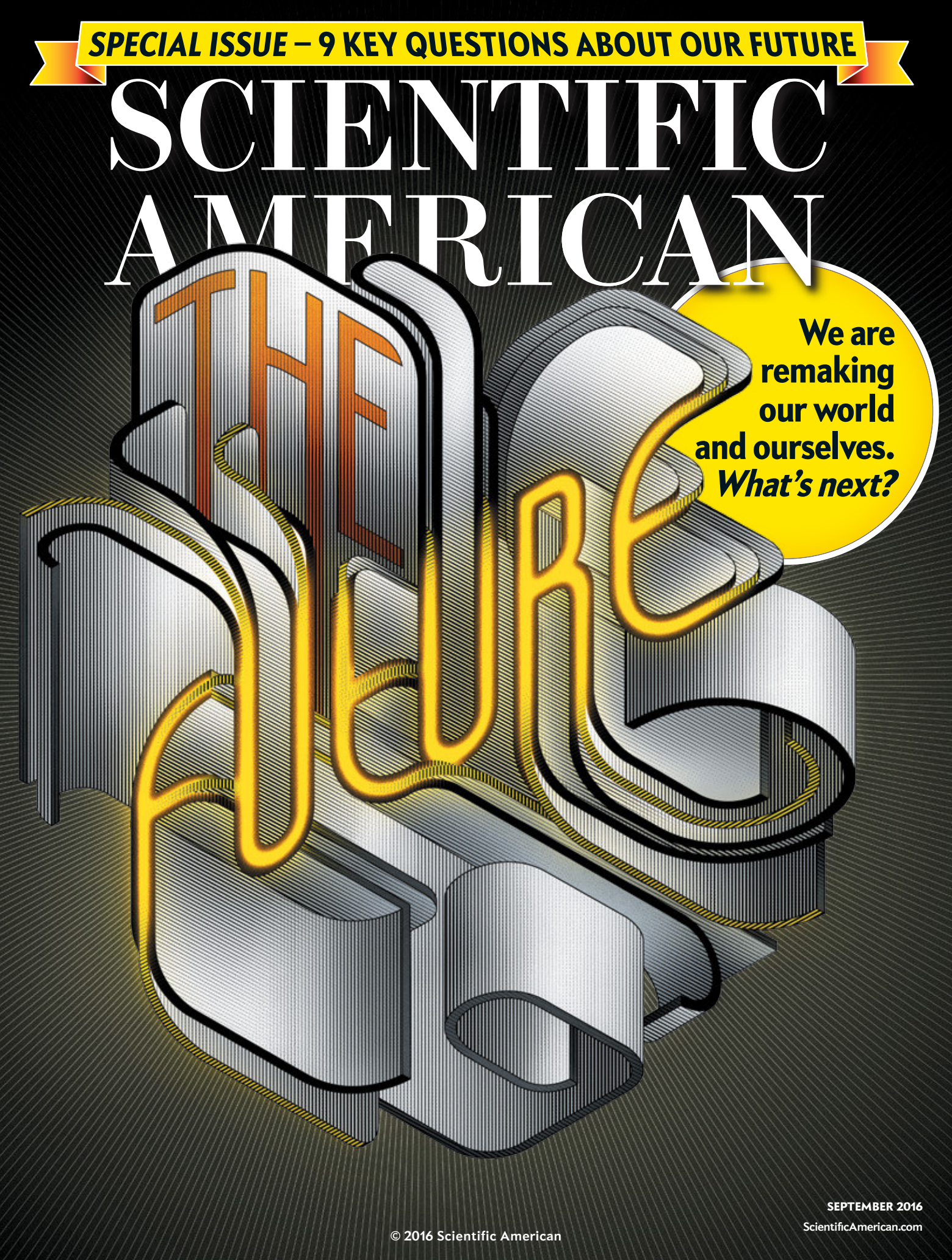
SPECIAL ISSUE – 9 KEY QUESTIONS ABOUT OUR FUTURE

SCIENTIFIC AMERICAN



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SEPTEMBER 2016

VOLUME 315, NUMBER 3

SCIENTIFIC AMERICAN

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THE FUTURE IN 9 BIG QUESTIONS

How smart are we? We changed the world irrevocably and may soon transform ourselves as a species. Here's a status report on the human experiment.

ON THE COVER

"Prediction is very difficult, especially if it's about the future." With this caveat from physicist Niels Bohr in mind, we look at what science has to tell us about the trajectory of the human species. **Illustration by Charles Williams.**

On the Web: What Else Is in Store?

Scientific American took to the streets to ask people what they most want to know about the future. Find the video, plus interactive maps and more predictions from experts, at **ScientificAmerican.com/report/future-of-humanity**

Photograph by Andrew Myers

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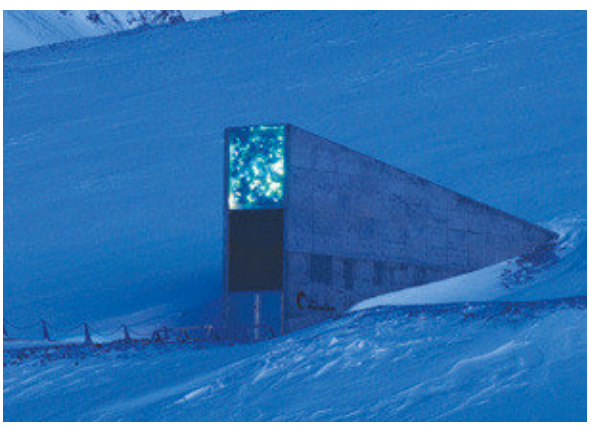

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ON THE WEB

2016 Summer Olympics
Scientific American investigates artificial enhancements, Zika fears and the limits of human achievement at the Games of the XXXI Olympiad in Rio de Janeiro.
Go to www.ScientificAmerican.com/sep2016/olympics

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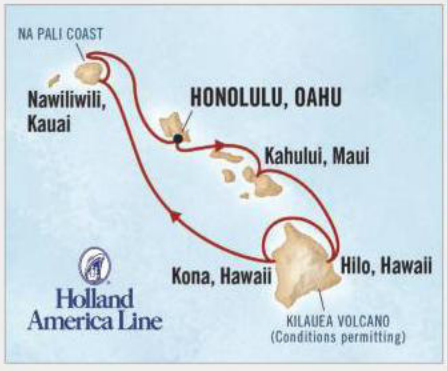

SEMINARS

DINOSAURS

- The Paleobiology of Meat-eating Dinosaurs
- Alberta, Land of Dinosaurs
- What Killed the Dinosaurs?

SPEAKER:

François Therrien, Ph.D.

Dr. François Therrien is the Curator of Dinosaur Palaeoecology at the Royal Tyrrell Museum of Palaeontology in Drumheller, Alberta. He holds a B.Sc. in Geology from the Université de Montréal, a Master's degree in Geosciences from the University of Rhode Island, and a Ph.D. in Functional Anatomy & Evolution from the Johns Hopkins University School of Medicine. Fresh out of his Ph.D., Dr. Therrien came to the Royal Tyrrell Museum as a NSERC postdoctoral fellow and was hired as a curator in 2006. Dr. Therrien's primary research interests focus on the study of faunal and environmental changes that occurred just before the extinction of the dinosaurs as well as the study of dinosaur behavior, particularly that of extinct predators. Over the years, he has conducted field research in Canada, the USA, Romania, and Mongolia and has participated in numerous documentaries. In 2012, Dr. Therrien was involved in the discovery and study of the first feathered dinosaurs from North America.

HUBBLE AND KEPLER TELESCOPES

- Exploring the Milky Way with Hubble
- How the Universe Began
- The Search for Other Earths

SPEAKER:

David M. Meyer, Ph.D.

Dr. David M. Meyer is Professor of Physics and Astronomy and Director of Dearborn Observatory at Northwestern University. He received a B.S. degree in astrophysics (1980) at the University of Wisconsin and earned his M.A. (1981) and Ph.D. (1984) in astronomy at UCLA. Dr. Meyer's research focuses on the composition, structure, and physical conditions of interstellar gas clouds in the Milky Way and other galaxies, and often makes use of observations obtained with the Hubble Space Telescope. At Northwestern, Dr. Meyer has specialized in designing and teaching introductory undergraduate courses in astronomy, cosmology, and astrobiology for non-science majors. His success in such efforts has led to a number of teaching awards including Northwestern's highest teaching honor — the McCormick Professorship of Teaching Excellence (in 2009). He has also developed and recorded two video courses for the Great Courses.

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Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Looking Forward

Since its founding in August 1845, 171 years ago, *Scientific American* has been a magazine with an obsession: how the process of scientific research and innovation not only fosters discoveries but also helps human society shape our own destiny. In that first issue, for instance, the editors promised to be the "advocate of industry and enterprise." They reported on the latest in transportation (an illustration of an aerodynamically improved railway car decorated the cover), communication (the editors praised Samuel Morse's telegraph as a "wonder of the age") and many patents aimed at easing human labors. And—given that the titles of most publications have an aspirational quality—the weekly broadsheet clearly sought to nurture more "scientific" Americans.

Moreover, for almost as long as *Scientific American* has been published, the editors have at least annually (and sometimes even more often) decided to devote an entire issue to looking at emerging topics and technologies that demonstrate how science provides solutions to societal challenges. An 1899 special edition touted bicycles and automobiles, which were changing the face of transportation. As the magazine developed alongside the young U.S., it found other ways to highlight and encourage our progress to a better tomorrow. It created trophies to goad the Wright brothers and others to increase the lengths of aircraft flights, for instance. The magazine covered radio and television decades before they arrived. A 1954 article on "Computers in Business" speculated about the benefits—and possible dangers—of thinking machines. I could go on.

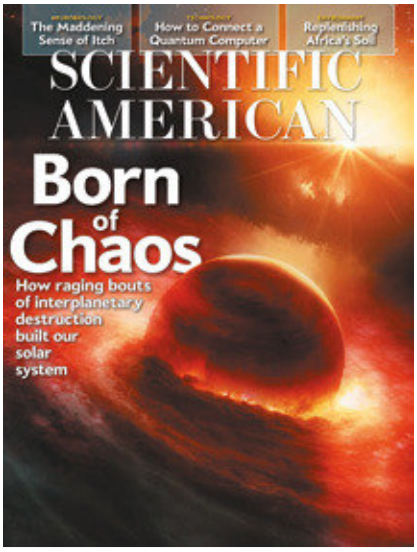
Supporting that prescience: *Scientific American* has always had a mix of award-winning writers, both journalists and scientists (now up to 158 laureates, who have collectively written more than 250 articles about their disciplines).

So about a year ago, when the editors gathered to discuss the focus of our 2016 single-topic issue, the team members, as always, proposed and then talked about lots of great ideas. But among the many compelling themes, one clearly dominated. Humans, in what is now increasingly commonly called the "Anthropocene," have become the major driving force in shaping our planet's future, as well as our own, toward uncertain ends. In effect, as executive editor Fred Guterl dubbed it, we are running "The Human Experiment." In this issue, Guterl, senior editor Seth Fletcher, design director Michael Mrak and their colleagues have put together a dynamic look at the tales of our times, exploring nine big related questions in the feature articles and the companion pieces. Turn to page 28 to begin.

Borrowing from Pogo: "We have met the future, and it is us." SA

SCIENTIFIC AMERICAN (covers)

Illustration by Nick Higgins



May 2016

DRUG ADVERTISING

Your criticism of televised ads for prescription drugs in "This Drug Ad Is Not Right for You" [Science Agenda] is right on. These ads lead patients to push prescriptions on their doctors by saying that they will find another physician if their request is not met, and together with the extraordinary pricing in the drug industry, they are huge burdens on the American public.

I was in active practice for 40 years. I recall vividly the expensive gifts, vacations, sports tickets and rounds of golf offered to physicians. This was drastically reduced a few years ago, but now TV "health education" is on day and night.

JOHN PEARSON
via e-mail

A more reasonable middle ground between reining in increasing prescription drug costs and preserving freedom of speech would be to forbid mentioning specific products that are not easy to purchase legally in "educational" advertising. That would allow drugmakers to send out messages to inform people with particular symptoms that their problems may now be treatable. Then doctors and their patients could confirm that guess with expert diagnosis and sort through the treatment options—including the one that prompted the drugmaker to send the message.

EVANIE CRONQUIST
via e-mail

"Together with the extraordinary pricing in the drug industry, drug ads are huge burdens on the American public."

JOHN PEARSON *VIA E-MAIL*

I am not a big fan of TV or magazine drug ads, but I was very disappointed in the solutions the editors proposed (including a moratorium for new drugs or an outright ban). We are talking about prescription drugs here, so I have to wonder about the role of my doctor. The editors state that a survey shows that 12 percent of ad viewers walked out of a doctor's office with that drug prescribed, but they say nothing about whether it was the right drug for the patient, the right diagnosis or, most important, whether it turned out to be successful.

We need to find a way for doctors to be fully aware of new drugs and how they fare compared with similar treatments. We also need doctors who will prescribe the right medicine for the diagnosis. If we can't do that, then stopping ads will have no effect, because drug company agents will still be their primary source of information on new medicine.

RICHARD BRUNS
Humble, Tex.

SPACE ODDITY

"Born of Chaos," by Konstantin Batygin, Gregory Laughlin and Alessandro Morbidelli, asserts that our solar system is unusual in its large orbits and small inner planets and that the typical planetary system has one or more super Earths orbiting closely to a star. But given that the era of discovering extrasolar planets is still in its infancy, with methods that more easily detect planets if they are massive and in tight orbits, how can we be certain that the exoplanets discovered so far are typical?

PETER FARSON
via e-mail

Parts of the scenario for the formation of the solar system that the authors describe appear to violate the law of conservation of energy. I can see how planets could migrate inward from aerodynamic drag in the early solar system, but where did all the large planets receive the energy to boost them into much higher orbits? And if Jupiter and Saturn were locked in some resonance duet—for one to move out, the other must move in—they could not both move out or in without the law of conservation of energy again being violated.

BRANDON COLE
Seattle

THE AUTHORS REPLY: Farson is right that analogues to our solar system cannot be discovered yet, given the limitations of our current observational techniques. But observations show that 70 to 80 percent of the stars we look at have planets with characteristics that we don't have here. We do not know yet whether systems like ours represent the remaining 20 percent, 1 percent or 0.01 percent, because we have not discovered any. So while waiting for an observational answer to this question, we use theoretical modeling to understand which processes sculpted the solar system as it is and how generic these processes could be. If our understanding is correct, its history has been marked by specific events, each of which looks improbable. Thus, we are inclined to think that our solar system is rare, although we are not able to quantify how rare it is.

Regarding Cole's questions: The planets do not migrate by gas drag but rather by their gravitational interaction with the planet-forming disk of gas and dust that surrounds a newborn star. Because the disk inside the orbit of a planet rotates faster than the planet around the star, it pushes that planet outward. Meanwhile the outer disk, which rotates slower than the planet, pushes it inward. Thus, the direction of migration of a planet depends on the relative importance of the inner versus outer disks. In the case of a lonely planet, the inner disk is significantly depleted relative to the outer disk because the planet blocks part of the gas flow from the outer to the inner part, so the outer disk wins.

In the case of Jupiter and Saturn, the gas is conveyed efficiently from the outer to the inner disk, and the inner disk is therefore more massive and moves the

two planets outward. The migration of Jupiter and Saturn violates no conservation laws because it is balanced against movements of the disk. If Jupiter and Saturn move outward, the disk moves inward, and vice versa.

DRIVERLESS DELAY

In "Who's Responsible When a Car Controls the Wheel?" [Advances], Corinne Iozzio discusses automakers' current plans for, and setbacks in, developing driverless cars. As a practicing engineer, I have to say that all those involved in meaningful research relating to developing safer driving technology should be very proud of the results that are being obtained.

I also have to add that, over the years, I have seen a number of promising areas of research discarded because they were released to the public too soon and without sufficient developmental testing. Iozzio states that "later this year Volvo will roll out the U.S.'s first semiautonomous highway driving feature, called Pilot Assist, on the 2017 S90 sedan." This "rush to market" approach by Volvo is similar to other catastrophes that I have witnessed in the past.

Because computers are capable of virtually instantaneous communication with other computers (relative to human reaction time), then perhaps the idea of autonomous vehicle operation should be restrained until all the similar computers in all the vehicles within a half-mile radius can communicate with one another. This approach could enable cooperation among vehicles without the need for human intervention.

PAUL HEANEY
Honeoye Falls, N.Y.

ERRATA

"Show Venus Some Love," by Alexander Rodin [Forum], stated that Venus "rotates on its axis once every 224 days." It does so every 243 days.

"Drawing for a Remedy," by Jessica Wapner [Advances], incorrectly spelled the name of Sheela Shenoi of Yale University.

"Saving Eden," by Rachel Nuwer, referred to the WWF as the "World Wildlife Fund for Nature." The full name of the international organization is the World Wide Fund for Nature.

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The Tweets We Hold to Be Self-Evident

The U.S. presidential election shows how far the political conversation has degenerated from the nation's founding principles of truth and evidence

By the Editors

"If it disagrees with experiment it is wrong."
—Richard Feynman

Four years ago in these pages, writer Shawn Otto warned our readers of the danger of a growing antiscience current in American politics. "By turning public opinion away from the anti-authoritarian principles of the nation's founders," Otto wrote, "the new science denialism is creating an existential crisis like few the country has faced before."

Otto wrote those words in the heat of a presidential election race that now seems quaint by comparison to the one the nation now finds itself in. As if to prove his point, one of the two major party candidates for the highest office in the land has repeatedly and resoundingly demonstrated a disregard, if not outright contempt, for science. Donald Trump also has shown an authoritarian tendency to base policy arguments on questionable assertions of fact and a cult of personality.

Americans have long prided themselves on their ability to see the world for what it is, as opposed to what someone says it is or what most people happen to believe. In one of the most powerful lines in American literature, Huck Finn says: "It warn't so. I tried it." A respect for evidence is not just a part of the national character. It goes to the heart of the country's particular brand of democratic government. When the founding fathers, including Benjamin Franklin, scientist and inventor, wrote arguably the most important line in the Declaration of Independence—"We hold these truths to be self-evident"—they were asserting the fledgling nation's grounding in the primacy of reason based on evidence.

Scientific American is not in the business of endorsing political candidates. But we do take a stand for science—the most reliable path to objective knowledge the world has seen—and the Enlightenment values that gave rise to it. For more than 170 years we have documented, for better and for worse, the rise of science and technology and their impact on the nation and the world. We have strived to assert in our reporting, writing and editing the principle that decision making in the sphere of public policy should accept the conclusions that evidence, gathered in the spirit and with the methods of science, tells us to be true.

It won't come as a surprise to anyone who pays even superficial attention to politics that over the past few decades facts have become an undervalued commodity. Many politicians are hostile to science, on both sides of the political aisle. The House Committee on Science, Space, and Technology has a routine practice of meddling in petty science-funding matters to score political points. Science has not played nearly as prominent a role as it should in informing debates over the labeling of genetically modified foods, end of life care and energy policy, among many issues.

The current presidential race, however, is something special. It takes antiscience to previously unexplored terrain. When the major Republican candidate for president has tweeted that global warming is a Chinese plot, threatens to dismantle a climate agreement 20 years in the making and to eliminate an agency that enforces clean air and water regulations, and speaks passionately about a link between vaccines and autism that was utterly discredited years ago, we can only hope that there is nowhere to go but up.

In October, as we did four years previously, we will assemble answers from the campaigns of the Democratic and Republican nominees on the public policy questions that touch on science, technology and public health and then publish them online. We will support ScienceDebate.org's efforts to persuade moderators to ask important science-related questions during the presidential debates. We encourage the nation's political leaders to demonstrate a respect for scientific truths in word and deed. And we urge the people who vote to hold them to that standard. SA

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Illustration by Chris Gash

Paul Davies is director of BEYOND: Center for Fundamental Concepts in Science at Arizona State University and author of *The Eerie Silence: Renewing Our Search for Alien Intelligence* (Houghton Mifflin Harcourt, 2010).

Many Planets, Not Much Life

We still have no idea how easy it is for life to arise—and it may be incredibly difficult

By Paul Davies

When I was a student in the 1960s, almost all scientists believed we are alone in the universe. The search for intelligent life beyond Earth was ridiculed; one might as well have professed an interest in looking for fairies. The focus of skepticism concerned the origin of life, which was widely assumed to have been a chemical fluke of such incredibly low probability it would never have happened twice. "The origin of life appears at the moment to be almost a miracle" was the way Francis Crick described it, "so many are the conditions which would have had to have been satisfied to get it going." Jacques Monod concurred; in his 1976 book *Chance and Necessity* he wrote, "Man knows at last that he is alone in the indifferent immensity of the universe, whence which he has emerged by chance."

Today the pendulum has swung decisively the other way. Many distinguished scientists proclaim that the universe is teeming with life, at least some of it intelligent. Biologist Christian de Duve went so far as to call life "a cosmic imperative." Yet the science has hardly changed. We are almost as much in the dark today about the pathway from nonlife to life as Charles Darwin was when he wrote, "It is mere rubbish thinking at present of the origin of life; one might as well think of the origin of matter."

There is no doubt that SETI—the search for extraterrestrial intelligence—has received a huge fillip from the recent discovery of hundreds of extrasolar planets. Astronomers think there could be billions of Earth-like planets in our galaxy alone. Clearly, there is no lack of habitable real estate out there. Yet because we do not know the process that transformed a mishmash of chemicals into a living cell, with all its staggering complexity, it is impossible to calculate the probability that life has actually arisen on these planets.

Carl Sagan once remarked that the origin of life cannot be that hard, or it would not have popped up so quickly once Earth became hospitable. It is true that we can trace the presence of life on Earth back 3.5 billion years. But we cannot draw any statistical significance from a sample of one.

Another common argument is that the universe is so vast, there just *has* to be life out there somewhere. But what does that statement mean? If we restrict attention to the observable universe, there are probably 10^{23} planets. Yes, that is a big number. But it is dwarfed by the odds against forming even simple organic molecules by random chance alone. If the pathway from chemistry to biology is long and complicated, it may well be that fewer than one in a trillion trillion planets ever spawns life.

Affirmations that life is widespread are founded on a tacit assumption that biology is *not* the upshot of random chemical reactions but the product of some kind of directional self-organization that favors the living state over others—a sort of life principle at work in nature. There may be such a principle, but if so we have found no evidence for it yet.

Maybe we do not need to look far. If life really does pop up readily, as Sagan suggested, then it should have started many times on our home planet. If there were multiple origins of life on Earth, the microbial descendants of another genesis could be all around us, forming a possible shadow biosphere. Nobody has seriously looked under our noses for life as we do not know it. It would take the discovery of just a single "alien" microbe to settle the matter. SA

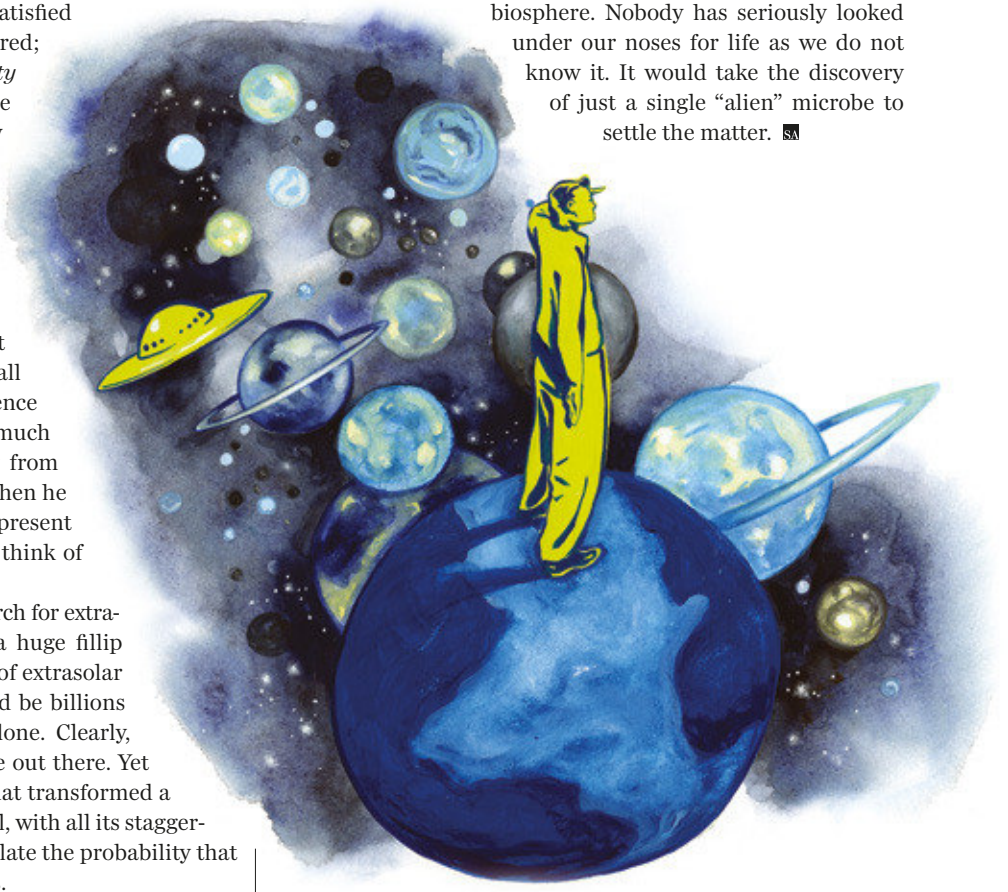

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Illustration by Tim Bower

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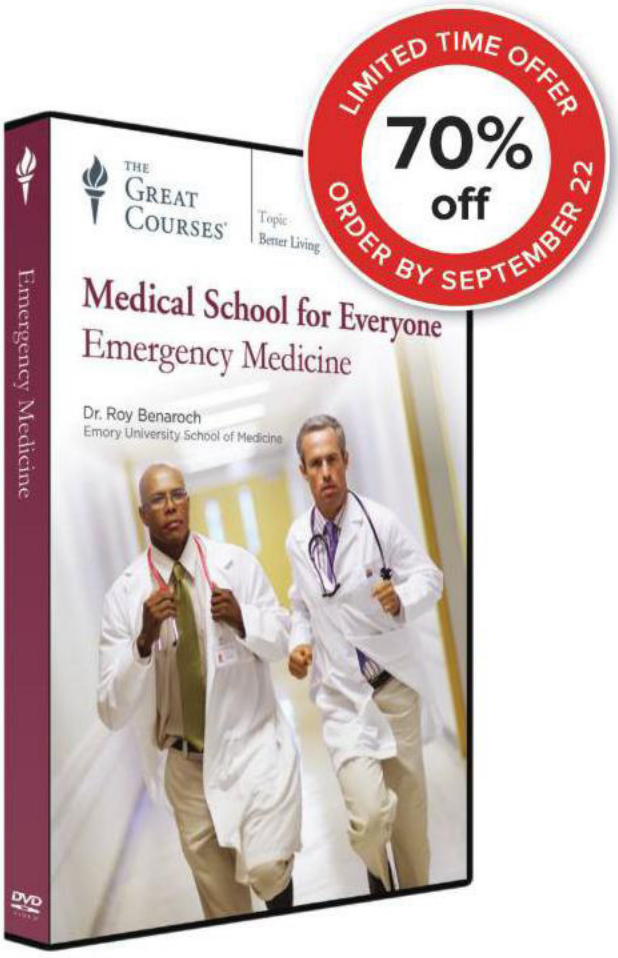

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ADVANCES

INSIDE

PUBLIC HEALTH

Can Medical Cannabis Break the Painkiller Epidemic?

Researchers fight red tape to study whether medical marijuana could substitute for addictive opioids

Six days before Prince died, the iconic pop star was hospitalized after possibly overdosing on Percocet. His death on April 21 involved overdosing on another painkiller, fentanyl. Both are among the prescription opioids that alleviate the pain of millions of Americans every year—often at the price of their needing ever greater amounts and the risk of overdose. The U.S. "is in the midst of an unprecedented opioid epidemic," according to the Department of Health and Human Services. Prescription opioid overdoses killed more than 165,000 Americans between 1999 and 2014, and the health and social costs of abusing such drugs are estimated to be as much as $55 billion a year. The problem has led experts to scramble for a less dangerous alternative for pain relief—and

some research points to medical marijuana.

As early as 15 years ago physicians began hearing that patients were using cannabis instead of prescription opioids for pain. These anecdotes inspired a research team led by Marcus Bachhuber, assistant professor of medicine at the Montefiore Medical Center in New York City, to examine whether some states' legalization of medical cannabis had affected the number of opioid overdose deaths. Published in 2014, the study revealed an intriguing trend: between 1999 and 2010, states that permitted medical marijuana had an average of almost 25 percent fewer opioid overdose deaths each year than states where cannabis remained illegal.

Bachhuber's research could not prove that medical cannabis use directly led to fewer opioid overdoses. In addition, the overdose count included both prescription opioids and illegal heroin. But the study opened the eyes of many researchers to a possible relation between marijuana and painkiller use. "I think medical cannabis could fall into the category of alternatives for treating chronic pain so that people don't use opioids or use a lower dose of opioids than they otherwise would," Bachhuber says.

Various wide-ranging new studies back him up. As reported in the June issue of the *Journal of Pain,* researchers at the University of Michigan conducted a retrospective survey of 185 patients who frequented a medical marijuana dispensary in Ann Arbor, Mich. Those patients reported cutting their opioid use by more than half in treating their chronic pain. Meanwhile animal studies have shown that cannabinoid chemical compounds found in marijuana can work synergistically with opioids to mitigate pain.

Medical cannabis was also a hot topic at the 2016 meeting of the American Pain Society, says Simon Haroutounian, chief of clinical research at the Washington University Pain Center in St. Louis. He co-authored a study, published online in February in the *Clinical Journal of Pain,* that followed a group of 176 chronic pain patients in Israel over seven months and found that 44 percent of them stopped taking prescription opioids within seven months of starting medical cannabis. The research is among several recent observational studies showing an association between medical cannabis use and decreased dependence on opioids.

Each of these analyses has its limitations. Retrospective studies cannot reveal crucial details such as whether overdose deaths involved patients who were using medically prescribed opioids or people who got the drugs illegally and were using them recreationally or to self-medicate. And although Haroutounian's observational study was carried out in real time, the participants were prescreened for psychiatric conditions and the potential for drug misuse. That means they were less likely to suffer complications from medical cannabis than a general population of chronic pain patients. "We don't have good data on the long-term effects and in larger populations that are not so carefully selected," Haroutounian explains.

1


2

In 2014 at least 240 million prescriptions were written for opioids—enough to give every American adult a bottle of pills (*1*). More than 500 licensed medical marijuana dispensaries operate in Colorado alone (*2*).

As for the safety of medical marijuana as an opioid alternative, one of the most extensive reports to date was published late last year in the *Journal of Pain* and followed about 200 patients using cannabis for chronic pain over 12 months. Unlike most previous research, this study directly compared medical cannabis users with a control group of chronic pain patients who did not use the drug. The results showed some increased risk for nonserious adverse effects in the medical cannabis group but no difference in the risk of serious adverse events.

Experimental clinical trials would provide the most definitive proof on any cause-and-effect relation between medical cannabis and reduced opioid use, says Mark Ware, director of clinical research at the Alan Edwards Pain Management Unit at McGill University and lead author of the *Journal of Pain* safety study. But experimental research with medical cannabis remains difficult because the U.S. classifies it as a Schedule I substance that has "no currently accepted medical use and a high potential for abuse." Most other countries have similar restrictions, which pose challenges for researchers to legally obtain cannabis or to get approval for clinical trials.

Such trials are also a necessary next step because they would help determine safety. All experts interviewed for this article see medical cannabis as a potentially viable treatment option for chronic pain, but many also worry about rushing ahead without a better understanding of the long-term effects of marijuana—which carries its own risks of substance abuse and unwanted side effects.

"We have all these states that have legalized medical cannabis," says Kevin Boehnke, a Ph.D. candidate in environmental health sciences and public health at the University of Michigan and co-author on the Ann Arbor study. "At this point, we really need a policy on the ways that cannabis can be researched and accessed by the scientific community to catch up with that reality."

Political attitudes toward cannabis have been shifting fast as of late. On June 8, Ohio joined 24 other states and the District of Columbia in legalizing medical cannabis. Even the U.S. Drug Enforcement Administration has been reconsidering marijuana's Schedule I status after receiving scientific and medical evaluations from the Food and Drug Administration earlier this year.

Medical cannabis is unlikely to prove a replacement for opioids in all medical situations. For example, prescribing opioids is relatively uncontroversial in end-of-life care and in treatment of acute pain from cancer, major surgery or broken bones. But for pain not caused by cancer, medical cannabis may prove a better candidate in the long run. Even the most severe critics, Bachhuber says, would accept that medical cannabis is safer than opioids when it comes to the risk of fatal overdose. —*Jeremy Hsu*

PRECEDING PAGES: JON PACIARONI *Getty Images*; THIS PAGE: MATTHEW STAVER *Getty Images* (*1*); LAWRENCE K. HO *Getty Images* (*2*)

CHEMISTRY

Mirror Molecules in Space

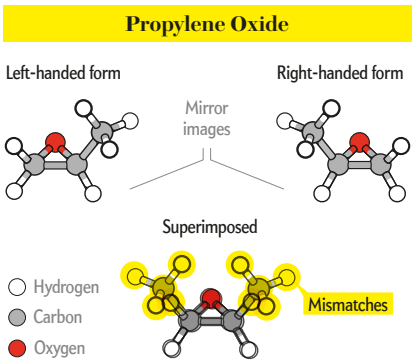
Astrochemists detect chiral molecules in interstellar space for the first time

Chiral molecules are those that come in two forms: versions that are mirror images of one another but cannot be superimposed, like right and left hands. Life seems to prefer molecules of a single chemical handedness, however. All DNA, for example, twists clockwise like the threads on a right-handed screw. Nearly all amino acids, meanwhile, are left-handed. Why one or the other? "It's pretty well established that once an excess [of one chirality] is present, life is going to go with it," says Brett McGuire, an astrochemist at the National Radio Astronomy Observatory in Charlottesville, Va. For instance, if DNA came in both forms, its strands would not fit together, and life probably would not have gotten far.

Although it is possible such an excess originated with meteors that brought mostly one type of molecule or another to Earth early in its history, another hypothesis suggests the origins of chirality are much older. As reported in *Science,* McGuire and his colleagues have discovered a chiral molecule in interstellar space. The compound, propylene oxide, exists in Sagittarius B2, a cloud of gas and dust near the center of the Milky Way.

The observation shows that chiral molecules were present "way before solar systems," says P. Brandon Carroll of the California Institute of Technology and a co-author of the paper. If these types of molecules were mostly right-handed, they could have seeded the formation of other right-handed molecules, ultimately including DNA, long before our sun first shone. If so, that right-handed excess could have been baked into Earth's chemistry as it was forming rather than being added by meteors after the fact.

NASA astrochemist Stefanie Milam says the implications are "huge" for astrobiology



because they suggest that at least some of the complex chemistry associated with life is present elsewhere in the universe. Others are skeptical. Arizona State University biochemist Sandra Pizzarello, who has studied chiral molecules in meteorites, says connecting the observations to DNA chirality could be difficult. "We are still left wondering what happens" on the long path between molecular clouds and the origins of life, she says.

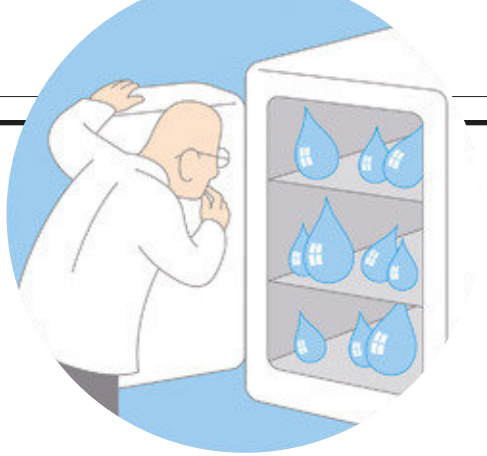
McGuire is now testing whether a majority of the propylene oxide molecules are right- or left-handed. —*Nathan Collins*

Illustration by Amanda Montañez

BIOLOGY

A Flood of Tears

Researchers want to build a tear bank to better understand why we weep



Compared with other bodily excretions, tears are vastly understudied. Collecting the salty drops is tedious—weepy donors are rare, men hardly ever sign up and tears must be "fresh" for their makeup to be properly analyzed. As a result, researchers lack a consensus about the purpose of a basic human behavior. Is crying a primal way to communicate that many species share, as some chemists hypothesize? Or is it, as psychologists have put forth, a uniquely human key to social bonding? Israeli neurobiologist Noam Sobel has a plan to advance the field: he has perfected a way to flash-freeze tears and is now working to create a "tear bank" for researchers around the world.

Sobel, who is based at the Weizmann Institute of Science in Rehovot, discovered in 2011 that women's tears contain pheromones that lower the testosterone levels of nearby men. But building on that research has been slow because the molecules easily degrade.

To keep the chemical composition of tears intact, Sobel and his team have developed a way to systematically freeze the droplets. The method involves liquid nitrogen, which rapidly lowers the temperature of a sample below –80 degrees Celsius. The process preserves most of the tears' chemicals, say the researchers, who plan to publish their results later this year. Next they will start building a cryogenic repository of tears, categorized by source and orderable online. "Just as other biobanks exist for amniotic fluid, blood and urine, we'll have a biobank of tears," Sobel says. "This would let you do studies in two weeks instead of six months."

A tear bank for research "has tremendous possibilities," says Saad Bhamla, a bioengineer at Stanford University who often has to use animal tears in his own investigations into how tears create a film on the eye. As examples of applications, he points to Silicon Valley's interest in contact lenses that double as a heads-up display, among other functions, and the rising cases of dry eyes from prolonged sessions of staring at a computer screen.

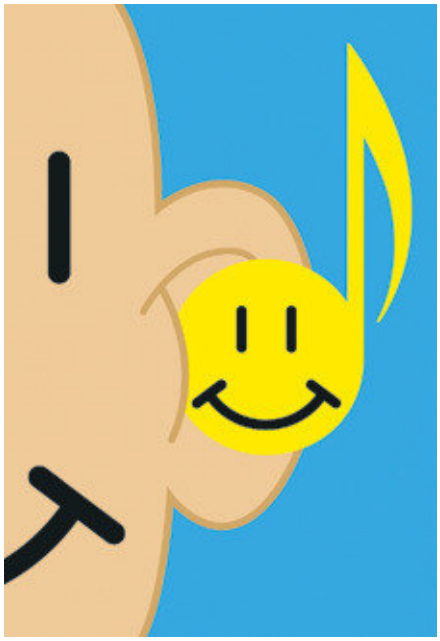
Sobel hopes interested researchers will eventually be able to select tears by age and gender from the repository—say, 200 samples from white males, 18 to 25 years old. This customized access could expedite experiments tackling the chemistry of crying's many unanswered questions: Do tears affect mood or appetite? Do the tears of men and women differ? How do emotional and nonemotional tears—from, say, cutting onions—compare? For Sobel, the more people who cry their eyes out, the better. —*Noah Caldwell*

Illustrations by Thomas Fuchs

HEALTH

An Auditory Component to Autism

New evidence suggests people with autism are savvy about the social cues that voices convey



"The face is the index of the mind," according to an ancient proverb. People with autism, however, are often unable to judge when a face conveys emotions such as happiness or sadness, and many researchers take this as evidence that autism involves serious deficits in processing social information. Yet the voice, too, can provide emotional cues, and several recent studies indicate that when listening to voices, people with autism can actually recognize feelings and other traits of humanness as well as—or even better than—neurotypical people do.

The studies were small and focused exclusively on high-functioning adults with autism, whose abilities are not necessarily representative of the broader autistic population, points out Andrew Whitehouse, head of autism research at Telethon Kids Institute in Australia. And success on a laboratory task does not necessarily translate into success in real-world social interactions, adds Helen Tager-Flusberg, a professor of psychological and brain sciences at Boston University. Nevertheless, the studies suggest that at least for some subgroups of autistic people in certain situations, deficits in identifying emotions could be confined primarily to vision. "This is great news from a treatment perspective," says Kevin Pelphrey, director of the Autism and Neurodevelopmental Disorders Institute at George Washington University. "It is much easier to help someone overcome an inability to read emotion from faces than it would be to treat a fundamental lack of understanding of emotion from all modalities." —*Anne Pycha*

THREE STUDIES ON AUTISM AND EMOTION

Daniel Javitt of the Nathan Kline Institute for Psychiatric Research in New York State and his colleagues displayed photographs of faces expressing happiness, sadness, fear or anger. The 19 participants with autism did a poor job of identifying these emotions. But when researchers played audio clips of voices conveying similar feelings, these same participants identified the relevant emotions just as well as a control group. The results were published in August in the *Journal of Psychiatric Research.*

Neuroscientist **Tamami Nakano** of Osaka University in Japan and her colleagues asked participants to rate real and computer-generated singing voices. Although the performance of the autistic and control groups differed for the real voices, the 14 participants with autism nonetheless gave the artificial voices the same low ratings for humanness and emotional qualities as their neurotypical peers did. The results were published in August in *Cognition.*

A team led by **I-Fan Lin** of Tokyo Metropolitan University measured how quickly people could judge whether or not a particular sound came from a human. (Audio examples included a violin playing a note and a person pronouncing the vowel "i.") The 12 participants with autism not only performed the task faster than their neurotypical peers, they also did it better, readily responding to human voices even when important acoustic components were missing. The results were published online in May in *Scientific Reports.*

FORENSICS

Blood Left at Scene Can Indicate Criminal Age

DNA found at a crime scene can help forensic investigators identify suspects. The genetic information may lead to a match in an existing criminal database or offer clues about physical attributes, such as eye and hair color. But DNA testing takes time—a rare commodity in many cases. Jan Halamek, a chemist at the University at Albany, is searching for new ways to rapidly reduce a pool of suspects: he recently identified a chemical biomarker in blood that can provide a rough estimate of a person's age.

Alkaline phosphatase (ALP) is an enzyme that is released during bone growth; its levels generally peak by 18 years of age in women and by 19 in men and then decline with age. As reported in *Analytical Chemistry,* Halamek and his colleagues have successfully used the enzyme as a proxy for age. So far they have been able to predict, with about 99 percent accuracy, whether a mock blood sample spiked with varying concentrations of ALP hypothetically came from a healthy person who is older or younger than 18. Halamek is now trying to narrow the age range.

The study was small—involving fewer than 200 samples—and the technique has not yet been tried in a real-world setting. Plus, there are already (slower) DNA-based methods that can more precisely indicate a person's age, says Manfred Kayser, a molecular biologist at the Erasmus MC medical center in the Netherlands. Ultimately, though, Halamek thinks his test could complement existing analyses and other types of evidence. He hopes these enzyme tests resemble point-of-care diagnostics that offer immediate results. Find high levels of ALP, he says, and investigators could quickly rule out an older suspect: "You can exclude a lot of samples so that they don't need to go to the DNA lab."

In earlier experiments, his team found that other biomarkers, including creatine kinase and alanine transaminase, could be used to indicate whether blood came from a man or a woman. —*Peter Andrey Smith*

GETTY IMAGES

PHYSICS

The Kilogram Makeover

Finally a better standard for the fundamental unit of mass

CASPAR BENSON Getty Images

The kilogram is a 127-year-old relic. It is the last remaining standard of measurement in the International System of Units that is still based on a physical object—a single, golf ball–sized cylinder of platinum and iridium that sits in a vault just outside Paris. It is kept under lock and key—and secured underneath three vacuum-sealed, glass bell jars—in a temperature-controlled room in the International Bureau of Weights and Measures. The slightest amount of dust, moisture, oil from fingerprints, or contraction or expansion could alter the mass of the cylinder. In fact, the so-called *Le Grand K* is so well protected that caretakers remove it only every 40 years so that other prototypes from around the world can be compared with it. Even then, it is impossible to tell if changes are caused by the fact that *Le Grand K* lost mass or that one of its copies gained some from contamination.

This is a serious problem for modern science, given that many technologies depend on an accurate measurement of the kilogram, says Stephan Schlamminger, a physicist at the National Institute of Standards and Technology. That is why scientists, for decades now, have wanted to redefine the kilogram in terms of constants found in nature—an achievement that would provide a more stable (and accessible) unit of measurement.

Schlamminger and his team recently reported that they have paved the way for such a feat by using Planck's constant, a mathematical value that describes the link between the energy of a photon and its frequency and that can be related to mass through Einstein's famous equation $E = mc^2$. As detailed in the *Review of Scientific Instruments*, the NIST team measured Planck's constant with a high-tech scale called a watt balance.

The researchers placed a known mass on one end of the scale and then counterbalanced it by sending an electric current through a movable coil of wire suspended in a magnetic field. They then used that electromagnetic force to measure

A BRIEF HISTORY OF THE INTERNATIONAL SYSTEM OF UNITS

1799
The metric system was created at the time of the French Revolution. Two platinum standards representing the meter and the kilogram were chosen in an effort to standardize trade.

1889
The first General Conference on Weights and Measures sanctioned international prototypes for the meter and the kilogram. Along with the second as a unit of time, these became the three base units of measurement.

1954
The 10th conference added the kelvin to the system of units as a measure of temperature.

1960
The 11th conference replaced the physical meter with a definition based on the radiation of krypton 86. This was later changed (in 1983) to the distance light travels in a given time.

Planck's constant down to an accuracy of 34 parts per billion.

Before the world redefines the kilogram based on Planck's constant, however, multiple teams must publish independent measurements by July 2017. At the 2018 General Conference on Weights and Measures, the data from each group will then be evaluated, including a constant calculated by counting the atoms in a silicon sphere. A complex computer program will subsequently sift through the numbers to arrive at a final value. Only then may *Le Grand K* be retired to the Louvre, next to the old meter and other artifacts. —*Knvul Sheikh*

BY THE NUMBERS

$6.626\,069\,83 \times 10^{-34}$ kg m^2/s

Planck's constant as measured using the NIST-4 watt balance

$0.000\,000\,22 \times 10^{-34}$ kg m^2/s

(or 34 parts per billion)

Level of uncertainty in the measurement by Stephan Schlamminger's team

230 miles

Driving distance between Washington, D.C., and New York City

0.5 inch

Level of uncertainty in the measurement of distance that is comparable to 34 parts per billion

SOURCE: NATIONAL INSTITUTES OF HEALTH

1967

The 13th conference changed the definition of a second from 1/86,400 of an average solar day to a particular number of periods of radiation produced by a cesium 133 atom.

2018

The year in which the physical kilogram is set to be replaced by a definition based on Planck's constant.

CONSERVATION

Cleanup on Isle Nine

Every year U.S. biologists visit some of the most remote islands in the world to monitor and conserve flora and fauna

To reach Nihoa, an uninhabited 171-acre piece of land in the northwestern Hawaiian Islands, scientists must take a 30-hour boat ride, leap ashore from an inflatable dinghy amid violent waves and then scale a cliff. Until recently, the critically endangered millerbird lived nowhere else on earth but Nihoa. But in 2011 and 2012 Sheldon Plentovich led a team that brought 50 of the tiny songbirds on a three-day voyage to Laysan, a sister island where introduced rabbits had driven a different millerbird subspecies to extinction roughly a century ago. At one point, "I thought [a few of] the birds were going to drown," says Plentovich, a U.S. Fish and Wildlife Service (FWS) biologist and former professional kiteboarder. "But somehow we were able to pull it off." As documented in July in *Biological Conservation*, the Laysan population has since swelled to about 164, providing a bulwark should disaster ever strike Nihoa's birds.

For Plentovich and other researchers focused on remote U.S. Pacific islands—most of which have no permanent residents and are off-limits to the public—such adventures are par for the course. All their conservation projects share a common theme: undoing damage caused by careless humans (such as the ones who transported rabbits to Laysan). "It is so humbling and disconcerting to see the obvious effects of humans—even in the middle of nowhere," Plentovich says. —*Jesse Greenspan*

U.S. PACIFIC ISLAND CONSERVATION PROJECTS

Palmyra Atoll: Some 30,000 rats (52 per acre) overran this former military base until the FWS and two nonprofit organizations wiped them out five years ago in an operation involving helicopters, slingshots and poisoned bait. Stefan Kropidlowski, who manages the atoll's wildlife refuge and spends half the year there in near-complete isolation, has since turned his attention to similarly destructive coconut palms, which crowd out the native trees on which many seabird and crab species depend.


1


2

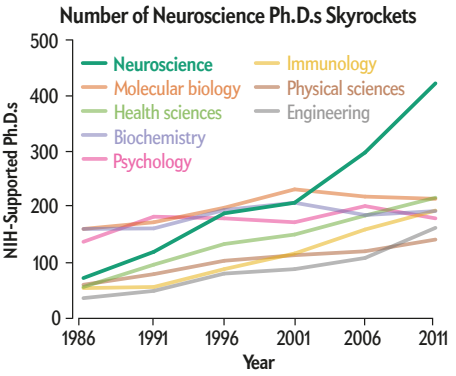
Frigate bird on Kure Atoll (*1*). Big-headed ants swarm sooty tern chick (*2*).

Johnston Atoll: A one-time nuclear weapons testing site, this four-island cluster serves as a seabird haven despite being highly contaminated with plutonium, asbestos and other toxic substances. The arrival of yellow crazy ants, however, threatened to devastate nesting populations. The invasive insect sprays acid as it swarms its prey—a tactic that frequently deforms chicks. Over the past six years FWS volunteers on six-month tours of duty have managed to beat back the infestation with poison-laced cat food and corn syrup. The latest strike team, which arrived in June, had uncovered only one small crazy ant nest as of press time.

Midway Atoll: Last winter FWS scientists on the three-island chain discovered that mice were eating albatross alive (the birds resist leaving their nests during incubation for any reason). The agency has initiated a program to remove the nonnative rodents from this location, best known for a World War II naval battle.

Kure Atoll: Strewn with garbage carried by ocean currents, this northernmost Hawaiian landmass hosts researchers as well as year-round volunteers who pick up the debris that is most likely to entangle wildlife. Cynthia Vanderlip, Kure's field camp manager, and her team are also working to demolish an unused airplane runway, eradicate invasive big-headed ants and golden crownbeard (a type of daisy), and plant native grasses and shrubs with an eye toward bolstering seabird populations. Meanwhile endangered Laysan ducks have been reintroduced, and the U.S. Coast Guard plans on cleaning up toxic PCBs it left behind decades ago.

CYNTHIA VANDERLIP



SOURCE: NATIONAL INSTITUTES OF HEALTH

EDUCATION

Where Will All the New Neuroscientists Go?

In recent decades neuroscience has emerged as a star among the biological disciplines. But its enormous popularity as an academic career choice has been accompanied by a drop in the percentage of trained neuroscientists who actually work in academic research positions—largely because of a lack of funding.

In 2014 the National Academies organized a workshop to ponder the question of whether this trend bodes well for the scientists-to-be who are now getting their Ph.D.s. The findings were published this summer in *Neuron*.

Steven Hyman of the Broad Institute of the Massachusetts Institute of Technology and Harvard University, who helped to plan the workshop and was recently president of the Society for Neuroscience (SfN), welcomes the flood of doctoral students choosing the field but warns: "Insofar as talented young people are discouraged from academic careers by funding levels so low that they produce debilitating levels of competition or simply foreclose opportunities, the U.S. and the world are losing an incredibly precious resource."

Because there are not enough academic positions to go around, it is now the responsibility of professors to prepare students for alternative careers, says Huda Akil of the University of Michigan Medical School, lead author of the paper. "It's not just academia and industry" where trained neuroscientists can make contributions to society, says Akil, also a former SfN president: "It's nonprofits. It's social policy. It's science writing. It's man-machine interfaces. It's Big Data, or education, or any area where knowledge of the brain is relevant." —*Gary Stix*

To read a complete Q&A with Huda Akil, visit the Talking Back blog at ScientificAmerican.com

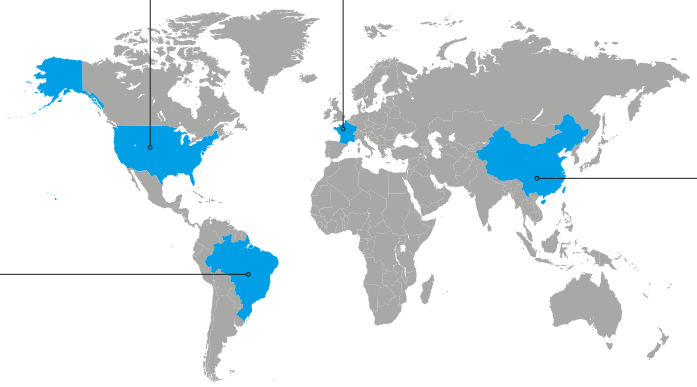
Graphic by Amanda Montañez

IN THE NEWS

Quick Hits

U.S.
The National Institutes of Health approved the first clinical trial that involves the gene-editing technique CRISPR. The trial will evaluate whether CRISPR is safe to use in humans as it applies to a cancer therapy that relies on the patient's own cells. It is set to begin by the end of this year.

FRANCE
Paris instituted a city ban on all cars built before 1997 in an effort to combat its growing smog problem. A regulation from earlier this year allows even- and odd-numbered license plates within city limits only on alternating days.



BRAZIL
Online requests for abortion pills spiked dramatically this year in Brazil, Ecuador and other Latin American countries that ban or restrict abortions, according to a report in the *New England Journal of Medicine*. The uptick suggests that women may be choosing to end pregnancies rather than risk birth defects caused by the Zika virus.

CHINA
The world's largest radio telescope, built in a natural basin in the Guizhou province, is scheduled to begin operations this month. The Five-Hundred-Meter Aperture Spherical Telescope, or FAST, has a dish the size of 30 football fields and will be used to hunt for gravitational waves, among other tasks.

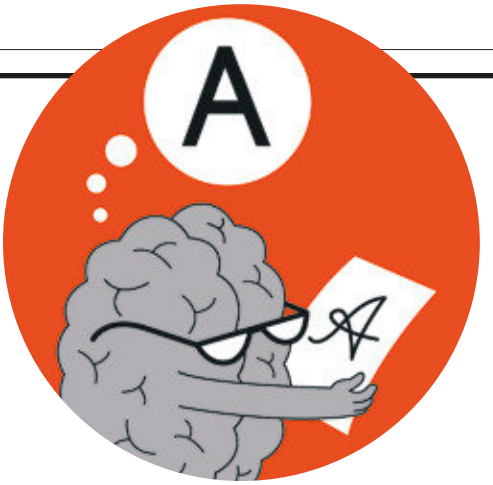
ANTARCTICA
Researchers reported the first clear evidence that the ozone layers above Antarctica are replenishing. They expect the current ozone hole, which was created by the use of now banned chlorofluorocarbons (CFCs), to close by 2060.

For more details, visit
www.ScientificAmerican.com/sep2016/advances

NEUROSCIENCE

We All Speed-Read

The brain doesn't sound out words it already knows



When children first learn to read, they painstakingly sound out every letter—C-A-T—before mentally stringing them together and connecting the result to a word and its meaning. With practice, however, we begin to recognize words on sight. In fact, our brain compiles a visual dictionary that is housed in the rear temporal lobe, adjacent to the area that recognizes faces, according to a new study published in *Neuroimage*. This dictionary eventually supersedes the responsibilities of the brain's phonics center, the researchers say, and is critical to becoming an advanced reader.

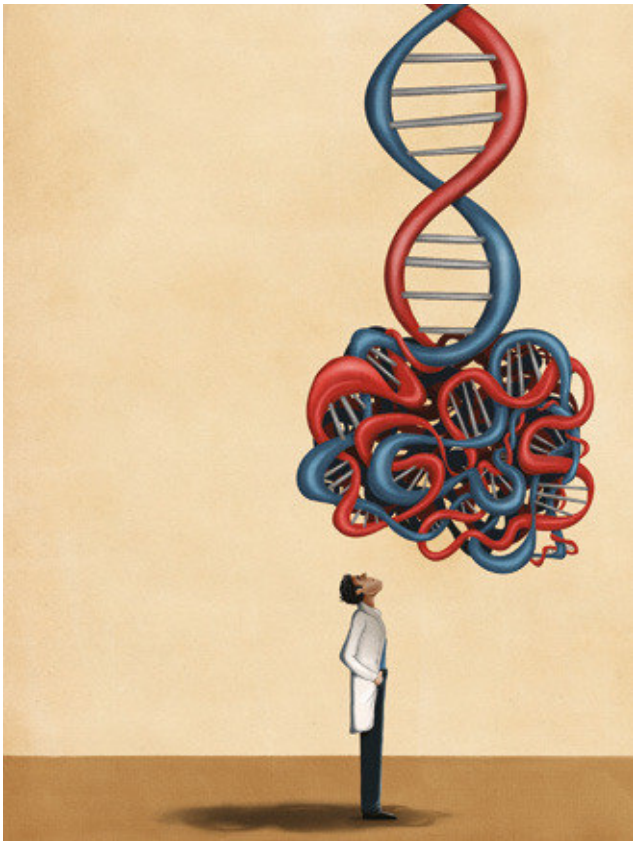
Laurie Glezer, a postdoctoral research fellow at San Diego State University, and her colleagues analyzed the brain activity of 27 participants—all native, monolingual English speakers reading at an advanced level—as they read homophones, words that sound alike but have a different meaning, such as "hair" and "hare." They found that the homophones activated different groups of neurons in the rear temporal lobe—an observation that suggests separate visual "entries" for the words. The same group of neurons would have lit up if the brain was sounding the homophones out.

"From this work it looks as if there are regions that are separately computing these visual and phonological aspects that are both incredibly important for reading," Glezer says.

The study's results could inform new teaching techniques. "In the debate about what's the best way to learn to read, there's this idea that phonics is the way to go," says Maximilian Riesenhuber, who leads the Laboratory for Computational Cognitive Neuroscience at Georgetown University Medical Center and is a co-author of the paper. This study refutes that idea, he adds, because it shows that skilled readers build up a visual vocabulary that they tap into when viewing a familiar word as a whole.

Similarly, the research may offer insight into dyslexia, notes Fumiko Hoeft, a psychology professor at the University of California, San Francisco, who was not involved in the study. For instance, perhaps people with this reading disorder have problems developing or accessing the visual dictionary. At this point, however, it is "hard to say where the breakdown is," Glezer says. She is now planning similar studies involving subjects who are dyslexic and others who are deaf—individuals who also tend to have trouble learning to read.

—Roni Jacobson



Cancer Gene Tests Provide Few Answers

Despite progress, genetic profiling of tumors has a long way to go

By Jessica Wapner

Genetic tests for cancer have come a long way since they first entered the clinic in 1995. Back then, mutations in two genes—known as *BRCA1* and *BRCA2*—hinted at the crucial role that genetics can play in treatment decisions. Women carrying one of those mutations (and having a family history of breast or ovarian cancer) were much more likely than the general population to develop tumors in their breasts or ovaries. Then, as now, some of these women opted to have their breasts and ovaries removed before any malignant growths could arise.

In the intervening decades, researchers have come to recognize that most cancers are driven largely by abnormalities in genes. Genetic analysis of tumors has, therefore, become standard practice for many malignancies—such as breast, lung and colon cancer—because the information may help guide therapy. Clinicians have amassed a modest arsenal of drugs able to counteract some of the most common mutations.

Jessica Wapner is a science writer and author of *The Philadelphia Chromosome: A Genetic Mystery, a Lethal Cancer, and the Improbable Invention of a Lifesaving Treatment* (The Experiment, paperbound, 2014).

Yet many patients learn that their cancers have mutations for which no drug exists. In fact, the roles many of these genetic changes play in cancer growth are poorly understood. Complex analyses of DNA done across a range of cancer types have revealed a landscape rife with genetic mutations, and very little of this encyclopedic information is helping doctors to make treatment decisions. To date, the U.S. Food and Drug Administration has approved just 29 tests for specific mutations that can directly influence therapy.

Several major research collaborations are now making heroic efforts to identify more mutations that can serve as drug targets and to collect the information that will allow doctors to match many more patients with such targeted therapies. And earlier this year President Barack Obama announced the National Cancer Moonshot, a $1-billion initiative that includes funding for such efforts. The task is so large and complicated, however, that the gap between genetic knowledge and patient benefit is likely to widen for some time before the promised revolution in care becomes a reality for most people afflicted by cancer. "We're in a transition period," says Stephen Chanock, who directs the Division of Cancer Epidemiology and Genetics at the National Cancer Institute.

DRIVERS VS. PASSENGERS

THE GENETIC CHANGES that eventually trigger cancerous growth fall into two main groups. First, there are hereditary germ-line mutations, which people inherit from their parents. Second, there are somatic mutations, which arise over the course of one's life as a result of advancing age, cigarette smoking or other environmental influences. Although hereditary changes in DNA often lead to aggressive tumors, including some childhood cancers, these kinds of germ-line mutations are relatively uncommon. The vast majority of human cancers arise from somatic mutations.

Most somatic mutations turn out to be harmless; many are even repaired by the body's own quality-control processes. But some manage to wreak havoc, causing cells to reproduce uncontrollably. Many genes code for proteins, which do much of the work in cells. In the case of cancer, the harmful mutations tend to result in proteins that either actively promote excessive replication or fail in their usual job of putting the brakes on cell proliferation.

Researchers refer to the abnormal changes that are integral to a tumor's growth and survival as driver mutations; the others are known as passenger mutations because they appear to be unimportant and seemingly are just along for the ride. No one knows how many driver mutations are needed to promote each of the different kinds of cancers. One study determined that the average tumor requires as few as two or as many as eight driver mutations, whereas other studies found that tumors may frequently contain as many as 20 driver mutations.

Illustration by Charlie Padgett

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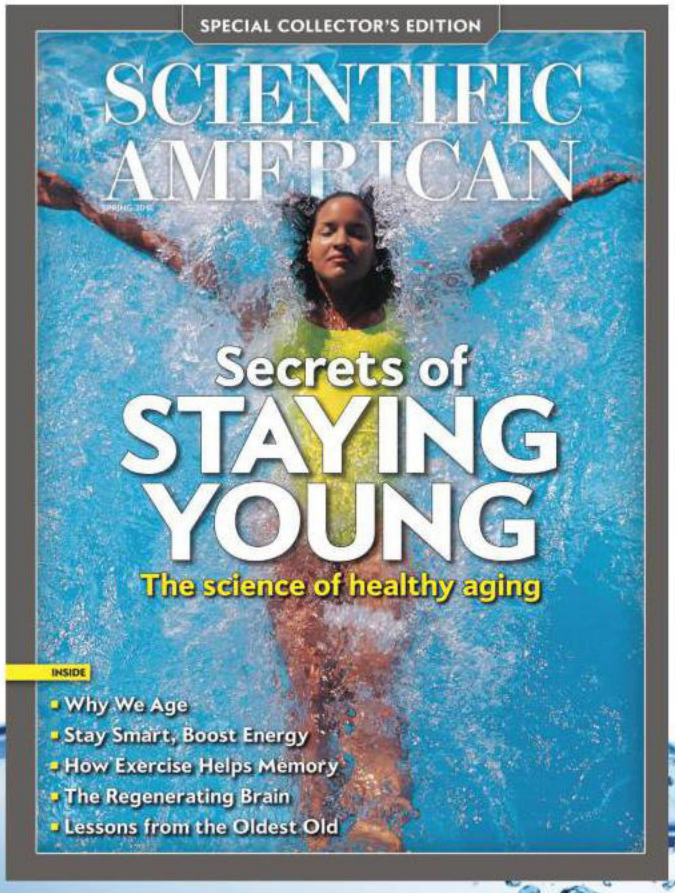

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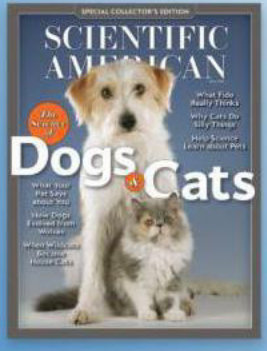

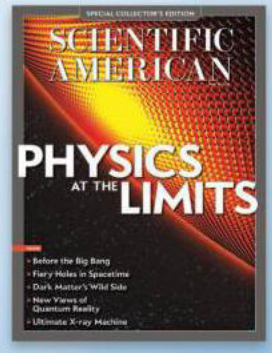

EARLY SUCCESSES

DESPITE THE DIFFICULTIES of figuring out which genetic mutations are important in a given tumor, researchers began making progress in targeting specific cancer mutations by the late 1990s. Among the first such treatments were imatinib mesylate (brand name Gleevec), which undermines a common driver of chronic myeloid leukemia, and trastuzumab (brand name Herceptin), which addresses the *HER2* mutation responsible for about a quarter of breast cancers. Other customized therapies soon followed.

For the past three years patients with lung cancer have routinely been tested for an abnormality in a gene known as *ALK*. In as many as 7 percent of such patients, a genetic mistake that melds the *ALK* gene with another gene yields an abnormal protein that drives the tumor's growth. Drugs that block this mutant protein typically do a better job than standard chemotherapy at slowing the disease. Patients with normal *ALK* genes in their tumors do not benefit from anti-*ALK* drugs at all.

Routine genetic tests have also helped people with melanoma, a form of skin cancer. About half of patients with melanoma have a mutation in the *BRAF* gene, which plays a role in the spread of cancer from the tumor to other parts of the body. In 2011 the FDA approved the first drug that inhibits the mutant BRAF protein. A recent study found that nearly 80 patients with metastatic melanoma who responded to the new treatment lived for an average of two years, much longer than the 5.3 months typically seen in such patients whose skin cancer has spread.

Sometimes a particular mutation allows doctors to steer clear of prescribing certain drugs. For example, colorectal cancers with mutations in the *KRAS* or *NRAS* gene typically do not respond to particular medicines because these genetic changes render those agents ineffective.

But there are several obstacles to further progress. Finding a genetic abnormality in a cancer is not enough—the aberration must be integral to the cancer's growth and survival. A reliable test for the mutation and a treatment that can exploit the mutation must exist. These requirements, it turns out, are a very tall order. Beyond the difficulty of figuring out which mutations drive the cancer, researchers also need to know which mutations tend to act later on. As a tumor grows, new mutations may appear. Each crop of abnormalities means separating the drivers from the passengers all over again, so that if one drug stops working, a subsequent genetic test can steer physicians to the next option.

Creating drugs to block driver mutations, likewise, is no small feat. Many abnormal proteins encoded by somatic mutations sit on the surface of cancer cells, within easy reach of drugs. But others are buried deep within cells, and compounds small enough to slip inside a cell are typically too small to stick to their target proteins. This conundrum has left the most common driver mutations, such as *p53, RAS* and *MYC,* impossible to combat.

And the drugs that do successfully target somatic mutations have often led to meager extensions in survival time. If a single drug targeted to a specific driver mutation manages to shrink a tumor but leaves even one cell resistant to the drug behind, that cell can proliferate and create additional tumors unresponsive to the medicine. It may be, then, that certain cancers, as is true of HIV, will need to be treated with multiple drugs. Yet each drug that is added will come with its own costs and potential side effects. Researchers will need to figure out the optimal strategies.

The rarity of many somatic mutations also slows the transition from the laboratory to the clinic. Some mutations occur in less than 1 percent of patients with a certain type of cancer. Evaluating whether a drug could possibly address that mutation requires a clinical trial, but finding enough patients willing and able to enroll in such a study can take a long time.

NEW DIRECTIONS

ALL THESE CHALLENGES are spurring research methods, drug designs and infrastructure meant to hasten the expansion of precision genetic medicine. The approaches are also taking into account a new realization. Traditionally cancer has been defined by the location of where it first arose in the body—for example, in the breast or lung. But it turns out that mutations known to drive a particular type of malignancy in one part of the body are sometimes involved in cancers typically found elsewhere in the body.

Defining cancer not only by its body part but also its genes is prying treatment options loose from old restrictions. A drug conventionally used for one cancer may turn out to work in another driven by the same abnormality. When the drugs trastuzumab and lapatinib, approved for breast cancer harboring a *HER2* mutation, were given to a group of patients with late-stage colorectal cancer with the same mutation, for example, nearly half lived for about a year, an unusually long time. Although such connections are still rare and preliminary, they indicate that it may be time to reconsider standard definitions of cancer.

The NCI launched one of the new collaborations—called MATCH—in August 2015. This study, which expects to enroll 840 volunteers, aims to provide the data needed for doctors to prescribe drugs to more patients based on tumor genetics. DNA from up to 5,000 tumor specimens will be sequenced to find suspicious abnormalities with matching gene-targeted drugs. When the trial started, eligible patients received one of 10 gene-drug combinations; that number has now expanded to 24. Meanwhile the American Association for Cancer Research has put an initial $2 million into a two-year project called GENIE, which will collect both tumor gene profiles and medical results for many thousands of patients from seven major cancer centers in the U.S. and Europe. This registry aims to provide information that investigators can use for many purposes, including identifying more mutations that might be amenable to targeted drugs and finding markers that can help with diagnosis or staging of tumors.

These and other efforts augur well for future improvements in genetically customized care for cancer patients. At present, however, they are dogged by skepticism about how quickly they will lead to meaningful changes. In addition, the push for targeted drugs could be undermined if pharmaceutical companies shift their focus to other up-and-coming approaches, such as immunotherapy. For now the gulf between the promise of precision medicine and the reality remains frustratingly large. SA

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David Pogue is the anchor columnist for Yahoo Tech and host of several *NOVA* miniseries on PBS.

What to Do with All Those Cassettes

Bite the bullet and have them digitized—I wish I'd done it sooner

By David Pogue

I hereby stick out my tongue at everyone who's ever accused me of filming too much.

Yes, I was that dad with a camcorder, on every vacation, at every birth, wedding and graduation as my kids grew up. More times than I can count, I've been chastised for "hiding behind that damn machine instead of living the moment" and told that "you'll never even watch those tapes."

Even Steve Jobs essentially said I was an idiot. (I had reviewed a new version of the MacBook and had criticized it for no longer including the port that allowed you to upload, and thus edit, videotape from a camcorder. Jobs called me at home to inform me that nobody used tape camcorders anymore and that if I truly thought that I would someday edit down all my tapes, I was deluded.)

But for decades, all of those people were pretty much correct. Recording video was easy. Watching it, though, was hard. Nobody wants to see raw, unedited home movies—but editing them is a time-consuming pain. So what happens? The world's VCR and camcorder tapes sit, at this moment, rotting in boxes.

And I mean rotting. Depending on the storage conditions, magnetic recording tapes might start degrading after 10 or 20 years.

Deep down, your conscience knows that you should rescue them before they're gone. But doing that yourself requires technical expertise, playback equipment you may no longer have, and free time that you almost *certainly* don't have. Sending it all out for conversion is convenient and usually yields better results, but it's pricey—usually $12 to $20 a tape. Worse, and bizarrely, most of today's conversion outfits transfer your old tapes onto DVD-R discs—which *themselves* begin to "rot" in as little as 10 years—instead of digital files that you can store online or on hard drives.

Not all of them, though, so I finally bit the bullet and shipped my 275 audio and videotapes to a company that converts them to digital. (You've still got plenty of choices: You can bring in your tapes in a box to Costco and Walmart, for example; they send them on to YesVideo for conversion. I sent mine to Southtree, a huge conversion facility in Tennessee. Almost all of them work the same way—playing your tape in regular old VCRs, in real time. It takes two hours to convert a two-hour video.)

When it was all over, I had a hard drive that could have been named "My Life, 1979–2010." It teemed with neatly labeled folders containing the digital conversions of all those videos. I rapidly fell down a time-suck rabbit hole, double-clicking, fast-forwarding, reliving.

Until you go through it, you can't imagine how powerful an experience this is—the closest you'll ever come to having a time machine. There you are, and your family and friends, in younger days. You see which parts of your character and personality have always been present and which were cultivated as you grew. You may even let yourself off the psychological hook in certain deep-seated ways; maybe you discover you weren't quite the naive doofus you've always imagined you were back then, or you realize some disastrous performance wasn't actually as bad as you remember it.

In digital form, videos are incredibly easy to edit. You can snip out the boring parts in seconds and post to YouTube with a click. I sent notes to old classmates, co-workers and family members, treating them to private YouTube links for resurrected scenes that I knew would delight them.

My children were blown away. They're encountering the concept of home movies for the first time, as teenagers. They're fascinated to see their relatives with dark hair and no wrinkles and themselves as tiny tots.

So I encourage you, right here, in writing, to rescue your family's videotapes (and films, and slides, and prints). You can't imagine the freaky sense of time travel and second youth it will bring you to watch them. SA

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Illustration by Tim Peacock

1

WHAT MARK WILL WE LEAVE ON THE PLANET?

By Jan Zalasiewicz

A HISTORY IN LAYERS

Photograph by Andrew Myers

Jan Zalasiewicz is a professor of paleobiology at the University of Leicester in England and is chair of the Anthropocene Working Group of the International Commission on Stratigraphy. He has a particular fondness for graptolites—an extinct form of plankton.

The idea was born in Mexico, in the year 2000. It was pure improvisation, by Paul Crutzen, one of the world's most respected scientists. The Dutch scholar was widely known for arguing that all-out atomic war would trigger a "nuclear winter" lethal to plant and animal life across the earth, and he had won a Nobel Prize for research into another global threat: human-caused destruction of the earth's ozone layer.

IN BRIEF

Humans have altered the earth's systems, yet scientists are debating whether the changes will leave permanent signatures in geologic layers of rock, which define formal epochs and eras.

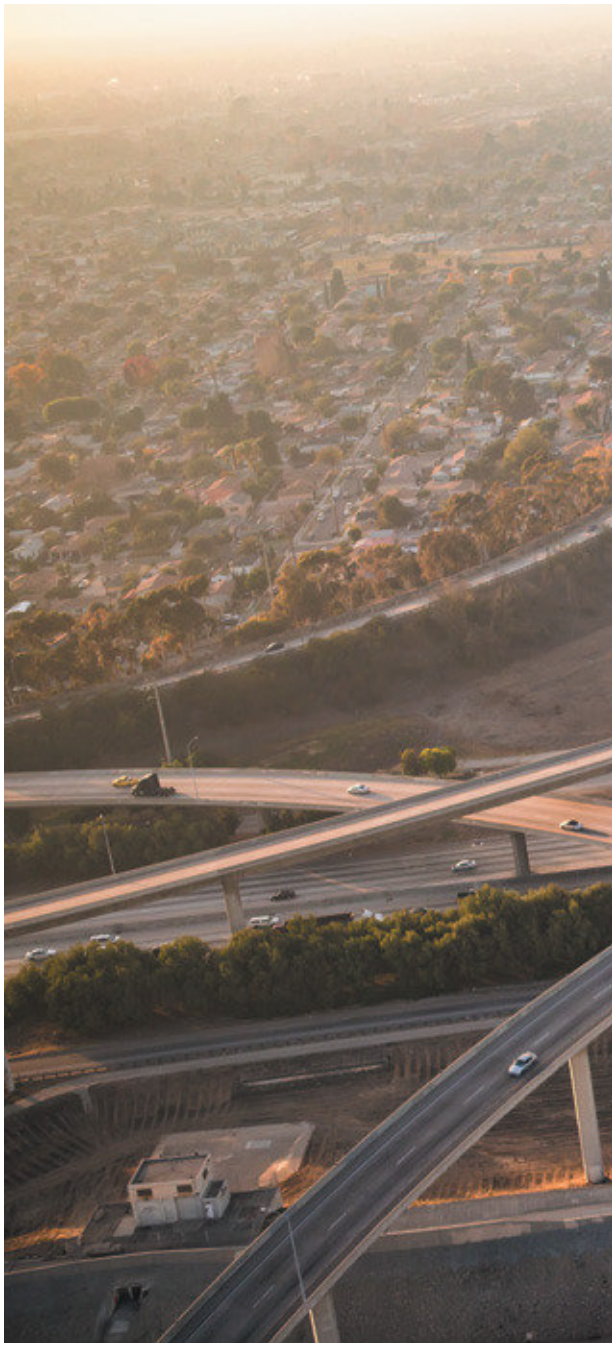
We have spread aluminum, plastics, concrete, carbon particulates (from burning fossil fuels), insecticides and radioactive particles (released by nuclear bombs) widely across the landscape and oceans—all evidence favoring the declaration of a new Anthropocene epoch.

Questions remain about whether such an epoch would have begun thousands of years ago, when human impacts were first discernible, or may only begin at some future time, when the full impact of humans will have played out.

In Mexico he was listening to experts discuss evidence for changes in the global environment that had occurred throughout the Holocene, a distinct epoch that geologists say began 11,700 years ago and continues today. Growing visibly more frustrated, he burst out: "No! We are no longer in the Holocene. We are in"—he paused to think—"the Anthropocene!"

The room went silent. The term had apparently hit home. And it kept coming up, again and again, for the rest of the meeting. That year Crutzen co-wrote an article with Eugene Stoermer (since deceased), a specialist in microscopic algae called diatoms who had independently coined the term "Anthropocene" some years earlier. The evidence, the two men said in the article, was clear: industrialized humanity had changed the composition of the earth's atmosphere and oceans and had modified the landscape and biosphere—including diatom populations. We were living on a new human-driven earth, quite different from the old one. Spurred by Crutzen's prestige and vivid, persuasive writing, the concept spread rapidly among the thousands of scientists in the International Geosphere-Biosphere Program, which had sponsored the Mexico meeting. "The Anthropocene" began to appear in scientific papers around the world.

But was this really *geologic* change—change so profound that its signals are imprinted into geologic strata across the planet? Could humans really wreak change as dramatic as the transformations that started the Holocene 11,700 years ago, when extensive glaciers covering much of the earth were retreating, melting so much they raised sea level globally by 120 meters? Were human influences on the dirt beneath our feet as significant as when the Pleistocene epoch began, 2.6 million years ago, as the Ice Age tightened its grip? Could human effects only a few centuries old truly be measured alongside the great shifts of our planet's tumultuous geologic past, where time units are measured in millions—and even billions—of years?



The idea had appeared before. In the 19th and early 20th centuries scholars such as Italian cleric Antonio Stoppani and American naturalist Joseph LeConte floated terms such as Anthropozoic and Psychozoic, but geologists were dismissive, even scathing. How could human activity—no matter how impressive—compare with profound changes such as the creation and destruction of entire oceans and mountain ranges, massive volcanic eruptions and monstrous collisions by incoming meteorites? Against such a scale, human actions appeared fleeting and ephemeral.

There was another problem, too. Geologic terms such as Jurassic, Cretaceous, Pleistocene and Holocene are not just labels. They are formal names that are part

PAGE 30: PROP STYLING BY ANGELA CAMPOS; *Stockland Martel*; THIS PAGE: GETTY IMAGES

HUMANS are paving paradise, transforming the planet's strata and defining a new geologic epoch: the Anthropocene.

of a complex geologic time scale that fundamentally characterizes how the earth evolved, thrived and struggled over 4.6 billion years. The names were accepted only after decades of evidence gathering and discussion by the International Commission on Stratigraphy. "Epochs" and the "eras" they belong to have specific technical meanings, and geologists take them seriously. Declaring a new epoch would imply that scientists believe humans were altering the course of the earth's evolution.

The Anthropocene had gone through none of the usual assessments. And esteemed as Crutzen is, he was an atmospheric chemist working on environmental stresses, not a geologist who was an expert in rock strata. Yet by 2008 members of the Stratigraphy Commission of the Geological Society of London realized that the term was increasingly being used in the literature as if it *were* a formal epoch. The society decided it had to confront the trend.

This cautious and conservative group meets in the old-world Council Room in London's Burlington House, complete with solemn portraits on the walls, where Victorian giants of the sciences such as Charles Darwin once walked. In this heavily traditional setting, the scientists began the geologic assessment of the Anthropocene. Perhaps to their own surprise, most of them agreed that the term "had merit" as a potentially formal unit of the proper geologic time scale and should be examined. Geologist Philip Gibbard, who also chaired the Interna-

MOUNTAINS of plastics in Jakarta and of concrete in New York City will persist long enough to permanently impregnate the earth's crust.

tional Commission on Stratigraphy's Subcommission on Quaternary Stratigraphy—which has power over the geological time scale—proposed a working group that has been exploring the question ever since.

To make a case, scientists must show that human impacts will leave a clear mark, fossilized in strata, that could be readily recognized tens or hundreds of millions of years from now by some geologist in the far future. The focus on strata is important. To a geologist, geologic strata *equal* geologic time. The key is a "time-rock" interval—a layer of strata that can be hammered, sampled or dug in (as for dinosaur bones) and that defines a new course of history. For the Anthropocene epoch to have such deep geologic meaning and to have any chance of being made formal, it must show its own time-rock unit. Is there enough evidence to pass muster? One could make a good case.

ROCKS AND 'OIDS

LET'S START WITH MINERALS, the fundamental components of rocks. Metals, for example, are almost always bound up in various oxides, carbonates and silicates (with rare exceptions such as gold). Humans have learned to separate metals out of these compounds, in huge quantities. We have manufactured more than 500 million metric tons of aluminum since World War II, enough to coat the entire U.S. in kitchen foil. As we scatter billions of cans, appliances, cigarette pack liners and other refuse across the landscape and into landfills, pure aluminum is becoming part of modern sediment layers.

The last great rise in mineral forms occurred about 2.5 billion years ago, when the earth's atmosphere became oxygenated. The event produced an array of oxides and hydroxides, including rust—which, incidentally, changed the color of the landscape from gray to red. But humans have now created another great rise by synthesizing many mineral compounds, such as tungsten carbide, common in tools and ballpoint pens. Perhaps the most striking inventions are "mineraloids" such as glasses and plastics. Before WWII plastics were limited to a few products such as shellac, Bakelite and rayon, but after the war they rocketed to the 300 million metric tons now made annually—roughly equivalent to the total human body mass. The qualities we find so useful in plastics—durability and resistance to decay—mean that they persist in the environment for many years.

The signature of plastic litter in the ground is strong enough, but it is even more geologically significant in the oceans. Because many sea creatures eat plastics, much of it ends up in the muds of the seafloor when the animals die—a first step to fossilization. Invisible to our eyes but more pervasive still are microplastics, such as the fibers detached from synthetic clothes. Even on remote ocean floors, far from land, researchers are finding thousands of fibers in every square meter of mud.

Human-made rocks are everywhere, too. For sheer bulk, concrete now reigns supreme; we have manufactured something like half a trillion metric tons to date. That is about a kilogram of concrete for every square meter of the earth's surface. Concrete forms the superstructures of our buildings, roads and dams, and broken-up fragments are now common in the turned-over ground underneath our towns and cities. It is already a signature rock of the Anthropocene, together with human-made bricks and ceramics. The enormous masses of the rocks we make impregnate the top part of the earth's crust, which we are also redistributing as big machines dig and plow soil to construct buildings and grow food. Humans now shift more sediment than natural forces such as rivers and wind do.

CHEMICAL FINGERPRINTS

IN THE PAST CENTURY or so, the burning of fossil fuels has largely powered the accelerated production and plane-

ULET IFAQNSASTI Getty Images

GEORGE HAMMERSTEIN *Getty Images*

tary deposition of new strata materials such as aluminum, plastic and concrete. The by-products of combustion are themselves so voluminous that they, too, leave a variety of chemical signals in sediments worldwide. The rise of carbon dioxide in the atmosphere since the industrial revolution began is about 100 times faster than the rate of rise when the glaciers retreated at the start of the Holocene. The emissions are captured and recorded in bubbles of air trapped in layer on layer of snow and ice frozen in the world's polar caps.

Combustion also produces smoke—incompletely burned particles that are tiny and inert. Falling to the ground worldwide, they form a geologically lasting smoke signal. The fires ignited by the meteorite impact that defines the boundary between the Cretaceous and Tertiary intervals left a similar trace in the rocks. The carbon from burned fossil fuels is also distinctly rich in the light carbon 12 isotope (^{12}C), which plants and animals readily absorb. As these life-forms die, they will be fossilized, leaving a permanent ^{12}C mark of the Anthropocene.

Widespread agriculture is casting its own chemical shadow. Humankind started farming about 10,000 years ago, but only since the early 1900s have farmers applied vast quantities of nitrogen fertilizer, extracted from the air by a technique known as the Haber-Bosch process, together with phosphorus dug from the ground. The enormous perturbations in soil, water and air leave clear chemical signatures. Lakes at high latitudes become polluted by these compounds, blown in by winds from distant farming regions. Fertilizer runoff from farm fields into streams and rivers and out to the sea overstimulates plankton production; as the huge blooms die and decay, they create "dead zones" that now suffocate seafloor life over hundreds of thousands of square kilometers every year. The devastated marine biology will tell its story as fossils in future strata.

Other chemical signals include persistent organic pollutants such as insecticides and toxic industrial chemicals such as dioxins, which now contaminate many sediments. Some of these may persist over geologic time scales, as did the long-chain carbon compounds produced by some ancient algae that paleontologists now use as tracers of climate tens of millions of years ago.

Tiny radioactive particles that spread around the globe after every nuclear bomb explosion are also detectable. Although only a couple of such bombs were dropped as part of war, various countries detonated more than 500 test bombs in the atmosphere between the mid-1940s and the late 1990s. The particles fell into soil, polar ice and seafloor sediment alike, and they were absorbed by animals and plants at the surface. This radioactive layer is one of the most abrupt Anthropocene signatures.

FOSSIL TRANSITIONS

WE HUMANS have obviously left our mark on the earth's biological landscape as well. In particular, our species—a very minor player amid the planet's biota even a few thousand years ago—is now the dominant predator on land and sea. We appropriate roughly a quarter of the earth's total biological production for our needs. As a result, we make up about a third of the mass of all land vertebrates (based simply on body weight), and the handful of animal species we have engineered to become our food make up most of the other two thirds. Wild animals, pushed to the margins, constitute 5 percent or less. In colonizing so much of the planet's land, we have comprehensively reshuffled what is left of wildlife, too, purposely or accidentally transporting animals and plants across the

TOP SCIENTISTS PREDICT OUR FUTURE

DOES HUMANITY HAVE A FUTURE BEYOND EARTH?

"I think it's a dangerous delusion to envisage mass emigration from Earth. There's nowhere else in the solar system that's as comfortable as even the top of Everest or the South Pole. We must address the world's problems here. Nevertheless, I'd guess that by the next century, there will be groups of privately funded adventurers living on Mars and thereafter perhaps elsewhere in the solar system.

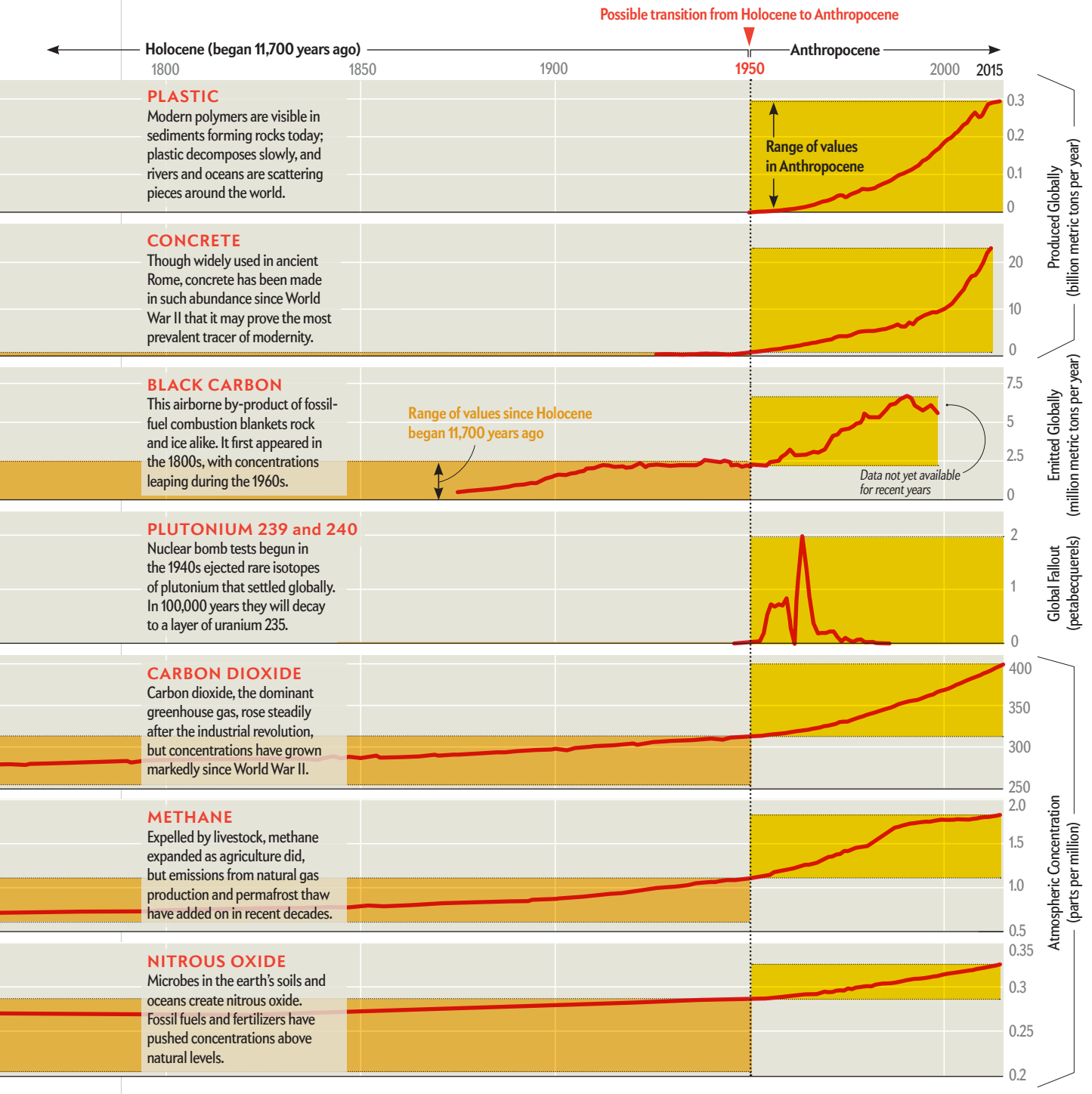
We should surely wish these pioneer settlers good luck in using all the cyborg techniques and biotech to adapt to alien environments. Within a few centuries they will have become a new species: the posthuman era will have begun. Travel beyond the solar system is an enterprise for posthumans—organic or inorganic.

MARTIN REES
British cosmologist and astrophysicist

Portrait by Kyle Hilton

When Did the Anthropocene Begin?

The detritus of modern humanity is so pervasive that our "techno-fossils"—such as plastic and concrete—will permeate the rock that is forming today. Mounting evidence collected by scientists supports the idea that human activity has pushed the planet into a new geologic epoch: the Anthropocene. They say the epoch will prove distinct from the Holocene, which began when glaciers retreated 11,700 years ago—and that 1950 may be the logical threshold between the two. Markers of the Anthropocene (*shown below*) have spread across the globe, says Colin Waters of the British Geological Survey. "We've in effect become a new geologic force." —*Katie Peek*



SOURCES: "THE ANTHROPOCENE IS FUNCTIONALLY AND STRATIGRAPHICALLY DISTINCT FROM THE HOLOCENE," BY COLIN N. WATERS ET AL., IN *SCIENCE*, VOL. 351; JANUARY 8, 2016; AND REFERENCES CONTAINED THEREIN; U.S. ENVIRONMENTAL PROTECTION AGENCY

Graphic by Katie Peek

globe, homogenizing biology worldwide. We are also killing so many species that in another century or two the planet's biodiversity could take as catastrophic a hit as the one that happened when the dinosaurs disappeared. These transformations will show up in the distant future as a switch from one assemblage of fossils to another.

Humans have meanwhile taken the manufacture of "trace fossils"—such as footprints by dinosaurs and burrows by sea worms—to completely new levels. Our mines and boreholes penetrate several kilometers into the ground, so deep that these traces permanently scar the planet. The towns and cityscapes that have made over the earth's surface are also mirrored in subsurface foundations, pipelines and subway systems.

PERMANENT OR FLEETING?

ALL IN ALL, we humans have left a formidable catalog of new geologic signatures. Will these effects *permanently* reconfigure the earth's strata and future history, defining a formal new epoch? Or, with humans gone, will the earth system spring back to normal, eroding our constructions into dust, like the fate of the mighty Ozymandias empire in Percy Bysshe Shelley's poem of the same name? It is still early days.

Luckily, four billion years of strata have left us a few lessons. Where the earth's crust is rising, such as on growing mountain ranges, surface structures are indeed eroded and washed away as sedimentary particles into some far-off sea. Where the crust is subsiding—as below many of the world's major deltas—the strata piling up can preserve even seemingly ephemeral traces, such as leaves, twigs and footprints. Therefore, San Francisco, pushed up by tectonic forces, seems destined to be weathered away. Sinking New Orleans, Shanghai and Amsterdam, however, will leave ample traces of their massive, complex structures, together with aluminum, plastic, ceramics—and skeletons with metal-filled teeth and artificial hips. When these strata are ultimately pushed up high by tectonic forces, millions of years from now, the newly minted cliffs will reveal a distinctive Anthropocene layer.

The permanence of fossils, and of long-term consequences of our actions, figures in the answer, too. The meteorite strike that ended the Cretaceous period was instantaneous; the immediate shock wave was over in hours. But its effects reshaped biology for millions of years, and the reverberations are still with us today. Without that meteorite we might not be here now; dinosaurs might still be ruling the earth.

Humanity's impact, swift though not that sudden, could likewise change the planet in ways that will be felt long after we disappear. Many trends are accelerating, and some—species extinction, climate change and sea-level rise—are only in their early stages. Regardless of when the fossil-fuel era finally ends, its effects will diminish only slowly, over many millennia. (And human civilization, which developed in the environmentally stable Holocene, will have to adapt to an unstable, changing planet for many generations.)

We may exert a long-term influence in another way as well. Humanity is a much more complex, protean planetary force than a meteorite strike or glacial retreat. Our extraordinary geologic power is driven by our intelligence, our manipulative ability and our hypersocial interactions that pass on new knowledge. These traits have allowed us to develop the technology that now keeps us alive, and that itself is evolving at an accelerating rate, literally from year to year.

This emergent technosphere, as Duke University professor emeritus Peter Haff calls it, can be considered an outgrowth of the biosphere. It has its own dynamics, over which we have only partial control. It includes the possibility that a silicon-based intelligence could soon vie with our own. Among all the ongoing global changes that will determine the geologic future of the earth, the technosphere is the wild card. It could produce a revised Anthropocene planetary state—only humans may no longer be calling the shots. For now scientists can decide only how to characterize the present. Should an earth that is rapidly, profoundly and permanently being transformed by humans be formally recognized in a new epoch in the geologic timescale?

For the geologists who would make the determination, the jury is still out. Important decisions need be made. When would the Anthropocene have begun, for instance? Suggestions have ranged from thousands of years ago, when human impacts first became discernible, to far into the future, once our impacts are fully expressed. For practical purposes, the most suitable boundary seems to be the extraordinary "great acceleration" of population, energy use and industrialization begun in the mid-1900s. Strata after that time are marked by strong rises in concrete, plastics, plutonium and the remains of a transformed biology.

Geologists are searching for a suitable "golden spike"—a carefully selected reference that serves as a global marker for a new epoch. Would that be provided by the radioactive nuclei or carbon particles trapped in the snow and ice layers of Greenland and Antarctica, in sediment layers in far-flung lakes and fjords, and on undisturbed seafloors? Or might it be some other indicator, a telltale change in living chemistry preserved within tree rings and annual coral growth bands? The hunt is on. SA

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2 HOW WILL CLIMATE CHANGE US?

By Katie Peek

COPING SKILLS

No one knows whether human consciousness will reside on a computer chip by the end of the century or even if self-driving cars will rule the road. But this much is certain: Earth is going to get hotter. The maps displayed here forecast how much warmer our planet will be in the year 2100 and how precipitation patterns will change. To make the figures, *Scientific American* worked with earth scientists at the NASA Ames Research Center. The researchers used high-resolution climate models from the Intergovernmental Panel on Climate Change to generate climate data for nearly every point on the planet, for every month of every year, through the end of the century. Our graphic presents a middle-of-the-road emissions scenario—it assumes that the world curbs greenhouse gases by midcentury but that substantial warming still takes place.

An estimated 10 billion people will inhabit that warmer world. Some will become climate refugees—moving away from areas where unbearable temperatures are the norm and where rising water has claimed homes. In most cases, however, policy experts foresee relatively small movement within a country's borders. Most people—and communities, cities and nations—will adapt in place. We have highlighted roughly a dozen hotspots where climate change will disrupt humanity's living conditions and livelihoods, along with the strategies those communities are adopting to prepare for such a future.

NEWTOK, ALASKA, U.S.

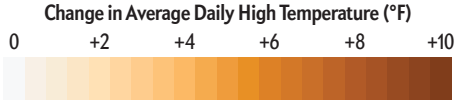
If current predictions play out, the Arctic will see more dramatic warming than anywhere else on Earth. The Eskimo village of Newtok is already facing the effects, as coastal storms and thawing permafrost have worn away the land it is built on. The town's roughly 400 residents voted in 2003 to relocate to higher ground nine miles away, but progress has been slow as residents try to secure approval and funding for roads, houses and an airport at the new site. Newtok's plight shows that even when a community wants to move, bureaucratic barriers can make the shift difficult.

TUVALU

As seas rise, low-lying island nations may seem like goners—and indeed, the president of the Maldives is trying to relocate much of his country's population. But geomorphologists in New Zealand have found that the atolls in Tuvalu—a nation of 11,000 people all living within 16 feet of sea level—are instead expanding. Storms and tides erode the shorelines in some places but create land in others when they deposit sand and gravel. On Tuvalu, villages may face the biggest challenge, as they try to reconcile their built environment with shifting landforms.

KEY

Maps show how much the average daily high temperature and annual rainfall are expected to shift by the end of the 21st century. Present-day values are based on an average from 2006 to 2010; future values are based on a projected average from 2091 to 2100. The data shown reflect averages across 20 models of what is called the RCP 4.5 prediction scenario, in which greenhouse gas emissions peak in 2040 and then decline. (Heating will continue to increase long after emissions drop.)

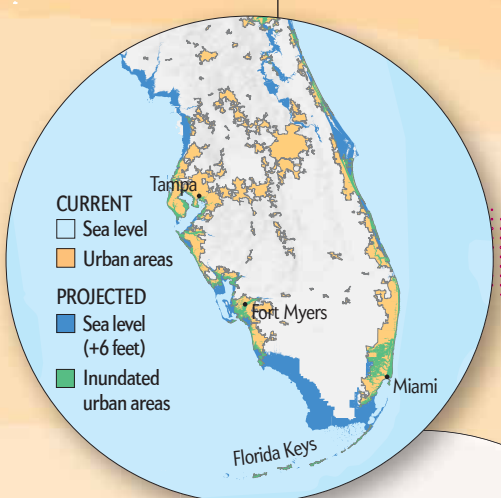


SOURCES: NASA EARTH EXCHANGE GLOBAL DAILY DOWNSCALED PROJECTIONS (NEX-GDDP) (*main map and monsoon insets*); NOAA OFFICE FOR COASTAL MANAGEMENT (*Florida inset*)

WESTERN U.S.

Over the next century wildfires will occur more routinely and rage more intensely—a trend already apparent in much of western North America, which is growing warmer and drier. Such fires threaten human lives and property. To adapt, experts say forest managers will need to thin high-risk woodlands, and homeowners and engineers will need to build with fire-safe materials and design fire-resistant landscaping.

Katie Peek, formerly the information graphics editor at *Popular Science*, is a science journalist and data-visualization designer. Peek also holds advanced degrees in astrophysics.



FLORIDA, U.S.

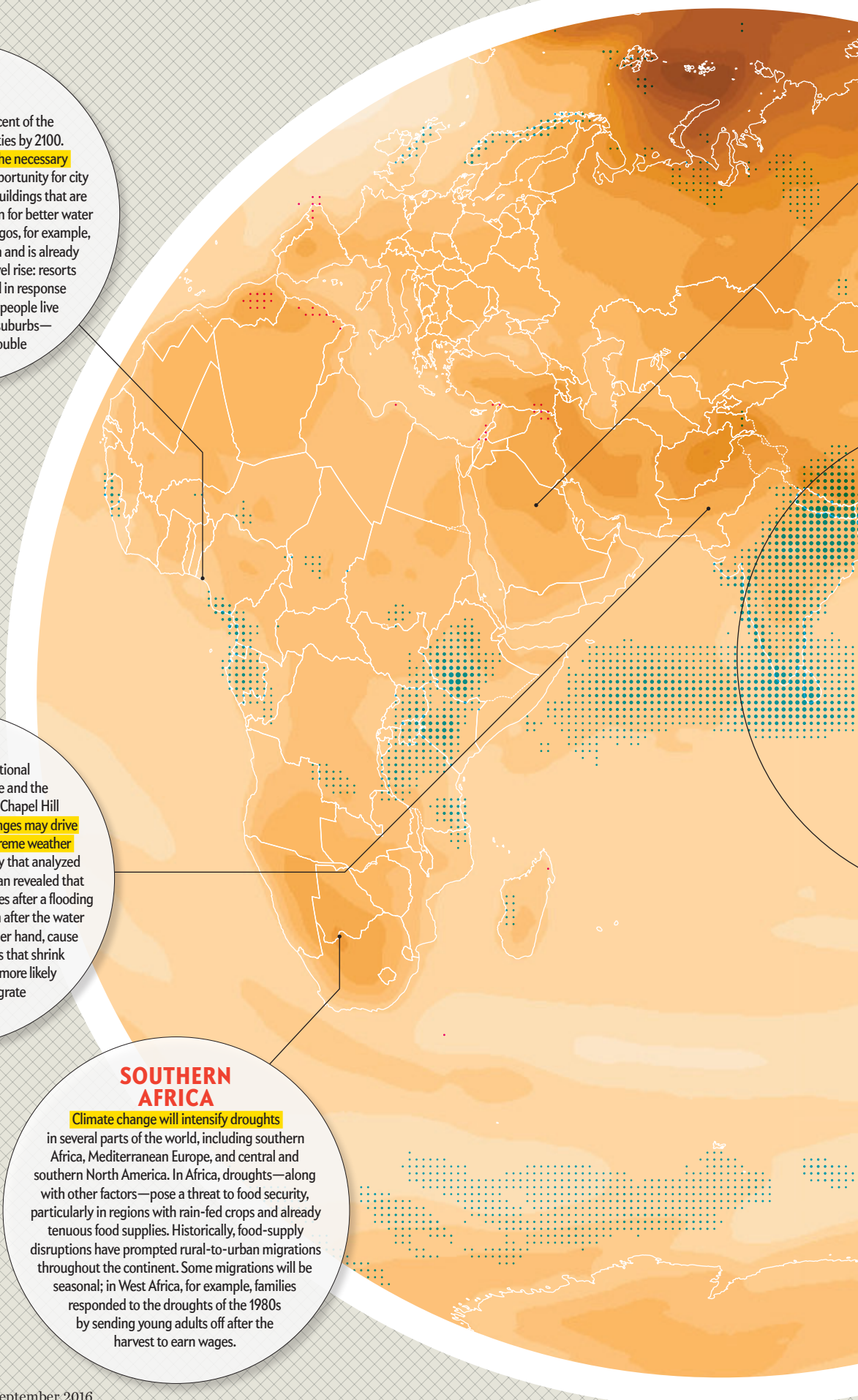
By 2100 demographers predict six million people in Florida will live in areas vulnerable to sea-level rise (*blue* and *green areas above*). A bipartisan alliance of four southeast Florida counties is currently working to help the region prepare. Efforts include a plan to develop infrastructure that keeps potable water available when seawater floods the drinking-water supply. The group is also working to change the building-height regulations in Key West so that homes could be raised above flood levels.

BRAZIL

By midcentury, fishery yields in many tropical oceans may drop by half as fish ranges shift—the result of warming temperatures, salinity variations and changes in habitat. This trend will likely continue through 2100. The fall-off will put economic pressure on people who rely on making catches for income. (In some high-latitude oceans, in contrast, fish populations may double.) Brazil has responded with Marine Extractive Reserves, wherein fishers, managers and researchers attempt to balance conservation with the need for small-scale fisheries to continue operating. The model is still under development in Brazil, but its principles could guide management in other countries with small fisheries.

LAGOS, NIGERIA

According to the U.N., 84 percent of the world's population will live in cities by 2100. Yet an estimated 65 percent of the necessary housing has not been built—an opportunity for city officials and planners to construct buildings that are resilient to climate change and to plan for better water and transportation infrastructure. Lagos, for example, is built around a flat coastal lagoon and is already experiencing the effects of sea-level rise: resorts on Victoria Island have relocated in response to erosion. Twenty-one million people live in Lagos and its surrounding suburbs—a number that is set to double by midcentury.



PAKISTAN

Economists at the International Food Policy Research Institute and the University of North Carolina at Chapel Hill have found that temperature changes may drive migration more strongly than extreme weather events. For example, a recent study that analyzed decades of migration data in Pakistan revealed that although people may leave their homes after a flooding event, they usually move back again after the water recedes. Warm winters, on the other hand, cause the kind of repeated crop failures that shrink the incomes of farmers and are more likely to prompt a family to migrate away permanently.

SOUTHERN AFRICA

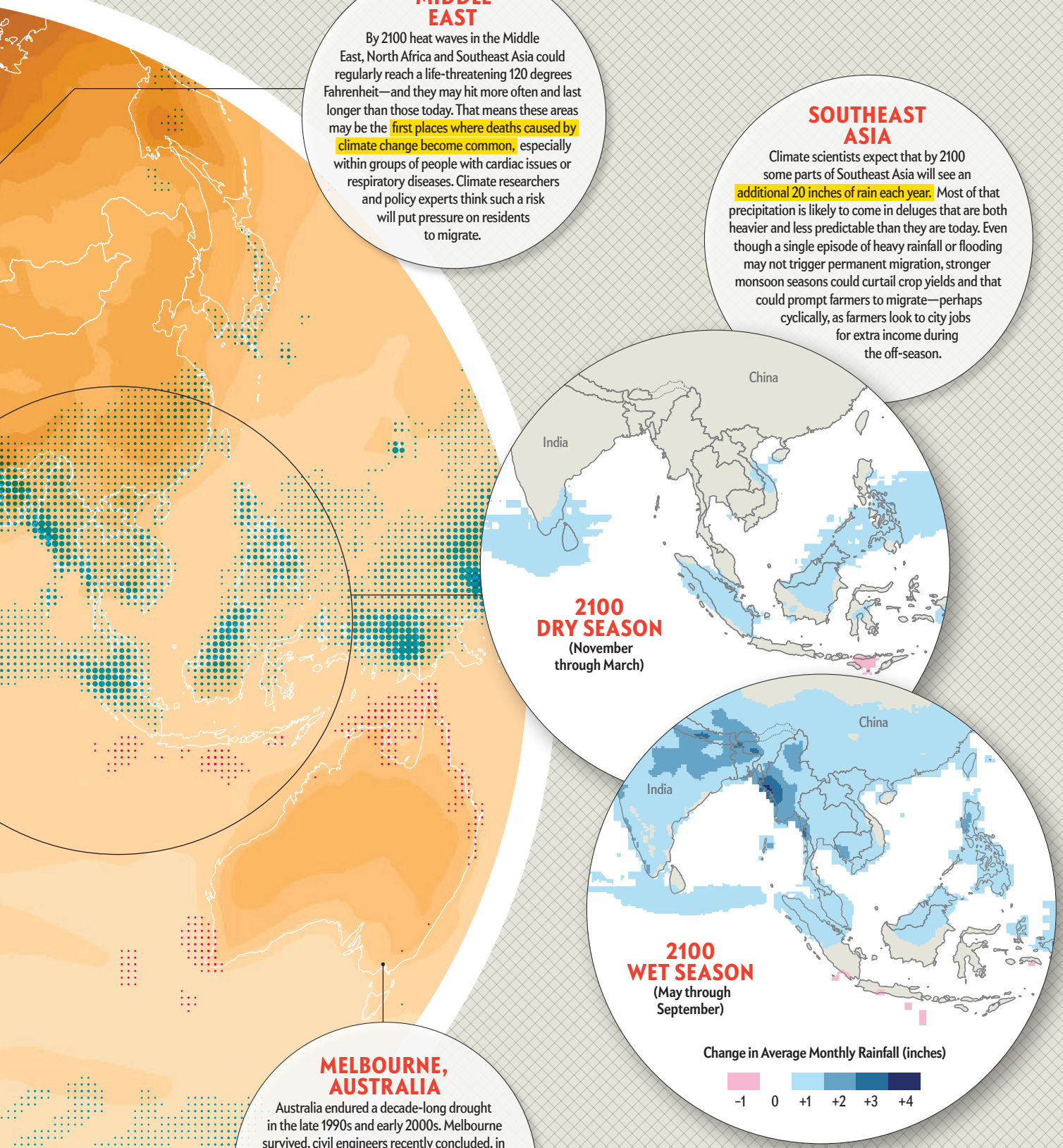
Climate change will intensify droughts in several parts of the world, including southern Africa, Mediterranean Europe, and central and southern North America. In Africa, droughts—along with other factors—pose a threat to food security, particularly in regions with rain-fed crops and already tenuous food supplies. Historically, food-supply disruptions have prompted rural-to-urban migrations throughout the continent. Some migrations will be seasonal; in West Africa, for example, families responded to the droughts of the 1980s by sending young adults off after the harvest to earn wages.

MIDDLE EAST

By 2100 heat waves in the Middle East, North Africa and Southeast Asia could regularly reach a life-threatening 120 degrees Fahrenheit—and they may hit more often and last longer than those today. That means these areas may be the first places where deaths caused by climate change become common, especially within groups of people with cardiac issues or respiratory diseases. Climate researchers and policy experts think such a risk will put pressure on residents to migrate.

SOUTHEAST ASIA

Climate scientists expect that by 2100 some parts of Southeast Asia will see an additional 20 inches of rain each year. Most of that precipitation is likely to come in deluges that are both heavier and less predictable than they are today. Even though a single episode of heavy rainfall or flooding may not trigger permanent migration, stronger monsoon seasons could curtail crop yields and that could prompt farmers to migrate—perhaps cyclically, as farmers look to city jobs for extra income during the off-season.



MELBOURNE, AUSTRALIA

Australia endured a decade-long drought in the late 1990s and early 2000s. Melbourne survived, civil engineers recently concluded, in part because residents were willing to change their water habits—flushing toilets less often, for example. Australia, the U.S. Southwest, southern Africa and the Amazon basin may all see mega droughts—dry spells lasting two decades or longer—in the coming century, and Melbourne's success could guide their adaptation plans.

3

WHO WILL PROSPER, AND WHO WILL FALL BEHIND?

By Mara Hvistendahl

A TALE OF TWO WORLDS

Lena and Saheed have never met; they probably never will. Lena lives in 2050 Leipzig, a placid and historic German city of middle-aged professionals. At 51, she is midway through a career as a pharmacist, with retirement more than two decades away. She and her husband no longer have to support their only child, a daughter who recently graduated from college, but they worry about caring for their aging parents, who are in fairly good health in their 80s and 90s. Saheed, unattached and unemployed at 22, lives in a decrepit slum on the outskirts of Lagos, Nigeria, where he is one of four siblings. He and his brothers and sisters face

Photograph by Andrew Myers

Mara Hvistendahl is a contributing correspondent at *Science* and author of *Unnatural Selection: Choosing Boys over Girls, and the Consequences of a World Full of Men* (PublicAffairs, 2011). She is currently writing a book on the rise of economic and cyberspying and the global battle over technological secrets.

IN BRIEF

Global population growth is slowing but continuing nonetheless. In 2050 the world might be home to 9.7 billion people. But the distribution of that growth is more revealing than the aggregate number.

Some rich nations will become smaller and less dynamic, the consequence of falling birth rates and aging citizenries.

The developing world, meanwhile, will become more crowded and, on average, younger. This demographic shift represents an economic opportunity as well as a political, infrastructural and public health challenge.

a very different kind of struggle: finding jobs in a tight labor market overrun with young workers, along with obtaining housing and clean water.

Lena worries about chronic diseases. Saheed is more likely to contract malaria. Germany scrambles to adapt its pension, health care and utility systems to a shrinking population that is living longer than ever before. Nigeria struggles to build roads, schools and sanitation facilities as its cities swell.

Lena's and Saheed's lives could hardly be more different. But these two divergent fictional figures embody many challenges that lie ahead. The distribution of the human population stands to change in unprecedented ways over the next few decades, forcing governments and the international community to rethink what it takes to protect the health and well-being of people around the globe. The decisions they make today will determine whether people like Lena and Saheed have a bright, or a bleak, future.

POPULATION MOMENTUM

ROUGHLY HALF A CENTURY AGO popular attention fixed on just one global population trend: sheer size. In his 1968 best seller *The Population Bomb,* Stanford University entomologist Paul R. Ehrlich warned that rapid population growth would outstrip production of food and other resources, with hundreds of millions dying of famine. Ehrlich's fears were not realized, however. The green revolution soon improved food security, and a mixture of economic development and access to education and family planning brought down birth rates in much of the world. By 1970 annual population growth had begun to decline from its 1960s peak of 2 percent.

And yet population growth is like a moving train—even as it slows, it possesses great momentum. Today the global growth rate continues to decline, but billions more will still be added to the human population over the next few decades. The United Nations estimates that by 2050, it will swell to 9.7 billion. The chance that the train will finally come to a stop and world population will stabilize or begin declining before 2100 is only 23 percent.

If we focus on such big-picture projections alone, though, we miss important nuances. Half of the population growth between now and 2050 will occur in nine countries, five of which are in Africa. Across the industrial world, meanwhile, birth rates are falling and life spans increasing. The number of people aged 60 and older in the world will more than double in the next 34 years, according to the U.N. The number aged 80 and older will triple. Many of those elderly will live in Europe, where by 2050 the 60 and over demographic is projected to account for more than a third of the population. Jack A. Goldstone, a political scientist at George Mason University and director of the Hong Kong University of Science and Technology's Institute for Public Policy, calls this disruption of the world order as we know it "the new population bomb."

Germany and Nigeria represent opposite extremes of this changing global dynamic. On one end is a wealthy but rapidly aging country where cities are shrinking and governments are facing ballooning pension costs. On the other is a youthful nation that will need to accommodate both more urban migrants and more babies—trends that could compound existing problems such as climate change and infectious diseases. Particularly in Nigeria, says Hans Groth, chair of the World Demographic and Ageing Forum in Saint Gall, Switzerland, history is no guide for what lies ahead: "We are not prepared as human beings to manage or accept such big changes."

GROWING PAINS

BY 2050 NIGERIA IS EXPECTED to overtake the U.S. to become the third most populous country in the world. Its population will more than double, to 398.5 million, according to the U.N. Over the course of Saheed's young adult years, then, he will watch as Nigeria's already thin resources spread even thinner. "Think about it," says John Bongaarts, vice president of the Population Council in New York City. "Everything man-made in the country has to be duplicated. Every school, every clinic, every bridge."

In 2015 the U.N. Population Division revised upward its estimates for population growth in Africa. To some extent, the change reflected positive news. Thanks to advances in public health, including measures that reduced infant mortality and death from AIDs, life expectancy in sub-Saharan Africa had risen.

But the other half of the story is that fertility has not declined as rapidly as many had hoped. Continent-wide, the total fertility rate—the average number of children a woman has over a lifetime—remains stuck at 4.7. In Nigeria, it is 5.7. The country could, in theory, gain from what is called a demographic transition—a phase during which fertility falls and a nation has a large number of working-age adults with few elderly and children to support. Countries that successfully complete a demographic transition, by lowering both birth rates and mortality while boosting education, employment and other drivers of economic development, can experience a "demographic dividend" that catapults them into the next level of development. But in Nigeria, as in other parts of sub-Saharan Africa, fertility has declined only slightly before stalling at a high level.

Demographers cite a range of possible factors for that intransigence, from the lingering influence of tribal culture to a longer window during which women customarily have children. Says Akinrinola Bankole, a demographer at the Guttmacher Institute in New York City: "People are still thinking in terms of old-age security"—having a large number of children to care for them as they age. "They think less about the need to invest in the children who will provide that security."

Stubbornly high fertility rates will compound the daunting array of threats already facing Nigeria: poverty, hunger, the prevalence of communicable diseases and the effects of climate change. Close to 240

PAGE 42: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

million people in sub-Saharan Africa, or one in four, lack adequate food, and 30 million children are currently underweight, according to the Population Reference Bureau. As Saheed and his siblings age, the region will add hundreds of millions more mouths to feed. Among those now working to improve food security is the Alliance for a Green Revolution in Africa. Founded in 2006 and led for more than six years by former U.N. secretary-general Kofi Annan, the organization lobbies for changes in agriculture policy and helps smallholder farmers obtain improved seeds, organic fertilizers and basic equipment. Sub-Saharan Africa will need all the help it can get. "The concentration of population growth in the poorest countries could make it harder for some countries to eradicate poverty, combat hunger and malnutrition, expand services in the area of education and health systems, and improve the provision of basic services and infrastructure," says Francois Pelletier of the U.N. Population Division.

Within countries such as Nigeria, moreover, population growth will not be evenly distributed. Birth rates are currently much higher in the north, which is largely resource-poor. As a consequence, growing numbers of northerners are joining Saheed and family in Lagos—a change that is part of a larger global trend. Urbanization and overall growth are expected to add more than 2.5 billion people to the world's urban population by 2050, with around 90 percent of the increase happening in Asia and Africa.

Urbanization is often a positive phenomenon, accompanied by an increase in education, a decrease in the birth rate and steady economic growth. Well-planned cities reduce land use and boost energy efficiency. Henrik Urdal, a political scientist at the Peace Research Institute Oslo in Norway, and his colleagues have found that urbanization may even decrease the risk of conflict.

But the fact that countries like Nigeria are urbanizing at a much lower level of economic development than they once did means that by 2050 much of the world's population will be concentrated in cities unequipped to provide adequate health care, sanitation and other services. That could increase Saheed's exposure to infectious diseases, which can thrive in densely populated areas with large numbers of migrants. Urbanization is believed to have been a major contributing factor to the early spread of HIV/AIDS in Africa. By 2050 the slums of Lagos could become hotbeds for tuberculosis and malaria.

CAN WE FEED THE PLANET WITHOUT DESTROYING IT?

"Yes. Here's what we need to do: reduce crop waste, consumer waste and meat consumption; integrate appropriate seed technologies and management practices; engage consumers about the challenges farmers face in both the developed and the developing world; increase public funding for agricultural research and development; and focus on advancing the socioeconomic and environmental aspects of farming that characterize sustainable agriculture."

PAMELA RONALD
Professor emerita in the Genome Center and the department of plant pathology at the University of California, Davis

EDWINA PICKLES *Getty Images*

SOME AFRICAN countries will undergo rapid population growth between now and 2050, putting pressure on food supplies and possibly leading to shortages like the current crisis in South Sudan.

Portrait by Kyle Hilton

CAN WE AVOID A "SIXTH EXTINCTION"?

"It can be slowed, then halted, if we take quick action. The greatest cause of species extinction is loss of habitat. That is why I've stressed an assembled global reserve occupying half the land and half the sea, as necessary, and in my book *Half-Earth,* I show how it can be done. With this initiative (and the development of a far better species-level ecosystem science than the one we have now), it will also be necessary to discover and characterize the 10 million or so species estimated to remain; we've only found and named two million to date. Overall, an extension of environmental science to include the living world should be, and I believe will be, a major initiative of science during the remainder of this century."

EDWARD O. WILSON
University Research Professor emeritus at Harvard University

As Nigeria moves up the economic ladder and more people buy cars and consume electricity, air pollution could pose another health threat. The explosion of megacities in Asia over the past few decades provides some guide of what could happen in Africa. Recent data from the Global Burden of Disease, Injuries, and Risk Factors Study suggest that air pollution contributed to 1.2 million deaths and 25 million lost years of life in 2010 in China alone.

Ironically, if Nigeria manages to lower its birth rate—the source of many of its problems—the shift could produce an unfortunate side effect. As the birth rate falls, the proportion of the total population composed of teenage and twentysomething men will increase. If the economy cannot provide enough jobs, Bongaarts says, "you have unemployed and underemployed young men who are unhappy. They are readily exploited, and they contribute to crime and lack of security." Political scientists believe that such so-called youth bulges contributed to the Arab Spring uprisings across North Africa and the Middle East.

To succeed in coming years, countries like Nigeria will need to simultaneously boost education, youth employment and access to family planning—a mammoth undertaking but one that is not impossible. Forty years ago few foresaw the rapid decreases in fertility that have occurred in Bangladesh, Indonesia and Iran. If Saheed finds a job and gets married, he may decide to have fewer children than his parents so that he can afford their schooling costs. As more and more men like him do the same, Nigeria has a shot at turning a potential liability into an advantage and achieving a demographic dividend. Such population changes have been crucial to the economic ascent of other countries, including Brazil, China and South Korea.

IN THE OLD COUNTRY

A VERY DIFFERENT SORT OF SHIFT is under way in Germany. Lena was born in 1999, when the German economy was the engine for European economic growth and workers abounded. By 2050 the population is projected to fall from 80.7 million to fewer than 74.5 million. Nearly 40 percent of Germans will then be 60 and older, whereas people aged 15 to 59, who make up most of the working-age individuals, will account for a mere 48 percent, a 19 percent decrease from today. Parts of Germany already offer a preview of what is to come. Last year the septuagenarian mayor of Ottenstein, a community in the northwest of the country, announced that he would give away land to couples with young children. The goal: to keep the village's school open.

Germany's situation is reflected throughout Asia, Europe and Latin America. The U.N. projects that 11 countries, including Japan and Ukraine, could lose 15 percent or more of their populations by 2050. Media reports already make much of the declining birth rate in Germany and neighboring countries. By 2050 policy makers could be worrying about a sustained economic slowdown caused by a shortage of young workers and taxpayers.

It might be tempting to turn to immigrants to fill the labor pool. The U.N. predicts that between 2015 and 2050, Germany will be one of the world's top receivers of migrants. The hundreds of thousands of desperate Syrian families crossing into Europe, their possessions strapped to their back, have already brought this issue into focus. As the population continues to grow in sub-Saharan Africa—and especially if young men like Saheed do not find jobs in their home countries—the tide of migrants may increase, linking the futures of Germany and Nigeria. Pundits sometimes argue that this trend will help counteract the aging population. But, Goldstone notes, "it would take tens of millions of migrants to offset the shrinking youth cohorts in Germany, Netherlands and other low-growth countries"—and conversely, to relieve population pressure in fast-growing countries in sub-Saharan Africa.

That means that even with modest rates of immigration, the population of Leipzig will decline. In the process, the city will struggle to adapt its utility system and other services to less use, perhaps by raising fees—a change that would be borne by working-age people like Lena. The shrinking city could be an expensive one.

Germany is also likely to face new health challenges, as improvements in health and longevity shift its disease burden. Lena's parents, for example, are part of an "oldest old" group of people, aged 80 and older, that is projected to include 14.4 percent of Germans in 2050. They will be less likely than previous generations to die of cancer or a heart attack. But they will be more susceptible to dementia, a disease that is becoming more prevalent as life expectancy increases and that will only become more common unless a cure is found. "Before, people simply died before they con-

Portrait by Kyle Hilton

tracted Alzheimer's," says Axel Börsch-Supan, director of the Munich Center for the Economics of Aging and principal investigator for the Survey of Health Ageing and Retirement in Europe, a longitudinal study of more than 45,000 Europeans aged 50 and older. "Now that doesn't happen."

Economically, aging in Western Europe is a mixed bag. It is not only the result of low birth rates: it has also been brought on by marked jumps in life span and individual health and well-being. People are not merely living longer; they are staying healthy and employable much longer as well. Over the past two decades life expectancy at birth in Germany increased by nearly five years to just over 80. Health metrics are improving across Europe, Börsch-Supan says: "Longevity is increasing linearly. There's no sign of the curve flattening out." (In the U.S., in contrast, discussion about the slower aging rate tends to obscure a disappointing trend in life expectancy, which has actually worsened among some groups in America, Börsch-Supan notes.)

In Europe, some say nothing short of a redefinition of what it means to be elderly is now required. Sergei Scherbov, a demographer at the International Institute for Applied Systems Analysis in Laxenburg, Austria, has proposed considering a person to be "aging" during only the last 15 years of life, as measured by a country's life expectancy at birth. Such a measure better reflects ability and health than the U.N.'s definition of aging as 60 and older, he says: "In the 1950s the oldest person to climb Mount Everest was 39 years old. A couple of years ago a Japanese guy of 80 climbed it."

Indeed, pension systems are being overhauled across much of Europe. In Germany, the retirement age, which is now 65 and five months, will be gradually increased until it reaches 67 in 2029. But to provide for people like Lena's parents who are living past 80, the country's retirement age ultimately will need to be linked to life expectancy, as has happened in Norway and Sweden—a change that will likely prove unpopular. "The issue in Europe is that people love to retire early," Börsch-Supan says. "That is not sustainable."

THE GRAVITY OF DEMOGRAPHY

THE FATES OF SAHEED AND LENA depend in no small part on what transpires now. By planning well for the future, demographers say, both Nigeria and Germany can tackle coming population changes. Demography, Goldstone says, is like gravity—you have to acknowledge its force and act accordingly. "If you manage to deal with gravity, you can make planes fly," he says. But you have to design your airplane well and fly it competently. "You can have a stable government and growing economy in the face of population growth or population decline. But you have to invest wisely, manage the economy well, educate the labor force to be more productive and plan for the welfare needs of different age groups as they change over time."

JOHN MOORE Getty Images

"YOUTH bulges" have been blamed for social unrest, but a sudden boom in able young workers can also be an economic boon.

In a way, Nigeria and Germany sit at two ends of a global continuum. Between these two extremes are dozens of other nations whose role in the world will also shift with changes in population distribution—including the U.S., which will both age and grow in overall population. By acting now on issues such as health care, urban infrastructure, education, and food and pension security, countries across the spectrum can ensure better lives for generations to come.

Efforts at maintaining global stability, meanwhile, will need to better involve populous emerging economies, among them Brazil, China, India and Mexico. That means reconfiguring global governing bodies such as the G7 and NATO so that they better reflect the changing face of the world—and ensuring that money flows toward the public health, resource and infrastructure challenges of the entire world, not just those of industrial nations. By thinking creatively and acting early and decisively, humanity might prevent the new population bomb from exploding. SA

MORE TO EXPLORE

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WILL CIVIL SOCIETY ENDURE?

By Angus Deaton

THE THREAT OF INEQUALITY

Photograph by Andrew Myers

Sir Angus Deaton, who is Dwight D. Eisenhower Professor of Economics and International Affairs, Emeritus, at the Woodrow Wilson School of Public and International Affairs and the department of economics at Princeton University, received the 2015 Nobel prize for economics. He holds British and U.S. citizenship and is a Fellow of the British Academy and a member of the National Academy of Sciences.

Today's world is full of threats. Two of the great bulwarks of our recent prosperity—the postwar European project and a (reasonably) well-functioning democracy in the U.S.—are under siege. Waves of refugees from the civil war in Syria are engulfing Europe and stretching to breaking the long-standing generosity of northern Europeans toward those in distress. We see horrors in the Middle East, faltering growth in China, and global warming. Substantial fractions of the populations in Europe and in the U.S. have seen little growth in living standards for many years, and they are disengaging from the political processes that have delivered so little for them. And across the rich world, growth rates of per capita income are falling, whereas almost everywhere, income and wealth inequalities are rising.

It may not be obvious that inequality deserves its place among these threats, but it would be a mistake to underestimate its potency. Every problem I mentioned is tied to inequality; if extreme and rising inequality has not caused that threat, it certainly makes it worse.

And so it may seem that the world is going to hell in a handbasket. To realistically assess our future prospects, however, it is a mistake to extrapolate only from the present. First we need to look back and to see how far we have come.

IN BRIEF

The gap between the rich and the poor has grown wider over the past few decades in many countries for a variety of reasons.

Not all income inequality is socially destructive, but if it allows small groups to change the rules in politics or economics in their favor, innovation and growth may falter.

Society is unlikely to achieve greater prosperity without tackling income inequality and taming the harmful behaviors it promotes.

We—meaning the inhabitants of the rich world and many of the inhabitants of the poor world—are enormously wealthier and healthier now than at any time in human history.

The usual interpretation of "prosperity" is spending power or material well-being, and that is certainly an important part of the story. But human well-being depends on much more. Material well-being is of limited value if you are dead or disabled, and good health is an important part of well-being in its own right. Education contributes to earnings and thus to material well-being, but it also enables one to lead a richer and better life. Like wealth, health and education, freedom—including the freedom to participate in civil society, the freedom of movement, and the freedom from discrimination, from violence, from arbitrary arrest and imprisonment—is part of prosperity. All these freedoms are more prevalent today than at any time in history.

If we go back 250 years, to the second half of the 18th century, we see that a few countries were beginning to emerge from a past in which poverty and ill health were the norm. For most of history, many children died before their fifth birthday. Plagues and epidemics were a constant threat. Only after the industrial revolution and the accompanying health revolution did sustained economic growth and improvements in health become widespread.

Even then, life got better in only a few countries at first before slowly transmitting to the rest of the world. Progress created new inequalities, driving living standards in London and Amsterdam away from those in Jakarta and Beijing, increasing life expectancy and decreasing child mortality in northwestern Europe but leaving it unchanged in Africa and Asia. The afterglow of this "great divergence" remains today, even after the remarkable recent catch-up growth in India and China and the even more remarkable increase in life expectancy in poor countries. Today per capita incomes in the U.S. are four times higher than in China, 10 times higher than in India or Nigeria, nearly 20 times higher than in Kenya, and more than 90 times larger than in the Central African Republic (all these figures have been adjusted for the lower cost of living in poorer countries). These vast international inequalities are a consequence of progress: it is almost always the case that some benefit before others. But they also threaten future progress.

It is unlikely that historians will ever come to a final agreement on the causes of the industrial revolution, but the Enlightenment was a crucial precursor, especially the Enlightenment notion of "useful knowledge." Useful knowledge starts from the interrogation of nature and the development of basic science and turns science into techniques, machines and understanding that make life better and promote the "pursuit of happiness." New knowledge does not simply drop from the heavens; the social environment and the needs of the time deeply influence the rate and direction of new understanding. Markets also play a role. High prices for goods incentivize people to economize, and one way to do that is to invent new methods that use less. High wages in Britain before the industrial revolution were likely one of the factors promoting the methods that were the core of the industrial revolution itself.

Political and intellectual freedom also helped us

PAGE 48: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

prosper. Inventions often work through what Joseph Schumpeter called "creative destruction." New techniques destroy not only previous ways of doing things but also the livelihoods of those who depend on those previous methods. Change will be fiercely resisted, often successfully, especially when the incumbents are politically powerful. Political arrangements can modify this resistance, however. One reason sustained growth happened in Europe and not in China is that the political fragmentation of Europe allowed those with new but unpopular ideas—or religions—to flee one political jurisdiction and set up elsewhere. Recent globalization has brought a greater and cheaper freedom to move goods, services and (to a lesser extent) people, which has played a role in allowing the recent great escapes from poverty in India and China.

The question for today is whether the growth since 1750 can be relied on indefinitely or whether the black clouds around us are a sign that we are done, that the well has run dry. We cannot assume, just because the history of the past quarter of a millennium has been one of progress (albeit with some horrific interruptions), that such progress must necessarily continue. Episodes of progress have come and gone before.

I do not see inequality as harmful in and of itself; my well-being does not change simply because someone else gets better or worse off. Inequality is sometimes just another word for incentives; those whose innovations make us all better off are often rewarded with great riches, and it is hard to see why this is socially destructive in and of itself. The dangers of inequality are in its instrumental effects, and it is those that are threatening our future.

The rate of per capita economic growth, long running at a little under 2 percent a year in the U.S., has been falling. Similar declines are observed in other industrial countries. This was true before the financial crisis that began in 2008, from which there has been a much less than complete recovery in the U.S. and no recovery at all in much of Europe. The Great

> The very size of the health care and financial sectors in the U.S. gives them political power that makes them difficult to control.

WHEN AND WHERE DO YOU THINK WE WILL FIND EXTRATERRESTRIAL LIFE?

"If there is abundant microbial life on Mars, I suspect that we will find it within 20 years—if it is enough like our form of life. If an alien life-form differs much from what we have here on Earth, it is going to be difficult to detect. It's also possible that any surviving Martian microbes are rare and located in places that are difficult for a robotic lander to reach. Jupiter's moon Europa and Saturn's moon Titan are more compelling places. Europa is a water world where more complex forms of life may have evolved. And Titan is probably the most interesting place in the solar system to look for life. It is rich in organic molecules but very cold and has no liquid water: if life exists on Titan, it will be very different from life on Earth."

CAROL E. CLELAND
Philosophy professor and co-investigator in the Center for Astrobiology at the University of Colorado Boulder

Illustration by Lorenzo Gritti, Portrait by Kyle Hilton

Recession may be just one more of the episodes that mar market economies, or it may be worse than that, a sign of things to come.

The growth of per capita GDP, imperfect as the measure is, remains our leading indicator of improving prosperity. At 3 percent a year, incomes double in 25 years, a single generation; at 2 percent a year, it takes 35 years; and at 1 percent, it takes 70 years. Americans and many European families in the middle of the distribution have already lost the chance of being better off than their parents; instead they are struggling not to do worse. Politics become more difficult with slower growth. With a growing pie, everyone can have more, but if the pie is fixed, I can only benefit at your expense. The same goes for public goods such as health care, social security systems, education and infrastructure. With growth, these goods can be repaired and expanded without reducing what anyone gets; without growth, someone must give up some of what he or she already has.

Slow growth rewards the formation of groups that enrich their members at the expense of the larger population, for example, by agitating for laws and regulations that increase their incomes or otherwise protect them, inhibiting innovation and beneficial change and further reducing growth. These activities are what economists call "rent seeking." Economic and political thinker Mancur Olson believed that rent seeking would bring down rich nations. It is easy to find examples of it today. To name one among many, the National Institutes of Health, one of the U.S. government's most important research institutions, declared in 2015, at the urging of a Congress that is well funded by the health care industry and deeply opposed to Obamacare, that it would not pay for research whose primary goal is to "assess the cost and efficiency" of the health care system.

When whatever growth exists is not shared, new problems arise. Those who are left behind may be patient when they are getting something, but if their incomes are flat or declining, they are unlikely to remain patient for long. Inequality becomes a political issue. Ideally, such dissatisfaction will bring political change. But if the political system is sensitive only to the needs of the wealthy—something that is arguably true of the U.S. Congress—there is a direct threat to political stability and, ultimately, to democracy itself. If the main political parties offer nothing to those who are excluded, they may turn to political remedies or candidates that threaten liberal democracy.

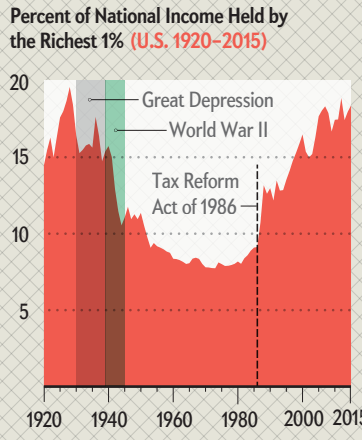
For those who are left behind, the loss of well-being is far from abstract. In the U.S., those in the middle of the distribution have not only seen stagnant incomes. There is now a health crisis among non-Hispanic middle-aged whites, who are destroying themselves through drug addiction, suicide and alcoholism. Most increases in life expectancy in recent years have accrued to the top of the income distribution.

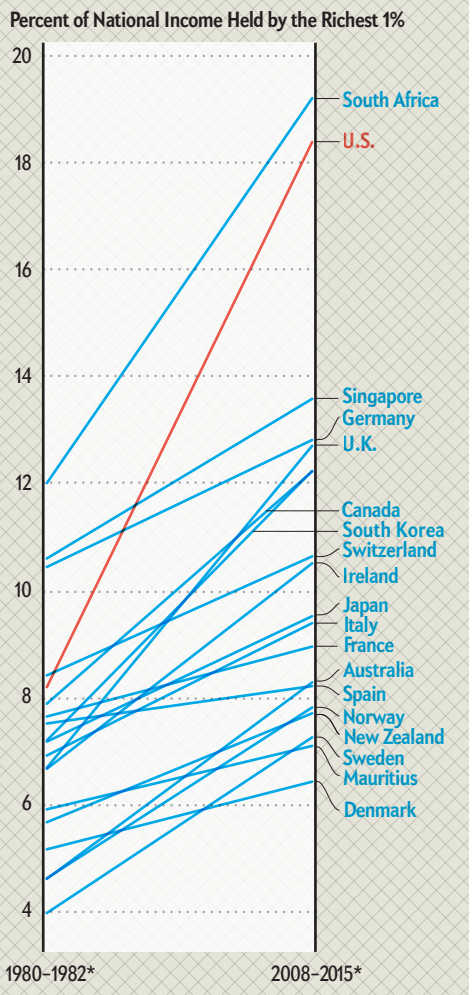
Understanding the causes of slowing growth is crucial for thinking about the future. Here there is much disagreement, although there are some direct reasons why we are growing so slowly, and they are all connect-

INCOME EXTREMES

Widening Gap

Although large differences in income are not socially destructive by themselves, they are fueled by and can further feed self-serving actions by well-placed groups to increase their own income at the cost of both economic growth and democratic governance. Limiting such pernicious effects—such as by funding programs that help individuals who are left behind—becomes more difficult as income inequality rises. As the following charts indicate, income inequality has increased markedly over the past few decades in the U.S. and at a much faster rate than in other countries.





*Annual information is not available for every country. Data shown are the most recent available within the indicated range. Data exclude capital gains.

SOURCE: *THE WORLD WEALTH AND INCOME DATABASE.* FACUNDO ALVAREDO, ANTHONY B. ATKINSON, THOMAS PIKETTY, EMMANUEL SAEZ AND GABRIEL ZUCMAN; DATA FROM JULY 6, 2016 www.wid.world

Graphic by Tiffany Farrant-Gonzalez

ed to rising inequality. In the U.S., though less so elsewhere, we spend enormous sums on health care, much of which has little or no effect. That money comes from wages and incomes, so citizens are paying more for health care than they think. This system is fiercely defended by those whose incomes and power come directly or indirectly from the nearly one fifth of American GDP that health care absorbs.

The financial sector is another key contributor to our well-being, but it is also too large. The enormous private rewards this sector generates outstrip its social returns. Many of our best minds are working in this sector instead of actually making things or coming up with new treatments for disease. At the same time, the instability of an overly large financial sector brings the risk of financial crises, which have disastrous negative effects on economic growth.

The very size of the health care and financial sectors gives them political power that makes them difficult to control. These sectors then become engines of inequality, generating huge rewards for some while slowing growth and undermining innovation.

If this analysis is correct, we are unlikely to restore prosperity without tackling income inequality and taming behaviors, such as rent seeking, that are both its causes and its consequences. Like the 15th-century Chinese emperor who banned potentially world-conquering seagoing exploration for fear of ceding power to others, we run the risk of stifling the innovation and growth that are the roots of our future prosperity.

One indication that inequality will be hard to reverse is that rising inequality is so widespread across rich countries in spite of differences in national policies and in spite of aggressive social welfare policies in some countries that seek to limit it. One concern is that technical progress, automation, globalization and the offshoring of jobs have not only had the traditional effect of displacing workers temporarily, so that, in the long run, they, too—or at least their children—can benefit from the higher prosperity that such forces can bring. Instead these changes seem to have created a process in which the benefits never come, or accrue only to foreigners, or to the owners of the machines. Such concerns have been raised throughout history in similar situations, and they have always proved baseless, so we have to be very careful in interfering if we believe, as I do, that technical advance is the bedrock of our rising prosperity and lengthening life spans. It is also doubtless the case that, in the aftermath of the long-prolonged Great Recession, it is easy to be pessimistic. That said, the fears are real, and there is more concern among economists than for many years.

LEFT BEHIND: Many people who voted in June for the U.K. to leave the European Union felt the purported benefits of membership had passed them by or were reserved for others.

CHRISTOPHER FURLONG *Getty Images*

What are the positives to offset all this pessimism? One is that democracy will win out in the end, that those who are not being well represented currently will use the democratic process to install leaders who are more responsive to their will. That will be difficult, and there are dangers to democracy along the way, but it is not impossible.

The second and most powerful ray of hope is in the history with which I began: it is the fact that people shape their circumstances to their needs, at least in the long run. It is not as if a rogue planet is approaching Earth and threatening to destroy it. Social arrangements can be changed, and they will need to be. I believe that, if left unaddressed, current levels of rent seeking and the extremities of national and international inequality that they create are likely to bring us down. Yet I am optimistic because the pursuit of happiness remains as powerful a desire today as it was in the 18th century. SA

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WILL WE CONTROL OUR GENETIC DESTINIES?

By Stephen S. Hall

THE RED LINE

Photograph by Andrew Myers

Stephen S. Hall is an award-winning science writer. He has authored six books, including histories of recombinant DNA and cancer immunotherapy, and teaches science communication at New York University.

Kyle Orwig has been itching to do an experiment that would, in his words, "piss people off." Orwig, a professor at the University of Pittsburgh, is an expert on the intricate biology of sperm cells—in particular, how specialized "stem" cells located in the male testes produce sperm. Every so often, however, a genetic flaw prevents these stem cells from completing this process, thus rendering the male infertile. The experiment Orwig has in mind is to use gene-editing technology to fix this flaw in the sperm-forming stem cells and then transplant them back into infertile mice, thereby demonstrating a potential treatment for male infertility.

IN BRIEF

New gene-editing techniques may soon be used in treatments for male infertility that involve altering the genetic code of sperm cells. Such alterations would be passed down to future generations, constituting a permanent change in the human genome.

Scientists seeking to quell the public's fears that such a step would cross an ethical red line have argued that the technology is not yet feasible, but others believe the line will be crossed soon.

The demand for infertility treatments has for decades fueled the adoption of new biotechnology, for better and worse.

It sounds simple enough, and, according to Orwig, it would be relatively straightforward to try—indeed, he has been transplanting sperm-forming stem cells into mice for 20 years. The consequences, however, could be momentous. The kind of experiment Orwig is contemplating would, if successful, push society right up to the brightest red line in contemporary biology: altering the genetic text of the human species in a way that is passed down to future generations.

If shown to be safe, effective and ethically acceptable, germ-line modification would confer unprecedented power on scientists—the power to edit the susceptibility to disease out of our species' DNA, for example, but also the power to manipulate human inheritance and "improve" the species, an aim that darkly harkens back to the eugenics movement of the early 20th century that reached its nadir in Nazi Germany.

Orwig, a broad-shouldered, burr-headed Oregonian who seems genial and determined, has no intention of crossing ethical lines. But he is something of a provocateur. By demonstrating that infertility in mice could be cured with a modest amount of genetic tinkering, he hopes to trigger a wider awareness that editing human genes is not an abstract, long-term technical challenge, as some have suggested, but a near-term possibility with practical medical consequences. Which is why Orwig recently told a colleague, "Let's just do this and piss some people off. Show them that it's possible, so nobody can say it's impossible. And get people talking about it."

The issue of germ-line modification has assumed great urgency in the past two years because of a powerful gene-editing tool called CRISPR/Cas9, which allows scientists to alter the DNA of any organism—including, potentially, humans—with unprecedented precision and ease. In April 2015 Chinese researchers reported the first attempt to edit the genes of human embryos. The headlines—"Embryo Editing Sparks Epic Debate," in *Nature;* "Eugenics Lurk in the Shadow of CRISPR," in *Science*—signaled broad social unease. In the alarmist shorthand of media accounts, the possibility of gene editing triggered fears of "designer babies" and "genetic enhancement."

The humble sperm cell, however, is a less controversial target. And whereas editing genes in an embryo remains a big challenge, many experts believe that approaching germ-line modification upstream of the embryo, in the sex cells that merge to form a zygote, is easier and arguably safer. Once you modify these cells, however, you are essentially modifying the human genome because the changes are permanently inscribed in the genetic text of the embryos they create. Orwig is among a handful of biologists who have experience genetically modifying and transplanting spermatogonial stem cells, the testicular cells that churn out sperm.

The field of reproductive medicine has a well-established track record for pushing headlong into the clinic with technological innovations. Infertility is also big business. If Orwig were to demonstrate in animals that a simple genetic fix is possible, it would be a tempting procedure for the tens of thousands of men who cannot make their own sperm, for whom options are currently limited, as well as for the in vitro fertilization (IVF) industry, which did an estimated $2 billion in business last year in the U.S. (and perhaps 10 times that amount worldwide).

Before administering any treatment, there must be proof that it works and causes no undue harm. Scientists would require such proof before even contemplating creating a human being with edited genes. Animal versions of those experiments are already under way, however, and the red line may be crossed soon. It could happen in China, where researchers have already taken the first tentative steps in editing human (albeit nonviable) embryos. It could happen in the U.K., where the government has legalized a form of germ-line modification known as mitochondrial re-

PRECEDING PAGE: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

placement therapy and, this past February, approved gene-editing experiments on human embryos. And it could happen in an IVF clinic anywhere, building on recipes developed in laboratories such as Orwig's.

"This isn't theoretical," Orwig says. "The mouse is here, and the human is not too far in the future. The pieces are already in place."

KEEP CALM AND CARRY ON

THE CURRENT DEBATE over germ-line modification may feel familiar, but it treads on fundamentally new ground. Scientists began to acquire the Promethean ability to rewrite the language of heredity in the early 1970s, when biologists discovered that they could crudely cut and paste DNA with the use of enzymes harvested from bacteria, a technique called recombinant DNA. That advance caused unease about dangerous, genetically engineered microbes escaping the lab, prompting a voluntary—and unprecedented—moratorium on recombinant DNA research in 1974 and a historic meeting in 1975 of scientists at the Asilomar conference in California. Prominent molecular biologists such as David Baltimore, then at the Massachusetts Institute of Technology, debated the safety of the new technology, which led to federal guidelines governing the research. The Asilomar meeting was correctly viewed as a watershed cultural moment: Michael Rogers published a richly detailed account of "The Pandora's Box Congress" in *Rolling Stone,* and by the time the guidelines were in place, biotechnology emerged as one of the transformative industries of the 20th century.

Although society applauded the scientific community's decision in 1974 to hit the pause button on the headlong rush of research, many scientists felt it was an overreaction to hypothetical safety concerns. James D. Watson, co-discoverer of the DNA double-helix structure, called it "senseless hysteria."

Since Asilomar, controversial biology has often landed in the public square with a bang, prompting big meetings with messy background noise. When the National Academy of Sciences debated recombinant DNA in 1977, protesters opposed to genetic engineering unfurled a banner quoting Adolf Hitler: "We Will Create the Perfect Race." A meeting on human cloning in 2001 became a media circus. Maverick IVF doctors vowed to clone human babies. Television crews followed the would-be cloners everywhere (including to the bathroom). *Wired* magazine, in 2001, proclaimed on its cover: "Someone Will Clone a Human in the Next 12 Months."

This time around there is palpable unease among scientists, but they are also wary that another self-imposed moratorium might hold up progress. The result? Another meeting. Last December the National Academy of Sciences and the National Academy of Medicine co-hosted an international "summit" in Washington, D.C. (with the Royal Society and the Chinese Academy of Sciences). Baltimore acknowledged that altering human inheritance had remained "unthinkable" because of the cumbersome and inefficient first-generation tools of genetic engineering. "Over the years, however, the unthinkable has become conceivable," he said, "and today we sense that we are close to being able to alter human heredity." The overriding question, Baltimore continued, is, "How, if at all, do we as a society want to use this capability?"

GENE EDITING: Scientists have tried to modify the genes of human embryos (*1*), but sperm cells (2) may be easier targets.

The answer, to anyone who sat through the three-day meeting, as I did, seemed to be: we're not sure, but there's plenty of time to think it through. Numerous talks, including a plenary address by genome scientist Eric Lander of the Broad Institute of M.I.T. and Harvard University, stressed the technical hurdles and the lack of compelling medical needs for human germ-line modification in the near future. "It might, might, might be a good idea that before we make permanent changes to the human gene pool," Lander warned, "we should exercise considerable caution."

The organizers deftly steered clear of an Asilomar-like moratorium. Baltimore read a carefully worded statement from the meeting organizers acknowledging that it would be "irresponsible" to pursue human germ-line editing in the clinic at this time. At the close of the summit, he went on to explain that the organizers had deliberately avoided calling for a ban or moratorium. "Neither word did we want to use," he said. "Neither word have we used." Basic research

NEIL HARDING *Getty Images* (1); GETTY IMAGES (2)

could, and should, proceed unimpeded, but the public need not be concerned about imminent developments: human applications of germ-line editing were implausible, unnecessary, unwise and certainly not right around the corner.

That is not the way everyone in the scientific community sees it. The organizers of the Washington meeting framed the issue as "when, if at all." But a different word often crops up in private conversations with biologists when you ask about the prospects for germ-line editing. That word is "inevitable."

THE TIMELINE

SOME SCIENTISTS viewed the National Academies meeting as an effort to "reinforce the status quo," according to biologist George Church of Harvard Medical School. "They basically want the public to calm down," he says. "That was their goal. And no matter what we said, that was going to be the goal. I don't want to stir [the public] up, and I don't want to calm them down, either. I want them to have an accurate view of where things are going." And the public needs to start thinking about gene-editing the human genome now, Church says, because science is already bumping up against the red line.

Despite a thicket of international provisions regulating human embryo research, Church and others believe that the creation of gene-edited sex cells in the test tube (the technical term is "in vitro gametogenesis," or IVG) has made great strides in recent years without attracting the same public scrutiny, or provoking the same ethical discomfort, as gene editing in embryos.

"In terms of the technology, that's ready to go now," says I. Glenn Cohen, a bioethicist at Harvard Law School. "In vitro gametogenesis is much closer to the mark than any other way to do it." And Ina Dobrinski, an expert in reproductive biology at the University of Calgary who works on gene editing of large animals such as pigs, adds, "Theoretically, we can do it. Practically [speaking], nobody is even touching it because of the ethical issues."

If human germ-line editing is inevitable, despite the ethical concerns (and indeed legal prohibitions in many countries), how might it happen? Speculation among biologists has become something of a parlor game, but I turned to Church, a card-carrying futurist, to lay out a plausible scenario. He was happy to oblige.

Church sees the germ-line Rubicon being crossed because sperm do not seem to arouse the same ethical passions as embryos or even egg cells. (Bioethicist Cohen agrees: "People do not believe that masturbation is genocide.") He also thinks gene therapy, not CRISPR per se, will set the table for this momentous change because it is already accepted: the U.S. Food and Drug Administration has allowed many trials of gene therapy in somatic (nongerm-line) cells. "Gene therapy is happening in young children already and will happen in younger and younger children," Church says.

In a highly publicized case last fall, for example, British researchers used gene-editing techniques to alter the immune cells of an infant battling leukemia. And the leap to germ-line gene therapy, according to Church, will occur not in human embryos but in the most proletarian, plentiful and expendable cell in the human body: sperm. Gene-editing sperm will spare couples the agony of destroying IVF embryos that, on preimplantation screening, are shown to possess variants that forecast some devastating single-gene disorders, he believes. "Maybe half the people in the U.S. already feel that they're not comfortable killing embryos, but I think people would be comfortable genetically altering sperm," he observes. "No embryos die."

Two obvious targets, Church adds, would be single-gene disorders (such as Tay-Sachs disease) and infertility. "You could also do it in human spermatogonial stem cells," he says, referring to the specialized adult stem cells in male testes that generate sperm cells—millions on millions of mindless, headlong swimmers—every day. "People don't really care about spermatogonia. Most people don't even know how to pronounce it. So they're going to let you mess around with them, right?" Church continues. "You will be able to do all kinds of things to show that they are functionally normal—that you've taken the sperm that can't swim, and that you've now taken their stem cells and made sperm that can swim. You can test that in a lab without any eggs being involved. And then in the fertility clinic, the dad will say, 'Hey, those are pretty awesome sperm. Let's try them out and see what they can really do.' And I don't know who's going to stop them from doing that."

As for the timeline, Church says, "I think there will be multiple clinical infertility solutions involving gene therapy soon."

How soon?

WILL SEX BECOME OBSOLESCENT?

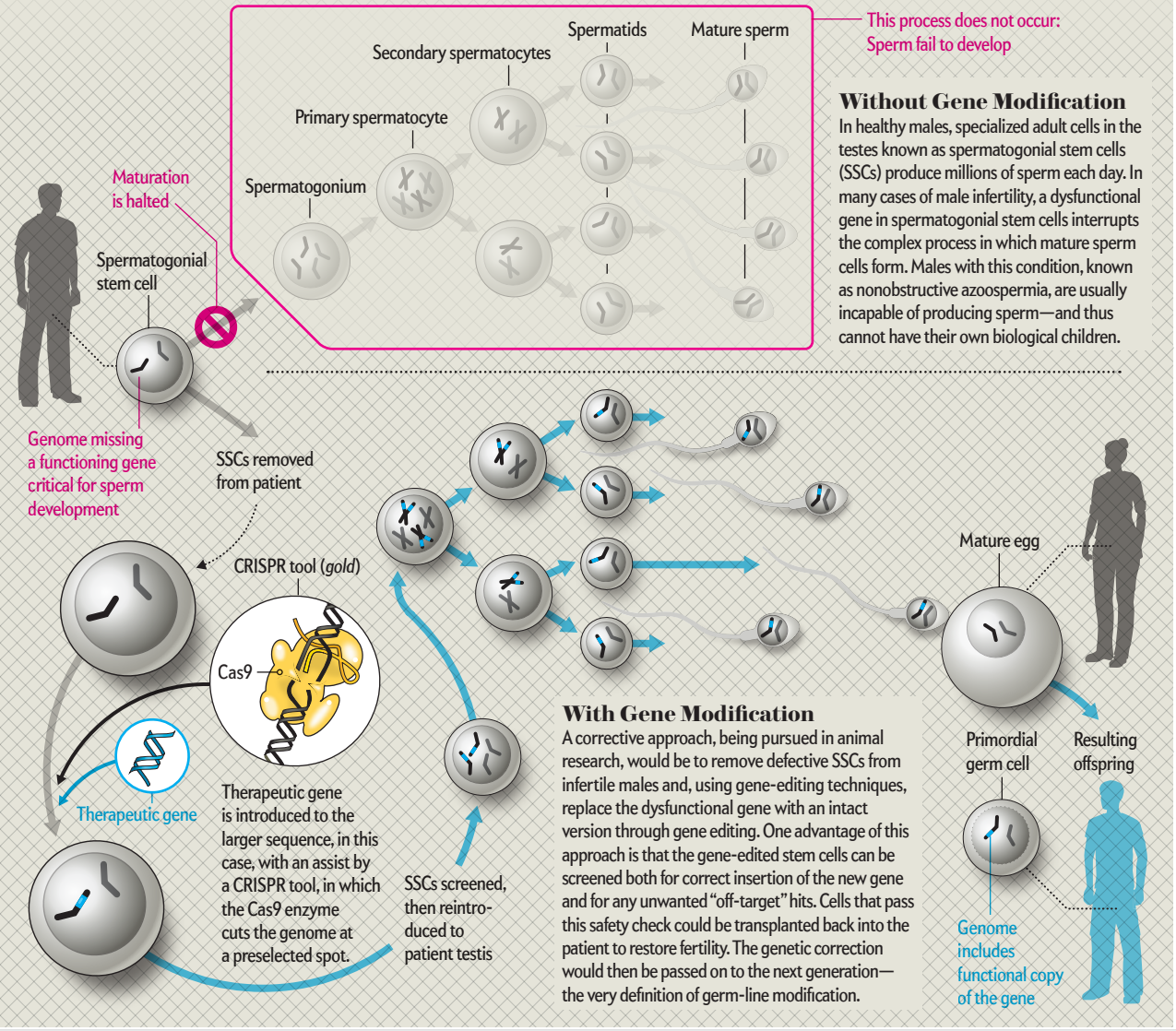
"No, but having sex to conceive babies is likely to become at least much less common. In 20 to 40 years we'll be able to derive eggs and sperm from stem cells, probably the parents' skin cells. This will allow easy preimplantation genetic diagnosis on a large number of embryos—or easy genome modification for those who want edited embryos instead of just selected ones."

HENRY GREELY
Director of the Center for Law and the Biosciences at Stanford University

Portraits by Kyle Hilton

How to Modify the Germ Line

Scientists in China have reportedly tried to edit the genes of human embryos for research purposes. They are also exploring the possibility of modifying genes in sex cells (sperm or egg), which would produce changes that are passed to the next generation. One potential route is to modify genes in the stem cells that produce sperm, which could lead to treatments for both male infertility (*below*) and single-gene disorders. (In 2015, for example, China researchers used such an approach to fix a mutation that causes cataracts in mice.)



Without Gene Modification

In healthy males, specialized adult cells in the testes known as spermatogonial stem cells (SSCs) produce millions of sperm each day. In many cases of male infertility, a dysfunctional gene in spermatogonial stem cells interrupts the complex process in which mature sperm cells form. Males with this condition, known as nonobstructive azoospermia, are usually incapable of producing sperm—and thus cannot have their own biological children.

With Gene Modification

A corrective approach, being pursued in animal research, would be to remove defective SSCs from infertile males and, using gene-editing techniques, replace the dysfunctional gene with an intact version through gene editing. One advantage of this approach is that the gene-edited stem cells can be screened both for correct insertion of the new gene and for any unwanted "off-target" hits. Cells that pass this safety check could be transplanted back into the patient to restore fertility. The genetic correction would then be passed on to the next generation—the very definition of germ-line modification.

"The next couple years," he says. "It would be very hard to resist."

In his talk at the National Academies meeting, Orwig flashed a slide that said: "Germ-Line Gene Therapy Is Technically Feasible Today." Afterward, according to Orwig, a member of the planning committee sidled up to him backstage and said, "Germ-line gene therapy is going to happen, I guarantee it." That sentiment never made it into the final meeting communiqué. But it galvanized Orwig.

"Whereas it might have been something I wanted to do hiding under a rock, it's now like, 'You go, man!' Let me get to work and prove to you that I can do it."

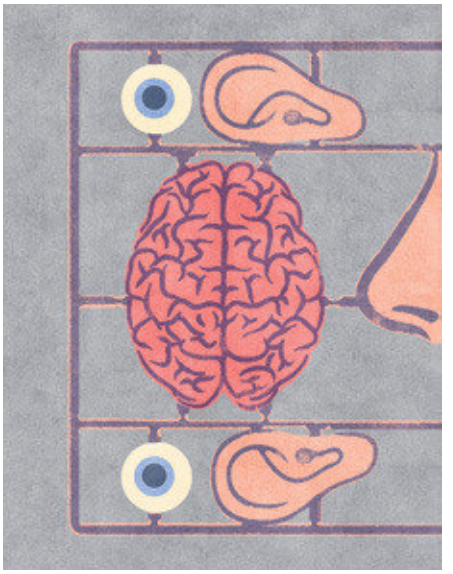
In animals, of course.

A GENTLE NUDGE DOWN THE SLOPE

A FEW STEPS DOWN the hallway from Orwig's office is a complex of rooms that houses hundreds of mice. You have to don a gown and booties and a mask to enter—not because you might catch something from the mice but because they might catch something from you. Many of the cages contain what are called nude

Illustration by Jen Christiansen

COULD WE ONE DAY REPLACE ALL OF THE TISSUES IN THE HUMAN BODY THROUGH ENGINEERING?



"In 1995 Joseph Vacanti and I wrote for this magazine about advances in artificial pancreas technology, plastic-based tissues such as artificial skin, and electronics that might permit blind people to see [see "Artificial Organs," by Robert Langer and Joseph P. Vacanti; Scientific American, September 1995]. All of these are coming to pass, either as real products or in clinical trials. Over the next few centuries it is quite possible that nearly every tissue in the body may be able to be replaced by such approaches. Creating or regenerating tissues such as those found in the brain, which is extremely complex and poorly understood, will take an enormous amount of research. The hope is, however, that research in this area will happen quickly enough to help with brain diseases such as Parkinson's and Alzheimer's."

ROBERT LANGER
David H. Koch Institute Professor at the Massachusetts Institute of Technology

mice—pink, wrinkled little rodents that resemble scrotums with eyes and feet. They are nude in the sense that they were bred to have compromised immune systems that accommodate cells transplanted from other species—for instance, human spermatogonial stem cells with mutations—to allow researchers to better understand the biology of male infertility.

If, as Church says, "everything is going to be done in animals first," the road to human germ-line modification runs through rooms like these. CRISPR makes the task more efficient ("It is so freaking easy!" Orwig says), but scientists have been able to alter the genes of sperm-making cells for more than two decades, beginning in 1994, when University of Pennsylvania biologist Ralph Brinster (Orwig's mentor) did the pioneering experiments in mice.

Male infertility has many causes, including obstructive "plumbing" issues, glitches in the incredibly complex process of sperm creation, and underachieving sperm. But in many cases, males simply can't make sperm at all; the condition, known as nonobstructive azoospermia, affects roughly 350,000 men in the U.S., according to Orwig. Several genes have been associated with the failure to produce sperm, including *tex11* and *sohlh1,* and those cases form the backdrop of the experiment Orwig is eager to do.

What Orwig wants to do is take infertile mice, which have a dysfunctional version of one of these genes, remove the sperm-forming stem cells from their testes and correct the defect in those cells by using the new gene-editing techniques. Once the altered stem cells are grown to sufficient numbers in the test tube and screened for precisely the correct alteration, they can be transplanted back into the testes of the animals. And at least in animal experiments of this kind, there is no need for any fancy molecular tests—if the gene editing is successful, Orwig will know within a couple of months because the infertile males will unambiguously demonstrate their ability to become fathers.

"We've been transplanting stem cells for 25 years in almost every species—mice, rats, hamsters, sheep, goats, pigs, dogs and monkeys," Orwig says. "That's a pretty broad swath of evolution, and in all this time, in all these animals, as far as we know, nothing bad has happened." That is why Orwig is optimistic he can demonstrate that editing the genes of stem cells in mice can reverse infertility.

This may seem like an innocuous animal experiment, but to edit a sperm-forming stem cell is to permanently modify the germ line because the resulting sperm cells pass the correction along to the next generation. A potential treatment for male infertility would cross the red line. And although Orwig has no plans to do the obvious human follow-up in his Pittsburgh lab, a successful preclinical demonstration in mice and primates would provide the impetus for an attempt in the private sector—which is where Church believes the final steps will unfold. "Sperm-editing efforts will be privately funded," he says, "just like other therapies."

Developing such a clinical treatment would face technical hurdles, of course. For one thing, scientists would have to find a way to maintain human spermatogonial stem cells long enough to select the right ones for transplantation—still not a trivial task. But these male stem cells offer much less of a moving target than embryos, which are dynamic and change rapidly. The Chinese researchers who have attempted gene editing in embryos with CRISPR, for example, have reported both "untoward mutations" and "mosaicism," meaning that some cells in the embryos show successful editing, whereas others do not. Moreover,

Illustration by Lorenzo Gritti

the DNA of gene-edited stem cells can be screened before an embryo is produced.

That is what makes Orwig's potential mouse experiment so politically inconvenient. Because of prohibitions enacted by Congress in the 1990s, the National Institutes of Health cannot fund any research that involves the destruction of human embryos. A human version of Orwig's proposed mouse experiment might sidestep that prohibition, but it would probably fall under a new obstacle that the House of Representatives introduced two weeks after the December summit on gene editing. In a two-sentence passage buried in the 2,009-page omnibus spending bill of 2015, Congress inserted language forbidding the FDA to consider any medical intervention relying on the use of gene-edited embryos; the wording does not explicitly prohibit editing germ cells, but Stanford University law professor Henry Greely believes "the FDA would take the position that those sperm were more than minimally manipulated human cells that would require FDA approval as a drug or biological product." The regulatory piece, he thinks, could add a decade or two to Church's timeline.

That does not mean Orwig's mouse experiment would be against the law—just a gentle nudge down the slippery slope toward germ-line modification. The step across the red line could happen in private IVF clinics, which have a long (and blemished) history of pushing the envelope on new reproductive technologies. "It's such an easy technology to apply that it would only take somebody with a little chutzpah to get together with someone in an IVF clinic and, you know, take a shot at it," says George Daley, a stem cell biologist at Boston Children's Hospital. "This is coming down the pike, and people need to start thinking about it," he notes. "This is a potentially disruptive reproductive technology."

It probably will not happen in the U.S. unless the public—and political—perception of germ-line modification becomes more accommodating, but Orwig is quietly preparing for that day. "We're going to work real hard behind the scenes," he says, "until the worldview changes."

CROSSING BORDERS

THE "WORLDVIEW" on germ-line editing is complicated and contradictory. A majority of Americans do not like the idea of editing genes in either embryos or germ cells, according to a recent analysis of 17 public opinion polls published in the *New England Journal of Medicine*. Yet paradoxically, most people support gene editing in adults "aimed at preventing one's children from inheriting certain diseases." (Robert J. Blendon, lead author of the study, says any intervention on the adult side that is positive for the next generation, including germ cells, would have "considerable public support.") Moreover, the *NEJM* study also pointed out that many of these public opinion polls pose their questions using language that "might not be scientifically precise." In other words, although the National Academies meeting adjourned last December with a pledge to continue the public conversation about germ-line editing, it is not clear that the public even understands the terms of that conversation. And while public forums struggle to find an effective vocabulary, the science races ahead.

As we spoke in his office last spring, Orwig nodded at a scientific reprint sitting on his desk. "I really, really love this paper," he said. He was referring to research published this past February in the journal *Cell Stem Cell* by a group headed by Qi Zhou of the Chinese Academy of Sciences. The experiment basically provided a recipe for the in vitro creation of germ cells.

The researchers showed that they could create sperm-forming stem cells in a dish; with a technique currently used in IVF clinics, these cells could be injected into egg cells to create fertile male mice. Harvard's Daley says of this advance: "With the addition of CRISPR, you've got the brave new world."

When Aldous Huxley imagined his brave new world in 1932, the story unfolded under one totalitarian regime, with neither national boundaries nor local regulations. In today's world, germ-line editing in any one place means the germ line is edited everywhere. "Regulation is country-specific, but science crosses borders," Harvard Law's Cohen says. Even if there were laws against germ-line modification in the U.S., you would have to build a wall much higher than the one proposed by Donald Trump to keep American germ lines insulated from an eventual influx of modified DNA.

"If you play out the world to 100 years from now, if anybody does this anywhere, that's the end game," Cohen says. "Over time those people will mate and create offspring and will cross borders and enter our shores. And if the safety and efficacy are worked out, it's inevitable that you're going to have people walking around in the world, and they're going to be reproducing, and they will end up in this country, and those changes will enter the U.S. gene pool."

As I am concluding my visit with Orwig, he glances at the computer on his desk. A reporter has sent an e-mail seeking comment on yet another experiment cozying up to the red line: a group in China has just reported its attempt to edit human embryos (nonviable) to be resistant to HIV infection. "Eventually we'll learn a vocabulary that acknowledges that we're there," Orwig says. "But I feel we're already there." SA

MORE TO EXPLORE

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FROM OUR ARCHIVES

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scientificamerican.com/magazine/sa

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WILL WE DEFEAT AGING?

By Bill Gifford

LIVING TO 120

In March, officials from Guinness World Records traveled to Haifa, Israel, to visit a retired candymaker named Israel Kristal. They came to proclaim him, at the age of 112 years and 178 days, the world's oldest man. Kristal has led an extraordinary life. When he was born, in 1903, life

Photograph by Andrew Myers

Bill Gifford is author of *Spring Chicken: Stay Young Forever (Or Die Trying),* a book about the science of aging.

expectancy for a boy in Poland was only about 45 years. As a child, he remembers throwing candies to Emperor Franz Josef of Austria-Hungary. As an adult, he ran a candy factory near Lodz. He lived through two world wars and survived nearly a year in various concentration camps, including a three-month stint at Auschwitz. His wife and two children were killed. After remarrying, he immigrated to Israel, where he made artisanal confections by hand. He now has something like 20 great-grandchildren. Born in the era of gas lamps, the centenarian now lives in the age of Twitter.

"Mr. Kristal's achievement is remarkable," said Marco Frigatti, head of records for Guinness, in an official statement. Indeed, the average life expectancy of a male in the developed world is close to 80 years. Only about two in 10,000 people live to age 100, and the vast majority of centenarians are female. At 112 and change, Kristal is near the limit of maximum observed life span for men. No human being has ever outlived Jeanne Calment of France, who died in 1997 at the age of 122.

What if, instead of dying at 80 or 85, the average person lived to be 100 or even 112 like Kristal? False promises of longer lives, even immortality, date back to the days of the alchemists, of course. So far there has not been much evidence to support such optimism. But some scientists believe centenarians such as Kristal really do age more slowly than the average person. Legitimate findings of current biological research hint that periods of extreme calorie restriction—perhaps like those experienced by the candymaker—affect the life spans of cells. This research is showing more precise ways to stretch those limits, not with diets, but with drugs.

Half a dozen medications or supplements, all of which have already been approved for human use for other purposes, turn out to target mechanisms within our cells that seem to improve internal damage control and thus help to prolong life. Some of these substances, including an anticancer drug, have already been shown to increase average and maximum life span in mice and other laboratory animals. This year a popular diabetes drug called metformin is headed for the first clinical trial ever designed to reveal whether a medication works to slow aging in people.

Because of this activity, a small coterie of well-established aging researchers is beginning to say that serious life extension could become a reality within the lifetimes of people reading this magazine. "There's been so much crazy talk about living forever and 'hacking' aging that it kind of drowns out what we know is possible now," says Matt Kaeberlein, a leading biogerontologist at the University of Washington. "The way the research is going, I see maybe 25 to 50 percent increases in healthy longevity as plausible in the next 40 or 50 years."

"There's been a huge response and huge interest, and a feeling that something big is going to happen," says Nir Barzilai, a leader of the metformin trial and the director of aging research at the Albert Einstein College of Medicine. "I think we'll get significant results. And the next drugs will be better."

IN BRIEF

Diets and other strategies, despite promising results in simple organisms and even mice, have failed to reliably extend healthy life spans in humans and other primates.

Mechanisms within cells triggered by dietary deprivation, however, are proving to be promising life-extension targets.

Drugs, including an antidiabetes medication and an anticancer drug, aim at these mechanisms and are now being tested for antiaging potential.

BEYOND DIET

AGING, AT LEAST IN PART, is rooted in our appetites. Scientists have known since the 1930s that underfeeding lab animals such as mice and rats can enable them to live longer—in some experiments, as much as 40 percent longer. Even nonscientists like Kristal think that the episodes of hunger in his life, during and after World War II, may have contributed to his longevity. In an interview with the newspaper *Haaretz,* he said, "I eat to live, and I don't live to eat. You don't need too much. Anything that's too much isn't good."

Unfortunately—or fortunately, depending on one's point of view—experiments with extreme caloric restriction in monkeys, animals more similar to people, have had mixed results. Low calorie consumption seemed to work well in one study, but then another well-designed trial showed that simply eating a more natural, whole-foods based diet, with a low sugar content, seemed to help just as much, regardless of calorie count. And in any event, very few humans can stick to a diet that requires cutting calories by 25 percent.

But experiments in lower organisms have revealed specific, beneficial cellular pathways—chains of molecular interactions—that are triggered when nutrients are scarce. These pathways evolved to allow organisms to survive long periods without food. In theory, activating such pathways with drugs could yield the same benefit without the pain of starving oneself. One example involves the enzyme AMPK, which acts as a kind of cellular fuel gauge. When nutrients are low, as happens during intense exercise or caloric restriction, AMPK jumps into action, transporting glucose into cells for energy and increasing cells' sensitivity to hormones that aid in this transport, such as insulin. It also helps break down fat for more energy. During exercise, AMPK stimulates the creation of new mitochondria, the energy producers within cells. All of these things improve health.

There is compelling evidence that aging and the rate of metabolism—the process by which a body converts food to energy—are directly linked. In 1993 Cynthia Kenyon of the University of California, San Francisco, discovered that mutations in just one specific gene called *DAF-2* could double the life span of the *Caenorhabditis elegans* worm. That gene is also linked to metabolic rates. But scientists still know relatively little about the genetics of aging, so for now their preferred targets are the higher-level mechanics of the cell.

One of the most promising antiaging mechanisms was discovered by accident. In 2001 biologist Valter Longo of the University of Southern California went away for a weekend and forgot to feed yeast cells that he was using in an experiment. He was surprised to discover that starving them completely for a time

PAGE 62: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

Aging's Off-Switch

In the soil of Easter Island in the 1970s, researchers found a compound that stopped the growth of fungus cells. They called the substance rapamycin after Rapa Nui, the native name for the island. What the compound did, scientists eventually learned, was interfere with an enzyme within cells that is essential for such activities as growth and replication. Because these activities eventually degrade cell functions, blocking the enzyme stretched out the prime of cellular lives. The enzyme, dubbed mTOR for "mechanistic target of rapamycin," seems to be a switch to turn aging off and on in cells and to make animals live longer.

When TOR Is On

The enzyme has two complexes, and the one called mTORC1 acts like a sensor for the cell's environment. When nutrients are abundant and energy for growth is easy to find, mTORC1 kicks the cell into high gear. It helps the cell take up glucose for energy, growth factors that trigger replication, and amino acids that can be used to make proteins essential to all of this labor.

When TOR Is Off

The drug rapamycin shields mTORC1, keeping it from detecting glucose or growth signals or nutrients, even when they surround the cell. As a result, the cell behaves as if it is living through a time of scarcity and slows down to conserve its resources. Major cellular functions are ramped down, in particular growth and replication.

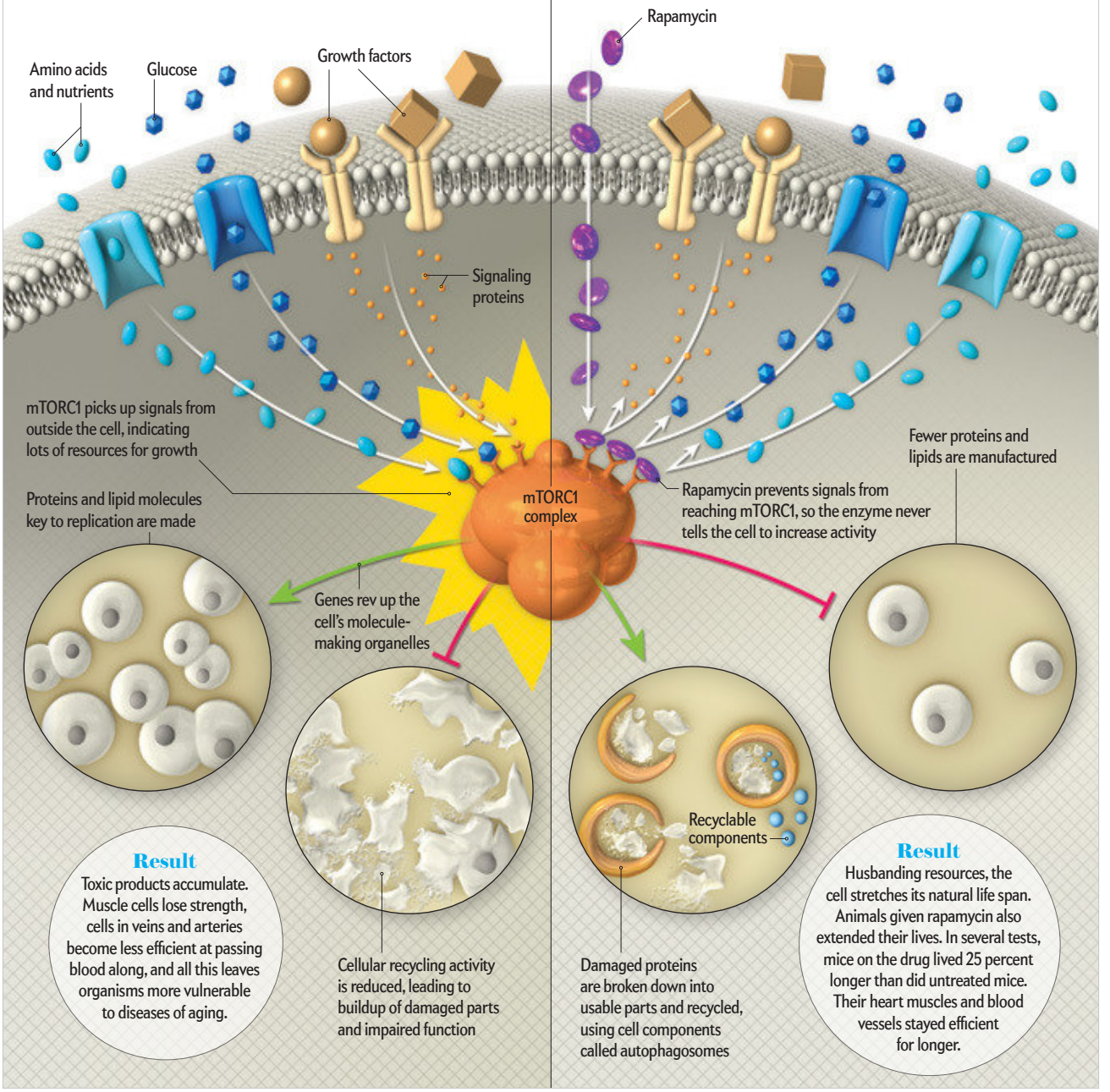
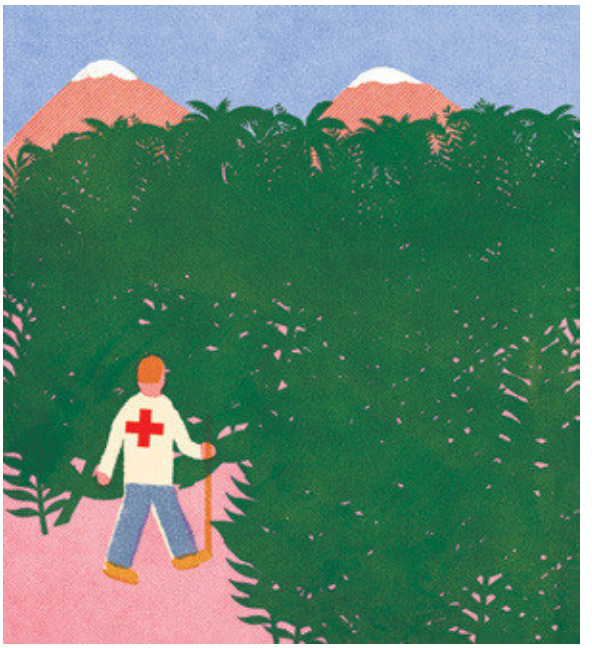


Illustration by Emily Cooper

WILL THE ENTIRE WORLD ONE DAY HAVE ADEQUATE HEALTH CARE?



"The global community has made tremendous progress toward health equity over the past 25 years, but these advances have not reached the world's most remote communities. Deep in the rain forest, where people are cut off from transportation and cellular networks, mortality is the highest, access to health care is the most limited and quality of care is the worst. The World Health Organization estimates that one billion people go their entire lives without seeing a health worker because of distance. Health workers recruited directly from the communities they serve can bridge the gap. They can even fight epidemics such as Ebola and maintain access to primary care when health facilities are forced to shut their doors. My organization, Last Mile Health, now deploys more than 300 health workers in 300 communities across nine districts in partnership with the government of Liberia. But we can't do this work alone. If the global community is serious about ensuring access to health care for all, it must invest in health workers who can reach the most remote communities."

RAJ PANJABI
Co-founder and chief executive at Last Mile Health and instructor at Harvard Medical School

made them live longer than usual. The reason, he learned, lay in a cascade of molecular actions usually referred to by the enzyme at its center, which is called mTOR.

This pathway was originally discovered years earlier thanks to a drug called rapamycin, which was found in soil bacteria. The drug, scientists learned, affected a major pathway regulating growth and division in the cell, like the circuit breaker in a tiny factory. Researchers named the path mTOR because it is a "mechanistic target of rapamycin." When mTOR is activated, the "factory" (that is, the cell) is humming along, producing new proteins, growing and ultimately dividing. When mTOR is blocked, such as by rapamycin—or by short-term fasting—cell growth and replication slow down or stop. This is why rapamycin has been effective as an immunosuppressor to protect transplanted organs and more recently as a cancer therapy; these conditions involve runaway cell division.

Longo's work led to the revelation of mTOR's crucial role in aging. When nutrients are scarce, mTOR is inhibited, and the factory goes into a more efficient mode, recycling old proteins to make new ones, ramping up the production of cellular cleaning and repair mechanisms and hunkering down to wait out the famine. Cell division slows down. And the animal is better able to survive until its next meal.

"What mTOR really does is, it senses the environment, and if there's lots of food around, then it gets cranked up—and in simple organisms, it causes them to develop really quickly and reproduce," Kaeberlein explains. "That makes a lot of sense because when there's lots of food, that's a really good time to make babies." No wonder the mTOR mechanism has been such a big evolutionary hit, used and reused by creatures up and down the tree of life, from single-celled yeast all the way up to humans and whales.

The activity change affects survival. In 2009 a team of scientists reported in *Nature* that rapamycin made lab mice live longer. This was a stunning finding: No other drug had ever lengthened the life span of mammals in this way in a controlled experiment. And this was not just one group of mice but *three* sets of genetically heterogeneous animals. All groups lived longer and not only on average: the animals' *maximum* life span was lengthened, which some considered clear evidence that the drug was slowing the aging process itself.

The mice given rapamycin generally seemed to stay healthier and more youthful for longer than rodents that did not get the drug. Their tendons, for example, stayed more flexible and elastic. So did their hearts and blood vessels. Even their livers were in better shape than the control mice's. They remained more active, even as they got older. What is more, rapamycin extended average and maximum life span even though mice only got it starting at the age of 20 months. It was like giving 70-year-old women a pill that let them live past 95. Or to put it another way, imagine a drug that would have let Kristal live into his 130s.

Other labs were able to reproduce the results and to extend them. Mice given rapamycin throughout their adult lives ended up living 25 percent longer—about the same as if they had been calorically restricted. Mice are not people, of course, but rapamycin raised the possibility, at least, that *something* might slow aging and delay the onset of age-related diseases. "Rapamycin was the first robust hit, the first drug that

Illustrations by Lorenzo Gritti, Portraits by Kyle Hilton

everybody said that this might be the real thing," says Brian Kennedy, CEO of the Buck Institute for Research on Aging in Novato, Calif.

Rapamycin is not without drawbacks, however. It can have unpleasant side effects, notably the appearance of mouth sores in some patients, and more frequent infections (because it suppresses immune response). In the mouse studies, the males appeared to suffer from testicular shrinkage. Those effects were acceptable for cancer and transplant patients, who were already quite sick, but they might disqualify it as an antiaging drug for otherwise healthy people. The cure might actually be worse than the disease. But what if you gave it to those healthy people in a different way or in lower doses? Could it, somehow, extend human life span as well?

To try and answer those questions, Kaeberlein and his colleague Daniel Promislow are starting an unusual clinical trial of low-dose rapamycin in middle-aged pet dogs. Our canine companions, they figure, are reasonable stand-ins for us: "They share our environment, and they get all the same diseases we get as they get older," Kaeberlein says. According to their preliminary data, dogs treated with rapamycin for just a few weeks displayed more youthful cardiac function, as measured by an echocardiogram. "We can clearly see that the heart is contracting better in the dogs that have gotten rapamycin than in the ones that haven't," Kaeberlein says. "In aging animals, poor blood flow is probably a factor in the decline of other body tissues."

One encouraging sign for the drug's potential as an antiaging agent, Kaeberlein says, is that in small amounts rapamycin may be working more as an immune modulator rather than a suppressor. It actually appears to *enhance* some kinds of immune function at these lower doses. A small human trial by Novartis, which markets a version of rapamycin as a cancer treatment called Afinitor, showed that older adults who took the drug actually responded better to a flu vaccine. This would indicate that it might enhance the immune response in some cases. One other interesting piece of evidence: a Dutch study found that healthy nonagenarians had lower levels of mTOR activity.

The next step, funds permitting, is to do a longer-term longitudinal study of rapamycin in older dogs, tracking their progress as they age. If the results reflect those achieved in mice—if the dogs live longer and healthier lives—they could justify a human clinical trial. "We could know, five years from now, to what extent it is actually working," Kaeberlein says.

STRETCHING LIVES

CONNECTING "HEALTHIER" to "longer" is key. Our life spans have been stretching out, but the latter part of our lives is prone to periods of disease and disability. As demographers James W. Vaupel and Jim Oeppen demonstrated in a 2002 *Science* paper, life expectancy for the longest-lived populations has been growing more or less linearly since the 1840s (currently Japanese females are at the top of the list). People have been living longer than ever before in human history.

At the same time, however, health span—defined as the length of healthy life—has not been growing quite as fast. This means that the period of disease and disability at the end of life, the dreaded decline of old age, has actually been getting longer. The only thing that changes, as we live longer and longer, is that we fall victim to different ailments. As mortality rates from heart disease and cancer drop, more of us become vulnerable to Alzheimer's disease. One in nine Americans older than 65 is affected by Alzheimer's or other forms of cognitive decline, with risk rising drastically after age 80.

"The rise of Alzheimer's disease has been astonishing, but it's exactly what you would expect if you push people into age windows where this disease is common, the late 70s and 80s," says S. Jay Olshansky, a demographer at the University of Illinois at Chicago. "If we continue this path, I think that it will get worse. The alternative is to slow aging and compress morbidity and mortality into a shorter time period."

Olshansky has not met Kristal, but the Guinness record holder seems to be the kind of old person he has in mind. At 112, Kristal is still sharp mentally and a witty conversationalist. He has managed to resist the deadly illnesses of aging—not only cancer and heart disease but also Alzheimer's and diabetes, which together account for about half of deaths in the developed world. In centenarians like him, researchers find, the period of sickness at the end of life is often much shorter than for people who die in their 70s. A successful antiaging drug would need to mimic the same effect, rather than merely prolong life at the expense of health and well-being, Olshansky says.

But until very recently, investigators have faced a formidable stumbling block to developing that kind of drug: the U.S. Food and Drug Administration has not considered aging to be a disease. Therefore, it would

WILL BRAIN SCIENCE CHANGE CRIMINAL LAW?

"In all likelihood, the brain is a causal machine, in the sense that it goes from state to state as a function of antecedent conditions. The implications of this for criminal law are absolutely nil. For one thing, all mammals and birds have circuitry for self-control, which is modified through reinforcement learning (being rewarded for making good choices), especially in a social context. Criminal law is also about public safety and welfare. Even if we could identify circuitry unique to serial child rapists, for example, they could not just be allowed to go free, because they would be apt to repeat. Were we to conclude, regarding, say, Boston priest John Geoghan, who molested some 130 children, 'It's not his fault he has that brain, so let him go home,' the result would undoubtedly be vigilante justice. And when rough justice takes the place of a criminal justice system rooted in years of making fair-minded law, things get very ugly very quickly."

PATRICIA CHURCHLAND
Professor of philosophy and neuroscience at the University of California, San Diego

not approve any drug that targeted the aging process itself. From the agency's point of view, this policy made sense: There is no objective way to "measure" aging—no blood test, for example, that can determine whether a person is aging more quickly or slowly than normal. So how would we know if an antiaging drug was working? That official stance eliminated any incentive for a drug company to invest in research into aging and drugs that might slow it down. There was simply no path to approval and to market.

The path began to clear in 2015, however, when the agency gave approval to a clinical trial meant to assess the antiaging properties of metformin. Approved for type 2 diabetes (the most common form) in the U.K. in the 1950s, metformin passed FDA review in the U.S. in 1994. It has since been prescribed to millions of patients as a first-line treatment. Now available as a cheap generic, it is one of the world's most common prescriptions, so much so that the World Health Organization has declared it an "essential" medication. It increases cells' sensitivity to insulin, the hormone that signals them to take in sugar (glucose) from the blood.

Because so many people take the drug, researchers have been able to detect intriguing patterns among patients. In particular, epidemiological studies have found that those on metformin seem to have a lower incidence of cancer. Other studies have suggested that metformin may have beneficial cardiovascular effects. Moreover, whereas diabetics generally lose several years of life expectancy, a 2014 analysis of British patient data found that older diabetics who were taking metformin were actually living 18 percent *longer* than matched nondiabetic controls. They also lived longer than diabetics using another common class of medications, the sulfonylureas, indicating that it was the metformin itself, and not just control of diabetes, that conferred a longevity advantage.

How exactly that works is not entirely clear. The mechanism of action of metformin, which is derived from an ancient herbal remedy called French lilac or goat's rue, has been debated among scientists for decades. One thing it is known to do is activate the AMPK pathway and its favorable metabolic changes. It also seems to affect insulin through other paths and even to inhibit mTOR somewhat.

The possibility that metformin might enhance longevity caught the attention of Albert Einstein's Barzilai, among others. As head of a major study of Ashkenazi Jewish centenarians, Barzilai knew that long-lived people rarely have problems with high blood glucose or diabetes; ultraefficient processing of blood glucose in fact is a marker for longevity. Metformin, he thinks, might alter our metabolism to more closely resemble that of a centenarian. "A lot of its antidiabetic activity is also antiaging, just improving cellular function and insulin sensitivity," Barzilai says. He actually takes the drug himself as a preventive because his parents both had diabetes. He stops just short of saying that everyone older than 50 should think about getting a prescription (he is 60). "It looks like a superdrug," Barzilai says. "It looks like it's involved in many things related to aging."

"There are 60 years of data in humans showing that it targets a whole lot of conditions that, in aggregate, would have you believe that it's targeting fundamental aging processes," agrees James L. Kirkland, director of the Robert and Arlene Kogod Center for Aging Research at the Mayo Clinic and a collaborator on the metformin studies.

Yet to test suspected antiaging drugs in people, researchers have to deal with another obstacle: time. A conventional life span study would require decades to complete—literally, a lifetime. The trial approved in

WILL WE EVER UNDERSTAND THE NATURE OF CONSCIOUSNESS?

"Some philosophers, mystics and other *confabulatores nocturni* pontificate about the impossibility of ever understanding the true nature of consciousness, of subjectivity. Yet there is little rationale for buying into such defeatist talk and every reason to look forward to the day, not that far off, when science will come to a naturalized, quantitative and predictive understanding of consciousness and its place in the universe."

CHRISTOF KOCH
President and CSO at the Allen Institute for Brain Science; member of Scientific American's *advisory board*

2015, called TAME, for Targeting Aging with Metformin, takes a different approach. Rather than simply comparing longevity in healthy subjects who get the drug with those who do not, the scientists will instead look at the progression of aging-related diseases in each subject.

One of the hallmarks of aging is the way that older people often develop more than one chronic condition, such as high blood pressure and diabetes or heart disease and cognitive impairment. These so-called comorbidities, one disease on top of another, are a major cause of misery in the elderly (not to mention a driver of increased health care spending). In the TAME trial, scientists plan to give metformin to elderly patients who already have one aging-related condition, such as diabetes or high blood pressure. The subjects will be monitored for five to seven years and compared against a control group that has agreed not to take the drug to see whether or not they go on to develop other age-related diseases at a faster or slower rate. If metformin is really slowing the aging process, then it should be able to stave off the progression of comorbidities.

The TAME trial, then, will really be measuring metformin's effect on health span—evaluating it as, in essence, preventive medicine. "The same kind of process occurred with, for example, giving antihypertensives to people who haven't had a heart attack," says Kirkland.

If the TAME study is successful, and the drug agency shows an openness to test new medications that target aging, Barzilai thinks, pharmaceutical companies will begin to move into the space—and not just traditional pharma, but ventures like the Google-backed Calico project, where none other than Cynthia Kenyon, who discovered the *DAF-2* aging gene two decades ago, is vice president of aging research. Calico, some reports have speculated, may be investing more than $1 billion in a search for drugs that will extend health span, an amount close to to the entire budget of the National Institute on Aging.

"If longevity is a side effect" of extending health span, Barzilai says half-jokingly, "we'll apologize for that."

PILLS FOR THE AGES

THE PIPELINE of potential antiaging medications is already beginning to fill. Another antidiabetic agent called acarbose has extended life span significantly in male mice, for example. Like metformin, acarbose is already approved for human use, so it, too, could be a candidate for a clinical trial against aging. Still another drug, the hormone alpha-estradiol, has also had good results, in the same kinds of trials that discovered the antiaging effect of rapamycin.

A newer and perhaps even more promising group of antiaging drug candidates does not work on metabolic pathways but by clearing out so-called senescent cells, which have stopped dividing but have not actually died. Like cellular zombies, they sit there and secrete small proteins known as cytokines that can damage the cells around them. Kirkland believes that their true function is as a cancer defense mechanism—a way for the body to kill neighboring cells that may be malignant. Senescent cells also play a role in wound healing because the cytokines they secrete help to marshal the immune system. Unfortunately, their toxic effects reach far beyond the immediate neighborhood, contributing to the low-grade inflammation that characterizes aging bodies—and, paradoxically, increasing cancer risk in surrounding tissues. Kirkland and others see them as a key driver of the aging process.

Even worse, the older we get, the more senescent cells we harbor in our bodies. What if we could get rid of them? Kirkland and his colleagues, including molecular biologist Jan van Deursen of the Mayo Clinic, have shown that eliminating senescent cells from genetically modified mice seems to increase their health span. The problem is that senescent cells are very hard to isolate—they are dispersed among healthy cells—and even harder to kill. "They're very resistant to dying," Kirkland says. "They're hardy as all get-out."

A team of researchers at Mayo, the Scripps Research Institute and other institutions looked for drugs that could kill senescent cells by inducing apoptosis, or cell suicide. In 2015 they reported in a paper that they found three, including two cancer drugs, dasatinib and navitoclax, as well as quercetin, a naturally occurring flavonoid. This is an antioxidant and pigment-carrying compound that is found in, among other things, the peel of apples and in capers (among many other foods).

In one experiment, animals had one leg disabled by irradiation, which caused muscle atrophy that was similar to the loss of muscle caused by aging. The radiation also created lots of senescent cells in the muscle, a condition that has also been observed in cancer patients after radiation or chemotherapy. After a short treatment with the drugs, the animals' leg function was restored almost completely. The dramatic effect, Kirkland believes, was because the drugs killed more senescent cells than other types. "We only gave a single dose, and treadmill endurance improved considerably—and stayed improved for seven months," Kirkland says. "That gives us reassurance that it's actually clearing senescent cells. And once they're dead, they're dead."

They have to die, perhaps, so that we might live. SA

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IF WE COULD, WOULD WE WANT TO LIVE FOREVER?

By Hillary Rosner

ALL TOO HUMAN

Photograph by Andrew Myers

Hillary Rosner is a freelance writer based in Colorado. She has written for *National Geographic,* the *New York Times* and *Wired,* among other publications. Rosner won a AAAS Kavli Science Journalism Award in 2010 and 2013.

Recently, at a wedding reception, I polled some friends about immortality. Suppose you could upload your brain tomorrow and live forever as a human-machine hybrid, I asked an overeducated couple from San Francisco, parents of two young daughters. Would you do it? The husband, a 42-year-old M.D.-Ph.D., didn't hesitate before answering yes. His current research, he said, would likely bear fruit over the next several centuries, and he wanted to see what would come of it. "Plus, I want to see what the world is like 10,000 years from now." The wife, a 39-year-old with an art history doctorate, was also unequivocal. "No way," she said. "Death is part of life. I want to know what dying is like."

IN BRIEF

Some scientists believe that one day technology will make it possible to achieve immortality by uploading our neural connections into robots' bodies; others believe this is impossible.

Regardless, legitimate philosophers are engaged in a debate over how such an eventuality would change our humanity.

Their dialogue is important because even if the "singularity" falls short, human augmentation and improvements may raise similar issues.

I wondered if his wife's decision might give the husband pause, but I diplomatically decided to drop it. Still, the whole thing was more than simply dinner-party fodder. If you believe the claims of some futurists, we'll sooner or later need to grapple with these types of questions because, according to them, we are heading toward a postbiological world in which death is passé—or at least very much under our control.

The most well-imagined version of this transcendent future is Ray Kurzweil's. In his 2005 best-selling book *The Singularity Is Near,* Kurzweil predicted that artificial intelligence would soon "encompass all human knowledge and proficiency." Nanoscale brain-scanning technology will ultimately enable "our gradual transfer of our intelligence, personality, and skills to the nonbiological portion of our intelligence." Meanwhile billions of nanobots inside our bodies will "destroy pathogens, correct DNA errors, eliminate toxins, and perform many other tasks to enhance our physical well-being. As a result, we will be able to live indefinitely without aging." These nanobots will create "virtual reality from within the nervous system." Increasingly, we will live in the virtual realm, which will be indistinguishable from that anemic universe we might call "real reality."

Based on progress in genetics, nanotechnology and robotics and on the exponential rate of technological change, Kurzweil set the date for the singularity—when nonbiological intelligence so far exceeds all human intelligence that there is "a profound and disruptive transformation in human capability"—at 2045. Today a handful of singulatarians still hold to that date, and progress in an aspect of artificial intelligence known as deep learning has only encouraged them.

Most scientists, however, think that any manifestation of our cyborg destiny is much, much farther away. Sebastian Seung, a professor at the Princeton Neuroscience Institute, has argued that uploading the brain may never be possible. Brains are made up of 100 billion neurons, connected by synapses; the entirety of those connections make up the connectome, which some neuroscientists believe holds the key to our identities. Even by Kurzweilian standards of technological progress, that is a whole lot of connections to map and upload. And the connectome might be only the beginning: neurons can also interact with one another outside of synapses, and such "extrasynaptic interactions" could turn out to be essential to brain function. If so, as Seung argued in his 2012 book *Connectome: How the Brain's Wiring Makes Us Who We Are,* a brain upload might also have to include not just every connection, or every neuron, but every *atom*. The computational power required for that, he wrote, "is completely out of the question unless your remote descendants survive for galactic timescales."

Still, the very possibility of a cyborg future, however remote or implausible, raises concerns important enough that legitimate philosophers are debating it in earnest. Even if our technology fails to achieve the full Kurzweilian vision, augmentation of our minds and our bodies may take us part of the way there—raising questions about what makes us human.

I ask David Chalmers, a philosopher and co-director of the Center for Mind, Brain and Consciousness at New York University who has written about the best way to upload your brain to preserve your self-identity, whether he expects he will have the opportunity to live forever. Chalmers, who is 50, says he doesn't think so—but that "absolutely these issues are going to become practical possibilities sometime in the next century or so."

Ronald Sandler, an environmental ethicist and chair of the department of philosophy and religion at Northeastern University, says talking about our cyborg future "puts a lot of issues in sharp relief. Thinking about the limit case can teach you about the near-term case."

PAGE 70: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

And, of course, if there is even the remote possibility that those of us alive today might ultimately get to choose between death or immortality as a cyborg, maybe it's best to start mulling it over now. So putting aside the question of feasibility, it is worth pausing to consider more fundamental questions. Is it desirable? If my brain and my consciousness were uploaded into a cyborg, who would I be? Would I still love my family and friends? Would they still love me? Would I, ultimately, still be human?

One of the issues philosophers think about is how we treat one another. Would we still have the Golden Rule in a posthuman world? A few years ago Sandler co-authored a paper, "Transhumanism, Human Dignity, and Moral Status," arguing that "enhanced" humans would retain a moral obligation to regular humans. "Even if you become enhanced in some way, you still have to care about me," he tells me. Which seems hard to argue with—and harder still to believe would come to pass.

Other philosophers make a case for "moral enhancement"—using medical or biomedical means to give our principles an upgrade. If we're going to have massive intelligence and power at our disposal, we need to ensure Dr. Evil won't be at the controls. Our scientific knowledge "is beginning to enable us to directly affect the biological or physiological bases of human motivation, either through drugs, or through genetic selection or engineering, or by using external devices that affect the brain or the learning process," philosophers Julian Savulescu and Ingmar Persson wrote recently. "We could use these techniques to overcome the moral and psychological shortcomings that imperil the human species."

In an op-ed this past May in the *Washington Post* entitled "Soon We'll Use Science to Make People More Moral," James Hughes, a bioethicist and associate provost at the University of Massachusetts Boston, argued for moral enhancement, saying it needs to be voluntary rather than coercive. "With the aid of science, we will all be able to discover our own paths to technologically enabled happiness and virtue," wrote Hughes, who directs the Institute for Ethics and Emerging Technologies, a progressive transhumanist think tank. (For his part, Hughes, 55, a former Buddhist monk, tells me that he would like to stay alive long enough to achieve enlightenment.)

There is also the question of how we might treat the planet. Living forever, in whatever capacity, would change our relationship not just to one another but to the world around us. Would it make us more or less concerned about the environment? Would the natural world be better or worse for it?

The singularity, Sandler points out to me, describes an end state. To get there would involve a huge amount of technological change, and "nothing changes our relationship with nature more quickly and robustly than technology." If we are at the point where we can upload human consciousness and move seamlessly between virtual and non–virtual reality, we will already be engineering nearly everything else

WILL WE EVER COLONIZE OUTER SPACE?

"That depends on the definition of 'colonize.' If landing robots qualifies, then we've already done it. If it means sending microbes from Earth and having them persist and maybe grow, then, unfortunately, it's not unlikely that we've done that as well—possibly on Mars with the Phoenix spacecraft and almost certainly inside the Curiosity rover, which carries a heat source and was not fully baked the way Viking had been.

If it means having humans live elsewhere for a longer period of time, but not reproduce, then that's something that might happen within the next 50 years or so. (Even some limited degree of reproduction might be feasible, recognizing that primates will be primates.) But if the idea is to construct a self-sustaining environment where humans can persist indefinitely with only modest help from Earth—the working definition of a 'colony,' according to the various European colonies outside of Europe—then I'd say this is very far in the future, if it's possible at all. We currently have a very inadequate understanding of how to build closed ecosystems that are robust to perturbation by introduced organisms or nonbiological events (*Biosphere 2,* for example), and I suspect that the contained ecosystem problem will turn out to be much more challenging than the vast majority of space colonization advocates realize. There are a wide range of technical problems to solve, another being air handling. We haven't bothered to colonize areas underwater on Earth yet. It's far more challenging to colonize a place where there's hardly any atmosphere at all."

CATHARINE A. CONLEY
NASA planetary protection officer

Portraits by Kyle Hilton

in significant ways. "By the time the singularity would occur, our relationship with nature would be radically transformed already," Sandler says.

Although we would like to believe otherwise, in our current mere mortal state we remain hugely dependent on—and vulnerable to—natural systems. But in this future world, those dependencies would change. If we didn't need to breathe through lungs, why would we care about air pollution? If we didn't need to grow food, we would become fundamentally disconnected from the land around us.

Similarly, in a world where the real was indistinguishable from the virtual, we might derive equal benefit from digitally created nature as from the great outdoors. Our relationship to real nature would be altered. It would no longer be sensory, physical. That shift could have profound impacts on our brains, perhaps even the silicon versions. Research shows that interacting with nature affects us deeply—for the better. A connection to nature, even at an unconscious level, may be a fundamental quality of being human.

If our dependence on nature falls away, and our physical ability to commune with nature diminishes, then "the basis for environmental concern will shift much more strongly to these responsibilities to nature for its own sake," Sandler says. Our capacity for solving environmental problems—engineering the climate, say—will be beyond what we can imagine today. But will we still feel that nature has intrinsic value? If so, ecosystems might fare better. If not, other species and the ecosystems they would still rely on might be in trouble.

Our relationship to the environment also depends on the question of timescales. From a geologic perspective, the extinction crisis we are witnessing today might not matter. But it does matter from the timeline of a current human life. How might vastly extended life spans "change the perspective from which we ask questions and think about the nonhuman environment?" Sandler asks. "The timescales really matter to what reasonable answers are." Will we become more concerned about the environment because we will be around for so long? Or will we care less because we will take a broader, more geologic view?

"It's almost impossible to imagine what it will be like," Sandler says, "but we can know that the perspective will be very, very different."

Talk to experts about this stuff for long enough, and you fall down a rabbit hole; you find yourself having seemingly normal conversations about absurd things. "If there were something like an X-Men gene therapy, where they can shoot lasers out of their eyes or take over your mind," Hughes says to me at one point, then people who want those traits should have to complete special training and obtain a license.

"Are you using those examples to make a point, or are they actual things you believe are coming?" I ask.

"In terms of how much transhumanists talk about these things, most of us try not to freak out newbies too much," he replies obliquely. "But once you're past shock level 4, you can start talking about when we're all just nanobots."

When we're all just nanobots, what will we worry about? Angst, after all, is arguably one of our defining qualities as humans. Does immortality render angst obsolete? If I no longer had to stress about staying healthy, paying the bills, and how I'll support myself when I'm too old and frail to travel around writing articles, would I still be me? Or would I simply be a placid, overly contented … robot? For that matter, what would I daydream about? Would I lose my ambition, such as it is? I mean, if I live forever, surely that Great American Novel can wait until next century, right?

Would I still be me? Chalmers believes this "is going to become an extremely pressing practical, not just philosophical, question."

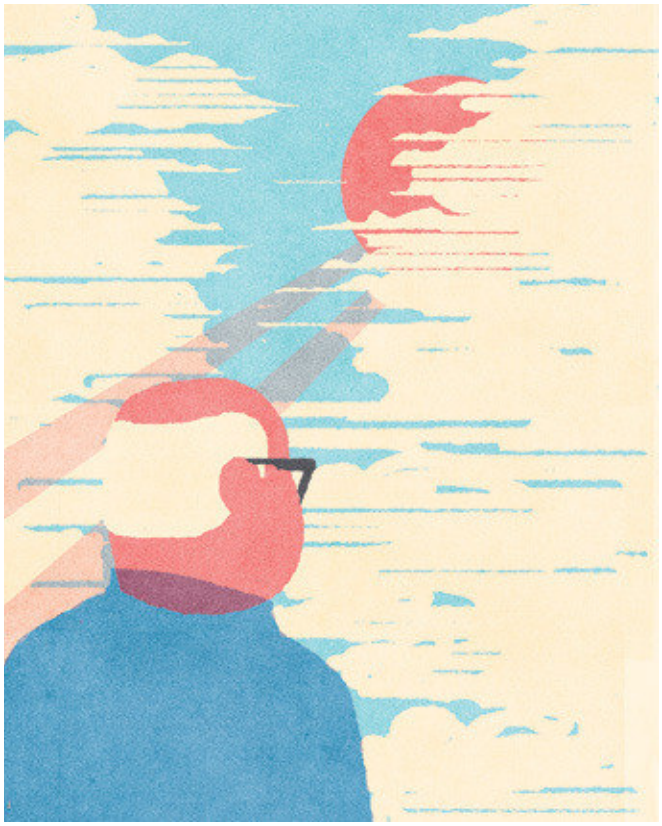
On a gut level, it seems implausible that I would remain myself if my brain was uploaded—even if, as Chalmers has prescribed, I did it neuron by neuron, staying conscious throughout, becoming gradually 1 percent silicon, then 5, then 10 and onward to 100. It's the old saw about Theseus's ship—replaced board by board with newer, stronger wood. Is it or isn't it the same afterward? If it's not the same, at what point does the balance tip?

"A big problem," Hughes says, "is you live long

WILL WE DISCOVER A TWIN EARTH?

"My money's on yes. We've found that planets around other stars are far more abundant and diverse than scientists imagined just a couple of decades ago. And we've also found that the crucial ingredient for life on this planet—water—is common in space. I'd say nature seems to have stacked the deck in favor of a wide range of planets, including Earth-like planets. We just have to look for them."

AKI ROBERGE
Research astrophysicist focusing on exoplanets at NASA Goddard Space Flight Center



WILL THERE EVER BE A CURE FOR ALZHEIMER'S?

"I am not sure if there will be a cure, per se, but I am very hopeful that there will be a successful disease-modifying therapy for Alzheimer's disease within the next decade. We have now started prevention trials that are testing biological interventions even before people show clinical symptoms of the disease. And we don't have to cure Alzheimer's—we just need to delay dementia by five to 10 years. Estimates show that a five-year delay in the terrible and expensive dementia stage of the disease would reduce Medicare dementia costs by nearly 50 percent. Most important, that would mean that many older people could die while out ballroom dancing rather than in nursing homes."

REISA SPERLING
Professor of neurology at Harvard Medical School and director of the Center for Alzheimer Research and Treatment

enough and you'll go through so many changes that there's no longer any meaning to you having lived longer. Am I really the same person I was when I was five? If I live for another 5,000 years, am I really the same as I am now? In the future, we will be able to share our memories, so there will be an erosion of the importance of personal identity and continuity." That sounds like kind of a drag.

Despite the singularity's utopian rhetoric, it carries a tinge of fatalism: this is the only route available to us; merge with machines or fade away—or worse. What if I don't want to become a cyborg? Kurzweil might say that it's only my currently flawed and limited biological brain that prevents me from seeing the true allure and potential of this future. And that the choices available to me—any type of body, any experience in virtual reality, limitless possibilities for creative expression, the chance to colonize space—will make my current biological existence seem almost comically trivial. And anyway, what's more fatalistic than certain death?

Nevertheless, I really like being human. I like knowing that I'm fundamentally made of the same stuff as all the other life on Earth. I'm even sort of attached to my human frailty. I like being warm and cuddly and not hard and indestructible like some action-film super-robot. I like the warm blood that runs through my veins, and I'm not sure I really want it replaced by nanobots.

Some ethicists argue that human happiness relies on the fact that our lives are fleeting, that we are vulnerable, interdependent creatures. How, in a human-machine future, would we find value and meaning in life?

"To me, the essence of being human is not our limitations … it's our ability to reach beyond our limitations," Kurzweil writes. It's an appealing point of view. Death has always fundamentally been one of those limitations, so perhaps reaching beyond death makes us deeply human?

But once we transcend it, I'm not convinced our humanity remains. Death itself doesn't define us, of course—all living things die—but our awareness and understanding of death, and our quest to make meaning of life in the interim, are surely part of the human spirit. SA

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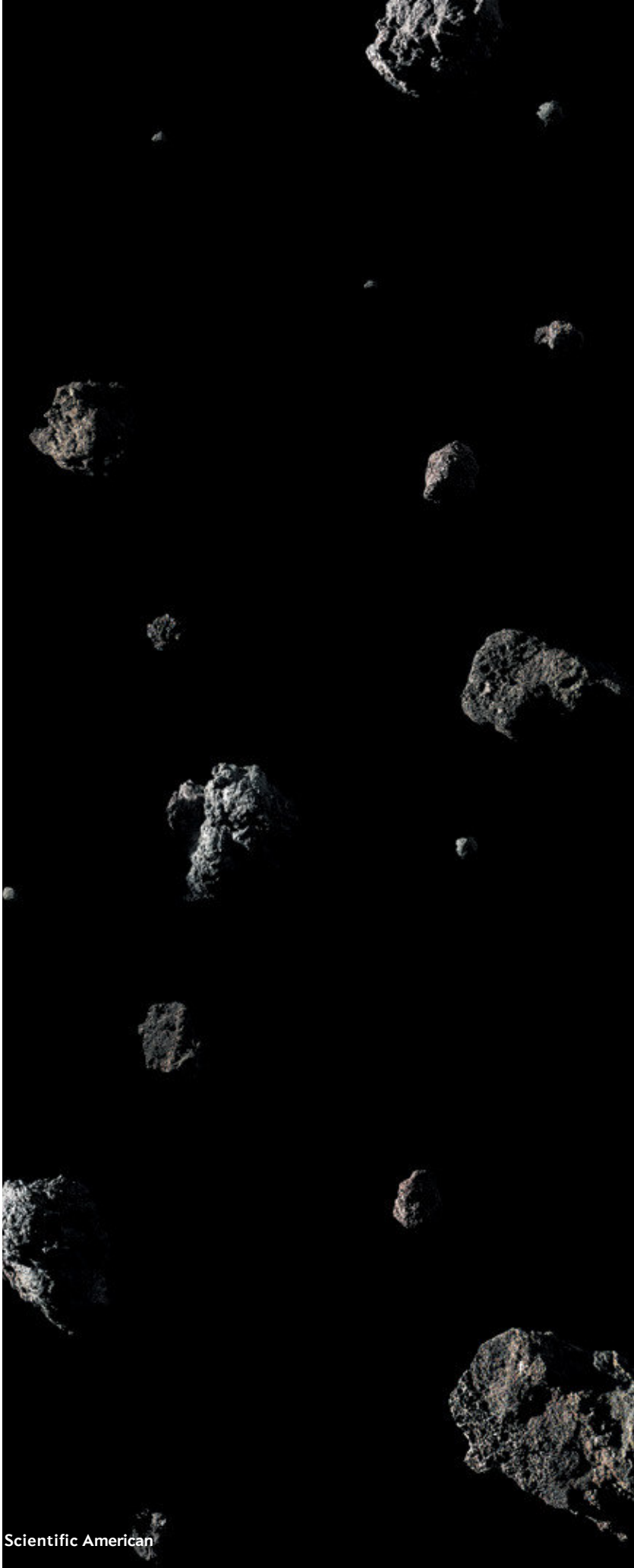
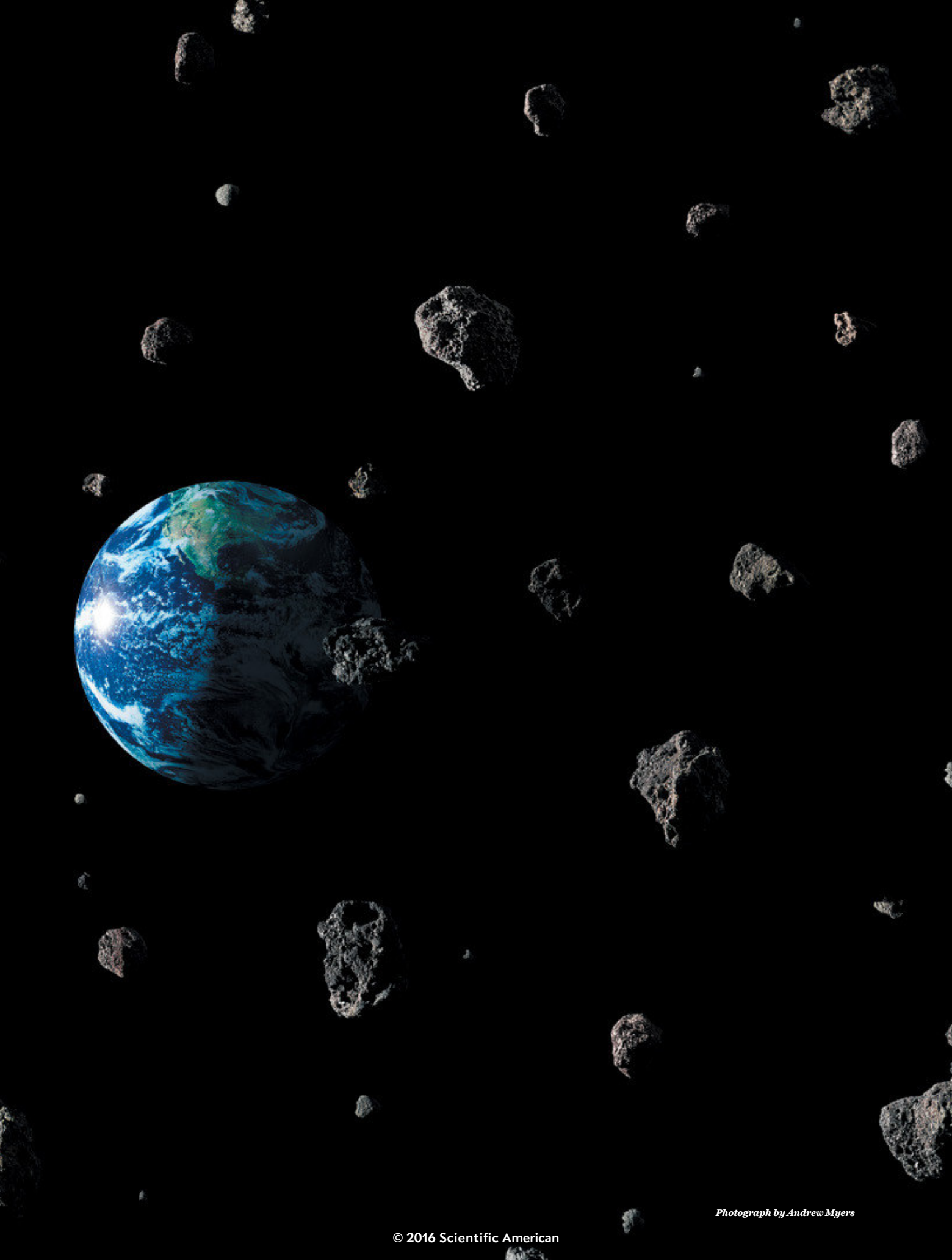
HOW LONG WILL WE LAST?

By David Grinspoon

DEEP TIME, DEEP SURVIVAL





Photograph by Andrew Myers

David Grinspoon is a senior scientist at the Planetary Science Institute in Tucson, Ariz. In 2012 and 2013 he served as the U.S. Library of Congress's first chair of astrobiology while researching his forthcoming book *Earth in Human Hands*.

The biggest debate among experts on the Anthropocene is when, exactly, a geologic epoch marked by humanity's influence began. As an astrobiologist who studies major historical transitions in planetary evolution, I am more interested in another question: When, and how, will the Anthropocene end?

Epochs are relatively short periods of geologic time. Much more consequential are the boundaries separating the geologic timescale's longest phases, the billion-year-scale chunks of history called eons. These transitions left the world permanently and profoundly changed. From the hellish conditions of the Hadean eon, Earth shifted to a cooler, quieter Archean eon that nurtured the emergence of life. During the Proterozoic eon, some of those microbes become a disruptive, planet-altering force, flooding the atmosphere with photosynthetic oxygen. This change in atmospheric chemistry poisoned much of the biosphere, but it also led to the flourishing of complex multicellular life, ushering in our current eon, the Phanerozoic.

The Anthropocene may be the beginning of another fundamental transition. This fifth eon could be defined by a radically new type of global change in which cognitive processes—the thoughts, deeds and creations of human beings—become a key part of the functioning of our planet. I propose we call this potential new eon the Sapiezoic, for "wise life." For the first time in Earth's history, a self-aware geologic force is shaping the planet.

But an epoch only becomes an eon if it endures for hundreds of millions of years or longer. For that to happen, *we* have to endure that long. Are we up to it?

IN BRIEF

The Anthropocene— the epoch in which humanity is a dominant force for global change—has just begun, but it will probably only last as long as we do.

Avoiding extinction requires overcoming existential threats such as population growth, resource scarcity, asteroid strikes, climate change and even the gradual senescence of the sun.

An enduring Anthropocene could push our planet into a new fundamental state—a billion-year-scale "Sapiezoic" eon in which our civilization's collective intelligence stabilizes Earth's natural systems and extends the biosphere to new cosmic realms.

AVOIDING EXTINCTION

OUR MOST IMMEDIATE CHALLENGES over the next century are to stabilize our population and to construct energy and agricultural systems that can provide for us without wrecking natural systems. There is no doubt that we will shift away from fossil fuels, but the speed with which we do so may determine whether the displacement and suffering caused by climate disruption in the 21st century will rival or surpass those caused by the wars, revolutions and famines of the 20th.

Anthropogenic global warming is waking us up to our inescapable role as planetary-scale operators, but it is not the only large-scale, long-term challenge we will face. Over the coming centuries, for example, we will need to devise effective defenses against dangerous asteroids and comets. A much smaller object than the 10-kilometer rock that did in the dinosaurs could devastate human civilization. Soon we will have catalogued most of the dangerous Earth-crossing asteroids. But a dark and dangerous comet can always come screaming from the fringes of the solar system with little warning. We should be ready to deflect such an interloper.

On a longer timescale—tens of thousands of years—we must learn how to prevent natural climate changes that dwarf the present warming spike. Civilization has developed during what is essentially a 10,000-year summer, a multimillennial period of unusually warm and stable climate. This will not last—unless we decide it should. Over tens of thousands to many millions of years, Earth goes through cycles of glaciation and global warming. Another ice age would wipe out most of our agriculture and thus our civilization while causing the extinction of countless other species. Geoengineering techniques to artificially cool (or heat)

WHAT IS THE CHANCE *HOMO SAPIENS* WILL SURVIVE FOR THE NEXT 500 YEARS?

"I would say that the odds are good for our survival. Even the big threats—nuclear warfare or an ecological catastrophe, perhaps following from climate change—aren't existential in the sense that they would wipe us out entirely. And the current bugaboo, in which our electronic progeny exceed us and decide they can live without us, can be avoided by unplugging them."

CARLTON CAVES
Distinguished Professor in physics and astronomy at the University of New Mexico

PRECEDING PAGES: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

ARE WE ANY CLOSER TO PREVENTING NUCLEAR HOLOCAUST?

"Since 9/11, the U.S. has had a major policy focus on reducing the danger of nuclear terrorism by increasing the security of highly enriched uranium and plutonium and removing them from as many locations as possible. A nuclear terrorist event could kill 100,000 people. Three decades after the end of the cold war, however, the larger danger of a nuclear holocaust involving thousands of nuclear explosions and tens to hundreds of millions of immediate deaths still persists in the U.S.-Russian nuclear confrontation.

Remembering Pearl Harbor, the U.S. has postured its nuclear forces for the possibility of a bolt-out-of-the-blue first strike in which the Soviet Union would try to destroy all the U.S. forces that were targetable. We don't expect such an attack today, but each side still keeps intercontinental and submarine-launched ballistic missiles carrying about 1,000 warheads in a launch-on-warning posture. Because the flight time of a ballistic missile is only 15 to 30 minutes, decisions that could result in hundreds of millions of deaths would have to be made within minutes. This creates a significant possibility of an accidental nuclear war or even hackers causing launches.

The U.S. does not need this posture to maintain deterrence, because it has about 800 warheads on untargetable submarines at sea at any time. If there is a nuclear war, however, U.S. Strategic Command and Russia's Strategic Missile Forces want to be able to use their vulnerable land-based missiles before they can be destroyed. So the cold war may be over, but the Doomsday Machine that came out of the confrontation with the Soviets is still with us—and on a hair trigger."

FRANK VON HIPPEL
Emeritus professor at the Woodrow Wilson School of Public and International Affairs at Princeton University and co-founder of Princeton's Program on Science and Global Security

the planet could free the Sapiezoic eon from these destructive fluctuations in climate.

Most discussions of geoengineering center on desperate short-term fixes for our self-inflicted climate woes, but our present ignorance of the complexities of Earth's climate makes such attempts exceedingly risky. Geoengineering is best regarded as a long-term project for the distant future, when we know much more about the Earth system and when that system will be pushed to the brink either by intrinsic climate fluctuations or—much further still in the future—by our home star reaching its senescence.

Stars like the sun grow more luminous as they age, meaning that a few billion years from now, our oceans will boil away like Venus's did billions of years ago. Fortunately, this is a long way off. Provided we overcome nearer-term existential threats, we will have plenty of time to work on that problem. Perhaps we could somehow rejuvenate the sun, move Earth to a wider orbit or partially shade our planet. Alternatively, we may decide to emigrate to another, younger star system.

THE WORLD IN OUR HANDS

IF INTELLIGENCE CAN ARISE as a self-aware geologic force here, then it can probably emerge elsewhere. As we peer deeper into the universe, we may find that there are three kinds of worlds: dead, living and sapient. Of course, there is a chance that ours is the only sapient world in a vast and silent cosmos. If so, then in addition to shaping the well-being of all future life on Earth, our choices dictate the fate of all sentient life in the universe. That is quite a responsibility.

History offers hope that we can handle it. One of humanity's most ancient hallmarks is our capacity to respond to existential threats. We seem to have survived a genetic bottleneck around 75,000 years ago, when climate change, probably caused by a "volcanic winter," led to the death of most humans. Earlier, between 200,000 and 160,000 years ago, anatomically modern humans arose in Africa after a devastating ice age almost eradicated all our predecessors. The secret to our ancestors' survival was probably our use of language to develop new modes of social cooperation.

Right now we are struggling to find our way through a dawning Anthropocene. If we endure, however, we could learn to protect Earth's biosphere almost indefinitely. In the long run, we could prove to be the best thing that ever happened to planet Earth. SA

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FROM OUR ARCHIVES

How Did Humans First Alter Global Climate? William F. Ruddiman; March 2005.

scientificamerican.com/magazine/sa

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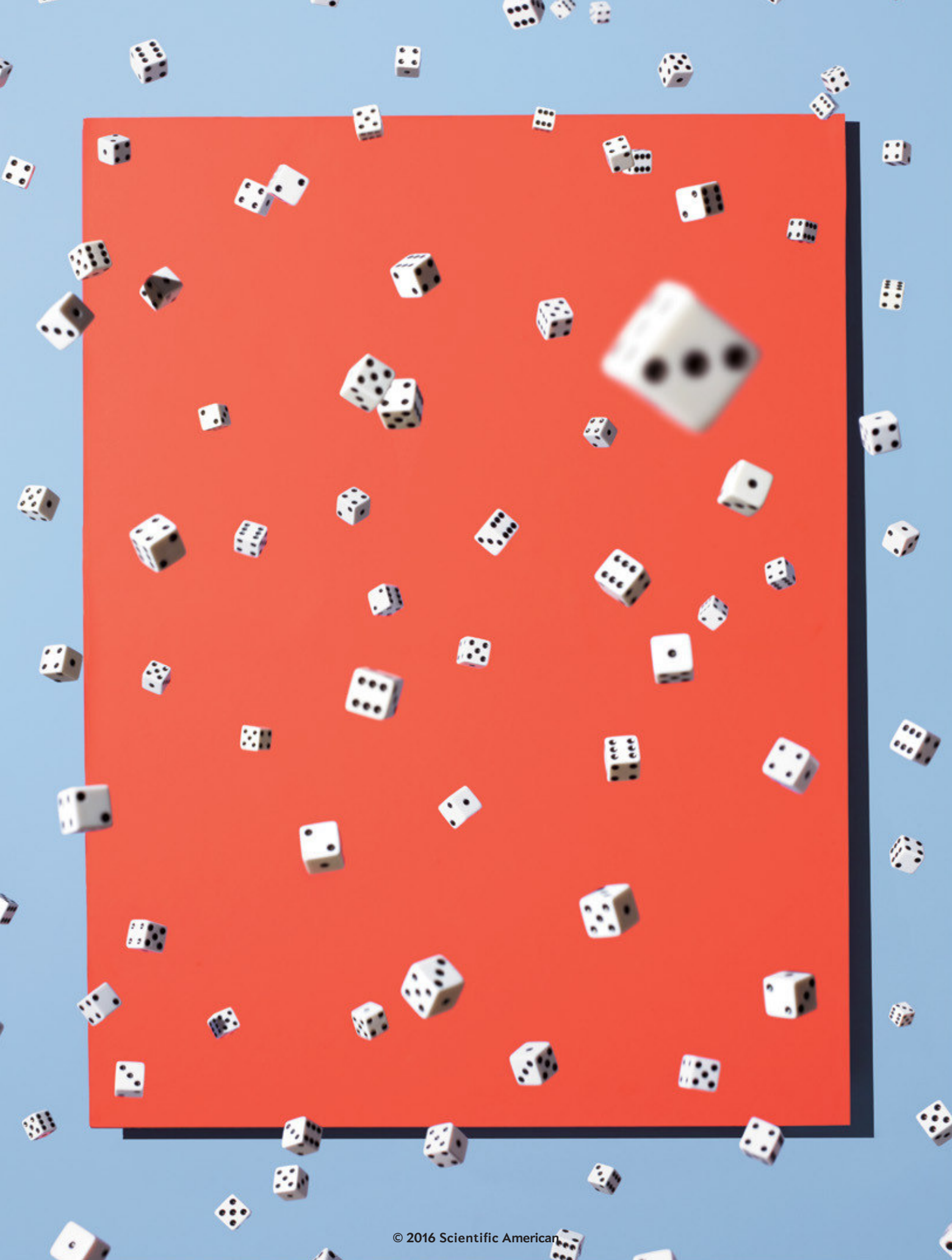

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CAN WE TRUST OUR OWN PREDICTIONS?

By Kim Stanley Robinson

THE GREAT UNKNOWN

Photograph by Andrew Myers

Kim Stanley Robinson is the best-selling author of many science-fiction novels, including the Nebula and Hugo award–winning Mars trilogy, *2312* and *Aurora*.

"I think you're making the very common mistake of imagining that a science-fiction writer knows something about the future."
—Iain Banks

I was on stage in 2012 with a great writer, the late Iain Banks, when he made this reply to a question from an audience at the British Library about what might be coming. It got a big laugh. We are all interested in the future. In our personal lives, when thinking about the future of humanity and even Earth itself, we keep trying to make predictions. But it never seems to work. We tend to hope there is a form of thought that can forecast successfully, and science fiction is often where we place that hope. But those of us who write science fiction have the firsthand experience to know that when it comes to foretelling, nothing is certain. Practice does not make perfect, although it does perhaps outline the parameters of the problem.

IN BRIEF

Science-fiction writers are no better than anyone else at predicting what is to come. The future, after all, is unknowable.

Often people try to extrapolate a recent trend straight into the future, but society and technology rarely change at a constant rate. Other foretelling techniques are similarly doomed to failure.

Science fiction, however, does recognize the value of prognosticating: it tends to reveal the preoccupations of the present.

In the project of constructing our own lives, prediction is a matter of modeling possible outcomes based on potential courses of action we can pursue in the present. That's precisely the kind of prediction science fiction does for society at large. It needs to be understood as a kind of modeling exercise, trying on various scenarios to see how they feel, and how deliberately pursuing one of them would suggest certain actions in the present. It's a very fundamental human activity, a part of decision making, which is crucial to our ability to act.

Yet all these possible futures that science fiction presents are not just forecasts but metaphorical statements about the feel of the present: "It feels like time is speeding up." "My job is robotic." "Computers are taking over." If they are mistaken for predictions only, the metaphorical power of science fiction gets lost. That would be a mistake because science fiction is always more about the present than it is about the future. It is at one and the same time an attempt to portray a possible future and an attempt to describe how our present feels. The two aspects are like the two photographs in a stereopticon, and when the two images merge in the mind, a third dimension pops into being; in this case, the dimension is time. It's history, made more visible than usual by way of science fiction's exercise of imaginative vision.

With the structure of the genre made clear, we can return to the idea of prediction. To get anything useful out of the exercise, you need not just one prediction but the whole spread of them, because there is not a single future already baked into our current moment. Given where we are now, everything from a horrible mass extinction event to a stable utopian civilization could come to pass. In such an open situation, describing the range of possibilities itself is useful, even striking. But given how wide this range is, is there any way to narrow the field and describe the futures that are most likely to occur?

One common method is to identify trends out of the recent past and suppose that these things will continue to change at the rate that they have been. This strategy is sometimes called straight-line extrapolation, and it is often charted on a graph, which some people find illuminating, or validating, or comforting, because it then looks like we are describing something that really can be graphed and made sta-

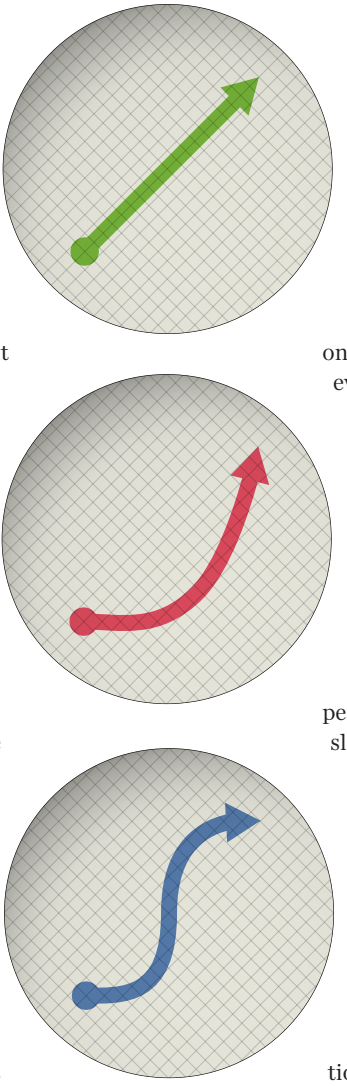
PAGE 80: PROP STYLING BY ANGELA CAMPOS *Stockland Martel*

tistically significant. Straight-line extrapolation follows its straight line into the future, trending either up or down as the case may be. It's simple, with a certain plausibility to it that comes from the physical property of inertia. But it's also the case that very few phenomena in biology or human culture do actually change in this consistent way, so using a straight line to predict the future most likely will turn out to be wrong.

Replacements or supplements to straight-line extrapolation then proliferate, as people try to match their models to the data in hand. Some might suggest increasing returns that create curves resembling a hockey stick, or the right side of a U, with growth headed for infinity. One real example that fits this pattern is the rise of the human population over history. Until very recently, it looked like it was headed toward infinity.

Another kind of trend is an asymptotic curve that flattens as it rises. Increases in food production since the green revolution tend to fit this curve, as do many other phenomena.

Combining a rapid rise with a flattening off creates the famous logistic growth curve, in which early new successes in some process create a rapid rate of change, but then exploitation of the various resources that made the change possible diminish as they are used up, and the change rate levels off. Many biological processes follow this curve for a while, and it is a staple of population dynamics for that reason. A classic example of this growth curve comes about when we chart the population of deer on reaching a new island and inhabiting it.



CURVES of various shapes can describe future trends. How to choose?

In the context of these curves, consider Moore's law; it proposes a straight-line rate of change in the size of computer chips over time. But in reality, this is just the straightest part of a larger pattern, with the slow gathering of the ability cut out of the start of the observation and the leveling off of the accomplishment also cut off. If the historical timeline were extended far enough in both directions, Moore's law would become a logistic growth curve and would be revealed as merely an observation about a certain number of years.

Other visual figures often used in predictions include circular or sine wave cycles, as well as bell curve parabolas, in which the up-down pattern seems more common than the down-up, although both must happen. Growth followed by a crash but then also a crash followed by regrowth. Then there are nonlinear breakpoints—that is, progressions with no clear pattern—as described by chaos math or the emergent qualities described in complexity studies. These latter two are often, in effect, attempts to model sudden rapid changes, so using them to predict exactly when something might happen is impossible. As with earthquake predictions, they attempt to define what is coming in the future without setting a time when it will happen, or they only suggest probabilities concerning when the event may occur.

There are other patterns and models one can invoke to aid prediction, but it's time to stop and remember that if you are trying to predict the course of human development, all kinds of processes are going on at the same time, each one possibly describable by one of the patterns mentioned above but not reliably until time has passed. And many of these processes are happening at different speeds, too—some fast, some slow—and they often cut against one another.

The upshot is that trend identification and pattern graphing are of very limited use in predicting what is going to happen. It's basically impossible to do quantitatively or with any feeling of certainty. What prediction really comes down to is studying history, looking hard at our current moment in its planetary, biospheric and human aspects, and then—guessing.

Sorry, but it's true. It's obvious on inspection, and it's worth acknowledging or admitting this to see what comes next.

Guessing is what science fiction admits to doing, and because science fiction is honest about this, it never says "this is what's going to happen, pay me $10,000 and adjust your business plan accordingly"—that's futurology, or futurism, or whatever its business card calls it. The difference is easy to identify because science fiction charges you not $10,000 per visitation but $10 and says only, "This could happen—take a look, it's interesting." When science fiction does shift into futurology, which happens from time to time, you get Scientology, frozen head companies, and so on, ranging from the ridiculous to the horrible. But for the most part, science fiction remains modest and playful in its so-called predictions because it knows they probably won't come true.

Given these realities, one thing the game of prediction can do is to try to identify those trends happening in human and planetary history that have such a large momentum they achieve a kind of inevitability, and one can confidently assert that "this is very likely to happen." This strategy could be called "looking for dominants." Examining a 1964 article Isaac Asimov wrote pre-

Illustrations by Jen Christiansen

dicting the year 2014 provides a pretty good example of this process, along with the other chancier aspects of prediction as well.

Asimov was great at this game: highly intelligent, extremely well educated in both the sciences and the humanities, and aware that prediction was an entertaining exercise at best. So he threw himself into an assignment from the *New York Times* with gusto, making about 50 specific predictions about what would happen in the coming half-century. In 2014 his essay was reprinted, and I was asked to write a commentary about it, which I was very happy to do.

What became apparent to me is that when it came to specific predictions for technological and historical developments, he was right a bit more than half of the time. Some of his predictions now seem obvious, others insightful, others misguided. But on the largest question, which might be formulated as "What will dominate history in the coming half-century?" his prediction was very impressive: he pointed to the demographic problem. The human population in 1964 was about three billion, but many public health problems had been solved, so that infant mortality was greatly lessened and, at the same time, the green revolution was arriving with its promise of much more food. Furthermore, the population of that time was relatively young.

Taken all together, a kind of historical dominant was evoked by this demographic surge: if the human population grew quickly, the pressure on the planet would increase. Asimov identified and explained these factors and indicated that without widespread "rational and humane" birth control, which was as far as he could imagine a change in the circumstances of women in particular, the problem would threaten progress in any other realm.

This outcome has substantially come to pass in the way Asimov predicted. Furthermore, if we try to imagine a similar historical dominant in our current era, it is to an extent a derivative of the one Asimov identified in 1964. Climate change has begun and is baked into our future: we are going to experience it, to one extent or another, no matter what we do from now on. Even more than population growth, which turns out to be quite variable depending on changes in our social systems, with the possibility of an abrupt drop already proved in some nations, climate change is an easy call to make; it's going to happen.

That said, we can't predict well how much of it will occur, nor can we foretell its local effects; these are contingent on a host of factors, including everything that we do from now on. So more specific predictions under the umbrella of this historical dominant are no easier than before, but it is possible to say that many things will happen based on our attempts to cope with climate change. We can at least cluster some likely guesses. We will generate power renewably, we will move slightly inland but also get better at living on the oceans, and so on. And by acknowledging the dominant factor, we avoid making unlikely predictions by steering clear of forecasting things that cannot happen in a post–climate change world.

> When people say that "a moment will come when artificial intelligence takes over human history," they are expressing a feeling, or a fear, that science and technology have taken on a momentum of their own.

Indeed, this leads us to an important principle to remember: what can't happen, won't happen. This fairly obvious rule or counterrule does seem to get lost in the shuffle sometimes, as we live in a culture of what might be called "scientism," which is another form of magical thinking. Many problems get waved away: we'll science our way out of them! The use of the word "science" as a verb is perhaps a giveaway to this form of magical thinking. But science is not magic, and some problems we are now creating, such as ocean acidification, are beyond our physical abilities to reverse in anything less than centuries or millennia, if ever.

So the rule "if it can't happen, it won't happen" is an important bordering function in the modeling exercises that we engage in when we play the prediction game. This principle might even help us to evaluate certain large-scale predictions that are pretty common in our culture today, such as "Humanity will go to the stars." This old chestnut deserves reexamination because the project is a lot harder than we thought when people first proposed it. Cosmic radiation, the fact that our microbiomes make us more dependent on the planet than we supposed, and other new findings mean that long-term isolation in spaceships will probably not work. As a prediction, humanity going to the stars turns out to be a bad one. As I've been saying lately, because it can't happen, it won't.

Another very common prediction these days, it

seems, is this notion of "the singularity." Very soon, some have asserted, artificial intelligence will become so smart it will decisively outstrip human intelligence, take over the world and then do—something. Head to the stars, cover the planet with computers, boss us around, whatever. Quite prominent public figures are warning us to beware of this possible future, including Elon Musk and Stephen Hawking. But business leaders and physicists are no better at prediction than anyone else; in essence, they are playing the science-fiction game, and that game is a great leveler. Such individuals are no doubt brilliant in their fields, but when they begin predicting the future among their other cultural pronouncements, it can get chancy. Albert Einstein and Richard Feynman were pretty good at it; James Watson and Ernst Haeckel were not. Asimov was distinctly better than any of them because he understood the methodologies of the game. So the authority of expertise in some other area is not a good reason to put much credence in anyone's prediction.

That said, the foretelling of the singularity is interesting because it's a prediction and therefore a science-fiction story. Indeed, it began as the 1981 novella *True Names,* by science-fiction writer Vernor Vinge. Now recall what I said at the beginning, about science fiction often being a metaphor for how our present feels. It's true here, too, and indeed, this rescues the notion of the singularity, which as a prediction ignores many realities of the brain, computers, will, agency and history. As a metaphor, however, artificial intelligence stands for science. Science itself is the artificial intelligence we fear will take over: collective, abstract, mechanical, extending far beyond individual human senses. What science knows, individuals could not sense or know themselves. And yet we invented science and deployed it.

So when people say that "a moment will come when artificial intelligence takes over human history," they are expressing a feeling, or a fear, that science and technology have taken on a momentum of their own that humanity no longer controls. In that sense, maybe the singularity has already happened!

When we read people, brilliant and prominent or not, warning us about the dangers of computer AI and the possibility of a singularity leaving us behind, we can roll our eyes (I do), or we can read them metaphorically, which is probably more productive, and understand them to be saying (even if they don't know it) this: we need to stay in charge of history; we have to make choices. Technology, though powerful and growing more powerful, is always a set of tools created as a result of human choices. When we don't make those choices, when they seem to "make themselves," it really means we are making our decisions based on old data, old assumptions and unexamined axioms that are like oversimple algorithms. And when we do that, bad things can happen. The singularity, in other words, is code for blind reliance on science or the notion that we can science our way out of anything, when in fact we must continue to make decisions about how we use science and technology to develop as a species.

Ergo a prediction: I expect that the global conversation about the scientific, environmental and political issues now facing us will grow. The inequality of our economic system, the destruction of our biosphere's ability to support us, the possibility of a sixth great mass extinction event in Earth's history being caused by us—all this will be well known to everyone alive. The necessity to change our technological and social systems to avoid catastrophe and create a just and sustainable world for all will be evident. And because necessity is the mother of invention, we will invent. The crux of the change will be in the laws we agree to live by, including the laws that define our economic system. Capitalism as we practice it now is the Chelyabinsk-65 plutonium plant of contemporary technologies: dirty, brutal, destructive, stupid. It isn't capable of solving the problems we're faced with and is indeed the name of the problem itself. So we will modify capitalism, law by law, until it is changed into a sustainable system.

Now, of course, one could predict the bad future and say we will screw up, fight one another, cause a mass extinction event, go nearly extinct ourselves and emerge blinking out of holes in the ground decades later, post-traumatic and brain-damaged as a civilization. This is possible, but its plausibility relies on assuming that human beings are stupid and cowardly and not good at cooperation. There are elements of truth in all these notions, perhaps; we are all things to ourselves.

But the record of the species so far, in adapting to radical climate changes and many other stresses, suggests these bad traits are weaknesses rather than defining elements. And many of us believe that the AI that is science is a benign force that we control. Thus, taking a straight-line extrapolation of our history so far—oh, but wait. Not the best method, as I've pointed out already. Instead, making a guess, based on an evaluation of all the trends we can see, I forecast that our intelligence and desire to do good for our children will see us through to the invention of a civilization in a stable relationship to the biosphere. After which I predict things will get even more interesting. SA

MORE TO EXPLORE

Visit to the World's Fair of 2014. Isaac Asimov in *New York Times,* pages 20–23; August 16, 1964. www.nytimes.com/books/97/03/23/lifetimes/asi-v-fair.html q

Kim Stanley Robinson on Isaac Asimov's 1964 Predictions. Kim Stanley Robinson in *SciFiNow*. Published online May 20, 2014. www.scifinow.co.uk/blog/kim-stanley-robinson-on-isaac-asimovs-1964-predictions

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Future Tense. Clara Moskowitz; Recommended, July 2016.

scientificamerican.com/magazine/sa

RECOMMENDED

By Clara Moskowitz

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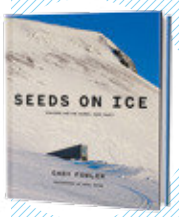
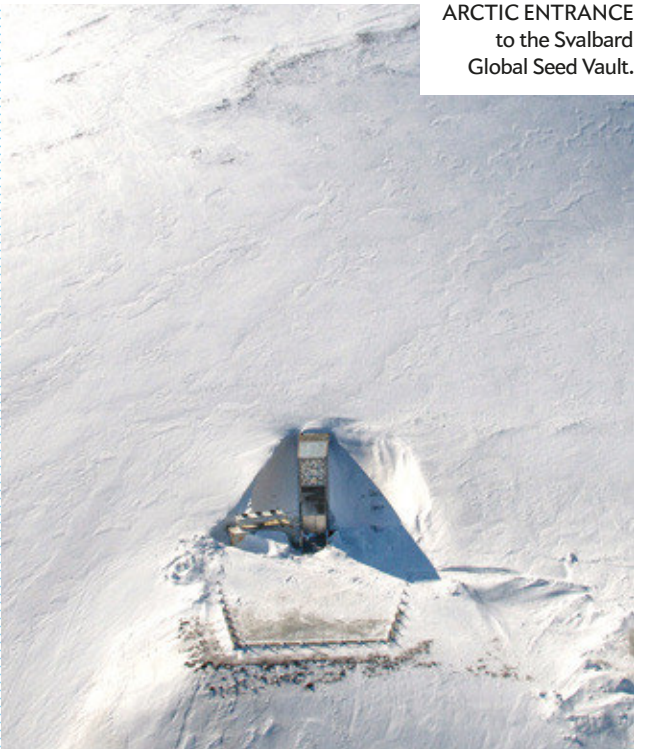
Seeds on Ice: Svalbard and the Global Seed Vault

by Cary Fowler. Photography by Mari Tefre. Prospecta Press, 2016 ($45)



To feed the world's growing population, global food production must soar by 50 percent by the middle of this century. That goal will be impossible if we do not protect and capitalize on the genetic diversity of the planet's crops. Enter the Svalbard Global Seed Vault, a repository of roughly half a million types of seeds buried inside the Arctic ice of the eponymous Norwegian islands. There variations from all the major food crops—including species we eat everyday and heirloom varieties no longer grown—are stored for safekeeping in case local versions are destroyed by natural or political disaster. One of the founders of the seed vault, agriculturist Fowler, describes the project's mission in this large-format book illustrated with photographs of the seeds, their repository and the stark beauty of the barren landscape that has become home to humanity's hope for a fecund future.



ARCTIC ENTRANCE to the Svalbard Global Seed Vault.

MARI TEFRE

Denying to the Grave: Why We Ignore the Facts That Will Save Us

by Sara E. Gorman and Jack M. Gorman. Oxford University Press, 2016 ($29.95)

Perfectly intelligent people refuse to vaccinate their children, believe that owning guns protects them from violence, doubt the safety of genetically modified foods and hold many other scientifically untenable positions. Why do so many cling to beliefs that run counter to evidence? Sara Gorman, a public health expert, and Jack Gorman, a psychiatrist, investigate the psychological factors that lead to such self-defeating denial of facts and conclude that normal, evolutionarily adaptive tendencies act against us. These include fear of complexity, misestimating risk, and our propensity to look for patterns that confirm our beliefs and to listen to charismatic leaders. "This means that simple education is not going to be sufficient to reverse science denial," the authors write, but countering the mental predilections that lead to it offers hope.

All These Worlds Are Yours: The Scientific Search for Alien Life

by Jon Willis. Yale University Press, 2016 ($30)

"The search for life beyond Earth is in the throes of a revolution," writes astronomer Willis in this primer on the prospects for finding E.T. The plethora of exoplanets recently discovered, as well as advances in telescope technology and solar system exploration, has transformed astrobiology in the past couple of decades, giving scientists their first hard data about worlds both within our solar system and outside it that might be hospitable to life. Willis describes the pros and cons of looking for creatures in several likely hotspots, among them Mars, Saturn's moons Titan and Enceladus, Jupiter's moon Europa and planets farther afield. He also makes what he calls "informed speculation" about what types of organisms might call such locales home and how they might differ from familiar life-forms.

Patient H.M.: A Story of Memory, Madness, and Family Secrets

by Luke Dittrich. Random House, 2016 ($28)

Much of what we know about memory comes from a man who lost his. Henry Molaison, known as patient H.M., the most studied subject in the history of neuroscience, had brain surgery in 1953 to treat epilepsy. Not only did the operation fail to cure him; it permanently robbed him of the ability to form new memories. Until he died in 2008, Molaison could recall life before the surgery, but he never created lasting impressions of anything that happened afterward. The tragic consequences for Molaison were a turning point for science—for the first time researchers could locate the seat of memory in the area of his brain that was removed. Journalist Dittrich, the grandson of the surgeon who performed the operation, recounts Molaison's life, grapples with the damage his grandfather caused and parses the knowledge that came of it.

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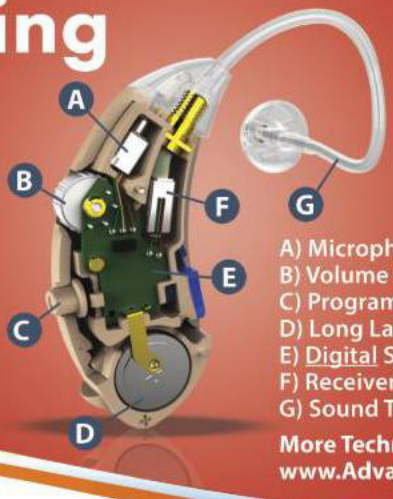

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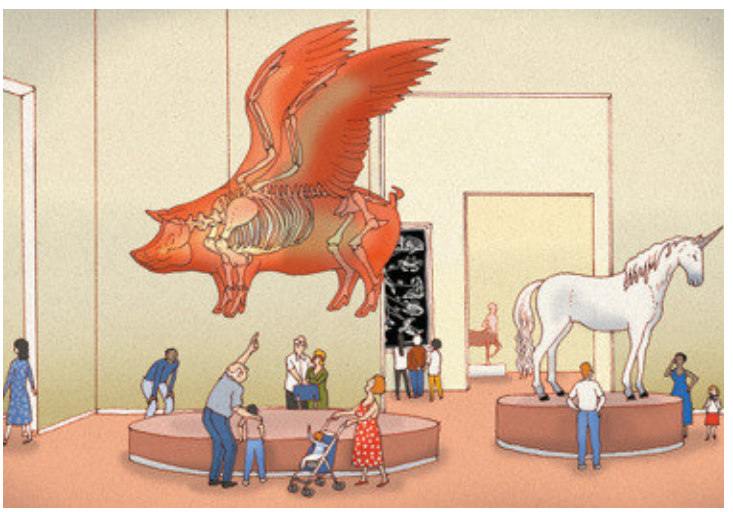
Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His book *The Moral Arc* is now out in paperback. Follow him on Twitter @michaelshermer

At the Boundary of Knowledge

Is it possible to measure supernatural or paranormal phenomena?

By Michael Shermer

The history of science has beheld the steady replacement of the paranormal and the supernatural with the normal and the natural. Weather events once attributed to the supernatural scheming of deities are now understood to be the product of natural forces of temperature and pressure. Plagues formerly ascribed to women cavorting with the devil are currently known to be caused by bacteria and viruses. Mental illnesses previously imputed to demonic possession are today sought in genes and neurochemistry. Accidents heretofore explained by fate, karma or providence are nowadays accredited to probabilities, statistics and risk.



If we follow this trend to encompass all phenomena, what place is there for such paranormal forces as ESP or supernatural agents like God? Do we know enough to know that they cannot exist? Or is it possible there are unknown forces within our universe or intentional agents outside of it that we have yet to discover? According to California Institute of Technology physicist Sean Carroll in his intensely insightful book *The Big Picture* (Dutton, 2016), "All of the things you've ever seen or experienced in your life—objects, plants, animals, people—are made of a small number of particles, interacting with one another through a small number of forces." Once you understand the fundamental laws of nature, you can scale up to planets and people and even assess the probability that God, the soul, the afterlife and ESP exist, which Carroll concludes is very low.

But isn't the history of science also strewn with the remains of failed theories such as phlogiston, miasma, spontaneous generation and the luminiferous aether? Yes, and that is how we know we are making progress. The postmodern belief that discarded ideas mean that there is no objective reality and that all theories are equal is more wrong than all the wrong theories combined. The reason has to do with the relation of the known to the unknown.

As the sphere of the known expands into the aether of the unknown, the proportion of ignorance seems to grow—the more you know, the more you know how much you don't know. But note what happens when the radius of a sphere increases: the increase in the surface area is squared while the increase in the volume is cubed. Therefore, as the radius of the sphere of scientific knowledge doubles, the surface area of the unknown increases fourfold, but the volume of the known increases eightfold. It is at this boundary where we can stake a claim of true progress in the history of science.

Take our understanding of particles and forces, which Carroll says "seems indisputably accurate within a very wide domain of applicability," such that "a thousand or a million years from now, whatever amazing discoveries science will have made, our descendants are not going to be saying 'Ha-ha, those silly twenty-first-century scientists, believing in neutrons and electromagnetism." Thus, Carroll concludes that the laws of physics "rule out the possibility of true psychic powers." Why? Because the particles and forces of nature don't allow us to bend spoons, levitate or read minds, and "we know that there aren't new particles or forces out there yet to be discovered that would support them. Not simply because we haven't found them yet, but because we definitely would have found them if they had the right characteristics to give us the requisite powers."

What about a supernatural God? Perhaps such an entity exists *outside* nature and its laws. If so, how would we detect it with our instruments? If a deity used natural forces to, say, cure someone's cancer by reprogramming the cancerous cells' DNA, that would make God nothing more than a skilled genetic engineer. If God used unknown supernatural forces, how might they interact with the known natural forces? And if such supernatural forces could somehow stir the particles in our universe, shouldn't we be able to detect them and thereby incorporate them into our theories about the natural world? Whence the *super*natural?

It is at the horizon where the known meets the unknown that we are tempted to inject paranormal and supernatural forces to explain hitherto unsolved mysteries, but we must resist the temptation because such efforts can never succeed, not even in principle. SA

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Steve Meowsky has been writing the Anti Gravity column since a typical tectonic plate was about 35 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

In Favor of Feline Felicity

A new book touts training your tabby

By Steve Mirsky

Habitual readers of this column may recall me mentioning that I have two cats. Or perhaps I should rephrase in light of the old adage "dogs have owners; cats have staff." So let's say that two cats have deigned to live with me in return for various services I provide, such as food delivery, health care and the administration of belly rubs. I contemplate cats to the point that when I see a reference to the chemical entity known as a phorbol, I pronounce it "fur ball."

I was thus inevitably intrigued when a review copy of the new book *The Trainable Cat* landed (cleanly, all four corners simultaneously) on my desk. The authors are John Bradshaw, foundation director of the Anthrozoology Institute at the University of Bristol, and Sarah Ellis, holder of a doctorate in feline behavior and a specialist with the charity International Cat Care in England. The book is subtitled *A Practical Guide to Making Life Happier for You and Your Cat.* As intimated above, I might have gone with *Making Life Happier for the Cat and Its Person,* but I just work here.

Real time aside: A neighbor's cat, appropriately named Jester, has just gamboled into my home office, as he does a few times every week. "[Another cat] may even be so bold as to actually enter the house," the Brits write. They go on to explain that "although cats learn a great deal from their owners, they can also learn from other cats … for example, how to use the cat flap." This interloper must have observed one of the resident cats employing said cat flap (we Americans usually call it the cat door). I assumed Jester was a copycat, but the authors note, "It's not clear whether the second cat actually learns how to perform the behavior directly from the other cat or whether the more skilled cat's actions simply draw the other cat's attention to the cat flap as something worth investigating."

If Jester (already gone) had to work out the cat door from first principles, he had plenty of time to suss out the problem. He's not binge watching dire wolves, dogs and dragons on *Game of Thrones;* he's not coming up with names for the orange tabby that lives atop Donald Trump's head; and he's certainly not writing a cat column on deadline.

Like an unemployed brother-in-law, Jester sometimes drops in just to see if there are any leftovers in the cat dish. "Cats are opportunists, and the chance of a free meal is something they rarely pass up," the authors assert. Indeed, I have never seen a cat pick up a check. Although "a free meal" here probably refers to food that comes out of a can rather than by virtue of some (calorically) expensive hunting expedition.

Real time aside: One of the resident cats has just commandeered my desk chair, leaving me to finish this composition with my derriere planted on a milk crate. Which leads to the first lines of the book's introduction: "Who on earth trains cats?" (Not me, obviously. In fact, I've been trained by them—I'm sitting on a milk crate.)

The authors then mention that big cats and domestics have been trained for performing, but "why would anyone want to train their *pet* cat, except perhaps to show off their feline accomplice's talents to their friends?" In truth, your friends will be less enthralled than you'd think by an exhibition of your cat chasing a laser light through the living room.

No, the book's serious purpose is "to show you how training can improve not just your relationship with your cat but also your beloved pet's sense of well-being." As I look at the cat sleeping contentedly in my chair, I wonder how its sense of well-being could possibly enlarge. Fortunately, I now have possession of an owner's—make that user's—manual. SA

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Illustration by Matt Collins

50, 100 & 150 YEARS AGO

INNOVATION AND DISCOVERY AS CHRONICLED IN *SCIENTIFIC AMERICAN*

Compiled by Daniel C. Schlenoff

SEPTEMBER

1966 Artificial Intelligence

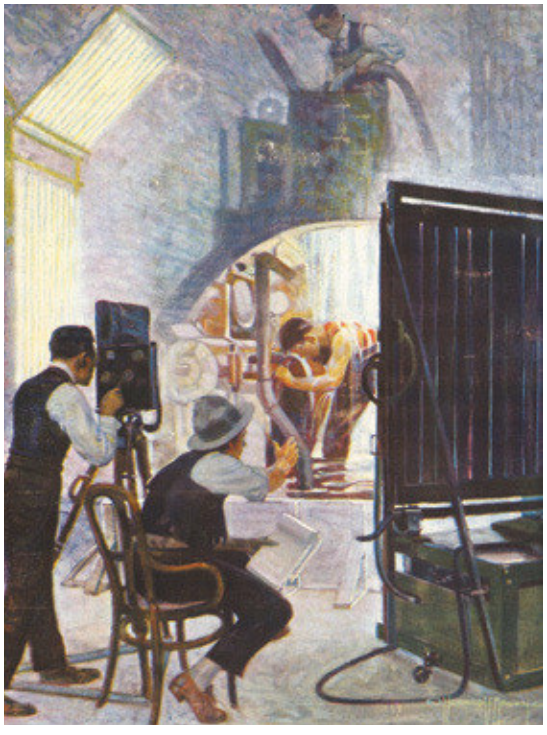
"In order for a program to improve itself substantially it would have to have at least a rudimentary understanding of its own problem-solving process and some ability to recognize an improvement when it found one. There is no inherent reason why this should be impossible for a machine. Given a model of its own workings, it could use its problem-solving power to work on the problem of self-improvement. The present programs are not quite smart enough for this purpose; they can only deal with the improvement of programs much simpler than themselves. Once we have devised programs with a genuine capacity for self-improvement a rapid evolutionary process will begin.... Whether or not we could retain some sort of control of the machines, assuming that we would want to, the nature of our activities and aspirations would be changed utterly by the presence on earth of intellectually superior beings. —Marvin L. Minsky"

1916 Motion Pictures

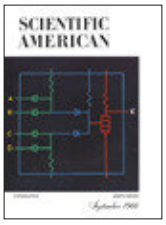
"The audience is tense with excitement as the hero in the film play struggles frantically with the control apparatus of a submarine that is fast sinking to the ocean bottom. Several months ago the scene in question was acted, not, as might be supposed, in the interior of a submarine, but in a quiet corner of a motion picture studio [*see illustration*]. For weeks the artisans of the studio workshops had worked on building this pseudo submarine; and before the camera crank was turned the technical director had gone over every detail of its construction to make sure that it emulated successfully the interior of a modern submarine. To-day the director strives to reinforce good story and fair acting with utmost realism of scenery."

Scourge of Polio

"The epidemic of infantile paralysis, or poliomyelitis, now ravaging the State and City of New York and extending over a great part of the United States is the most serious in medical history. On September 1st the number of victims in New York State alone had reached 10,000, while the largest reported in any previous epidemic was 3,840. This was in Sweden in the year 1911. This cruel disease has only lately attracted the attention of medical science. It must, of course, have existed from the earliest times; but it was not described until 1841 when eleven cases occurred in Louisiana. During the last thirty years it has rapidly gained ground, claiming ever larger and larger numbers of helpless children and not a few adults as well, until now it is one of the most dreaded of all diseases. In the United States we have had fourteen carefully described epidemics, beginning with that of Vermont in 1894."



1916: Moviemakers strive for realism in a tale of a sinking submarine.



1966

1916

1866

First Report of Tanks

"Strange tales are coming to us from the battlefields of northern France. We would almost believe that our old friend Baron Münchausen had come to life had not the extraordinary developments of the present war prepared us to accept the wildest yarns as possible. War correspondents have been telling us of a huge British machine that hurdles trenches and shell-holes, that prefers to smash through a tree rather than pass around it, that delights to crush into the brick walls of a house and wallow about inside, tramping on the enemy."

Tanks were used for the first time in the battle of Flers-Courcelette in France on September 15, 1916.

1866 The Far Future

"The moon must be drawing very slowly nearer to the earth, and the two bodies, in the far distant future, will come together. The solid crust of the earth will be broken up by the shock, and an immense quantity of heat will be generated by the destruction. At the same time, the earth is winding its way inward toward the sun, and must ultimately fall, an inconsiderable pebble, into that vast glowing mass. The same fate awaits all the planets, and our solar system must one day be but a single globe. When this globe is cooled, it may be covered with a multitude of inhabitants, and astronomers may arise who will watch its revolutions among the associated suns of our stellar system. If their knowledge and intellect are equal to the science of our astronomers, they will foresee the ultimate coming together of all these suns into one common globe. And all of the visible universe into one mass of matter."

To explore how Scientific American *looked at the future in past years, go to ScientificAmerican.com/sep2016/past-future*

SCIENTIFIC AMERICAN, VOL. CXV, NO. 10, SEPTEMBER 2, 1916

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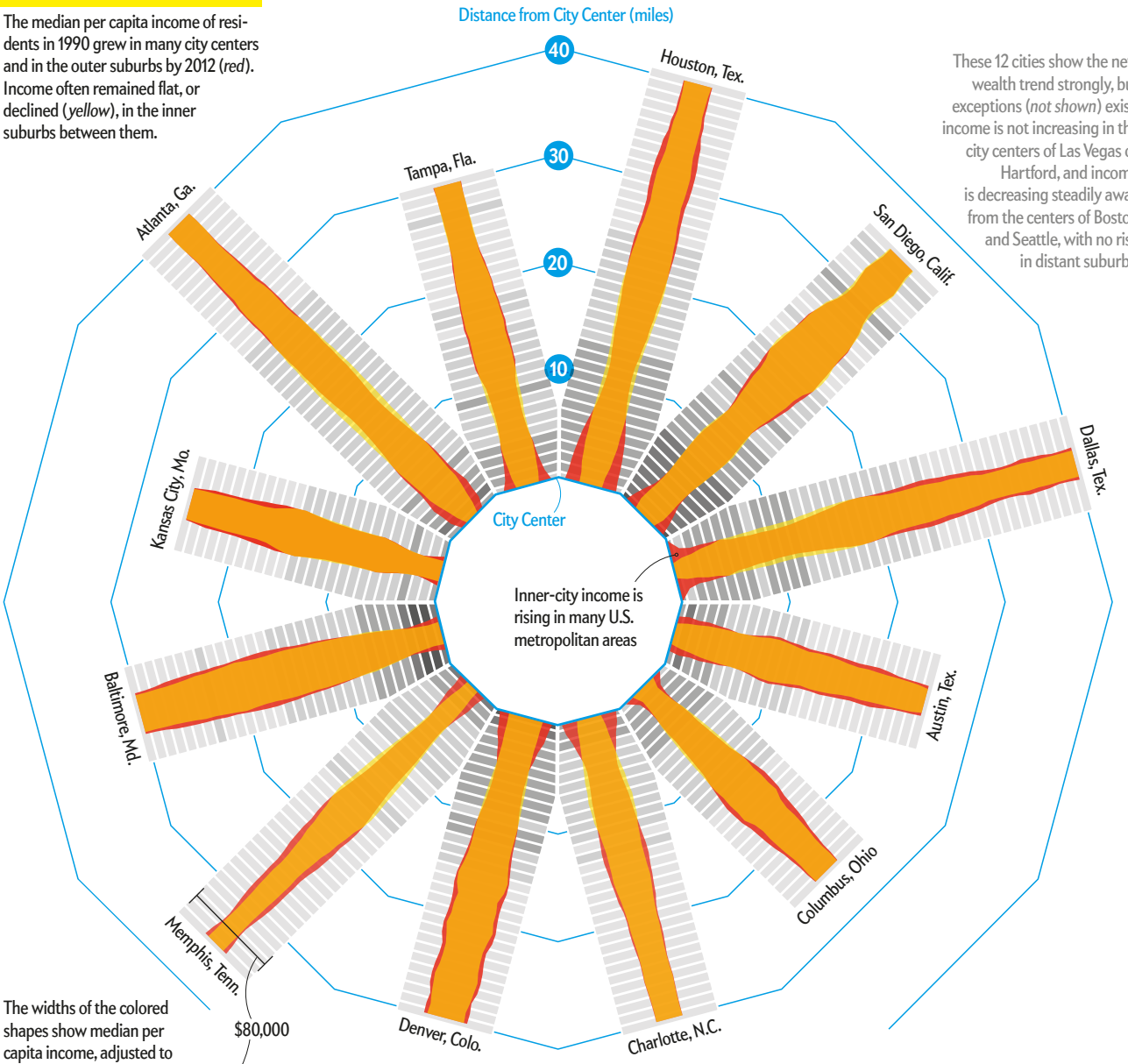
Inner Cities Get Wealthier

The median per capita income of residents in 1990 grew in many city centers and in the outer suburbs by 2012 (*red*). Income often remained flat, or declined (*yellow*), in the inner suburbs between them.



These 12 cities show the new wealth trend strongly, but exceptions (*not shown*) exist: income is not increasing in the city centers of Las Vegas or Hartford, and income is decreasing steadily away from the centers of Boston and Seattle, with no rise in distant suburbs.

The widths of the colored shapes show median per capita income, adjusted to 2012 dollars. The full width of the gray bars represents $80,000 a year

Median per Capita Income
- 2012 increase over 1990
- 2012 decrease from 1990
- Overlap of 2012 and 1990

Population Density (people per square mile)
- Rural
- 1,000–3,000
- 3,000–6,000
- 6,000–10,000
- ≥ 10,000

Urban Wealth

The young and affluent move downtown, pushing out the poor

For decades most U.S. cities had a decaying inner core surrounded by suburbs that grew increasingly wealthy with distance. But now many cities are showing a new pattern of affluence and poverty. Well-educated millennials in their 20s and 30s who have considerable income are moving into rejuvenated downtown areas (*red shapes at center of graphic above*). They are driving up rents, which is forcing some poorer residents to the inner suburbs, vacated by suburbanites who have moved farther out. These inner suburbs may pose the next big revitalization challenge for urban planners: postwar houses are aging, and basic city services such as mass transit are often lacking. *—Katie Peek*

SOURCE: *THE CHANGING SHAPE OF AMERICAN CITIES*, BY LUKE J. JUDAY. DEMOGRAPHICS RESEARCH GROUP, WELDON COOPER CENTER FOR PUBLIC SERVICE, UNIVERSITY OF VIRGINIA, MARCH 2015

Graphic by Katie Peek

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1884

Memorial Sloan Kettering Cancer Center

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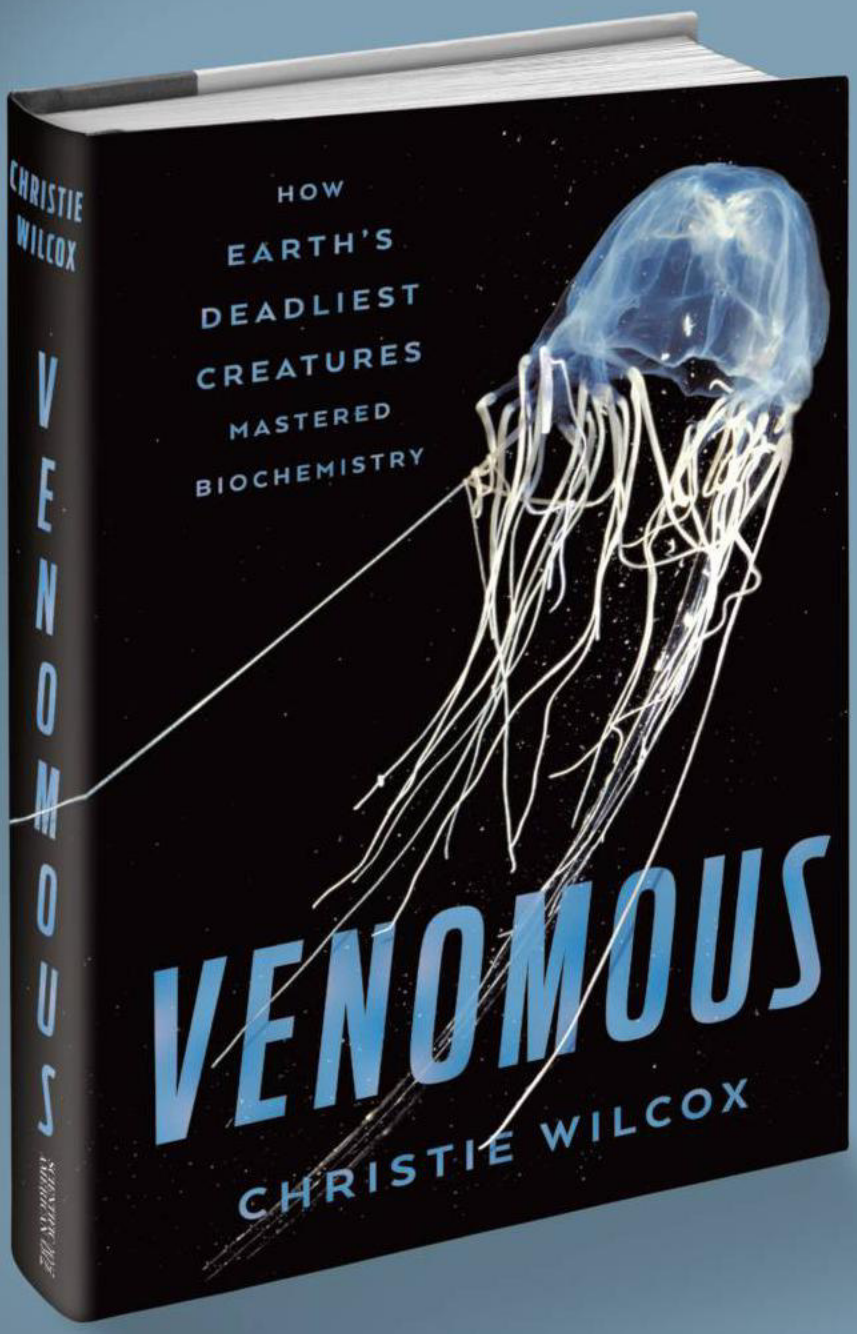

"Christie Wilcox is the perfect guide to the wild and weird world of venomous creatures—a scientist who knows how to tell a vivid story, a storyteller who understands the elegant science of poisons. As a result, *Venomous* succeeds both as an insightful study of the natural world and, equally important, as a fascinating read."
—Deborah Blum, author of *The Poisoner's Handbook*

"Even at its most sinister, nature can't help but be fascinating, and in *Venomous*, Christie Wilcox has created a fitting tribute to one of nature's most sinister creations of all. She not only provides a tour of the venomous world's most frightening specimens, but she also dives into the astonishing biology underlying their deadly success." —Carl Zimmer, author of *Parasite Rex*

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