stages or early clinical trials. This R&D, backed by investors' high expectations, fuels hopes for healthier elderly years.

EMERGING TECHNOLOGIES 2021

CHEMISTRY



GREEN AMMONIA Reducing the CO₂ footprint of fertilizer production By Javier García Martínez and Sarah E. Fawcett

The Haber-Bosch process—arguably one of the most important inventions of the 20th century that many people have never heard of—enables synthesis of ammonia on an industrial scale. This ammonia is used to produce the fertilizers that fuel 50 percent of global food production, making it a key to food security around the world. Ammonia synthesis, however, is an energy-intensive chemical process that requires a catalyst to fix nitrogen with hydrogen.

Unlike nitrogen, which makes up most of the air we breathe, hydrogen must be synthetically produced and is currently generated using fossil fuels. Natural gas, coal or oil is exposed to steam at high temperatures to generate hydrogen gas. Problematically, this process yields vast amounts of carbon dioxide, accounting for 1 to 2 percent of total global emissions.

Green hydrogen, produced by splitting water using renewable energy, promises to change that. In addition to

BIOINFORMATICS



BIOMARKER DEVICES GO WIRELESS

Continuous, noninvasive monitoring of chronic diseases

By Joseph Costantine

Nobody likes needles. But monitoring chronic diseases such as diabetes and cancer requires frequent blood work to identify and track certain biological markers, or biomarkers. Now more than 100 companies are developing wireless, portable and wearable sensors that will soon enable continuous monitoring of this vital information.

Monitors use a variety of approaches to detect biomarkers in sweat, tears, urine or blood. Some use light or low-power electromagnetic radiation (similar to cell phones or smart watches), combined with antennas and electronics, to peer into tissue. Others involve wearable, flexible electronic sensors atop skin. To detect a given biomarker, monitors seek a change in current, voltage or electrochemical concentration.

Diabetes is a top target for this technology, with 578 million people globally expected to be diagnosed with the diseliminating carbon emissions during hydrogen production, the process has a significantly purer end result. It is free of chemicals that are incorporated when fossil fuels are used, such as compounds containing sulfur and arsenic that can "poison" the catalyst, thereby reducing reaction efficiency.

Cleaner hydrogen also means that superior catalysts can be developed because they no longer need to tolerate the poisonous chemicals from fossil fuels. In fact, companies such as Denmark's Haldor Topsoe have already announced the development of novel catalysts from entirely renewable sources for green ammonia production.

Spanish fertilizer producer Fertiberia is partnering with energy company Iberdrola to vastly expand green ammonia plans, from a 20-megawatt pilot plant that will be operational in 2021 to a full 800 MW of solar-driven electrolytic hydrogen production by 2027. The investment, estimated at 1.8 billion euros, is expected to generate 4,000 jobs and save 400,000 tons of CO_2 a year, equivalent to the emissions of about 60,000 cars.

A major obstacle is the current high cost of green hydrogen. To help solve that problem, 30 European energy players have launched HyDeal Ambition, a project aiming to deliver green hydrogen at 1.5 euros per kilogram before 2030 through innovations in the production, storage and transport of hydrogen. If successful, the effort could unleash a whole range of new applications for green ammonia, including its ability to be decomposed back into hydrogen—enabling a virtuous green hydrogen-ammonia circle.

ease by 2030. To meet the rising need for checking glucose levels, one portable device promises noninvasive monitoring using wireless electromagnetic fields at millimeter waves and near-infrared sensing; the voltage variation in a patient's finger can be correlated to glucose level. In another approach, wearable electronics embedded in clothing detect glucose levels in the bloodstream with electromagnetic waves within the microwave range. In a third effort, tattoo-based circuitry evaluates glucose in sweat by employing electrodes to produce tiny amounts drawn from the interstitial fluids that naturally leak out of capillaries. Similar to glucose detectors, tattoolike circuits could sample sweat for changes in lactate, an application that is drawing investment from the athletics industry.

The wireless transmission systems can be paired with various types of sensors, including those made with densely aligned carbon nanotubes or ones that drive magnetic nanoparticles into tiny microfluidic channels to detect biomarkers through a change in voltage or current. Such technologies open the door for an "electronic tongue" that is able to distinguish various liquid samples.

Tears can be surprisingly revealing as well. Electronic, transparent contact lenses can wirelessly pick up cancer biomarkers or glucose levels for diabetes monitoring. Saliva biomarkers may indicate physiological and psychological stress or diseases such as HIV, intestinal infections, cancer and COVID. When integrated in a mouth guard that has radio-frequency identification technology, saliva sensors can also monitor oral health, detecting decay or anomalies.



MATERIALS SCIENCE

HOUSES PRINTED WITH LOCAL MATERIALS Concrete is swapped for soil By Bernard S. Meyerson and Carlo Ratti

Technologies such as childhood vaccines or LASIK eye surgery tend to dramatically improve quality of life for many people in the industrial world. But their influence in developing nations has often been far more limited or significantly delayed. Building houses with 3-D printers, however, could help tackle the challenge of inadequate housing for 1.6 billion people worldwide, according to a U.N. estimate.

The concept of 3-D printing houses is not new. Several enterprises have printed homes on Long Island in New York and in Austin, Tex., with promising results. Materials such as concrete and various mixtures of sand, plastics and binders are trucked to the building site and extruded through a massive 3-D printer. As a relatively simple and low-cost construction method, 3-D printing houses seems well suited to mitigating housing struggles in remote, impoverished regions. But the lack of infrastructure for transporting materials has precluded its use.

Recently various firms have taken inspiration from projects intended for Mars, where local materials are the only option available. In the small town of Massa Lombarda, Italy, one prototype designed by Mario Cucinella Architects uses local clay soil for printing housing components, dramatically reducing the complexity, cost and energy use of construction. The soil is mixed with hemp and a liquid binder, then extruded layer by layer by Italian 3-D printing company WASP into the complex shapes and surfaces required of a dwelling. Using native materials eliminates about 95 percent of the mass that would typically need to be transported to a site.

Another approach, demonstrated by WASP in collaboration with designer RiceHouse, is inspired by centuries of experience in creating mud bricks in arid regions. The process involves blending the traditional mixture of mud with a binding filament, which can be naturally occurring fiber. Instead of hand pressing the base material into a mold, the material is pumped through a 3-D printer supplied by WASP to create a house in far less time than required with traditional methods—and with extra strength granted by the rigid geometry of the printed walls. Much of the base material is sourced from the construction site itself.

With the WASP approach, structures that have reached the end of their usable life can simply be broken down to their base materials, and those materials can be reused. This zero-waste, or circular, model goes back thousands of years. Today homes still exist on Mount Erice in Sicily that were constructed of residual materials from 10 centuries of homes that came before them.





ENGINEERING AND COMPUTING



SPACE CONNECTS THE GLOBE

The Internet of Things goes into orbit By Rajalakshmi Nandakumar

Today at least 10 billion active devices make up the Internet of Things (IoT), a number that is expected to more than double in the next 10 years. Maximizing the IoT's benefits in communication and automation requires devices to be spread across the globe, collecting zettabytes of data. The data are assimilated in cloud data centers, using artificial intelligence to identify patterns and anomalies, such as weather patterns and natural disasters. There is a big problem, though: cellular networks span less than half the globe, leaving enormous gaps in connectivity.

A space-based IoT system could patch those gaps, using a network of low-cost, low-weight (less than 10 kilograms) nanosatellites that orbit a few hundred kilometers from Earth. The first nanosatellite launched in 1998; today roughly 2,000 CubeSats serve as orbiting monitors. Companies such as SpaceX Starlink, One-Web, Amazon and Telesat have used nanosatellites for the goal of providing global Internet coverage.

Soon it will be possible to communicate with these orbiting nanosatellites from small battery-powered IoT devices here on Earth. Data from a device—say, a location reading from a tracking sensor—would be sent to a satellite using low-power, low-cost communication protocols similar to long-range communication and Sigfox, which can decode even weak signals. It would then be transferred to ground stations where the data would be analyzed.

This technology is enabling various data-driven applications in previously unreachable or difficult-toconnect locations. Communications company Iridium, for instance, has a network of 66 low-Earth-orbit satellites that can connect ships to aircraft flying anywhere in the world. Battery-powered sensors from Lacuna Space in the U.K. can connect to their low-Earth-orbiting satellites to track assets such as packages in ships, as well as monitor farm data to enable agriculture that uses water, fertilizer and herbicide more efficiently. Myriota in Adelaide, Australia, uses space-based IoT to track endangered species such as rhinos. And to move data from a satellite to centralized servers in data centers, Microsoft partnered with SpaceX Starlink to launch a space-based cloud computing platform.

Space IoT still faces a multitude of challenges before becoming truly global. For instance, nanosatellites have a relatively short lifetime of about two years and must be supported by expensive ground station infrastructure. To confront the growing problem of orbiting space junk, plans are underway by NASA and others to either automatically deorbit satellites at the end of their functional life or collect them using other spacecraft.

It also will be important to provide secure, reliable, high-bandwidth communication links from satellites to maintain connectivity in different weather conditions and terrains. To do so, companies are working on a different frequency spectrum and developing coding schemes to improve the bandwidth and robustness of the communication systems.

SPACE WEATHER

Devastating geomagnetic storms may happen more frequently than scientists thought, and that has ominous implications for a wired global society

By Jonathan O'Callaghan

THE THREAT OF SOLAR SUPERF

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LARES

VERY NOW AND THEN OUR STAR PRODUCES immense flares of particles and radiation that can wreak havoc on Earth. For more than 150 years scientists studying these outbursts and how they affect our planet have placed great focus on a single, seemingly pinnacle

example: the Carrington Event of 1859. An eruption from the sun walloped Earth, pumping enough energy into our planet's magnetic field to set off a massive geomagnetic storm that created beautiful auroral displays but also sparked electrical fires in telegraph lines. The storm was seen as an odd, minor inconvenience that caused limited damage to the electrical infrastructure of the time. Researchers today, however, recognize the Carrington Event, along with a 1921 storm <u>of comparable strength</u>, as an ominous warning of future catastrophes.

> The first indication that solar storms could be even worse came in 2012, with the discovery of a mega storm some 10 to 100 times stronger than the Carrington Event that occurred around A.D. 775. "It was really, really astounding," says Nicolas Brehm of ETH Zurich. "We didn't think something of this magnitude could happen."

> The ancient mega storm might have come from a oncein-10,000-years "superflare," an event thousands of times more powerful than a regular solar flare, scientists speculated at the time. A direct hit by such a superflare today would have devastating consequences for our globally wired society.

> Now these phenomena appear to be even more common than we thought: researchers investigating the geochemical annals of Earth's recent history have now found evidence for two more.

In a paper led by Brehm, available as a preprint on Research Square, scientists reveal the possible discovery of two frightfully strong solar events. One occurred in 7176 B.C., when nomadic hunter-gatherer societies were giving way to agrarian settlements. The other happened in 5259 B.C., as the planet emerged from the last ice age. Both events are thought to have been at least as strong as the one in A.D. 775, and for the past decade scientists have been searching for similarly extreme occurrences. Brehm's team is the first to find some. "It's a great achievement," says Fusa Miyake of Nagoya University in Japan, who led the study in 2012 that revealed the 775 event. Scientists now refer to such superflares as "Miyake events."



Jonathan O'Callaghan is a freelance journalist covering commercial spaceflight, space exploration and astrophysics. To look for these solar flares, researchers rely on chemical analyses of samples from polar ice caps and from ancient trees preserved in waterlogged bogs or high on mountaintops. When solar particles hit the atmosphere, they can produce unstable radioactive forms of various elements, called isotopes, that accumulate in these places. For example, solar activity can form carbon 14, which is absorbed by trees as they





SOLAR FLARES and sheets of glowing plasma rise from a region of intense activity on the sun. grow. Because each ring within a tree's trunk corresponds to a single year of growth, scientists can determine the precise dates of any isotope spikes caused by increased solar activity: the more carbon 14 there is in one ring, the more solar particles were hitting our atmosphere at that time. Such rings "allow us to reconstruct patterns of radiocarbon through time," says Charlotte Pearson of the Laboratory of Tree-Ring Research at the University of Arizona, who is a co-author on Brehm's paper. "One of the key things that drives those fluctuations is the activity of the sun."

By studying the concentrations of beryllium 10 and chlorine 36 in ice cores, scientists can make similar though slightly less accurate measurements. Together the two methods can provide a precise account of historical events. We have tree-ring data for most of the Holocene—the current geologic epoch, which began about 12,000 years ago. Poring over them to search for carbon 14 spikes is time-consuming, however. Looking at just a single year typically requires weeks of analyzing and cross-correlating multiple tree-ring samples. "There's 12,000 years of the Holocene to do, and we've done 16 percent of it," says Alexandra Bayliss, head of scientific dating at Historic England and a co-author on the paper. "It's a matter of time and money."

Brehm and his team got lucky. For the event in 7176 B.C., they first saw preliminary evidence for a beryllium 10 spike in ice cores. The researchers followed up with tree rings and saw a corresponding spike of carbon 14. For the event in 5259 B.C., Bayliss had noticed a gap in archaeological data around this time period. Studying carbon 14 data in tree rings from this era, the team found another spike. "We found this huge increase" for both dates, Brehm says, each similar in magnitude to the spikes Miyake found in the samples that clinched the A.D. 775 event.

At first scientists were unsure what had caused these spikes, and some even thought solar events were unlikely. A 2013 study led by Brian Thomas of Washburn University, however, showed <u>solar flares were the probable culprit</u>. "There were people making suggestions [that the 775 spike] could be from a supernova or even a gamma-ray burst," says Thomas, who was not involved in the latest paper by Brehm and his colleagues. "But they're just too rare to cause this kind of frequency. It doesn't fit as well as the solar explanation." Such large, frequent spikes, he argues, were more likely the result of increased solar activity—possibly accompanied by a geomagnetic storm similar to the Carrington Event but far more powerful. "The Carrington Event isn't even detectable" in tree rings and ice cores, Bayliss notes, which suggests it was minuscule by comparison.

Even so, the exact correlation between spikes in solar particles and the intensity of any accompanying geomagnetic storm remains unclear. "A big particle event is often associated with a geomagnetic storm, but it doesn't necessarily have to be," Thomas says. It may even be that geomagnetic storms like the Carrington Event do not cause spikes in carbon 14 at all—that would explain its absence from tree-ring and ice-core data dated to the event. There are hints, however, that at least the event in 775 was accompanied by powerful auroras, <u>recorded in China</u>, pointing to a strong geomagnetic storm alongside this









A PLANET-DWARFING solar prominence

solar prominence erupts from our star, unleashing massive amounts of matter and radiation. huge influx of solar particles. "It's safer to assume all these events were big geomagnetic storms," Thomas says.

If that link is correct, it suggests that in the past 10,000 years alone, Earth has been battered by at least three solar superflares. (Evidence of more may eventually be found in the 84 percent of available tree-ring data that have yet to be analyzed for carbon 14 spikes.) "For there only to be one in the past 10,000 years didn't really seem realistic," Pearson says. "But up until this point, it could have just been a one-off. Now that we've found two more, I'm not sure that it's surprising—but it may be concerning."

The major worry is that if such an event happened today, it could be devastating to satellites in orbit and infrastructure on the ground. In March 1989 a geomagnetic storm much weaker than the Carrington Event <u>caused a 12-hour</u> <u>blackout in Quebec</u> when it overloaded the entire province's power grid. Today a geomagnetic storm resulting from a Miyake event would probably cause many more widespread effects, including potentially catastrophic power grid and satellite failures.

Sangeetha Abdu Jyothi of the University of California, Irvine, recently calculated that a Carrington Event-level storm today could even cause an "Internet apocalypse." Energetic particles from such a storm could knock out undersea cables between countries, disrupting worldwide Internet traffic for weeks or possibly months. In the U.S. alone, such a disaster could cost \$7 billion a day, Abdu Jyothi estimates. Something stronger, such as a Miyake event, could cause almost incalculable damage. "For something at a Carrington-scale, we could possibly recover because our data themselves will not be erased," Abdu Jyothi says. "With something 10 or 100 times stronger, I don't know. I don't think anybody has simulated that. I suspect it would cause significant data loss. We could lose all our records, bank information and critical health information and not have anything to go back to."

The odds that our global civilization will suffer a dark age from a Miyake event seems remote for the time being. But some estimates suggest the chance of a Carringtonlevel event may be as much as <u>12 percent in the next</u> <u>decade</u>. We can prepare for something of this magnitude by monitoring solar activity to shut down satellites and power grids ahead of the arrival of a superflare and its ensuing geomagnetic storm. But a Miyake event may be more difficult to protect against.

Meanwhile scientists continue to find evidence of additional extreme solar events in ancient tree rings and ice cores. "We're starting to realize that the sun can be much more energetic and active than we thought," Thomas says. "When people were studying these superflares on other stars, one discussion was whether the sun could do this. From these historical records, it seems the sun is capable of getting into that range."

FROM OUR ARCHIVES

The Mysterious Origins of Solar Flares. Gordon D. Holman; April 2006. scientificamerican.com/magazine/sa







A CHURNING MAELSTROM

of twisted magnetic fields drives the outbursts that define the sun's 11-year activity cycle.

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Warning Signs



CANCER, IN ALL ITS FORMS, IS MOST TREATABLE

when caught early. But despite the vast resources aimed at finding ways to detect the disease in its initial stages, many people who qualify for existing screenings still do not receive them. Some are unfamiliar with the constantly evolving guidelines on when and where to get tested. Others have never been informed that they need exams in the first place. And still others cannot get their physicians to refer them for screening even when

they request it. Equity and access are ever present barriers—race, socioeconomic status and education all play a role in who gets tested and who gets overlooked. Inevitably those in the most vulnerable communities face the greatest burdens.

Over the past 20 months the pandemic has made cancer screening even less attainable. In early 2020 many clinics temporarily shut their doors, health-care practitioners were reassigned, and masks and other protective equipment were reserved for those on the COVID front lines. Even when appointments were available, many put off scheduling regular mammograms, colonoscopies and other screenings for fear of exposure to the novel coronavirus. The result was an unintentional experiment in the importance of early cancer screening. Many predicted a drastic increase in diagnoses of advanced cancers, and some initial data indicate at least a modest rise. But the ultimate effects of the pandemic on cancer mortality are complex and difficult to measure—most now believe they will take years to parse.

One screening that has been particularly affected by the pandemic, for better and for worse, is for colorectal cancer. In-person screenings fell, but at-home tests, which can indicate the need for a followup colonoscopy, amassed new attention. Many researchers and practitioners hope that attention brings awareness to a disease whose incidence—for reasons no one fully understands—is growing at a surprising rate among younger adults, even while it declines in older demographics.

This puzzle has sent scientists wading through data and has garnered enough concern that the U.S. Preventive Services Task Force recently lowered its suggested age of first colonoscopy, from 50 to 45. Even that, however, will not detect the cases in younger age groups. If researchers could determine underlying reasons for this upswing—lifestyle, environmental or gestational influences—they might be able to identify higher-risk individuals who would benefit from early and regular screenings, thereby preventing a multitude of unnecessary deaths.

Lauren Gravitz, Contributing Editor

S3 The Equity Equation Eliminating disparities in

cancer screening will require outreach, availability and cultural consideration *By Melba Newsome*

S7 The COVID Cancer Effect Oncologists are grappling with predicting—and mitigating the effects of the pandemic *By Usha Lee McFarling*

S10 GRAPHIC:

Cancer Diagnoses before and during COVID in the U.S.

S12 The Colon Cancer Conundrum

Colorectal cancer rates in younger adults are climbing. The race is on to figure out why *By Cassandra Willyard*

S14 GRAPHIC:

Concerning Trends in Colorectal Cancer Incidence in the U.S.

This report, published in *Scientific American* and *Nature*, is sponsored by Johnson & Johnson. It was produced independently by the editors of *Scientific American*, who take sole responsibility for the editorial content.

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Cover and main illustrations by Harry Campbell


The Equity Equation Eliminating disparities in cancer screening will require outreach, availability and cultural consideration

By Melba Newsome

LA SHAWN FORD HAS ALWAYS BEEN METICULOUS about his health. He ate well, exercised regularly and never smoked. But last year, when the 48-year-old Illinois state representative learned that actor Chadwick Boseman had died of colon cancer, he decided to take his health-care game up a notch. In October 2020 Ford scheduled an appointment with his primary care physician for a colonoscopy and, while he was at it, a prostate cancer screening, too.

The colonoscopy came back clean, but his doctor refused to order the prostate-specific antigen (PSA) test, saying Ford wasn't in the recommended age range for screening. Although Ford had no indication that anything was amiss, he found another doctor to help him get the simple blood test.

FARLY DETECTION

Men with a PSA level between 4 and 10 have about a one-infour chance of having prostate cancer. That risk goes to one in two if the level is above 10. Ford's was 11, so high that his physician ran the test again to confirm. This time it registered a PSA of 12.

Black men like Ford are disproportionately diagnosed with, and die from, prostate cancer, says Edward M. Schaeffer, chair of the urology department at the Northwestern Feinberg School of Medicine. "I'm surprised that if you're a Black man and you say to your doctor 'I want to get screened for prostate cancer because I'm at higher risk' that they would say no," he says. "That's kind of shocking to me, but I do see people like Representative Ford in my clinic not that infrequently."

Ford's subsequent blood work and MRI found further irregularities, and a biopsy confirmed that he had prostate cancer. Schaeffer performed a radical prostatectomy to remove Ford's entire prostate gland. Months later he was declared cancer-free.

"My cancer was already in an aggressive stage. It covered a lot of my prostate, but fortunately it was still contained," he says. "If I had not advocated for myself and waited until I was 50, it could have been too late."

His experience illustrates two things: cancer screening can save lives, and cancer screening is not accessible for everyone who needs it. People of color, those of low wealth and residents of rural areas tend to be most vulnerable to screening disparities for reasons that are complex and often interrelated. Cost and lack of access, health illiteracy, implicit bias, and both cultural and structural barriers all play a role, as do disparities in cancer risk and vast differences in how screenings are integrated into patient care. The result is that too many cancers are detected too late, leading to too many avoidable deaths.

According to a report on cancer disparities from the American Association for Cancer Research, people of color receive significantly fewer recommended examinations than white people and are more likely to be diagnosed with advanced disease, lowering their chances of survival. "Cancer screening has huge inequities in this country," says Derek Raghavan, president of the Levine Cancer Institute in Charlotte, N.C. "The screening for breast, colon, prostate and lung cancer is way below what it should be in the African-American and Latino populations. If we could fix that, we could improve the death rate from cancer dramatically."

ONE SIZE DOES NOT FIT ALL

MEDICAL SOCIETIES AND EXPERT PANELS constantly reassess their screening guidelines in response to new research, using updated models and the most recent data. The result, however, may be confusing and seemingly inconsistent guidelines about who should be screened and how often, leaving many primary care providers unaware of the latest recommendations. It can mean huge variations in how these screenings are implemented—among both individual physicians and large health systems—as well as in how insurance companies reimburse for them. It can also mean huge variations in which patients receive the screenings they need.

Perhaps even more concerning, researchers such as Schaeffer say, is that medical groups often have homogeneous guidelines that do not account for variations among racial groups. With breast cancer, for instance, recent studies indicate that the incidence rate is higher in Black women younger than 45 and among white women older than 60. Yet the U.S. Preventive Services Task Force (USPSTF) and several other medical groups do not differentiate by race and recommend mammography screenings begin at age 50 for those at average risk. This does not acknowledge that Black women tend to have a more aggressive type of breast cancer that strikes at younger ages, argue researchers in a recent report in the *Journal of Breast Imaging*. For this group, those researchers recommend starting annual screening at age 40.

"The data surrounding the disparate incidence of breast cancer in Black women under 40 is compelling and must be considered as we look at cancer screening and diagnosis through the lens of health equity," says Monique Gary, chief medical adviser for Touch, the Black Breast Cancer Alliance and medical director of the cancer program at Grand View Health in Pennsylvania. "The current guidelines are an example of what happens when we 'don't see color.' They potentially place an already vulnerable group at significant risk for greater harm."

Similar disparities exist in cervical cancer. In 2018 both the USP-STF and the American Cancer Society (ACS) were recommending that women between the ages of 21 and 65 get a Pap smear every three years. Women between 30 and 65 were advised to have both a Pap and an hrHPV test, which screens for the presence of highrisk human papillomavirus—a major risk factor for cervical cancer—every three (ACS) to five (USPSTF) years. As though that weren't confusing enough, the ACS changed its stance in September 2020. Because cervical cancer is so rare in younger women, it suggested testing for hrHPV only and starting at age 25 rather than 21. The reasoning was that getting the more accurate HPV test every five years can reduce the risk of cervical cancer more effectively than a Pap test done every three.

That is troubling for some clinicians, who attribute disparities in cervical cancer incidence and mortality to lower access to screening. The incidence rate of cervical cancer among Hispanic women is 32 percent higher than for white women, and Black women are more likely to die of cervical cancer than any other racial or ethnic group. Limiting screening options could undermine cancerprevention programs in vulnerable populations. If the new guidelines—which increase the suggested age of first screening—are widely adopted, insurers are likely to change reimbursements to match, something that could further decrease screening rates in the most underserved communities.

As Ford discovered last fall, screening guidelines strongly in-

fluence who gets referred for screening and what tests insurance providers will cover for whom. The trouble is that those guidelines are based on clinical trials conducted with subjects who are predominantly white.

Research shows that Black people are at a higher risk of lung cancer even if they smoke less over time, and their inclusion in clinical trials could have a significant impact on any screening guidelines that result. Raghavan points to the 2011 National Lung Cancer Screening trial, which studied more than 53,000 current or former heavy smokers to determine the cost and effectiveness of a form of screening called lowdose computed tomography (LDCT). Fewer than

5 percent of their participants were Black. A European trial on the same topic, the NELSON lung cancer study, also studied LDCT screening with 7,557 participants. The researchers made no mention of people of African ancestry.

Clinical trials investigating the benefits of prostate cancer screening also excluded Black men, despite greater incidence and mortality in this population. These trials, which consisted exclusively of white men, showed little or no benefit from PSA screening. As a result, in 2012 the USPSTF—concerned about overdiagnosis and treatment of small, benign or slow-growing cancers—recommended against using prostate cancer screening for anyone. The organization partially reversed its decision in 2018, recommending instead that for men age 55 to 69, screening decisions should be left up to the individual.

But some researchers are finally beginning to acknowledge the importance of diversity both in clinical trial participation and in establishing more relevant screening guidelines. A 2019 study in *JAMA Oncology* found that fewer Black smokers with lung cancer met the criteria for screening than white smokers with the disease. That is because Black smokers develop lung cancer at younger ages

and at higher rates than white smokers. The researchers found that 68 percent of Black smokers were ineligible for screening at the time of their diagnosis, whereas 44 percent of white smokers were.

The USPSTF cited the study earlier this year as a factor in lowering its recommended screening age for lung cancer, from age 55 to 50, and reducing the number of pack years (years of smoking multiplied by the number of packs smoked per day) from 30 to 20, greatly expanding potential access. Nevertheless, only 5.7 percent of those at high risk are actually screened, in part because of the dearth of screening centers and lack of awareness.

THE COST BARRIER

IMPROVING ACCESS TO, AND AWARENESS and affordability of, cancer screenings is what the Lung Bus was built to do. This 35-foot motor coach is the brainchild of the Levine Cancer Institute and is equipped with an LDCT scanner to serve people in local North Carolina communities with the highest risk of advanced lung cancer. These patients traditionally tend to have high rates of inoperable lung cancer, and they may also face transportation barriers or lack insurance.

"You can overcome disparities of care if you really want to." —Derek Raghavan *Levine Cancer Institute*



Herbert Buff is one of them. Buff, 58, had smoked for more than 20 years but did not know it was possible to screen for lung cancer. In 2018 Buff went to the clinic in Morganton, N.C., for a routine doctor visit and casually mentioned that he sometimes had problems breathing. His doctor suggested a free screening on the Lung Bus. Buff's quick, noninvasive exam revealed a nickel-sized growth on his left lung that was later diagnosed as stage 1 lung cancer and was cured by surgery alone.

Since its first voyage in March 2017, the Lung Bus has achieved remarkable success in addressing health disparities. "We have used the bus exclusively to screen uninsured and underinsured people and the rural poor," says Raghavan, noting that they launched their screening program specifically to tackle the accessibility issues they saw in their patient population. They published the initial results in the *Oncologist* in 2020. "Our data show that of the 1,200 people we screened, 78 percent were rural poor and 20 percent were Black Americans. We found 30 lung cancers, of which 21 were at the potentially curable stage," he says. "You can overcome disparities of care if you really want to."

Cost factors into other screenings, too. The most advanced, ac-

curate technologies for breast and cervical cancer screenings are more expensive and less accessible. Rural and underresourced areas are most likely to lag in getting the newest technology. Screening guidelines have long recommended HPV testing in conjunction with the Pap test, and randomized clinical trials have shown it results in better detection, fewer false positives and decreased mortality than Pap smears alone. But HPV testing is limited in the communities that have disproportionately high rates of cervical cancer incidence, morbidity and mortality.

ARLY DETECTION

Three-dimensional mammograms are another advance that has been more accessible to those with means, despite the fact that doctors say traditional mammograms are still the standard for all patients. The technology, which digitally sews numerous two-dimensional scans into a detailed 3-D image, can detect more cancers with fewer false positives than traditional mammography. But it's only selectively available. According to a study published in *JAMA Network Open*, Black and Latina women, as well as those who have less education and less income, have not been able to obtain 3-D mammography as easily as women who are white, are well educated or have a higher income. Clinics that serve these patients simply do not have the necessary tools. "[The] equipment is more expensive, and it's not available everywhere," says Diana Dickson-Witmer, a breast surgeon and head of the BeeBe Center for Breast Health in Rehoboth Beach, Del.

STRUCTURAL AND CULTURAL BARRIERS

IN THE DECADE since the passage of the Affordable Care Act in 2010, more Americans than ever have gained access to health insurance. Expanded government coverage has gone a long way toward making cancer-screening access more equitable by eliminating many out-of-pocket costs, according to research by the ACS. As just one example, a report in the *Journal of Cancer* in July 2020 found that U.S. states that expanded Medicaid had fewer men with high PSA results, indicating they were getting screened earlier than those living in states that had not expanded Medicaid. In this case, at least, insurance appeared directly correlated to better screening outcomes.

Addressing cost is a good start, says Tomi Akinyemiju, a cancer epidemiologist and associate director for community outreach and engagement at the Duke Cancer Institute. Akinyemiju explores the interconnection of race, ethnicity, income and access to health care and develops outreach strategies for communities in North Carolina. "People in Black, Hispanic or Latinx communities are less likely to have received the screening that they are eligible for," she says. "Affordability ... is a big reason, especially for minorities and those of low income, but there are also other really important dimensions separate from the cost."

Eliminating screening disparities requires tackling structural barriers, Akinyemiju says. These can include knowing the location of the nearest facility, being able to get there and setting up hours that accommodate people with inflexible work schedules.

Education—of risk factors and, consequently, what screening is needed and when—is yet another structural issue. Many people lack basic understanding or a primary care provider to help inform them. When Tanya Weaver, an independent community health advocate, began working to get breast cancer screenings for underserved Black women in Portsmouth, Va., more than a decade ago, many did not even understand what care they needed or whom they should contact for information.

"Many of the women couldn't even pronounce the word 'mammogram,' and some confused mammograms with having breast cancer because no one had educated them," Weaver says. "When the city sent out informational pamphlets, they were all earmarked for the more affluent areas of Portsmouth."

Even once someone gets past all that, Akinyemiju says, interactions with providers are vital, too. "Do they talk down to you? Do they explain things in language that is easy to understand? Do they answer your questions respectfully and show concern and care for you?" If not, she says, then patients are far less likely to return for future screenings.

That is precisely what Weaver has seen with the women she works with. She arranged free mammograms for them at a local hospital, never imagining they would be derided for taking care of their health. "Many of the women came back dejected and said they would never go back because they felt like they weren't wanted there," Weaver says. "They overheard one person say, 'They keep coming in here with these coupons to get a free mammogram.'"

Today there is growing evidence—medical, epidemiological and sociological—that cancer-related disparities are closely linked to extensive influences known as social determinants of health, which involve the conditions in which people live and work that affect their health risks and outcomes. There is also a growing understanding by clinicians and other health-care providers that helping those most affected will require focused and coordinated social action. Academic institutions and health-care systems around the country are building multidisciplinary programs that prioritize health equity so that the most vulnerable people get the cancer screening tests they need.

One of those programs is at Northwestern, where Ford received his care. Northwestern Medicine's Project HOPE (Health Outreach Promoting Equity) educates local communities in the Chicago area about health disparities, aiming to increase equity in health outcomes. During primary care screenings, doctors now routinely talk with their patients about how they are doing financially and socially. They ask them to describe their living conditions to better understand and address any underlying issues. Ford, now a vocal proponent of regular health checks and of being one's own medical advocate, works with Project HOPE to reach others in situations similar to his.

Today Project HOPE and other programs are identifying ways to help close the cancer-equity gap, in screening and beyond. Patients who have good information, who are treated with respect and kindness, and who have people to help guide them through a confounding process are able to make better decisions, Schaeffer says. "By beginning to identify these different social determinants of health, we can impact this and make a difference," he says. "There are glimmers of hope for continued progress."

Melba Newsome is an independent journalist in Charlotte, N.C., whose work has appeared in *Prevention*, *Newsweek*, *Wired*, *Politico*, *Yale E 360*, *Oprah* and the *New York Times*, among other publications.

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The COVID Cancer Effect

Oncologists are grappling with predicting—and mitigating the effects of the pandemic

By Usha Lee McFarling

AS THE NOVEL CORONAVIRUS SWEPT THROUGH BOSTON LAST MARCH, Toni Choueiri was worried. He was concerned not only about the rapid rise in COVID infections but about the swift shutdown in cancer screenings.

In Boston—and around the nation—colonoscopy suites stood empty as patients refused to come in, terrified of setting foot in any hospital or clinic. Screening center schedules, once full of mammography appointments, cleared dramatically. Hospital corridors quieted; screening center workers were sent home. Hospital administrators struggled to find enough PPE to take care of urgent surgeries, and elective procedures fell to the wayside. As COVID cases surged frighteningly across the country, cancer detection seemed to be the last thing on anyone's mind.

ARI Y DETECTION

Choueiri, who directs the Lank Center for Genitourinary Oncology at the Dana-Farber Cancer Institute, saw a steep drop in new consultations in the pandemic's early months. The veteran oncologist feared that the lack of screenings, which aim to detect cancer at its earliest stages, would lead to a tidal wave of missed diagnoses. He worried about tumors seeding, taking hold, growing and metastasizing without being detected. He envisioned a future with streams of patients who had cancers so advanced he could no longer cure them.

Driven by these concerns and a desire to know exactly how bad the problem was, Choueiri and his colleagues turned to the data. Their study, published in *JAMA Oncology* in January 2021, showed a steep drop in screening from March to June of 2020 in his health system, Massachusetts General Brigham. More than 60,000 patients are typically screened there for cancer in a threemonth period; in the first three months of the pandemic, he says, fewer than 16,000 came in for tests. In those early days National Cancer Institute officials estimated the pandemic would result in 10,000 excess cancer deaths in breast and colon cancer alone over the coming decade.

Screenings for some cancers fell by 90 percent when COVID struck, making a postpandemic surge of cancer deaths seem a foregone conclusion. As the pandemic wore on, some cancer centers began to report a worrisome increase in advanced cancer diagnoses. But as more time passed and screenings resumed, the outlook grew less dire. COVID may prove to be a grand experiment assessing the import of cancer screening, and results are beginning to trickle in. But because both the disease and its epidemiology are so complex, those results may take years, or even decades, to become clear.

SKIPPED SCREENINGS

ONE PATIENT whose pandemic screening turned up early-stage breast cancer was Senator Amy Klobuchar of Minnesota. After delaying the procedure, she had a routine mammogram in February 2021. With surgery and radiation completed and a good prognosis in hand, Klobuchar is urging others not to put off their screenings. "I hope my experience is a reminder for everyone of the value of routine health checkups, exams and follow-through," she wrote in a recent blog post.

Cancer kills some 600,000 people in the U.S. every year. Screening tests such as Pap smears, mammograms, colonoscopies, lung scans and prostate-specific antigen tests clearly save lives: although rates vary by cancer type, five-year survival is consistently higher when the disease is caught in its early stages. Yet as the pandemic spread throughout the U.S. and the world, rates of those routine screenings fell precipitously. This was especially true for colonoscopies, the most invasive screening and an exam that many avoided even before the pandemic. Choueiri's health system usually performs more than 9,000 colonoscopies in any three-month period; in March, April and May of last year, there were just over 1,700 in total. Similar drop-offs were seen across the country, where in some cases up to 95 percent of colonoscopies were missed in the first months of the pandemic.

Screening rates synchronized with pandemic waves, bouncing back in the summer of 2020 before falling during subsequent surges. Those who never rescheduled may be up to two years behind. "Between the peaks, what we didn't see was sufficient recovery," says Karen E. Knudsen, chief executive officer of the American Cancer Society. "We've made progress getting people back in the door, but there's a large population that is underscreened. We don't know the impact of this yet, but it's definitely a problem."

One major issue, Knudsen says, is that people who miss screenings aren't always flagged for follow-up. And some tests, such as those for prostate cancer, are harder to track using medical records because of how they are coded. In fact, she says, determining how many people are overdue for screening is virtually impossible because of the diverse settings in which patients receive screenings and because there is no national infrastructure that tracks them in real time. "We don't know who didn't come back," Knudsen says.

According to a study published in *JAMA Oncology* in April, nearly 10 million people missed screenings for breast, colon and prostate cancer between March and May of 2020, but no one knows how many of those tests remain unscheduled. Those who missed screenings, Knudsen says, are likely to be people who haven't been screened before, because they either just became eligible during the pandemic or were already hesitant. "We can infer that hesitancy is only enhanced with COVID," Knudsen says.

TRACKING MISSING PATIENTS

COAXING OVERDUE PATIENTS into a clinic is one of Rachel Issaka's primary concerns. Issaka, a gastroenterologist and assistant professor at the Fred Hutchinson Cancer Research Center and University of Washington, says it is critical that health systems track down these missing patients. A study she published in June found that hundreds of colonoscopies were canceled between March and May 2020, and more than half of those people had not yet returned. Of those who did, more than 5 percent had new cancers. That implies that around 5 percent of the people who haven't returned may also have cancer, she says, but won't know it. Similar scenarios are likely playing out at health systems across the country; a study that surveyed gastroenterology practices last year found that two thirds did not yet have a plan in place to follow up on missed appointments, although some have now begun this work in earnest.

Issaka is working diligently to contact and shepherd in her more skittish patients. One powerful tool is at-home detection tests for colon cancer. A low-cost fecal immunochemical test, or FIT, can detect blood or tumor DNA in stools and catch 70 percent of colon cancer cases [see "The Colon Cancer Conundrum," on page S12]. But a positive FIT result requires a follow-up colonoscopy, and scheduling that, Issaka says, remains challenging.

Telehealth has proved a surprisingly effective way to persuade overdue patients to visit the clinic. A study published in *JAMA Oncology* last spring examined the precipitous drop in breast, colon and prostate cancer screenings and found that telehealth patients were more likely to come in for exams. Patients who are concerned about in-person screenings can use telehealth appointments to talk with their primary care physicians about setting up a plan based on personal and familial risk factors, says the American Cancer Society's Knudsen. "Screening is knowledge. It's power," she says.

Although much communication in oncology, particularly of bad

do screenings on Saturdays or in the evenings?" Knudsen asks. "Those turned out to be really popular times for mammography."

UNCERTAIN MORTALITY MODELS

THERE IS LITTLE DOUBT that the chaos ushered in by the pandemic will lead to more cancer deaths. But determining how many has been difficult: many cancers are slow-growing, their development can be complex, and factors such as treatment decisions play a big role in outcomes. To assess how missed screenings might affect cancer mortality rates, the National Cancer Institute turned to Oguzhan Alagoz, a professor of industrial and systems engineering at the University of Wisconsin–Madison whose research involves modeling both cancer epidemiology and infectious diseases.

"The question is really interesting because it's a combination of the two areas I work in," Alagoz says. His first estimates, unveiled in a widely read editorial published in *Science* in June by NCI director Normal E. Sharpless, showed that missed screenings might result in 5,000 additional deaths in breast cancer alone over the next decade. A separate group, looking at missed colon cancer screenings, predicted another 5,000 deaths.

When Alagoz produced his breast cancer estimates early in the pandemic, he thought the numbers might not be truly representative. So he worked to refine them, using better data with three powerful cancer models that incorporated numerous factors related to breast cancer—such as delayed screening, treatment effectiveness and long-term survival rates—and the nuanced ways they intersect to affect mortality over time. "Everyone can tell you what will happen immediately, but it's hard to say what's going to happen in five or 10 years," Alagoz says. "If there's a huge increase in smoking, you're not going to see more lung cancer right away. You're going to see that 10 or 15 years down the road."

After a more detailed analysis and after seeing screenings re-

news, is best done in person, the pandemic has shown that telemedicine can play an important role in cancer care and should remain in place, says Choueiri, who is also a professor of medicine at Harvard Medical School. "It's helped a lot," he says. "We can stay in touch with patients, maybe even better than before."

The pandemic-imposed challenges to screening prompted the American Cancer Society to create tool kits explaining current screening guidelines in clear and simple language. It is also spreading the word that patient access to screening must be made easier. One way is to move screenings out of hospitals and into clinics and, when possible, even mobile vans. Another is to open up scheduling in off-hours. "Can you

Case Study: Breast Cancer Screening before and during COVID in a San Francisco Hospital



When SARS-CoV-2 hit the U.S., the number of mammograms performed at a safety-net hospital in San Francisco dropped precipitously. Despite almost normal numbers during the first two months of the year, by the end of 2020 the number of screenings had dropped by nearly half.

bound from what he calls the "panic phase" of March and April 2020, Alagoz now says those early mortality numbers were far too high. In revised estimates, published in the Journal of the National Cancer Estimate last April, Alagoz and his colleagues suggested the pandemic could lead to 2,500 excess breast cancer deaths in the coming decade, half as many as they had first predicted. "The entire estimate was too pessimistic," he says. "Any individual death is sad, but if there is any silver lining, it's that this isn't as bad as we feared."

One reason death rates may be curbed, Choueiri says, is that oncologists did aggressive triage work to screen and treat patients who needed care most. His hospital system reported fewer missed cancer diagnoses than he expected, and he thinks this was because people at highest risk of cancer and those with palpable symptoms were most likely to be screened even during the pandemic's most dangerous peaks. "Screenings never stopped 100 percent," Choueiri says. "Who were the patients who continued to be screened? They were the highest, highest risk."

Some oncologists say this "risk stratification"—prioritizing screening, diagnosis and treatment for those most at risk or with obvious symptoms—should stay in place after the pandemic ends so treatment can be provided quickly to those who need it most.

COVID'S LONG SHADOW

UNDERSTANDING THE PANDEMIC'S EFFECTS on cancer mortality is a complicated task because delayed screenings aren't the only factor involved. Increased alcohol consumption and reduced physical activity—behaviors common during long pandemic lockdowns—can increase cancer risk as well. But postponing an exam can be a major danger. In November 2020 Vincent Valenti, a retired screenwriter in Brooklyn, noticed his voice was hoarse. He attributed it to all the screaming he did on election night. But it persisted for weeks, and his girlfriend encouraged him to get it checked. Valenti, 71, refused. He wasn't going near a hospital or doctor until he was vaccinated. "You walked by hospitals, and there were all these morgue trucks parked outside," he says. "I knew something was wrong, but I wasn't

going to go near a hospital." In February of this year, once he had received two doses of vaccine, he scheduled an appointment with an E.N.T. "She scoped me and jumped back," he says.

There was a tumor on his larynx, stage 3, that had almost reached his lymph nodes. It was a shock to both Valenti and his doctor. He wasn't considered high risk for laryngeal cancer because he doesn't drink heavily or smoke. After seven weeks of chemotherapy and radiation, Valenti says, there was no trace of the tumor, and a recent PET scan confirmed that the cancer did not metastasize. Valenti was told his cancer would likely have been caught at stage 2, or even stage 1, if he had gone in right away.

Research published in *JAMA Network Open* in August shows that Valenti is far from alone. The study reports that diagnoses of eight cancer types dropped nearly 30 percent during the first pandemic wave of 2020, rebounded somewhat during the summer and early fall, then fell by 20 percent during the pandemic's win-



As COVID surges waxed and waned, so did new cancer cases. A study of nearly 800,000 patients found that the pandemic dramatically curbed diagnoses in a variety of cancer types. Experts worry these late diagnoses may result in disease that is more advanced and difficult to treat.

ter surges. Such consistently low numbers indicate that many cases will continue to be undiagnosed, the authors wrote.

Some programs have already reported an increase in the detection of cancers. Lung cancer, the nation's leading cause of cancer death, is of particular concern because it can be so aggressive. The University of Cincinnati's lung cancer screening program was closed for three months. When screening resumed, patients remained scarce, and no-shows were frequent. But among those who did come in, "we noticed we were seeing many more suspicious lung nodules than usual," says Robert Van Haren, a thoracic surgeon and assistant professor of surgery at the University of Cincinnati Medical Center, who analyzed the effect of the pandemic on cancer screenings. "Even small changes in the size of a lung cancer can be important for overall survival," he says. "That's the reason we're concerned about any delays or stoppages."

Whether the pandemic has already caused an increase in dire cancer prognoses more broadly is still an open question. Choueiri hasn't run the numbers and is not sure yet whether his practice is facing more advanced cancer diagnoses. So far the picture is worrisome to him, but it is less so than he originally feared.

This is largely because screening did rebound. If the pandemic was turning out to be a natural experiment on the toll of missed cancer screenings, thankfully it was one that ended earlier than expected. "Testing for many cancers, such as mammograms, has

> largely returned," says Choueiri, who has co-authored several studies tracking the pandemic's effect on cancer screening. "Why did it return to normal? Simply because the hospitals, and all of us, put measures into place to make this as safe as possible."

DEEPENING HEALTH DISPARITIES

BUT TIMELY SCREENING hasn't returned for everyone. Those looking at the data see disturbing gaps in the populations that are coming back and those that aren't, gaps that may be deepening racial and ethnic disparities in cancer care and mortality. At his health system, Choueiri says, fewer Black and Hispanic patients rescheduled mammograms from June to December 2020, even after screenings rebounded in other groups. Van Haren saw something similar in his Cincinnati clinics: more screening noshows for patients at highest risk of lung cancer death, including those who were current smokers and those who were Black. "It's concerning," Choueiri says. "The

pandemic may have accentuated racial disparities related to cancer screening that already existed."

Black people are already 40 percent more likely to die from colon cancer than other groups. Issaka fears those numbers could now grow worse. "Before the pandemic, African-Americans, Hispanics and Native Americans were not screening at high rates. With COVID, my concern was that these same populations that were hard hit by the pandemic wouldn't come for screening," she says. "I worry that five to 10 years from now, we're going to see patients in those groups presenting with advanced disease and higher mortality."

Because colon cancers are usually slow-growing, it's not too late to prevent these deaths. "We need to be very proactive," Issaka says. "We still have the opportunity to turn the tide."

One of the people working to do so is Kathy Briant, assistant director for the Fred Hutchinson Cancer Research Center's office of community outreach and engagement. Cancer-screening outreach was one of the pandemic's biggest casualties, particularly among racial, ethnic and low-income groups that have historically had lower access to screening tests and are far less likely to be up-todate on cancer screening than white and high-income patients.

Briant has had to mothball the giant inflatable walk-through colon she used to send to events in tribal areas and gatherings of agricultural workers throughout Washington State. She has had to cancel all face-to-face meetings with at-risk older people, the same ones who are less likely to see her team's YouTube and Twitter messages. Hardest of all, she says, she had had to call off two years of health fairs that, prepandemic, provided information, cancer screenings, free health tests and colonoscopy scheduling.

The communities Briant works with are both the least likely to receive cancer screening and the hardest hit by COVID: minorities, frontline workers, and people who were losing jobs, struggling financially and dealing with SARS-CoV-2 infections. She learned relatively quickly that cancer screening was not a priority for many in these communities. There was fear of COVID, but there were other reasons, too: no time, no child care, a lack of health insurance or the inability to afford copays. In addition, their regular clinics often were too overwhelmed with COVID patients to provide wellness checks or screenings.

People had more immediate needs, such as finding transportation to vaccine appointments and someone to help if they had COVID. Briant's team pivoted from providing grants for cancer screening to helping in other ways. "Our agenda, yes, is cancer screenings, but we had to set that aside and listen to the community," she says. "They were thinking about survival. They were saying cancer screening is not important right now."

Issaka's research confirms what Briant was seeing. One study at her safety-net hospital found that patients already faced multiple obstacles to having a colonoscopy, including lack of transportation, no coordination among specialists to get tests scheduled, and difficulties with the bowel preparation needed for the test. The pandemic added more barriers, she says, such as requiring a negative COVID test before people could even walk through the door.

By responding to more immediate needs, Briant's team hoped to strengthen bonds and increase trust in communities they work with, something that will help them spread the cancer-screening message in the future. Sure enough, as restrictions loosened, she began fielding calls from community health leaders who wanted the inflatable colon sent over. The hypercontagious Delta variant has put those plans on hold—a colon is an enclosed space after all so they have resorted to a video version until Briant can once again unleash her colon into the world.

COULD WE BE OVERSCREENING?

ANOTHER PIECE of the cancer puzzle that the pandemic experiment may start to solve is a particularly contentious one. As cancerscreening programs continue to grow, an increasingly vocal group of physicians is arguing that too much screening might, at least for some people, be doing more harm than good.

These researchers contend that many patients, particularly those of advanced age, often receive more screening than they require. And those tests can result in more risk than benefit. "One of the biggest risks of cancer screening is the overdiagnosis of cancer tumors that are indolent and will never cause symptoms," says Jennifer Moss, an assistant professor in the department of family and community medicine at Pennsylvania State University, whose research has shown that 45 to 75 percent of older adults receive screening they do not need. She found that for colon, cervical and breast cancers a large percentage of patients were being screened after they had aged out of the recommended age limit. In all three cancers, overscreening was more common for people living in cities compared with those in rural areas.

Unnecessary screenings not only result in false positives but also come with other issues, including unnecessary medical procedures to remove cancers that might not cause harm and side effects, such as perforations during colonoscopies. Now they have the added threat of SARS-CoV-2 exposure. "Many older patients face greater risk from cancer screening than not screening," Moss says. "Especially in a time of COVID."

Moss wants to be clear that people who need screening, based on national guidelines and conversations with their physicians, should get it. And she believes that the pandemic will likely cause an increase in cancer deaths because of missed screenings. But she also thinks the past year and a half will yield important data on missed screenings that were not as consequential, data that could inform future guidelines. "The pandemic will definitely give us insight into when, and how often, and for whom, cancer screening is the most effective," she says.

Choueiri, for his part, is convinced that cancer screening is a singularly powerful tool that can catch cancers at their earliest and most treatable stages. "You don't want stage 1 to become stage 4," he says. "Or even stage 2."

These days his conviction is personal. Unlike many of his patients, who postponed their screenings during the pandemic, Choueiri did not. Because of the pandemic slowdowns, he had extra time on his hands. So, when he turned 45 last year, he took his doctor's advice and scheduled a routine colonoscopy. He didn't think it was urgent—he had no symptoms or family history of the disease. But his test turned up an unexpected precancerous polyp. Now, he says, he will not miss any future screenings.

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The Colon Cancer Conundrum

CER FARLY DETECTION

Colorectal cancer rates in younger adults are climbing. The race is on to figure out why

By Cassandra Willyard

IN 2012, A FEW DAYS AFTER Katie Rich gave birth to her third child, she started experiencing sharp pains under her ribs. When she brought it up at her postpartum checkup, her doctor thought it might be Rich's gallbladder. Instead a sonogram revealed a spot the size of a dollar bill on her liver. It might be a bruise, her doctor told her. "You are 33 years old. Do not worry about this," she remembers him saying.

Rich did not have time to worry. Her oldest child was three, and her newborn was only eight weeks. "We were so overwhelmed with the three little kids," she says. But she did follow up. A biopsy revealed stage IV colon cancer. Rich got the call on a Friday and spent the weekend crying. "I was in total disbelief," she says.

The diagnosis made no sense to her. Nobody in her family had ever had colon cancer. Rich, an athlete, ran and played volleyball. She exercised through all of her pregnancies. She made sure to eat a healthy diet. And she was young. Colon cancer was not even on her radar.

Stories like Rich's are increasingly common. Even as colorectal cancer rates for older adults have declined, rates in younger people have started climbing. In 2010 adults younger than 50 accounted for 5 percent of colon cancers and 9 percent of rectal cancers. By 2020 those proportions had grown to 11 and 15 percent, respectively.

The underlying reasons for this rise remain a mystery, one that is proving increasingly frustrating for those in the field. Experts now recommend that the general public start screening at age 45 instead of 50, a stopgap measure that they hope will identify many of these cases. But it is hardly a perfect fix. The new guidelines will not catch the increasing number of cases in people younger than 45—people like Rich. And some worry that the influx of newly eligible adults could strain the system and divert resources toward younger, healthier people and away from older adults in underserved populations, who are already less likely to be screened. If researchers could figure out who is at greatest risk, they could target those individuals for screening. The reality, however, is that the constellation of factors that are putting more younger people at risk has proved difficult to pin down.

RISING RATES

CANCER SCREENING IS DESIGNED to identify disease before someone develops symptoms. The rationale is simple: cancer is easier to treat when it is diagnosed early. And colorectal cancer screenings in particular can prevent cancer from ever taking hold. During a colonoscopy, doctors examine the colon with a flexible scope that allows them to take biopsies and remove precancerous polyps. These screenings have led to an overall decrease in colorectal cancer incidence and mortality—so much so that declines in the disease have often been touted as progress in the war on cancer.

But that progress masks a disturbing trend. In 2008 Rebecca Siegel was mired in data, deep in the latest update of a report by the American Cancer Society called "Cancer Facts and Figures." Siegel, a cancer epidemiologist with ACS, had run the numbers before. At the time the recommendation was that screening should begin at 50 for adults with no obvious risk factors. What would happen, she wondered, if someone broke down the numbers in a slightly different way and instead looked at incidence among people younger than 50?

To her surprise, that analysis showed that colorectal cancer rates were going up. Between 1992 and 2005 the overall incidence for people 20 to 49 years old increased 1.5 percent a year in men and 1.6 percent a year in women. (The rise was largely driven by rectal cancer, which rose 3.5 percent a year in men and 2.9 percent a year in women.) The numbers were even more stark when she broke them down by race: Per year, incidence had increased among white men by 2.0 percent and in white women by 2.2 percent. There was no statistically significant change in Hispanic women, but she found an increase in Hispanic men of 2.7 percent a year. The absolute risk for these younger people was small compared with the risk for older people, but Siegel found the trend troubling.

Declines in disease in the over-50 age groups had made it appear that colorectal



cancer incidence was going down overall. But, Siegel says, "What's going on in the younger age groups is really masked."

Siegel published her results in 2009. "It got a little bit of attention," she says, but reactions were mixed. The consensus at the time was that screening should begin at 50. Rather than seeing Siegel's results as concerning, some argued that the increase was probably good news and attributed it to more young people being screened.

Siegel did not buy it. She points out that if the increase were the result of more screening, doctors would be catching more early-stage cancers and seeing declining mortality rates in this younger group. Instead, as she collected more data over the next eight years, she found more late-stage diagnoses and mortality rates that were climbing by about 1 percent a year.

In 2017, as evidence for rising rates piled up, the ACS's Guideline Development Group began to reassess its screening guidelines for colorectal cancer, tweaking models to incorporate increasing incidence among younger adults. When it lowered the age to 45, the benefits outweighed the harms. ACS updated its recommendations accordingly the following year.

The move "caused quite a stir," says Aas-

ma Shaukat, a gastroenterologist at New York University's Grossman School of Medicine. At the time critics argued that colorectal cancer affects too few younger adults to warrant the change. Even today the risk of someone in their late 70s being diagnosed with colon cancer is about one in 500, whereas the risk for someone in their early 30s is about one in 17,500. And, the same critics said, there were not enough data to support such a shift in recommendations.

A PUZZLE UNSOLVED

TODAY IT IS CLEAR that the increase in earlyonset colorectal cancer is real. In the 20-to-49 age group, rates climbed from about one in 12,000 in 1992 to one in 9,300 in 2015. "It's not just a blip," says Folasade P. May, a gastroenterologist at the University of California, Los Angeles. Some groups have been hit harder than others. The upward trend has been steepest among people who are white, Native American and Alaska Native.

Black people have had higher rates of colorectal cancer across all age groups for decades. "We still see young-onset colorectal cancer in Black individuals," May says, "but they were already having those high rates." Mortality rates are highest in these groups, too. But in adults younger than 50, she says, it is white men who are driving the increase. Twenty-five years ago Black people between 20 and 49 years old had a 40 percent higher incidence of colorectal cancer than white people in the same age group. As of 2016, the two groups were the same: one in 7,000.

Exactly what factors are prompting this rise is still unknown, but they are apparently increasing with each generation. In the U.S., people born in the 1950s have the lowest incidence of colorectal cancer, and rates rise from there. Someone who is 41 today has a 47 percent higher risk of colorectal cancer than someone who was 41 in 1991over those 30 years the rate increased from 10.6 to 15.6 people per 100,000. In other words, the risk goes up with every subsequent generation and travels with those individuals as they age, something known as a birth-cohort effect. Other wealthy countries are experiencing similar increases. Siegel and her colleagues looked at rates worldwide and found that during the most recent decade of available data, trends in eight other countries resembled those in



the U.S., with incidence increasing among people younger than 50 and stable or decreasing in those 50 and older. Rates among younger adults declined in only three countries: Austria, Italy and Lithuania. Two of those, Austria and Italy, initiate colorectal cancer screening for average-risk adults in their 40s, the very group driving those declining rates.

Researchers are scrutinizing the usual suspects—obesity, sedentary lifestyle, smoking, alcohol, diets rich in red meat and processed foods. One study showed that diabetes might play a role. Another found a link to sugary drinks. But for Rich and many others, those explanations do not fit. Actor Chadwick Boseman, who died of colon cancer last year at age 43, "was not obese. He was not sedentary," says Kimmie Ng, director of the Young-Onset Colorectal Cancer Center at the Dana-Farber Cancer Institute in Boston. "And that is reflective of so many of the young patients we see in our center."

Some researchers speculate that human papillomavirus (HPV), the cause of most anal cancers, may explain some of the rise in colorectal cancers in younger adults. That would mean that the vaccines that prevent other HPV-caused cancers might be protective. But most research to date has been unable to conclusively make the connection, and more research is needed to confirm or rule out the link.

Because the birth-cohort effect in cancer suggests that exposures early in life, during childhood or young adulthood, may be crucial, some have begun looking closely at changes to the microbiome. "We know that diet and lifestyle significantly shape our microbiome. They also significantly shape our immune system, which we need to fight off the development of cancer. And so we are hypothesizing that it's a complex interplay among the microbiome, diet, lifestyle and your immune system," Ng says.

Several case-control studies suggest that antibiotic use may be partly to blame. These medications can have a profound impact on the gut microbiome, potentially tweaking it in ways that foster carcinogenesis. And prescriptions for broad-spectrum antibiotics nearly tripled from 1980 to 1992. One study presented at the 2021 European Society for Medical Oncology World Congress on Gastrointestinal Cancer found that antibiotic use was associated with an increased risk of both early- and late-onset colon cancer.

Another potential explanation that some are exploring is gestational influence. Caitlin Murphy, an epidemiologist at the University of Texas Health Science Center at Houston, and her colleagues have been studying the effect of prenatal exposures on colorectal cancer risk. In a cohort of about 14,500 mothers and their children, maternal obesity increased a child's future risk of colorectal cancer. High weight gain during pregnancy also contributed to the child's risk.

That might be one piece of the puzzle, Murphy says, but it is certainly not the only one. "When I first started working in this area, I was kind of convinced that there was this smoking gun," she says. "The more I get into it, the more I realize that's just not





Colorectal cancer is often touted as a success story in the war on cancer. Rates have dropped precipitously over the past two decades. But when you zoom in, it becomes clear that the decline is driven by older adults. Both colon cancer (*solid*) and rectal cancer (*dotted*) are rising in the younger age groups, and researchers don't yet understand why.

true." Figuring out how the pieces fit together and who is most at risk will be essential for screening to be used to best effect.

SCREENING DEBATE

THERE IS A GROWING CONSENSUS that the benefits of starting colon cancer screening at age 45 may outweigh potential harms. The American College of Gastroenterology, the National Comprehensive Cancer Network and now the U.S. Preventive Services Task Force have all endorsed the new lowered screening age. The U.S. Multi-Society Task Force on Colorectal Cancer, which is in the process of updating its guidelines, has also adopted the lower age for average-risk adults. (Those with a family history are advised to start screening even earlier.)

Lowering the age to 45 "really does make sense," Ng says. Because half of early-onset colorectal cancer cases occur in patients in their 40s, she says, "we will catch a lot more cancer in that earlier stage." At least one study hints that this may be true and that colorectal cancer incidence among people in their 40s might be even higher than anyone thought. A paper published in 2020 in JAMA Network Open reports an odd jump in the number of cases at age 50 compared with age 49. "That's not because there is something biologically different between 49- and 50-year-olds," says Swati G. Patel, a gastroenterologist at the University of Colorado Anschutz Medical Center, who was not involved in the study. Rather it is because when people start getting screened, cancers they may have had for years are detected.

The new screening guidelines should help doctors catch some of these cancers. Most adults younger than 50 have never been screened for colorectal cancer and can be slow to seek medical attention. One study found that for patients older than 50, a month passed from the onset of their first symptom to treatment. But for those younger than 50, the median delay was 217 days. Because they were not in the screening group and did not interpret the symptom as a potential problem, they waited to seek care or, if they did consult doctors, their physicians sometimes attributed their symptoms to something else such as hemorrhoids or fistulas.

Some researchers see the move to 45 as premature. If you look at the results of the modeling, Shaukat says, "the risk-benefit ratio is very, very thin." Screening programs are costly, and colonoscopies are not without risk. Scopes can cause bleeding or even perforate the bowel, something that occurs in about one of every 2,500 procedures. Plus, colonoscopies almost always require sedation, which may have its own complications. Stool tests can yield false positives—rates as high as 13 percent—which induce anxiety and lead to unnecessary procedures.

Increased screening poses hazards not just to individuals but to the entire system. Lowering the screening age by five years means 21 million people are newly eligible for screening. Many clinics already have a hefty screening backlog after halting colonoscopies as COVID cases surged in the spring and fall of 2020. Even where the procedure was available, some opted to postpone out of fear of exposure to the virus.

Now gastroenterologists must find a way to accommodate both the COVID backlog and people in their late 40s. If all these new recruits immediately schedule colonoscopies, they could overwhelm the system and lead to longer wait times for older patients who might have a more acute need. And screening compliance is already below what it should be in the over-50 crowd. According to Murphy's research from 2018, about 50 percent of white and Black adults in their early 50s are up-todate with screening, compared with only about 35 percent of Hispanic and 32 percent of Asian adults the same age. And, as Shaukat points out, the healthiest and wealthiest adults in their 40s-executives who run marathons and eat kale-may be the ones who come in for screening first.

There might be a way to strike a balance. At-home stool tests can also detect colorectal cancer, and Siegel believes they should be more widely adopted. One system using them is Kaiser Permanente Northern California, which mails patients annual fecal immunochemical tests-FITs for short-if they are not up-to-date with their screening. These tests detect blood in the stool, something that can be a sign of cancer or precancerous polyps. Only those with positive results need to follow up, typically with a colonoscopy. Since Kaiser launched the program in 2006, the percentage of eligible adults in their system who get screened has increased from 40 percent to more than 80 percent. The national screening rate, in contrast, is

just under 69 percent. Even better, cases of colorectal cancer fell by 26 percent among Kaiser's patients, and deaths related to colorectal cancer dropped by 52 percent.

The Veterans Health Administration has adopted FITs, too. When the pandemic hit, VA hospitals stopped performing screening colonoscopies for veterans with an average risk of colorectal cancer and instead began offering them a home stool test.

Siegel wishes more doctors would offer their patients stool tests as an option. "You don't have to get a colonoscopy. You can have a test that's less invasive," she says. "The reduction in mortality from colorectal cancer is comparable for both."

A newer test, Cologuard, combines FIT with DNA markers indicative of cancer. But although a single Cologuard test can detect up to 92 percent of cancers, compared with the FIT's 74 percent, it is much more costly and yields more false positives. Because it is recommended every three years rather than annually, the difference in accuracy over time may be negligible.

Neither test will help adults not yet eligible to be screened. "The rate of rise is actually the steepest in people in their 20s and 30s," Ng says. Colon cancer incidence is increasing by 2 percent a year in people 20 to 29 years old, compared with 1.3 percent in those 40 to 49 years old. Rectal cancer incidence is rising by 3.2 and 2.3 percent a year in those same groups. That is why we must figure out why rates are increasing. If researchers can determine those most at risk, she says, "we can target them for early screening rather than lowering the age."

Rich does not know why she got colon cancer so young and tries not to dwell on it. After her weekend crying jag when she was diagnosed, "I never looked back," she says. She put her energy into the fight ahead. After eight rounds of chemotherapy and the loss of 30 percent of her colon and 70 percent of her liver, Rich has been free of cancer for more than eight years. In 2015 she and her husband had another baby, a girl they named Hope. The chance the cancer will come back is small, but Rich still has an implanted pump her doctors can use to send chemo directly to her liver if it does return. "It's basically an insurance plan," she says.

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This section was produced independently with support from

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SPECIAL REPORT FROM

SCIENTIFIC AMERICAN **NATURE**

www.ScientificAmerican.com/InnovationsIn/cancer-early-detection

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NONFICTION

Oceans of Enchantment

A marine biologist who wrote poetically of the sea

Review by Cal Flyn

Before Rachel Carson wrote Silent Spring in 1962—a literary masterpiece and foundation of the modern environmental movement—she was a marine biologist and a prolific writer on the subject of the ocean. Carson first made her name with a trilogy of best-selling books about the sea, published between 1941 and 1955, books in which she exhibited her distinctive synthesis of complex science and lyrical landscape writing so rich and descriptive that it verges, at times, on the spiritual.

Republished this winter as a single tome by the Library of America, Carson's *Sea Tril*ogy is as gratifying to read today as it ever was; the science, once cutting-edge, may be long surpassed, but much of it will still be new to the lay reader. Each book achieves that rare feat of popular science: crafting a narrative so deceptively simple as to entice readers in and, once there, enchant them enough to stay as much for the prose as for the delicious morsels of data.

Under the Sea-Wind, the first in the sequence, was Carson's first published book. It is unusual and inventive—the flowing, shape-shifting story line taking the form of a succession of episodes seen through the eyes of nonhuman creatures, many of them named: Blackfoot and Silverbar, two sanderlings en route to the Arctic; a mackerel called Scomber; an eel called Anguilla; and so on.

This is a device more often found in children's literature, a signifier of a heavily anthropomorphized animal world, but Carson's intentions were in the opposite direction. Later she explained that she "wanted [her] readers to feel that they were, for a time, actually living the lives of sea creatures." Giving them names marks these animals as the protagonists of their own stories. subtly shifting the center of gravity away from human concerns and tempting us into investing more fully in the lives of other species. (Readers even take the perspective of the tattered tundra wildflowers at the close of the summer: "No more need of bright petals ... so cast them off ... let the leaves



Rachel Carson: The Sea Trilogy. Edited by Sandra Steingraber. Library of America, 2021 (\$40) fall, too, and the stalks wither away....")

The book was well received by critics but did not sell—and a few weeks after publication, Japan's attack on Pearl Harbor in December 1941 ensured that all else was pushed away from public attention. Among many things, it was a difficult time to be making your debut as a writer—something many pandemic-published authors can understand—and Carson faded back into obscurity as her ambitions were overtaken for a decade by her job at the Bureau of Fisheries (later the U.S. Fish and Wildlife Service) and the needs of her family, where she was the sole earner supporting her aging mother and two motherless nieces.

When finally she published *The Sea Around Us* in 1951, her persistence was rewarded. It shot into the best-seller charts and stayed there for 86 weeks. This second book took a more conventional form—a sweeping natural history of the ocean—and offered accessible summaries of what was



then the forefront of oceanographic science (fathograms, sonic sounding, hydrophonic recordings) while never losing that sense of almost mystical veneration for the interconnectedness of all things. "What happens to a diatom in the upper, sunlit strata of the sea may well determine what happens to a cod lying on a ledge of some rocky canyon a hundred fathoms below, or to a bed of multicolored, gorgeously plumed seaworms carpeting an underlying shoal, or to a prawn creeping over the soft oozes of the sea floor in the blackness of mile-deep water."

This sentence is typical of Carson's style: at once exact and expressive, with that same sense of zoomed-out, joined-up thinking that would later enable her to connect the disparate dots of the research into DDT as it existed in piecemeal form in the 1950s and 1960s.

The Sea Around Us was met with a rapturous reception and propelled Carson to literary celebrity. It is not hard to see why: the book is packed with captivating detail, and on almost every page one finds a passage of uncommon beauty. The dated science does not detract from one's enjoyment; if anything, it adds to it because it allows the reader to look afresh at the ocean and see it once more from a place of greater ignorance. Oh God, as the Breton prayer goes: Thy sea is so great, and my boat is so small.

The ocean summoned up in *The Sea Around Us* is an alien world, where "strange and fantastic" creatures lurk in its darkest recesses, their "eyes atrophied or abnormally large, their bodies studded with phosphorescent organs." It is a place where mists of plankton swirl through shafts of seagreen light, where flying squid hurl themselves onto the decks of passing vessels. To read it is to confront how we have coexisted alongside a vast realm almost unknown beyond our own small circle of light.

Carson tells us of the amazement felt by the crew of the *Bulldog* in 1860, when a sounding line was brought up from a depth of 1260 fathoms—a depth then suspected to be entirely devoid of life—with 13 starfish clinging to it. It was as if a space shuttle were now to return to Earth with unexpected stowaways onboard: "The deep has sent forth the long coveted message," as the ship's naturalist recorded it at the time. There was a whole other world down there.

We learn of the discovery in 1946 of the detection by echo sounding of a "phantom

bottom" of "wholly unknown nature," which appeared to hang suspended between the surface of the ocean and the sea bed, at a depth of around 1.500 feet. First mistaken for a chain of sunken islands, it was later detected to stretch across much of the ocean and was observed to moverising to near the surface at night and sinking into the depths during the day, "apparently strongly repelled by sunlight." This phenomenon we now call the deep scattering layer is made up of millions of small fish, but when viewed from 1951 its first detection retains enough proximity and mystery to send a shiver up one's spine. What Carson's descriptions most bring to mind is the sentient ocean of Stanisław Lem's 1961 sci-fi classic Solaris—and that same sense of being in the presence of an unknown, unnerving being with its own, incomprehensible agenda.

Of the trilogy, *The Sea Around Us* is by far the most vivid and intoxicating. Partly this is a function of the strangeness of its subject matter, the expanse of the great black deep. The relatively prosaic setting of the third book, *The Edge of the Sea*— the seashore, where so many of us have trundled with our little nets—perhaps inevitably pales in comparison. Still, Carson is our constant, erudite companion, who chatters companionably of the most interesting crabs and seaweeds, crustaceans and barnacles she knows, all prettily accompanied in this edition by the original illustrations by Carson's friend and colleague Robert W. Hines.

Truly, this third book is more of a field guide and was always intended as such, but it nonetheless was produced with Carson's trademark flair: snail shells are "coiled like a French horn"; comb jellies move with "elusive moonbeam flashes." She recalls one rock pool "only a few inches deep, yet it holds all the depth of the sky within it, capturing and confining the reflected blue of far distances."

Carson once declared that if there was poetry in her books about the sea, it was not because she put it there "but because no one could truthfully write about the sea and leave out the poetry." Perhaps. But one cannot help but think of Carson working late into the night, crafting her perfect sentences with the precision of a jeweler. She was a scientist, yes, but also a disciple of the sea. These books are devotional works.

The sea, through Rachel Carson's eyes, is a wild and majestic place. At its edges, contemplating the waves, she writes, "We have an uneasy sense of the communication of some universal truth that lies just beyond our grasp." Though I live on an island, this had not previously occurred to me. Now, having read Carson's *Sea Trilogy*, I look out my window and see the water as if for the first time.

IN BRIEF

Elephant Trails:

A History of Animals and Cultures by Nigel Rothfels.

Johns Hopkins University Press, 2021 (\$40)



Historian Nigel Rothfels traces the human relationship with elephants from prehistoric days to the present, writing with compassion for the

mighty mammals and condemnation for our abhorrent treatment of them. He captures the ache and cruelty of colonization and enslavement; it is, at times, a gruesome read but a sobering one. This book will appeal to those fascinated by the mythology and legacy of elephants, as well as animal lovers who fight for the liberation of all living creatures. —Jen Cox

The Making of Incarnation: A Novel

by Tom McCarthy. Knopf, 2021 (\$28)

Tom McCarthy's inventive latest novel follows Mark Phocan, an employee of a motion-capture firm assisting with the special effects of scifi thriller Incarnation. As Phocan deploys the company's technology across contexts from war to sex, he becomes entangled in a mystery involving a fictionalized version of industrial psychologist and engineer Lillian Gilbreth, whose time-and-motion studies may have uncovered something far more valuable than saved labor. Though intensely technical, these nested narratives are steeped in mysticism, linking time, light and energy to the nature of being. —Dana Dunham

The Forgotten Botanist: Sara Plummer Lemmon's Life of Science and Art

by Wynne Brown. University of Nebraska Press, 2021 (\$27.95)



Sarah Plummer Lemmon was a 19thcentury frontierswoman. She nursed wounded Civil War soldiers, estab-

lished the first library in Santa Barbara, lobbied for the golden poppy as California's state flower and became a prolific botanical illustrator. She also collected and described numerous plant specimens across the American West, but for years her scientific discoveries were credited only to "J. G. Lemmon & wife." In this attentive and richly researched portrait, writer Wynne Brown honors not just Plummer Lemmon's many accomplishments but her verve and courage. —*Tess Joosse* STATEMENT OF OWNERSHIP, MANAGEMENT, AND CIRCU-LATION 1. Publication title: Scientific American. 2. Publication number: 509-530. 3. Filing date: 10/1/2021. 4. Issue frequency: monthly. 5. Number of issues published annually: 12. 6. Annual subscription price: U.S. and its possessions, 1 year, \$49.99; Canada, 1 year, \$59.99; all other countries, 1 year, \$69.99. 7. Complete mailing address of known office of publication: Scientific Ameri-can. One New York Plaza, Suite 4600, New York, NY 10004-1562. USA. 7a. Contact person: Karen Dawson: telephone: (917) 460-5373. 8. Complete mailing address of the headquarters or general business office of the publisher: Scientific American, One New York Plaza, Suite 4600, New York, NY 10004-1562, USA. 9. Full names and complete mailing address of publisher, editor and managing editor: Publisher, Jeremy A. Abbate, Scientific Ameri-can, One New York Plaza, Suite 4600, New York, NY 10004-1562, USA. Editor, Laura Helmuth, Scientific American, One New York Plaza, Suite 4600, New York, NY 10004-1562, USA, Managing Editor, Curtis Brainard, Scientific American, One New York Plaza, Suite 4600, New York, NY 10004-1562, USA. 10. Owner: Springer Nature America, Inc., One New York Plaza, Suite 4600, New York, NY 10004-1562, USA. 11. Known bondholders, mortgagees and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages or other securities: none. 12. Tax status: has not changed during preceding 12 months. 13. Publication title: Scientific American. 14. Issue date for circulation data: September 2021. 15. Extent and nature of circulation: a. Total number of copies (net press run): average number of copies of each issue during preceding 12 months: 292,729; number of copies of single issue published nearest to filing date: 285,442. b. Paid circulation (by mail and outside the mail): (1) mailed outside-county paid subscriptions stated on PS Form 3541 (includes paid distribution above nominal rate, advertiser's proof copies and exchange copies): average number of copies of each issue during preceding 12 months: 175,171; number of copies of single issue published nearest to filing date: 170,829. (2) mailed in-county paid subscriptions stated on PS Form 3541 (includes paid distribution above nominal rate, advertiser's proof copies and exchange copies): average number of copies of each issue during preceding 12 months: 0; number of copies of single issue published nearest to filing date: 0. (3) paid distribution outside the mails, including sales through dealers and carriers, street vendors, counter sales and other paid distribution outside USPS®: average number of copies of each issue during preceding 12 months: 48,009; number of copies of single issue published nearest to filing date: 44,638. (4) distribution by other classes of mail through the USPS (e.g., First-Class Mail®): average number of copies of each issue during preceding 12 months: 0; number of copies of single issue published nearest to filing date: 0. c. Total paid distribution (sum of 15b (1), (2), (3) and (4)): average number of copies of each issue during preceding 12 months: 223,180; number of copies of single issue published nearest to filing date: 215,467. d. Free or nominal rate distribution (by mail and outside the mail): (1) free or nominal rate outside-county included on PS Form 3541: average number of copies of each issue during preceding 12 months: 157; number of copies of single issue published nearest to filing date: 154. (2) free or nominal rate incounty copies included on PS Form 3541: average number of copies of each issue during preceding 12 months: 0; number of copies of single issue published nearest to filing date: 0. (3) free or nominal rate copies mailed at other classes through the USPS (e.g., First-Class Mail): average number of copies of each issue during preceding 12 months: 0; number of copies of single issue published nearest to filing date: 0. (4) free or nominal rate distribution outside the mail (carriers or other means): average number of copies of each issue during preceding 12 months: 13; number of copies of single issue published nearest to filing date: 11. e. Total free or nominal rate distribution (sum of 15d (1), (2), (3) and (4)): average number of copies of each issue during preceding 12 months: 170; number of copies of single issue published nearest to filing date: 165. f. Total distribution (sum of 15c and 15e): average number of copies of each issue during preceding 12 months: 223,350; number of copies of single issue published nearest to filing date: 215,632. g. Copies not distributed: average number of copies of each issue during preceding 12 months: 69,379; number of copies of single issue published nearest to filing date: 69,810. h. Total (sum of 15f and 15g): average number of copies of each issue during preceding 12 months: 292,729; number of copies of single issue published nearest to filing date: 285,442. i. Percent paid (15c divided by 15f times 100): average number of copies of each issue during preceding 12 months: 99.9%; number of copies of single issue published nearest to filing date: 99.9%. 16. Total circulation does not include electronic copies. 17. Publication of statement of ownership: If the publication is a general publica-tion, publication of this statement is required. Will be printed in the December 2021 issue of this publication. 18. I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties). Signature and title of Editor, Publisher, Business Manager or Owner: (signed) Karen Dawson, Head of Logistics, Americas. Date: 10/1/2021.

Women on Ice

Once shut out of Antarctic research, female scientists now are doing vital work

By Naomi Oreskes

In 1981, as a young scientist, I applied for my dream job as a geologist with the British Antarctic Survey. As a child, I had adored snow and ice. Winter was my favorite season (and still is). My most cherished book was Wilson A. Bentley's atlas of <u>snow-flake photographs</u>, and I avidly read the accounts by Robert Falcon Scott and Ernest Shackleton of their Antarctic expeditions. As a teenager, I enjoyed hiking and camping. I studied earth science in college, and when I graduated with top honors from a premier university in Britain, it did not seem like a stretch to apply for a job as a geologist in a cold and snowy place.

The Survey promptly rejected me via a curt and slightly defensive letter. I could not be considered for that position—or, indeed, for any scientific position—because I was a woman.

The letter explained the rationale: Survey geologists had to sleep in tents. It did not explain why this was disqualifying for a woman. Perhaps they believed that a "lady geologist" (a common phrase at the time) could not use a tent. Or perhaps the Survey could not imagine hiring enough women to share a shelter. So despite my qualifications—and despite the fact that I had slept





Naomi Oreskes is a professor of the history of science at Harvard University. She is author of *Why Trust Science?* (Princeton University Press, 2019) and co-author of *Discerning Experts* (University of Chicago, 2019).

in tents many times-my application would not be reviewed.

Fast-forward to the present, and it may seem that things have not improved much. Women still struggle to be fully recognized in science. The top tiers of institutions are still populated primarily by men, typically white men. Harassment and hostility remain common. In a 2020 *Nature* survey of postdoctoral researchers, four out of 10 reported gender discrimination; 90 percent of those people were female. It is not just women who face big hurdles. It is young scientists broadly. And right now, on top of institutional challenges, scientists increasingly have to contend with public and government hostility—at times even harassment—when they work on socially contested subjects such as <u>environmental</u> science, the effectiveness of gun control and public health.

But inclusivity has gotten better in one scientific area, and because 2021 has been so brutal, I decided to try to close out this year by highlighting that field: polar science, the very discipline that once kept me out. Outright exclusion is gone, and scores of women are making major contributions.

<u>Caroline Gleich</u>, a ski mountaineer and climate activist leading an Antarctic expedition this month, has compiled a brief list of women active in cryospheric science today. She came up with more than two dozen. They include <u>Alison Banwell</u>, who studies ice-shelf stability, crucial for anticipating climate-induced sealevel rise; <u>Indrani Das</u>, who works with ice-penetrating radar to understand ice sheets; <u>Cécile Agosta</u>, who is using stable isotopes to understand climate variability in Antarctica; and many more. Several of these women are making extensive efforts to support others: Oregon State University's <u>Erin Pettit</u>, for example, uses field experience to build confidence among underprivileged women considering science careers. And of course, there are women who paved the way, such as Ellen Mosley-Thompson, who in the 1980s pioneered the use of ice cores in climate reconstruction.

It is striking that many in the current generation of women polar scientists are working on the stability of ice shelves and sheets. This is one of the most important areas of research at the moment because it speaks directly to the impacts of climate change. If the great ice sheets of Greenland and Antarctica start to disintegrate rapidly, they could add many additional meters of sea-level rise globally. Rapid ice-sheet disintegration is a frightening scenario. Once it starts, it will probably be impossible to stop, and people will have very little time to adapt. Women are not working at the margins of climate science; they are working to answer one of its central and most consequential questions.

None of this is to assume that all is well in Antarctic science. I'm sure that women doing research in that region—like women in all areas—continue to face many challenges. But it is to say that 40 years after the British Antarctic Survey refused to consider my application, women are now in the mainstream of polar science. So far as I know, nobody worries about them sleeping in tents.

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1971 How Birds Breathe

"A bird's respiratory system can deliver enough oxygen for the animal to fly at altitude. How do the birds do it? The bones of birds contain air. This is true not only of the larger bones but also often of the smaller ones and of the skull bones. Birds have two lungs that are connected to the outside by the trachea, but in addition they are connected to several large, thin-walled air sacs that fill much of the chest and the abdominal cavity. The sacs are connected to the air spaces in the bones. In this way it becomes apparent that the blood, as it is about to leave the lungs, can take up oxygen from air that has the highest oxygen concentration available anywhere in the system."

1921 Needed: Teachers Who Experiment

"What must America do to establish itself as the leader among nations for world trade? The principal essential is a body of trained investigators. Nowadays what most of us are doing depends upon some phenomenon or property of matter unknown a century ago, which has now become a pillar of civilization. We have splendid laboratories. We have a wealth of materials. We have abundant money. But we need more college professors who are not content to give their pupils merely the results of scientists of the past, but who are themselves experimenting to learn new scientific truths, and who encourage their pupils to experiment. -W. R. Whitney, Director, General Electric Research Laboratory"

Smoke, Not Fire

"A new form of fire alarm has been invented in England. It depends upon the presence of smoke and is not affected by temperature changes, which usually are the chief factors in the operation of most fire alarms. The smoke

DECEMBER







1871

detector consists of a metal cvlinder some eight inches long and two inches in diameter, open at each end, so that air can circulate freely, and containing two rectangular metallic capsules, one of which is considerably larger than the other. The smoke on the capsules causes one to bend more than the other, completing an electrical circuit, and a large electric bell or other alarm signal may be operated. The advantage is that its action is more rapid and reliable. In many fires dense smoke would be produced before any material rise in temperature occurred."

871 Also Needed: Practical Education

"The custom of learning everything by rote, and reciting like a parrot, has become so embedded in our system of education that it seems almost impossible to find any explosive sufficiently active to blow it up. It is probable that we must look to the West. At the University of Iowa, instead of teaching physics, chemistry, geology and astronomy by oral recitations and unillustrated lectures, they have established laboratories and workshops where practical things can be practically learned. The trustees have resolved to place the elements of physical science at the very beginning of the course. They do not propose to wait until the pupil, by droning over dry facts and abstract principles, has acquired a disgust for every branch of knowledge. They think it wiser to pursue the natural method, and begin when the mind is anxiously inquiring into the cause of things."

Dehydrated Meat

"At the meeting of the Lyceum of Natural History, Dr. H. Endemann gave an account of a process invented by himself. About 100 pounds of meat are placed in a suitable chimney, and air, heated to 140 degrees Fahrenheit, is drawn by an exhauster through it until it is entirely dry. The meat is subsequently ground into powder, and will keep in ordinary paper packages. It can also be compressed into hard cakes. Four to five ounces of the dry powder represents one pound of meat. Scattered upon bread, its flavor is excellent and preferable to that of raw meat. It has an agreeable aromatic odor. And, as all of the albumen and fibrin are present, all of the nutritious properties of the flesh are retained."







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INNOVATIONS TO DETECT CANCER AT ITS ORIGIN

What will it take to **IMPROVE CANCER DIAGNOSIS** such that oncologists have the best chance of curing the disease?



Amyloidosis (shown here in liver tissue) has non-specific symptoms and is often diagnosed late.

a single medical objective could be applied to the entire range of cancers, it would be detecting the disease as soon as possible. "At the highest level, finding any cancer early gives you the opportunity for curative treatments," says Andrea Ferris, CEO of research funding organization, LUNGevity.

Although the goal of early detection emerged decades ago, much work remains to be done. Low-dose computed tomography (CT) scanning, used to detect lung cancer, has not changed much in the past ten years, and Ferris says that another part of the problem is a lack of public awareness of the "importance of screening and that it can save lives."

There are other issues too. Clinicians need more powerful tools to detect and track these diseases, which can be hard to find and identify at the earlier stages before a patient develops symptoms. Cancers start small, often deep in tissues, where the malignancy evades early detection. Plus, even when symptoms develop, they can mimic non-cancerous diseases. Simply put, detecting cancer at its earliest stages presents challenges that vary from one type of cancer to the next.

Why time slips away

It's not easy to find tumors at early stages. "They're small and, in most cases, they're not causing any systemic effect," explains Michael Morrissey, global head, early detection & data science, Lung Cancer Initiative at Johnson & Johnson. No symptoms mean the person doesn't seek help for the growing tumor. "This makes screening programs crucial," Morrissey says. It's not just solid tumors that can evade detection. When asked what hematologic cancers are the most difficult to detect, Mark Wildgust — vice president, global medical affairs, oncology, Janssen Pharmaceutical Companies of Johnson & Johnson — says, "Almost all of them."

"FINDING ANY CANCER EARLY GIVES YOU THE OPPORTUNITY FOR CURATIVE TREATMENTS"

Andrea Ferris, CEO, of research funding organization LUNGevity.

For the rare bone-marrow malignancy AL amyloidosis, diagnosis can require multiple visits to physicians, often over a few years. Symptoms are non-specific and suggestive of heart or kidney failure. "It's a hard diagnosis," Wildgust says, "and delays in diagnosis result in the outcome of those patients getting worse." Without effective treatment, the expected survival time is only about a year¹.

Similar challenges arise in lung cancer: about 75% of patients are diagnosed at advanced stages (stage 3 or 4)². "These cancers usually start deep in the lung tissue, giving enough time for a lesion to grow into a cancer that is difficult to treat," Morrissey says.

In general, the longer that a cancer develops, the more mutations it acquires, enabling it to evade treatment. "The tumor gets more heterogeneous," says Wildgust. Plus, the evolving cancer can co-opt the patient's immune system to help or hide the cancer instead of fighting it.

Cancer screening is crucial to early detection, but even that healthcare tactic faces challenges. "You need to

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Computed tomography (CT) scanning, used to detect lung cancer, has not changed much in the past ten years.

balance the effectiveness of screening with risk of false positives and false negatives," says Wildgust. "The specificity is so important, and that's a balancing act that we need to work towards."

Building better tools for detection

In the next five to ten years, Ferris expects significant advances in detecting cancer. "There are a lot of really exciting things to come," she predicts. As one example, she mentions blood-based tests to determine if you have a cancer.

In the PROMISE study at Dana Farber, principal investigator Irene Ghobrial is using a blood test to look for warning signs of myeloma. "The traditional way of doing this would be with serum protein electrophoresis," she says, "but we're using a much more sensitive method of mass spectrometry."

Using this more sensitive method, Ghobrial only needs 500 microliters of blood. She hopes to find the risk factors that lead to myeloma and determine how common those factors are in high-risk populations, which include people of African descent, African Americans, or those with an immediate family member with blood cancer. The results from this study could reveal better biomarkers of risk and lead to better therapies, especially ones that can be used in early stages of this cancer.

Ghobrial hopes that this blood test becomes a standard of care for everyone who's at risk. She adds, "The notion that we wait for people to have symptoms and then we treat them needs to change — not just for multiple myeloma but for every cancer."

Some detection methods will combine technologies. In prostate cancer, the U.S. Food and Drug Administration recently approved a radioactive agent to use with positron emission tomography (PET) imaging in men with prostatespecific membrane antigen (PSMA)-positive lesions. This technology, says Wildgust, allows you to "find much more early disease, and you can find what I would call micrometastatic disease."

On top of combining technologies, Johnson & Johnson's Lung Cancer Initiative (LCI) — a cross-sector R&D engine — collaborates with teams across the company's medical device, pharmaceutical, and consumer health sectors, and with scientists from other companies and academia. These research teams hope to improve a variety of approaches to lung cancer detection. The ongoing work includes cuttingedge radiomic applications for chest CT images and analyzing circulating tumor DNA in a patient's blood. The group is also collaborating with California-based Veracyte in developing a nasal epithelialcell gene expression diagnostic.

We're really looking for technology that would provide — either by itself or in combination with other technologies — a highly sensitive and specific test for lung cancer, such that we can guide patients to earlier, less invasive, and potentially more effective treatments," Morrissey states.

For one thing, Johnson & Johnson scientists want to distinguish between early lesions that are cancerous or are likely to develop into cancer, from those which are likely to remain harmless. After that, Morrissey says that he and his colleagues hope to "understand what might lead to the transformation of a benign lesion into an early stage malignancy and ultimately to late stage disease.". After that, Morrissey says that he and his colleagues hope to "understand what might lead to a transformation of a lesion into an early stage malignancy." In thinking about the future of detecting lung cancer, he says. "Ideally, we'd like to identify lesions that have the potential to form cancer, but that remains to be seen."

Other tools in development will act even earlier: to assess a patient's risk. "This could be, for instance, a nasal swab to say that a person is at higher risk for a certain cancer and should be more vigilant about screening," Ferris says. "It will help us target the communications a lot more, and also target the follow up so that it's moving diagnostics toward precision medicine."

If detection can be improved to the point where the precise location of the tumor is known, then it opens the door to new treatment strategies. Technologies like a robotic bronchoscopy platform from Ethicon, part of the Johnson & Johnson Family of Companies, can "potentially deliver therapeutics to a precise location within the lung," Morrissey says, "and we're excited about such an approach because localized dosing may provide options that wouldn't necessarily be tolerated systemically."

Biology and big data

To improve the outcomes for patients, Johnson & Johnson scientists often go back to the basics. When asked about the best way to improve the detection of colorectal cancers, Wildgust says, "It's really backing down to looking at the underlying biology of the disease — biomarkers and other types of early signs and large datasets, to try to

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More sensitive blood tests are revealing risk factors for myeloma and other cancers.

understand it from a moleculardiagnostics perspective."

Clues to colorectal cancer development can also be found within the gut microbiome, which consists of the microorganisms in a person's gastrointestinal tract. "We are looking for signatures in the microbiome that help us understand who might have a particular kind of cancer," Wildgust says. Such a search involves extensive data. The MetaHIT (METAgenomics of the Human Intestinal Tract) project estimates that there are 3.3 million genes in the gut microbiome - 150-fold more than in the average human genome3.

Scientists already know that the gut microbiome impacts cancer care. "Certain patients with a specific microbiome within their GI responded better to checkpoint inhibitors," Wildgust notes. "Imagine if you could give somebody a type of treatment with a set of bacteria in it that suddenly makes the cancer drug far more effective." In some cancers, important additional data could come from traditional tests. One example comes from using electrocardiogram (EKG) data to diagnose AL amyloidosis.

"A particular signature of an EKG might suggest AL amyloidosis rather than congestive heart failure," Wildgust says.

To make a diagnosis even more specific, scientists sometimes turn to the basic biology of genes. In bladder cancer, which is diagnosed in more than half a million patients each year⁴, noninvasive malignancies that sit on the inner surface of the organ often express mutations of the gene for fibroblast growth factor receptor (FGFR). "Those driver mutations might be detectable in small amounts of tumor DNA that are circulating in the bloodstream," Morrissey says.

Knowing these features of bladder-cancer biology "sets you up to start thinking about how to deliver targeted therapy locally to a patient's bladder," Wildgust says. "That's where really understanding the biology helps us think about how we can build therapies."

Enhancing access and incentives

Enhanced understanding of cancer biology, and new diagnostic tools, are certainly a big part of the solution. But they are inadequate if nobody makes use of them. To get more people screened today and tomorrow, Ferris suggests an incentive structure, which could come in the form of reduced healthcare premiums or maybe even a tax break, that encourages people to take preventative measures. "It will help to shift the mindset," she explains. Then, people might even work harder to reduce their risk of getting cancer.

Moreover, some of the most important changes in cancer diagnostics could come from improving access. "They're so basic," Ferris says of some of the needed improvements. "It's just thinking about how to make it easier for people to get to a clinic to get screened." That could even include night and weekend hours at clinics to better accommodate patients' schedules, she adds.

Tomorrow's diagnostic techniques also need to do a better job — more accurately and precisely finding cancer as soon as possible. As Wildgust says, "If we could treat cancers before patients have symptoms, we can think about a world where there is no cancer."

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GRAPHIC SCIENCE

Text by Tess Joosse | Illustration by Beth Zaiken, Maps by Jen Christiansen

How Tusks Grow

After growing and losing a first set of "milk tusks" between six months and a year old, mammoths develop a permanent pair. Adult tusks grow outward by adding cones of bone to a hollow center extending from the mammoth's gums, continuing throughout the animal's life. The resulting tusk's tip is from the animal's younger years, and its inner layers are from its later years.

One Mammoth's Journey

The alkaline earth metal strontium comes in different versions called isotopes, each with a unique atomic mass. Proportions of these isotopes vary in soils around the world, and small amounts of strontium become part of a mammoth's bones, teeth and tusks when it eats plants. By analyzing each tusk layer's strontium isotopes, researchers traced where the mammoth roamed during each stage of its life.



500 kilometers

Older tusk

material

Pulp cavity

Newer tusk

material





Mammoth Travels

Chemical layers in a tusk reveal an epic journey across Alaska

Mammoths are among the best-known inhabitants of the last ice age. Fossils usually offer a static snapshot of an animal's life, but researchers recently used one to track every place a male mammoth traveled from birth to death. By analyzing the chemicals in a 17,100-year-old tusk, scientists found the mammoth walked far enough to loop around the world twice—likely in search of food and a mate.

"Tusks are like time lines," adding layers each year that contain chemicals from the environment, says Matthew J. Wooller, a paleoecologist at the University of Alaska Fairbanks. He and his colleagues sliced a five-and-a-half-foot-long tusk in half, then measured chemical ratios in each layer to re-create the mammoth's itinerary. Over 28 years the animal walked nearly 80,000 kilometers across what is now Alaska. The team plans to apply the same technique to more tusk fossils in the future. "We have hundreds," Wooller says.

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