SPECIAL **MIT Technology Review** EDITION

BEST IDEAS IN TECH

The key breakthroughs reshaping our society right now

Does this box offer a practical way to pull carbon dioxide from the air? See page 26.

Robots will change the way we work

Personalized medicine promises new cures

China is becoming a tech superpower

Tools for fighting global warming

Democracy is being reinvented

Gene editing will alter the human race

PLUS

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From the editor

At MIT Technology Review, we're always asking questions. Is a new technology truly groundbreaking—or just an incremental advance, likely of interest only to researchers in the lab? Has it been attempted before, and if so, what makes this attempt any more likely to succeed than earlier ones? We ask such questions every day, with every story we consider writing.

But then there are the larger, existential questions—cases where a new technology or trend in technologies might render the world as we know it unrecognizable. Then we ask whether our democracies or economies can withstand the change. Or if we'll even survive as a species.

It's these larger questions that we grapple with in this issue of Best Ideas in Tech—not only asking the question, but offering an in-depth, deeply reported attempt at an answer.

What will employment look like 20 or 30 years from now? We know automation and self-driving cars will be more prevalent, and we're told (by the robot makers, typically) that this is a good thing, that it creates new types of jobs and helps our economy grow. But does that bear any resemblance to what will really happen? Our writer Erin Winick got an inkling, as she writes in her essay "Confessions of an accidental job destroyer" (page 6). On an engineering internship, she was asked to quiz a longtime mold maker in the plant about how he did things so she could streamline the process. In this case "streamlining" meant replicating his work with a 3D printer, and the two of them realized, after the initial enthusiasm, that this would render the human mold maker redundant. Winick caught up with him recently to see how things had worked out.

Are we doing enough to stop climate change? In fact, carbon emissions are still increasing, and we're far away from making the cuts necessary to avoid devastating effects. Since carbon dioxide persists in the air for thousands of years, the damage we're doing now will be locked in for many future generations unless we can dream up a method of removing carbon straight from the air (see "Is carbon removal crazy or critical?" page 26).

There's another habit of ours responsible for a huge chunk of emissions, something most people rarely think about (or would prefer not to)—our tendency to eat meat. It's responsible for massive amounts of deforestation and water use and leads heavy doses of methane to be released into the atmosphere. We could probably trim a quarter of our emissions by cutting down on or giving up meat altogether, and yet most people don't seem to want to do that—which is why companies like Impossible Foods and Beyond Meat are attempting to create burgers that taste like the real thing but don't involve livestock (see "The meat without the cow," page 34).

Will gene editing change the human race? In a way it already has. Late last year our own Antonio Regalado was first to report that He Jiankui, a researcher in China, had used CRISPR to create the world's first gene-edited babies. In "The man who crossed the germline" (page 88) he takes a look at how whirlwind developments over the past few years have led us inevitably to this place, and asks if we're really prepared—legally, ethically, emotionally, and otherwise—for the changes they're likely to bring.

And there are other questions. Has democracy taken a hit from technology? Does the future belong to China, and if so, what does that mean for the rest of the world? Will we ever be able to harness what we know about the human genome to cure diseases, not only in embryos but in adults?

We tackle all of these questions inside.

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Will robots change the way we work?

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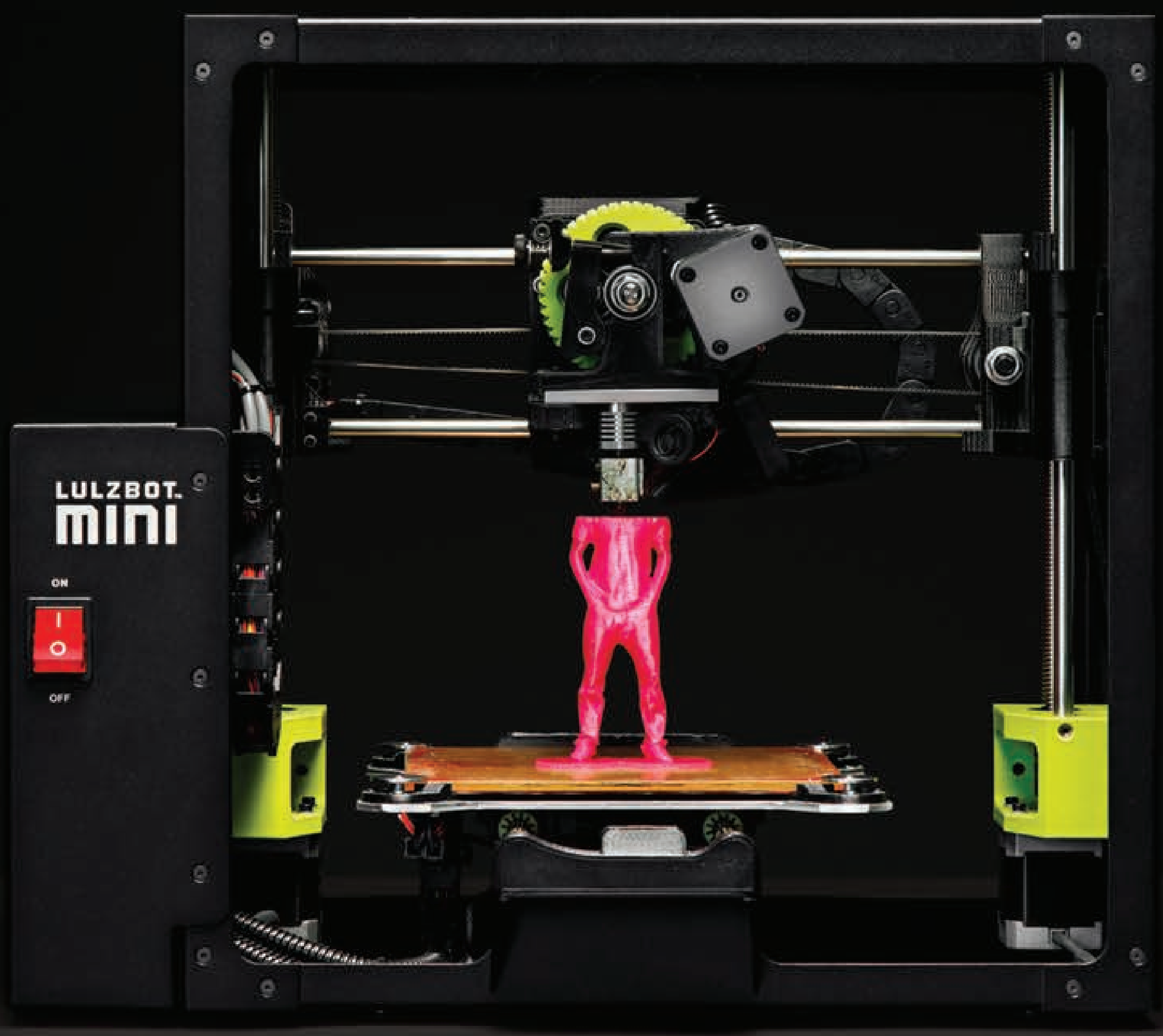
As robotic arms with better dexterity team up with artificial intelligence, robots will be found anywhere products are assembled, unpacked, or sorted (page 8). Driverless vehicles will not only displace truckers but also upend all sorts of services that rely on the car culture (page 14). How will we adapt? As one displaced worker put it, “You must stay current with the new processes ... even if it means doing it on your own time and at your own expense” (page 6).

Confessions of an accidental job destroyer

Behind every piece of automation is a human who made it happen.

By Erin Winick
Photograph by Bob O'Connor



I expected my summer engineering internship to include things like updating old 3D models, creating part designs, and learning the ins and outs of how a company works. I didn't expect it to involve learning to make my colleagues obsolete.

It was the summer after my sophomore year of college, at a company in Southern California. At the beginning of the internship, my manager asked me to implement 3D printing to streamline a complicated mold-making process. I have long been obsessed with 3D printing (I own two machines myself), so I was thrilled to introduce it into the business.

First I had to look at how the company currently made molds. So I sought out the man who did it. (We agreed not use his real name, so I'll call him Gary.) He was the only one who knew about the costs, the dimensions, and why these molds were made the way they were. The project wouldn't work without him.

As he described the process and his role in it, I realized that making molds was Gary's sole responsibility. He had spent over 30 years perfecting these tools and parts. If my project succeeded, I would be making him redundant.

At first he was friendly and eager to talk. But as I explained the goals of my project, his tone changed. He was still willing to talk, though, after venting a bit about our bosses and the company.

Throughout my internship, we built a sort of … relationship. I asked questions; he provided information. The conversations involved a lot of me smiling and nodding and acting as a sounding board. I seemed like one of the few people who cared about what he had to say. Since we both knew that my project could cost him his livelihood, I felt I at least owed him that attention.

Each time we spoke, I was closer to making a working product—and more nervous about telling him how things were going. I felt that by doing so, I was letting him know how close he was to losing his job. A few times I suggested he retrain to learn how to operate the 3D printer. That seemed far-fetched to him. He didn't think the company would be willing to invest in a worker his age.

I had built a workable prototype by the end of the summer. To show off my progress, I arranged a demo for my bosses, and I invited Gary. The higher-ups praised my creation and openly appreciated the money it would potentially save. But it felt ominous to flaunt my work in front of the guy whose job it threatened. I was proud of what I had made, but I knew what the repercussions could be if they decided to use it.

I left that internship without knowing the outcome. At the time I was happy to embrace the ignorance. I left the moral quandaries about the consequences of technological innovation to the execs.

But I still wondered what had happened to Gary. Last year, I contacted him to finally find out.

The company had used my project. It was improved until it was ready to hit the factory floor. When it did, Gary was assigned to a new area. However, he was unhappy in his new role and with the business in general. He retired—after 34 years with the company.

Essentially, although he wasn't laid off, he lost his job as a result of my work.

In society's narrative of the war between robots and humans, I'm probably the bad guy. But human vs. robot isn't always good vs. evil. Automation creates new roles for people. Humans will be the ones to install and create our new robotic coworkers. According to the International Federation of Robotics, the average proportion of robots to workers worldwide is 74 to 10,000, and this number is rising. The robotic workforce grew by 9% in Asia in 2017, with 631 robots per 10,000 employees in South Korea. Yet by 2030, according to predictions from McKinsey, technology spending alone will create 20 million to 50 million new jobs, some of which will introduce tech and tools like those robots to workplaces.

If you, too, are a job automator, or will be someday, here's my advice: talk to the people whose jobs you are automating. It's going to be uncomfortable, but they probably want to tell you their point of view. Dismissing them can reinforce the us-against-them mind-set and create opportunities for miscommunication. When I talked to Gary for this story, he told me the company had taken "a very aggressive stance with [him] and some other employees in similar positions" after I left. "I assumed, wrongly, that I would have an opportunity to follow along with the evolution of the process," he said.

While I did eliminate Gary's role, my 3D printer created opportunities at the company for workers who knew how to run the new machines. Gary said that was one of his biggest takeaways: "I learned that you cannot allow yourself to get complacent. You must stay current with new processes and technology even if it means doing it on your own time and at your own expense."

Connecting with him again was a cathartic but strange experience. Gary said he was surprised—pleasantly!—to hear from me. He moved states and is working in customer service now. I asked him what his initial reaction was when I approached him about the project all those years ago. "I was excited to find that somebody was willing to discuss what was happening," he said. "The 'official position' of the company was that there was no attempt to change anything about how things were being done."

Communication might not be enjoyable for either party, but it is necessary. People are a crucial part of the automation process. The robots won't take over without us.

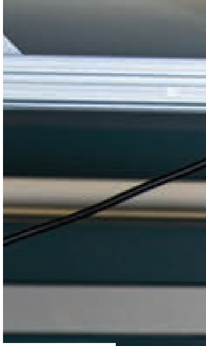
Erin Winick reports on all things related to the space industry for MIT Technology Review.

A robot arm in a San Francisco test facility picks up chicken parts and deposits them in bento boxes.

This is how the robot uprising finally begins

By Will Knight
Photographs by Winni Wintermeyer

AI and robotics have been separate fields up to now. Combining them could transform manufacturing and warehousing—and take AI to the next level.




A robot retrieves products from a bin.

The robot arm

is performing a peculiar kind of Sisyphean task. It hovers over a glistening pile of cooked chicken parts, dips down, and retrieves a single piece. A moment later, it swings around and places the chunk of chicken, ever so gently, into a bento box moving along a conveyor belt.

This robot, created by a San Francisco–based company called Osaro, is smarter than any you've seen before. The software that controls it has taught it to pick and place chicken in about five seconds—faster than your average food-processing worker. Before long, Osaro expects its robots to find work in a Japanese food factory.

Anyone worried about a robot uprising need only step inside a modern factory to see how far away that is. Most robots are powerful and precise but can't do anything unless programmed meticulously. An ordinary robot arm lacks the sense needed to pick up an object if it is moved an inch. It is completely hopeless at gripping something unfamiliar; it doesn't know the difference between a marshmallow and a cube of lead. Picking up irregularly shaped pieces of chicken from a haphazard pile is an act of genius.

Moreover, until recently, robots have been largely untouched by advances in artificial intelligence. Over the last five or so years, AI software has become adept at identifying images, winning board games, and responding to a person's voice with virtually no human intervention. It can even teach itself new abilities, given enough time to practice. All this while AI's hardware cousins, robots, struggle to open a door or pick up an apple.

That is about to change. The AI software that controls Osaro's robot lets it identify the objects in front of it, study how they behave when poked, pushed, and grasped, and then decide how to handle them. Like other AI algorithms, it learns from experience. Using an off-the-shelf camera combined with machine-learning software on a powerful computer nearby, it figures out how to grasp things effectively. With enough trial and error, the arm can learn how to grasp just about anything it might come across.

Workplace robots equipped with AI will let automation creep into many more areas of work. They could replace people anywhere that products need to be sorted, unpacked, or packed. Able to navigate a chaotic factory floor, they might take yet more jobs in manufacturing. It might not be an uprising, but it could be a revolution nonetheless. "We're seeing a lot of experimentation now, and people are trying a lot of different things," says Willy Shih, who studies trends in manufacturing at Harvard Business School. "There's a huge amount of possibility for [automating] repetitive tasks."

It's a revolution not just for the robots, but for AI, too. Putting AI software in a physical body allows it to use visual recognition, speech, and navigation out in the real world. Artificial intelligence gets smarter as it feeds on more data. So with every grasp and placement, the software behind these robots will become more and more adept at making sense of the world and how it works.

"This could lead to advances that wouldn't be possible without all that data," says Pieter Abbeel, a professor at the University of California, Berkeley, and the founder of Embodied Intelligence, a startup applying machine learning and virtual reality to robotics in manufacturing.

Separated at birth

This era has been a long time coming. In 1954, George C. Devol, an inventor, patented a design for a programmable mechanical arm. In 1961, a manufacturing entrepreneur named Joseph Engelberger turned the design into the Unimate, an unwieldy, awkward machine first used on a General Motors assembly line in New Jersey.

From the beginning, there was a tendency to romanticize the intelligence behind these simple machines. Engelberger chose the name "robot" for the Unimate in honor of the androids dreamed up by the science fiction author Isaac Asimov. But his machines were crude mechanical devices directed to perform a specific task by relatively simple software. Even today's much more advanced robots remain little more than mechanical dunces that must be programmed for every action.

Artificial intelligence followed a different path. In the 1950s, it set out to use the tools of computing to mimic humanlike logic and reason. Some researchers also sought to give these systems a physical presence. As early as 1948 and 1949, William Grey Walter, a neuroscientist in Bristol, UK, developed two small autonomous machines that he dubbed Elsie and Elmer. These turtle-like devices were equipped with simple, neurologically inspired circuits that let them follow a light source on their own. Walter built them to show how the connections between just a few neurons in the brain might result in relatively complex behavior.

But understanding and re-creating intelligence proved to be a byzantine challenge, and AI went into a long period with few breakthroughs. Meanwhile, programming physical machines to do useful things in the messy real world often proved intractably complex. The fields of robotics and AI began to go their own separate ways: AI retreated into the virtual, while robotics largely measured its progress in terms of novel mechanical designs and clever uses of machines with modest powers of reasoning.

Then, about six years ago, researchers figured out how to make an old AI trick incredibly powerful. The scientists were using neural networks—algorithms that approximate, roughly speaking, the way neurons and synapses in the brain


KUKA

The man behind Osaro's smarter robot

Osaro's CEO, Derik Pridmore, studied physics and computer science at MIT before joining a West Coast VC firm called Founders Fund. While there, Pridmore identified DeepMind, a British AI company, as an investment target, and he worked with the company's founders to hone their pitch. DeepMind would go on to teach machines to do things that seemed impossible at the time. Famously, it developed AlphaGo, the program that beat the top-ranked human grandmaster at the board game Go.

When Google acquired DeepMind in 2014, Pridmore decided that AI had commercial potential. He founded Osaro and quickly zeroed in on robot picking as the ideal application. Grasping objects loaded in a bin or rolling along a conveyor belt is a simple task for a human, but it requires genuine intelligence.

The techniques DeepMind pioneered, known as "deep reinforcement learning," let machines perform complex tasks without learning from human-provided examples. Positive feedback, like getting a higher score in a video game, tunes the network and moves the algorithm closer to the goal until it becomes expert.

The reasoning that makes this possible is buried deep within the network, encoded in the interplay of tens of millions of interconnected simulated neurons. But the resulting behavior can seem simple and instinctual. With enough practice, an arm can learn to pick things up efficiently, even when an object is moved, hidden by another object, or shaped a bit differently. Osaro uses deep reinforcement learning, along with several other machine-learning techniques, to make industrial robots a lot cleverer.

learn from input. These networks were, it turns out, direct descendants of the components that gave Elsie and Elmer their abilities. The researchers discovered that very large, or "deep," neural networks could do remarkable things when fed huge quantities of labeled data, such as recognizing the object shown in an image with near-human perfection.

The field of AI was turned upside down. Deep learning, as the technique is commonly known, is now widely used for tasks involving perception: face recognition, speech transcription, and training self-driving cars to identify pedestrians and signposts. It has made it possible to imagine a robot that could recognize your face, speak intelligently to you, and navigate safely to the kitchen to get you a soda from the fridge.

One of the first skills that AI will give machines is far greater dexterity. For the past few years, Amazon has been running a "robot picking" challenge in which researchers compete to have a robot pick up a wide array of products as quickly as possible. All of these teams are using machine learning, and their robots are gradually getting more proficient. Amazon, clearly, has one eye on automating the picking and packing of billions of items within its fulfillment centers.

AI gets a body

In the NoHo neighborhood of New York, one of the world's foremost experts on artificial intelligence is currently looking for the field's next big breakthrough. And he thinks that robots might be an important piece of the puzzle.

Yann LeCun played a vital role in the deep-learning revolution. During the 1980s, when other researchers dismissed neural networks as impractical, LeCun persevered. As head of Facebook's AI research until January 2018, and now as its chief AI scientist, he led the development of deep-learning algorithms that can identify users in just about any photo a person posts.

But LeCun wants AI to do more than just see and hear; he wants it to reason

COURTESY PHOTO

> “If you solve manipulation in its fullest, you’ll probably have built something that’s pretty close to full, human-level intelligence.”
>
> — Pieter Abbeel, UC Berkeley

An employee at Embodied Intelligence uses a virtual-reality rig to train a robot.

and take action. And he says it needs a physical presence to make this possible. Human intelligence involves interacting with the real world; human babies learn by playing with things. AI embedded in grasping machines can do the same. “A lot of the most interesting AI research now involves robots,” LeCun says.

A remarkable kind of machine evolution might even result, mirroring the process that gave rise to biological intelligence. Vision, dexterity, and intelligence began evolving together at an accelerated rate once hominids started walking upright, using their two free hands to examine and manipulate objects. Their brains grew bigger, enabling more advanced tools, language, and social organization.

Could AI experience something similar? Until now, it has existed largely inside computers, interacting with crude simulations of the real world, such as video games or still images. AI programs capable of perceiving the real world, interacting with it, and learning about it might eventually become far better at reasoning and even communicating. “If you solve manipulation in its fullest,” Abbeel says, “you’ll probably have built something that’s pretty close to full, human-level intelligence.”

Will Knight is a senior editor at MIT Technology Review and writes about AI and robots.

Going driverless in the city of cars

What will the adoption of shared autonomous vehicles do to the urban fabric of much of America?

By Ed Finn

Photographs by Brandon Sullivan


Courtesy
CHEVROLET
MEMORIAL DAY TENT SALE
CHEVROLET

Joe Helms, a service advisor at Chapman BMW on East Camelback Road in Phoenix.

THE CAR CULT

Sitting in the BMW dealership waiting for a flat to be replaced, I realize I've driven over 100 miles and spent five hours behind the wheel this week. And it's only lunchtime on Wednesday. In Phoenix, I am living the life this city has designed for me.

A sprawling grid fueled by swooping highways and generous arterial roads, the Phoenix metropolitan area is a gargantuan expression of the car culture that defines the urban experience for most Americans. To use this space, you need a vehicle. Anything else effects your passive or active exclusion from a host of activities and, more broadly, from the culture itself. You might choose to live downtown in one of the few patches of walkable urban space, but your access to groceries, drugstores, and other amenities will be severely limited. To meet friends, to send children to school, to attend a concert or a movie, is to buy into car culture and its attendant traffic jams, parking-space hunts, and maintenance responsibilities for a vehicle that is expensive to purchase and rapidly loses value.

Camelback Road, one of those major arteries, is a 33-mile temple to this cult of the car. Dealerships, auto repair shops, strip malls, and car washes, all ringed by vast parking lots, line a six-lane roadway that is deeply discouraging to navigate by foot. This world was designed by well-meaning urban planners, business owners, politicians, and private citizens who thought they were building the spaces where prosperity would grow, with the personal automobile as its driving force.

But Camelback is also ground zero for what may become the biggest disruption to cars' place in American life since they were invented. Thanks to Arizona's hands-off approach to regulation, firms developing self-driving cars—many of them headquartered in neighboring California—have begun to do their testing in the state.

Much of the debate has focused on safety, particularly after a self-driving Uber vehicle knocked down and killed a pedestrian in Tempe in March of 2018. Yet safety is only the first question. After all, if vehicular deaths were our primary concern, we might have banned cars from urban roads long ago; Arizona itself leads the nation in its rate of pedestrian fatalities.

Rather, as autonomous-vehicle companies continue testing and lobbying, we will find ourselves redesigning society to accommodate that technology in ways that go far beyond safety.

Autonomous vehicles won't merely eliminate the need to hold a steering wheel. They will enable entirely new modes of transportation and vehicle management that could accelerate the decline in private car ownership. What will then become of the rich ecosystem of infrastructure, services, retail, and cultural experience that has grown up around automobiles? What happens to Phoenix and hundreds of similar cities when we reinvent the car?

SHARING THE FUTURE

It's already possible to book a ride in a Waymo vehicle with no human behind the steering wheel. That won't just take work from human Lyft and Uber drivers; it will change life for millions of travelers in these cities.

That's because these cars will be not just driverless but also probably ownerless, at least in the customary sense. Waymo appears to be aiming squarely at a shared-transportation model. Its vehicles will operate in fleets (Waymo has already partnered with Avis to service and maintain its test vehicles in Arizona) as autonomous taxis. CEO John Krafcik described the company's vision in December: a small fleet of self-driving cars could serve an entire community because "you're accessing vehicles rather than owning them." A study envisioning such a fleet of vehicles at work in a simulated city based on Austin, Texas, found that running the network would cost about as much per mile as individual car ownership, and possibly less.

For Phoenix today, the most radical change in this future will be the nature of the car itself. Krafcik argues that cars "no longer have to be designed around the driver as the primary user." Instead you might step into a Starbucks Van, or a Burger King Coupe, to dine and commute at the same time. This could spell the end of drive-throughs like the Dutch Brothers coffee franchise, whose euphorically hands-on customer service seems to be irresistible to the millennial drivers who queue up tens of cars deep at the Camelback location.

In this vision of a shared-mobility future, the changes would ripple up and down thousands of streets like Camelback. The nearly trillion-dollar US auto industry may very well have to reinvent itself as cars evolve from consumer objects at rest an estimated 95% of the time to workhorses overseen by fleet management algorithms tasked with maximizing the value of every mile. Some companies would start offering cheaper ride-share

At Dutch Brothers, a drive-through coffee shop at Camelback and Central.

An Uber gets spiffed up at Jacksons Car Wash on East Highland Avenue.

services using no-frills vehicles designed for many years of continuous use.

If fewer people buy cars, many of the glittering auto showrooms on Camelback might close. Ford has announced that it will sell only two models of sedan going forward, concentrating on SUVs and trucks instead. But if oil prices rise, economics and physics may conspire to push people away from SUVs and further toward a shared model. Ford is "radically changing their ideas about cars" to accommodate a near future of selling car-related services rather than the cars themselves, says Larry Goldberg, a cofounder of the futures consultancy Experimental Design, which has been working with Ford and other industry players.

The phrase "mobility as a service" weaves together the business models of ride-sharing companies, the ambitions of manufacturers like Ford and Tesla, and the broader turn to a service economy. Cars may increasingly come to resemble smartphones—not just lumps of hardware, but consumer experiences that we pay monthly fees to use, and whose functions can be changed remotely by software updates, as Tesla already does with some cars. As more cars become autonomous, they'll drive to where they're needed and schedule their own maintenance checks, taking these decisions out of the hands of the consumer. All that code will funnel the currently vibrant ecology of auto-related businesses, from windshield replacement and custom detailing to mechanics, tire dealers, and parts retailers, into an increasingly narrow set of corporate fiefdoms and centralized systems of control.

CHANGING THE CAR ECONOMY

Consider the car wash, a mainstay of urban life in the dusty Southwest. A Waymo vehicle cannot go through a normal car wash for fear of damaging its many sensors. Instead the company's agreement with Avis includes specialized hand-washing.

The ripples of a changing car culture have already reached the local Jacksons Car Wash chain. At the Jacksons a block off Camelback at 20th Street, attendants in matching T-shirts vigorously towel off glossy cars as usual while a conveyor belt moves other vehicles through a noisy array of rotating brushes, sprayers, and mops. But there is also a banner celebrating a partnership with Uber. Its drivers can get discounted services and even subscriptions for unlimited car washes—essential when having a dirty car can cost a driver a five-star rating.

Jacksons is already upgrading its conveyor belts to safely handle Teslas, with their sensors and battery packs, and it is watching the evolution of autonomous vehicles closely. Sean Storer, the company's senior vice president, predicts that if they're individually owned, demand will grow for "full service" washes with hand toweling and customized human attention. But if Waymo, Lyft, or Uber owns them, the companies may see more profit in creating their own facilities where cars can be recharged, cleaned, serviced, and detailed all under one roof.

Variations on that prospect multiply as you move up and down Camelback. Alan Gershenfeld, a cofounder of Experimental Design, envisions a host of services for autonomous vehicles. Small companies might customize them for the specialized needs of landscapers or plumbers, for example, or to comply with a city's local regulations.

"The companies that adapt will thrive. But there will be pain in the transition," Gershenfeld says. Automation is likely to eliminate or transform over a third of the jobs in Phoenix, according to a recent report from the New America Foundation and Burning Glass, a labor-market data company. Transportation will account for a lot of them. These jobs are the lifeblood of Camelback Road: retail and services, stockers and servers, drivers and cashiers, all dependent in myriad ways on the current ecosystem of private cars, parking lots, and drive-up retail.

And that's not where the economic disruption ends. Many people now turn to Lyft, Uber, and the gig economy to make ends meet if they lose full-time employment. The automation that eliminates jobs along Camelback might also take part-time driving off the table, notes Megan Garcia, head of New America's recently launched Phoenix outpost. Already, contractors working for Waymo have taken to the employment reviews site GlassDoor to complain about poor working conditions, thwarted even from complaining to Waymo's HR because they are hired through intermediary companies. Waymo declined to comment.

BLAME IT ON THE YOUTH

Self-driving cars aside, Storer of Jacksons Car Wash says, what really worries him is generational change. Younger people are, in growing numbers,

A Ford Transit at the Camelback Ford dealership. Even in a driverless ecosystem, Ford will probably continue to make consumer service vehicles.

rejecting not just car ownership but even the once-mandatory rite of passage that is getting a driver's license. When they do buy cars, they don't care as much about washing, maintenance, or detailing.

However, this kind of cultural revolution—a rejection of the car as a central facet of American identity—could also present tremendous opportunities. The same forces leading sleek new condos and cafés to sprout up in downtown Phoenix could redirect the vast amounts of time, energy, and cash we put into the car cult toward a different kind of urban experience.

Cars may be privately owned, but the infrastructure they rely on is largely public: sidewalks and streets, traffic lights and parking requirements. Motivated city governments can legislate change: London, New York, and Barcelona, for example, have restricted or outright banned vehicles from certain areas. Widespread vehicle sharing would eliminate the need for most parking structures. All this can free urban space for parks, pedestrian shopping districts, housing, or urban farms. That could increase property values and create new local economies.

This is already starting to happen. San Francisco is nearly a decade into an experiment that lets local businesses convert parking spaces into "parklets" instead. In Arizona the city of Chandler, which has been working closely with Waymo, will let zoning authorities reduce parking space by up to 40% in anticipation of autonomous vehicles. If Waymo is even modestly successful in promoting shared transit, it should mean fewer vehicles and less urban congestion. Chandler's mayor, Jay Tibshraeny, argues that the changes will expand "the amount of property available for revenue-generating activity." And it is tantalizing to imagine a Phoenix that is greener, less polluted, less congested, and consequently less of a baked-concrete inferno six months of the year.

It is an inspiring vision. But there are good reasons why the only cities that have taken major steps toward it have densely packed urban cores. The fate of Phoenix as a temple to the car may have already been sealed by 60 years of concrete, bypasses, and car-oriented urban design.

PRY THE STEERING WHEEL FROM MY COLD DEAD HANDS

It may also have been sealed by personal choices. Phoenicians might simply refuse to abandon their vehicles because they've invested too much already: the cars, the generous garages, and all the equipage that goes with them. Not to mention the defining choices they have made about neighborhoods, school districts, commuting, friendships, and relationships—the whole fabric of work and life, dictated by cars and the urban layouts needed to travel in them.

That's why, while Waymo is banking on a future of shared-vehicle fleets, plenty of car companies aren't giving up on private ownership. Elon Musk foresees a Tesla Network, a "shared autonomy fleet" in which car owners can rent their vehicles out to others on their own terms—restricting access to friends and family, for example, or to certain hours of the day.

David King, an urban planner at Arizona State University, suggests that automation could even make private vehicle ownership *more* valuable. "What if my car takes me to work and then runs my errands for me?" he says. "You know what's used even less than 5% of the time? My toilet. There's a utility to having it there." King's point is that we are willing to pay for the perk of owning a vehicle where we can store paperwork, sports equipment, and spare outfits; it is how we reinvent and reposition ourselves as we move between home, office, rec team, and restaurant. Lugging all those costume changes between shared vehicles, or hiding them out of sight while a stranger is renting your car, might be a bridge too far for many drivers today.

But even if the number of vehicles on the roads doesn't drastically fall, the number of drivers will. At the same time, whole new modes of driving are slouching towards Camelback to be born.

PHOENICIANS MIGHT REFUSE TO ABANDON THEIR VEHICLES BECAUSE THEY'VE INVESTED TOO MUCH ALREADY: THE CARS, THE GARAGES, NOT TO MENTION THE DEFINING CHOICES THEY'VE MADE ABOUT NEIGHBORHOODS, SCHOOL DISTRICTS, COMMUTING, FRIENDSHIPS, AND RELATIONSHIPS—THE WHOLE FABRIC OF WORK AND LIFE, DICTATED BY CARS.

Waymo's autonomous technology will find some of its first customers in logistics: imagine a mobile grocery store that drives to you so you can pick out your own apples and carrots. Droids might follow us around to run errands and complete small purchases, says King: "Maybe we go back to the days of the milkman. You can schedule it or do it on demand, where the store comes to you." Autonomous vehicles might come in thousands of varieties, many of them small enough to roll along sidewalks and unobtrusively navigate suburban neighborhoods. The design and maintenance of these machines could become the basis of a new service economy and vehicular culture.

Whether or not you believe in this droid future, self-driving cars could be quite good for small businesses. Ford may be abandoning most passenger cars, but it's doubling down on the successful F150 truck. Such vehicles are business platforms as well as rolling storage units, and a plumber, electrician, or painter who can dispatch the truck to the store for supplies without interrupting work will be more efficient and presumably better paid. Perhaps Camelback will keep some of its car dealerships, and the more nimble service shops will start working with—even designing vehicles for—small-scale retail and service businesses.

Experimental Design imagines another scenario: neighborhoods eliminate the growing stream of delivery vehicles by organizing central locations or deploying a kind of package delivery van that comes around once or twice a day like an ice-cream truck. Neighbors might gather around the day's influx of retail goods and exchange news, transforming the hermetic life behind closed garage doors into a more open and collaborative kind of community.

These visions may seem overly idyllic, but consider the billions a year Amazon makes from Prime subscription fees alone (and that was before a 20% price hike). The company's "Treasure Truck" already invites Prime members in certain cities to rendezvous at one of several scheduled stops to get a special discount on a single item. There they meet up with Amazon employees driving a decked-out delivery truck to pick up their treasure. This is exactly the kind of logistical work Amazon has been perfecting for a decade. What would it take for services like this to start reshaping the layout and culture of Phoenix's neighborhoods?

It is through local actions like these that the transition from car culture to a new kind of collective mobility might actually work. Those who might not want to share a car with strangers might still be willing to share it with their neighbors, family, and friends. "It's not that you're going to zero cars, but it's less cars per family," says Thad Miller, co-director of the Center for Smart Cities and Regions at ASU. A gradual shift like that may be more plausible for a deeply car-centric city like Phoenix.

To make this change work across the vastly different urban spaces of America's coasts and its sprawling interior, companies and people will need to start telling new stories about autonomous vehicles that make sense of the spaces we have. We need a new dream about the romance of the car to convince us to let go of the old one.

Ed Finn runs the Center for Science and the Imagination at Arizona State University and is the author of What Algorithms Want: Imagination in the Age of Computing.

A Waymo car out in the wild: a Chrysler Pacifica hybrid.

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How can we fight climate change?

2

We're beyond the point where incremental changes will fix what we've done to the planet. It's time for desperation moves, like trying to draw carbon dioxide straight out of the air. But is that even feasible at the scale that will make a difference? And if it is, can we afford it? (page 26). Or, perhaps just as desperate a ploy, we can try to persuade people to change their eating habits—or invent a type of food that doesn't slam the environment quite so hard (page 34).

IS CARBON REMOVAL CRAZY OR CRITICAL?

Photographs by Spencer Lowell

By James Temple

YES.

The big metal container in Klaus Lackner's lab doesn't look as if it could save the planet. It most closely resembles a dumpster— which it sort of is.

As Lackner looks on, hands in the pockets of his pressed khakis, the machine begins to transform. Three mattress-shaped metal frames rise from the guts of the receptacle, unfolding like an accordion as they stretch toward the ceiling.

Each frame contains hundreds of white polymer strips filled with resins that bind with carbon dioxide molecules. The strips form a kind of sail, designed to snatch the greenhouse gas out of the air as wind blows through the contraption.

Crucially, that same material releases the carbon dioxide when wet. To make that happen, Lackner's device retracts its frames into their container, which then fills with water. The gas can next be collected and put to other uses, and the process can begin again.

Lackner and his colleagues at Arizona State University's Center for Negative Carbon Emissions have built a simple machine with a grand purpose: capturing and recycling carbon dioxide to ease the effects of climate change. He envisions forests of them stretching across the countryside, sucking up billions of tons of it from the atmosphere.

Lackner, 66, with receding silver hair, has now been working on the problem for two decades. In 1999, as a particle physicist at Los Alamos National Laboratory, he wrote the first scientific paper exploring the feasibility of combating climate change by pulling carbon dioxide out of the air. His was a lonely voice for years. But a growing crowd has come around to his thinking as the world struggles to slash climate emissions fast enough to prevent catastrophic warming. Lackner's work has helped inspire a handful of direct-air-capture startups, including one of his own, and a growing body of scientific literature. "It's hard to think of another field that is so much the product of a single person's thinking and advocacy," says David Keith, a Harvard professor who cofounded another of those startups, Carbon Engineering. "Klaus was pivotal in making the argument that [direct air capture] could be developed at a scale relevant to the carbon-climate problem."

The carbon-trapping materials work in various forms, including a grass-like structure used to fertilize greenhouses (previous pages).

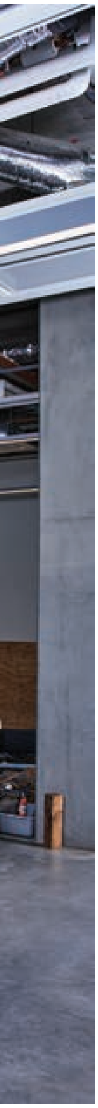
The latest prototype (right) unfolds to grab carbon from the air. Klaus Lackner (next page) pioneered the field of direct air capture.

No one, including Lackner, really knows whether the scheme will work. The chemistry is easy enough. But can we really construct anywhere near enough carbon removal machines to make a dent in climate change? Who will pay for them? And what are we going to do with all the carbon dioxide they collect?

Lackner readily acknowledges the unknowns but believes that the cheaper the process gets, the more feasible it becomes. "If I tell you, 'You could solve the carbon problem for $1,000 a ton,' we will say, 'Climate change is a hoax,'" Lackner says. "But if it's $5 a ton, or $1 a ton, we'll say, 'Why haven't we fixed it yet?'"

Narrowing our options

The concentration of carbon dioxide in the atmosphere is approaching 410



parts per million. That has already driven global temperatures nearly 1 °C above preindustrial levels and intensified droughts, wildfires, and other natural disasters. Those dangers will only compound as emissions continue to rise.

The latest assessment from the UN's Intergovernmental Panel on Climate Change found that there's no way to limit or return global warming to 1.5 °C without removing somewhere between 100 billion and a trillion metric tons of carbon dioxide by the end of the century. On the high end, that means reversing nearly three decades of global emissions at the current rate.

There are a handful of ways to draw carbon dioxide out of the atmosphere. They include planting lots of trees, restoring grasslands and other areas that naturally hold carbon in soils, and using carbon dioxide–sucking plants and other forms of biomass as a fuel source but capturing any emissions when they're used (a process known as bio-energy with carbon capture and storage).

But a report from the US National Academies in October 2018 found that these approaches alone probably won't be enough to prevent 2 °C of warming—at least, not if we want to eat. That's because the amount of land required to capture that much carbon dioxide would come at the cost of a huge amount of agricultural food production.

The appeal of direct-air-capture devices like the ones Lackner and others are developing is that they can suck out the same amount of carbon dioxide on far less land. The big problem is that right now it's much cheaper to plant a tree. At the current cost of around $600 per ton, capturing a trillion tons would run some $600 trillion, more than seven times the world's annual GDP.

In a 2018 paper, Harvard's Keith calculated that the direct-air-capture system he helped design could eventually cost less than $100 a ton at full scale. Carbon Engineering, based in British Columbia, is in the process of expanding its pilot plant to increase production of synthetic fuels, created by combining the captured carbon dioxide with hydrogen. These, in turn, will be converted into forms of diesel and jet fuel that are considered carbon neutral, since they don't require digging up additional fossil fuels.

If Keith's method can capture carbon dioxide for $100 a ton, these synthetic fuels could be sold profitably in markets with public policy support, such as California, with its renewable-fuel standards, or the European Union, under its updated Renewable Energy Directive. The hope is that these kinds of early opportunities will help scale up the technology, drive down costs further, and open additional markets.

Other startups, including Switzerland-based Climeworks and Global Thermostat of New York, think they can achieve similar or even lower costs. They are exploring markets like the soda industry and greenhouses, which use air enriched with carbon dioxide to fertilize plants.

However, selling carbon dioxide isn't an easy proposition.

Global demand is relatively small: on the order of a few hundred million tons per year, a fraction of the tens of billions that eventually need to be removed annually, according to the National Academies study. Moreover, most of that demand is for enhanced oil recovery, a technique that forces compressed carbon dioxide into wells to free up the last drips of oil, which only makes the climate problem worse.

A critical question for the carbon-capture startups is how much the market for carbon dioxide could grow. Dozens of businesses are exploring new ways of putting it to work. They include

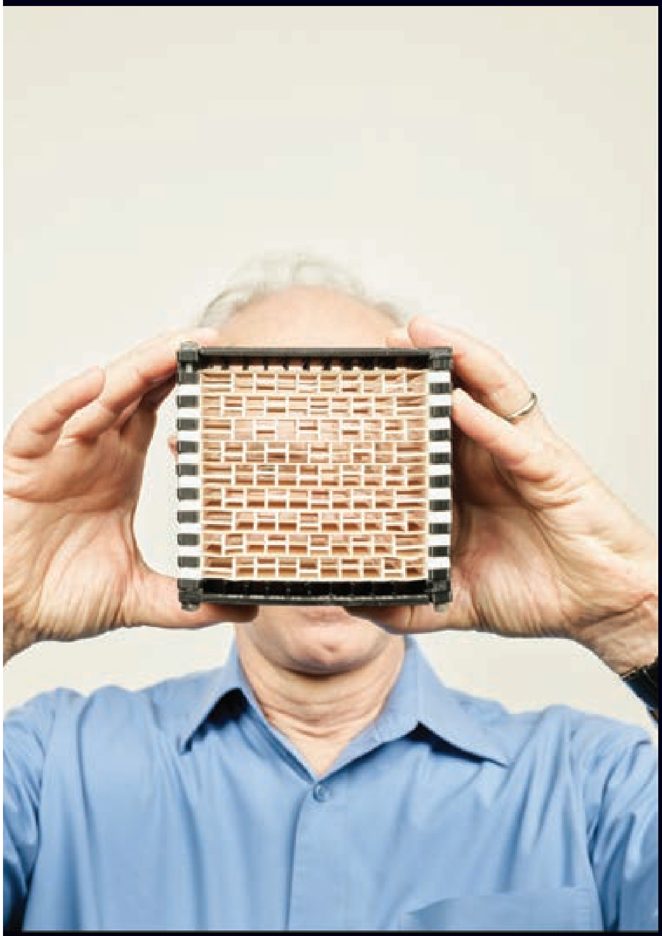
"THE IDEA THAT WE'RE GOING TO GET TO NEGATIVE CIVILIZATION-SCALE EMISSIONS THROUGH AIR CAPTURE, TO ME, JUST SEEMS LIKE A FANTASY."

California-based Opus12, which is using carbon dioxide to produce chemicals and polymers, and CarbonCure of Nova Scotia, which is working with more than 100 concrete manufacturers to convert carbon dioxide into calcium carbonate that gets trapped in the concrete as it sets.

A 2016 report by the Global CO_2 Initiative estimated that the market for products that could use carbon dioxide—including liquid fuels, polymers, methanol, and concrete—could reach $800 billion by 2030. Those industries could put to use some 7 billion metric tons per year—about 15% of annual global emissions.

Such projections are extremely optimistic, though. And even if such a vast transformation of multiple sectors actually occurs, it will still leave huge amounts of captured carbon dioxide that will need to be permanently stored underground.

That's only going to happen if society decides to pay for it, and some are skeptical we ever will. Capturing carbon dioxide out of the air—which means plucking a single molecule from amid nearly 2,500 others—is one of the most energy-intensive and expensive ways we could dream up of grappling with climate change. "Direct air capture is more expensive than avoiding emissions, but right now we're not even willing to spend the additional money to do that," says Ken Caldeira, a climate scientist at the Carnegie Institution. "So the idea that we're going to get to negative civilization-scale emissions through air capture, to me, just seems like a fantasy."



Lackner peers through an early model of an air-capture device, with the carbon-trapping materials shaped into a grid.

Robot-making robots

On a summer night in 1992, while Lackner was a researcher at Los Alamos National Laboratory, he and a fellow particle physicist were having a beer and complaining about the lack of big, bold ideas in science. One or two drinks later, they had one of their own: What would become possible if machines could build machines? How big and fast could you manufacture things?

They quickly realized that the only way the scheme would work is if you designed robots that dug up all their own raw materials from dirt, constructed solar panels to power the process—and made ever more copies of themselves.

The next morning, Lackner and his friend, Christopher Wendt of the University of Wisconsin–Madison, decided they had an idea worth exploring. They eventually published a paper working out the math and exploring several applications, including self-replicating robots that could capture massive amounts of carbon dioxide and convert it into carbonate rock.

The robot armada, solar arrays, carbon-converting machines, and piles of rock would all grow exponentially, reaching "continental size in less than a decade," the paper concluded. Converting 20% of the carbon dioxide in the atmosphere would generate a layer of rock 50 centimeters (20 inches) thick covering a million square kilometers (390,000 square miles)—an area the size of Egypt.

The hitch, of course, is that self-replicating machines don't exist. Lackner moved on from that part of the plan, and briefly focused on solar power as a replacement for fossil fuels. But the more he studied the problem, the more he came to believe that renewable sources would struggle to compete with the price, abundance, and energy density of coal, oil, and gasoline.

"This suggested to me that fossil-fuel-based power will not just roll over and die," he says. But perhaps if carbon removal technologies were cheap enough, he thought, you could "force fossil-fuel providers to clean up after themselves."

A few years later, Lackner published a paper titled "Carbon Dioxide Extraction from Air: Is It an Option?" He argued that it was technically feasible and might be possible for as little as $15 a ton. (He now believes the price floor is probably between $30 and $50 a ton.)

In 2001 Lackner moved to Columbia University, where he cofounded Global Research Technologies, the first effort to commercialize direct air capture. Gary Comer, founder of the clothing and furniture company Lands' End, handed the company $8 million of what Lackner describes as "adventure capital, not venture capital."

The company built a small prototype but soon ran out of money. A group of investors bought the controlling interest, moved it to San Francisco, and renamed it Kilimanjaro Energy. Lackner served as an advisor and board member. But it quietly closed its doors after failing to raise more money.

Despite these failures, Lackner continued to try to figure out how to do air capture cheaply and efficiently. He's published more than 100 scientific papers and editorials on the subject, and applied for more than two dozen patents.

SOME SCIENTIFIC CRITICS FOUND LACKNER'S PROJECTIONS NOT JUST WRONG BUT DANGEROUS. A PAIR OF CRITICAL PAPERS IN 2011 SOUNDED TO MANY LIKE A DEATH KNELL FOR DIRECT AIR CAPTURE. LACKNER WAS UNDAUNTED.

Some scientific critics, however, found Lackner's projections not just wrong but also dangerous. They feared that claiming direct air capture could be done cheaply and easily would reduce the pressure to slash emissions. In 2011, a pair of studies concluded that the technology would cost between $600 and $1,000 a ton.

Howard Herzog, a senior researcher at the MIT Energy Initiative, who coauthored one of the studies, took the added step of suggesting that "some purveyors" of the technology were "snake-oil salesmen." In an interview last year, Herzog told me he was mainly talking about Lackner. "He was the one who was really out there," he says.

Many read the two papers' conclusions as a death knell for direct air capture. Lackner stood firm, telling the journal Nature after the first of the studies was published: "They proved that one specific way to capture carbon dioxide from air is expensive. If you study penguins, you might jump to the conclusion that birds can't fly."

In 2014, he and his Global Research Technologies cofounder, Allen Wright, established the Center for Negative Carbon Emissions at Arizona State, where they've continued to try to get their own fledgling to take flight.

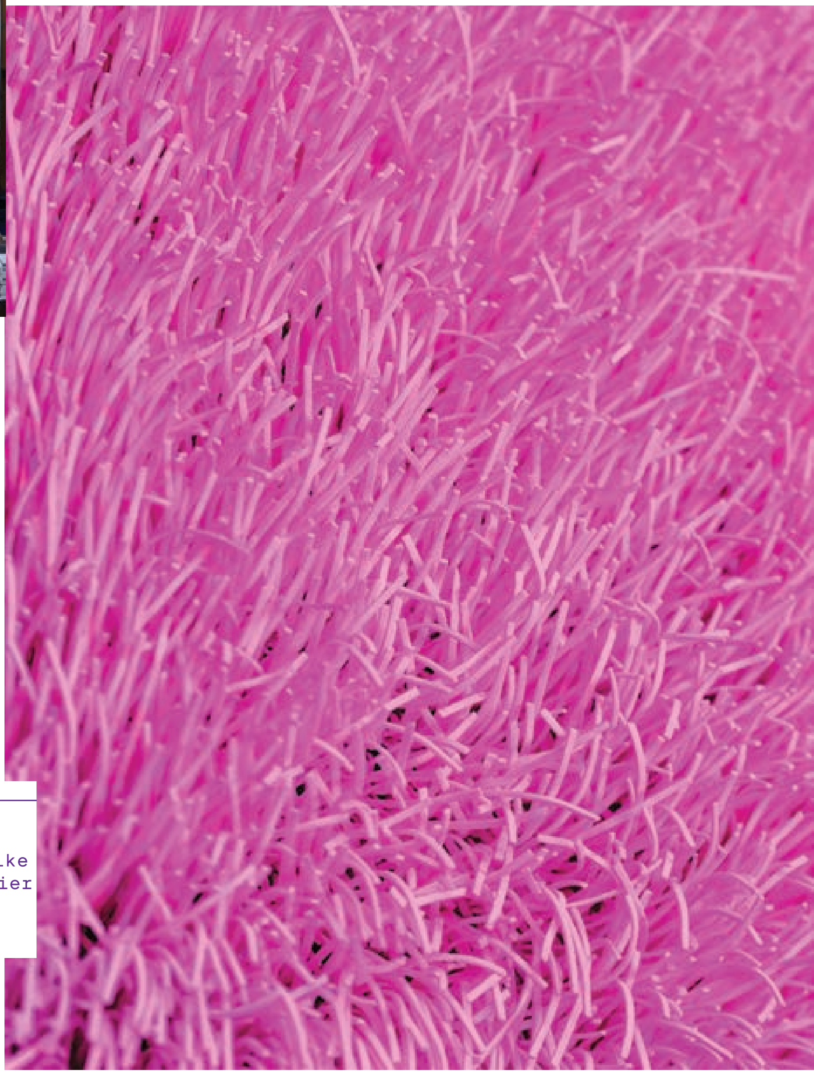
Planting synthetic forests

At the heart of the Center for Negative Carbon Emissions' design is a particular type of commercially available anion-exchange resin. As wind carries carbon dioxide in the air across those polymer strips, negatively charged ions bind with the gas molecules and convert them into bicarbonate—the main compound in baking soda and antacids.

The machine then retracts, pulling those saturated strips back into the container and pumping it full of water. The water begins converting the bicarbonate molecules into carbonate ions.

As the water drains away, those compounds become unstable and turn back into carbon dioxide in the air within the container. The now carbon dioxide–rich

The hundreds of polymer strips form a kind of sail that grabs carbon dioxide molecules as wind blows air through the device.



A close-up view of the carbon-capturing materials in a grass-like configuration, an earlier design that releases carbon dioxide when placed in a greenhouse.

"MY ARGUMENT HAS ALWAYS BEEN WE NEED TO BE PASSIVE," LACKNER SAYS. "WE WANT TO BE A TREE STANDING IN THE WIND AND HAVE THE CO_2 CARRIED TO US."

air can then be sucked out through a tube, and into an adjacent set of tanks.

Since carbon dioxide is relatively dilute in the air, most other direct capture approaches employ large fans to blow air over the binding materials to trap more of the gas. They then employ heat to drive the subsequent reactions that release the carbon dioxide. Both these steps use more energy. In contrast, Lackner says, his and Wright's approach just requires a little electricity to extend and retract the machine, pump the water, and vacuum out the air.

"My argument has always been we need to be passive," Lackner says. "We want to be a tree standing in the wind and have the CO_2 carried to us."

But there are big drawbacks to this method. It works only when the wind is blowing and makes sense only in dry areas, since humidity allows the carbon dioxide to escape. Moreover, the concentration of captured carbon in the resulting gas is less than 5%, compared with around 98% from a Carbon Engineering or Climeworks facility.

That low level is fine for fertilizing plants in greenhouses. But that's a tiny market, and Lackner has grander designs.

He envisions thousands of these machines plucking carbon dioxide from the sky in some dry and hot part of the world, while adjacent solar panels drive an electrolysis process that extracts hydrogen from water. The carbon dioxide and hydrogen could then be combined on site to produce thousands of barrels a day of synthetic fuel, which could be sold for heating or transportation, or used to feed the electric grid when renewables like wind and solar flag.

That plan, however, poses several challenges. Electrolysis is still very expensive. And they'd need to compress the carbon dioxide to the necessary concentration while removing water vapor, nitrogen, and oxygen.

That can be done, but it could substantially increase costs and energy needs. "This is a big, important piece that he's glossing over a bit," says Jennifer Wilcox, a professor at Worcester Polytechnic Institute and coauthor of the National Academies report.

Some believe Lackner's strengths as a theorist and big-picture guy haven't served him as well in translating those ideas into the necessary advances in materials science and chemistry. Notably, the Center for Negative Carbon Emissions project is trailing well behind Carbon Engineering, Climeworks, and Global Thermostat, which are amassing capital, hiring staffs, and building out demonstration if not commercial-scale facilities.

But Lackner remains confident that his approach will be less expensive than competing ones. "I can lay it out unit process by unit process, and in terms of first principles, at every step we're a little cheaper," he says.

Deep trouble

How does Lackner himself feel about the technology's prospects more than two decades after starting down this research path? It's not a simple answer. Lackner doesn't really do simple answers. During a walk across the university's palm-lined campus in Tempe, he says he remains confident that direct air capture is feasible and believes it could get much less expensive if it's able to reach commercial scale.

"But I'm less optimistic that we have the political will to go through that threshold," he says.

Given the high early costs and limited markets, he believes the technology will need significant government funding or tight regulations to be widely adopted—and more government support to cover the cost of capturing and burying the majority of the carbon dioxide that can't be used. He thinks we'll need to treat carbon dioxide like sewage, requiring consumers or companies to pay for its collection and disposal, whether in taxes or fees.

But after decades of relatively little political action on climate change, and fierce public resistance to carbon taxes, he fears the world isn't going to come around to that way of thinking until the suffering from climate catastrophes becomes too horrible to ignore.

What he is sure of, after spending more time than anyone else puzzling over carbon removal, is that we're going to need it. "I'm the first to admit that air capture isn't proven—and it certainly isn't proven at scale," Lackner says. "But we're in deep trouble if we can't figure it out."

James Temple is MIT Technology Review's senior editor covering climate change.

The meat without the cow

Meat production spews tons of greenhouse gas and uses up too much land and water. Is there an alternative that won't make us do without?

Memphis Meats CEO Ulma Valeti (center) and chief science officer Nicholas Genovese (right) watch a chef prepare one of their creations.

MEMPHIS MEATS

In 2013, the world's first burger from a lab was cooked in butter and eaten at a glitzy press conference. The burger cost £215,000 ($330,000 at the time) to make, and despite all the media razzmatazz, the tasters were polite but not overly impressed. "Close to meat, but not that juicy," said one food critic.

Still, that one burger, paid for by Google cofounder Sergey Brin, was the earliest use of a technique called cellular agriculture to make edible meat products from scratch—no dead animals required. Cellular agriculture, whose products are known as cultured or lab-grown meat, builds up muscle tissue from a handful of cells taken from an animal. These cells are then nurtured on a scaffold in a bioreactor and fed with a special nutrient broth.

Over five years later, startups around the world are racing to produce lab-grown meat that tastes as good as the traditional kind and costs about as much.

They're already playing catch-up: "plant-based" meat, made of a mix of non-animal products that mimic the taste and texture of real meat, is already on the market. The biggest name in this area: Impossible Foods, whose faux meat sells in more than 5,000 restaurants and fast food chains in the US and Asia and should be in supermarkets later this year. Impossible's research team of more than 100 scientists and engineers uses techniques such as gas chromatography and mass spectrometry to identify the volatile molecules released when meat is cooked.

The key to their particular formula is the oxygen-carrying molecule heme, which contains iron that gives meat its color and metallic tang. Instead of using meat, Impossible uses genetically modified yeast to make a version of heme that is found in the roots of certain plants.

Impossible has a few competitors, particularly Beyond Meat, which uses pea protein (among other ingredients) to replicate ground beef. Its product is sold in supermarket chains like Tesco in the UK and Whole Foods in the US, alongside real meat and chicken. Both Impossible and Beyond released new, improved versions of their burgers in January 2019.

In contrast, none of the lab-grown-meat startups has yet announced a launch date for its first commercial product. But when that happens—some claim as early as the end of this year—the lab-grown approach could turn the traditional meat industry on its head.

"I suspect that cultured meat proteins can do things that plant-based proteins can't in terms of flavor, nutrition, and performance," says Isha Datar, who leads New Harvest, an organization that helps fund research in cellular agriculture. Datar, a cell biologist and a fellow at the MIT Media Lab, believes cultured meats will more closely resemble real meat, nutritionally and functionally, than the plant-based kinds do. The idea is that a die-hard carnivore (like me) might not feel so put off at the thought of giving up the real thing.

A GLOBAL RISK

You might ask, why would anyone want to? The answer is that our meat consumption habits are,

"Without changes toward more plant-based diets," says Marco Springmann, a researcher in environmental sustainability at the University of Oxford and the lead author of the Nature paper, "there is little chance to avoid dangerous levels of climate change."

The good news is that a growing number of people now seem to be rethinking what they eat. A recent report from Nielsen found that sales of plant-based foods intended to replace animal products were up 20% in 2018 compared with a year earlier. Veganism, which eschews not just meat but products that come from greenhouse-gas-emitting dairy livestock too, is now considered relatively mainstream.

That doesn't necessarily equate to more vegans. A recent Gallup poll found that the number of people in the US who say they are vegan has barely changed since 2012 and stands at around just 3%. Regardless, Americans are eating less meat, even if they're not cutting it out altogether.

in a very literal sense, not sustainable. Livestock raised for food already contribute about 15% of the world's global greenhouse-gas emissions. (You may have heard that if cows were a country, it would be the world's third biggest emitter.) A quarter of the planet's ice-free land is used to graze them, and a third of all cropland is used to grow food for them. A growing population will make things worse. It's estimated that with the population expected to rise to 10 billion, humans will eat 70% more meat by 2050. Greenhouse gases from food production will rise by as much as 92%.

In January a commission of 37 scientists reported in The Lancet that meat's damaging effects not only on the environment but also on our health make it "a global risk to people and the planet." In October 2018 a study in Nature found that we will need to change our diets significantly if we're not to irreparably wreck our planet's natural resources.

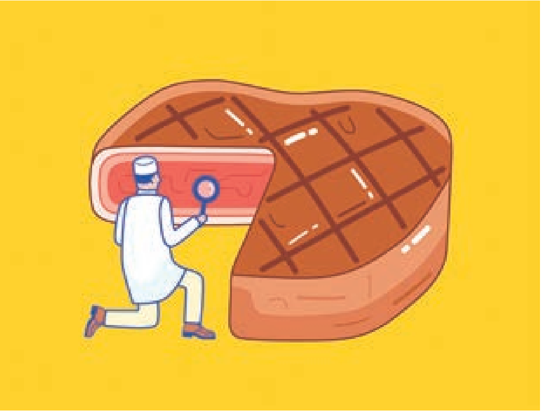
We'll need to change our diets to avoid wrecking the planet.

AND NOW FOR THE LAWSUITS

Investors are betting big that this momentum will continue. Startups such as MosaMeat (cofounded by Mark Post, the scientist behind the £215,000 burger), Memphis Meats, Supermeat, Just, and Finless Foods have all swept up healthy sums of venture capital. The race now is to be first to market with a palatable product at an acceptable cost.

Memphis Meats' VP of product and regulation, Eric Schulze, sees his product as complementing the real-meat industry. "In our rich cultural tapestry as a species, we are providing a new innovation to weave into our growing list of sustainable food traditions," he says. "We see ourselves as an 'and,' not 'or,' solution to helping feed a growing world."

The traditional meat industry doesn't see it that way. The National Cattlemen's Beef Association in the US dismissively dubs these new approaches "fake meat." In August 2018, Missouri enacted a law



that bans labeling any such alternative products as meat. Only food that has been "derived from harvested production of livestock or poultry" can have the word "meat" on the label in any form. Breaking that law could lead to a fine or even a year's jail time.

The alternative-meat industry is fighting back. The Good Food Institute, which campaigns for regulations that favor plant-based and lab-grown meats, has joined forces with Tofurky (the makers of a tofu-based meat replacement since the 1980s), the American Civil Liberties Union, and the Animal Legal Defense Fund to get the law overturned. Jessica Almy, the institute's policy director, says the law as it stands is "nonsensical" and an "affront" to the principle of free speech. "The thinking behind the law is to make plant-based meat less appealing and to disadvantage cultured meat when it comes on the market," she says.

Almy says she's confident their case will be successful and is expecting a temporary injunction to be granted soon. But the Missouri battle is just the start of a struggle that could last years. In February 2018, the US Cattlemen's Association launched a petition that calls on the US Department of Agriculture (USDA) to enact a similar federal law.

Traditional meat-industry groups have also been very vocal on how cultured meat and plant-based meats are to be regulated. Last summer a group of the biggest agricultural organizations in the US (nicknamed "The Barnyard") wrote to President Trump asking for reassurance that the USDA will oversee cultured meat to ensure "a level playing field." (The USDA has tougher, more stringent safety inspections than the Food and Drug Administration.)

In November 2018, the USDA and the FDA finally released a joint statement to announce that the two regulators would share the responsibilities for overseeing lab-grown meats.

"I think there will be lines outside the store that are longer than for the next iPhone."

THE BOVINE SERUM PROBLEM

Some cultured-meat startups say this confusion over regulations is the only thing holding them back. One firm, Just, says it plans to launch a ground "chicken" product this year and has trumpeted a partnership with a Japanese livestock firm to produce a "Wagyu beef" product made from cells in the lab. Its CEO is Josh Tetrick, who'd previously founded the controversial startup Hampton Creek, Just's forebear. (The FDA had at one time banned the firm from calling its signature product mayonnaise, as it did not contain any eggs.) Speak to Tetrick, a bullish, confident young man, and you get a sense of the drive and excitement behind the alternative-meat market. "The only [limit] to launching," he says, "is regulatory."

That's optimistic, to say the least. The lab-meat movement still faces big technical hurdles. One is that making the product requires something called fetal bovine serum. FBS is harvested from fetuses taken from pregnant cows during slaughter. That's an obvious problem for a purportedly cruelty-free product. FBS also happens to be eye-wateringly expensive. It is used in the biopharmaceutical industry and in basic cellular research, but only in tiny amounts. Cultured meat, however, requires vast quantities. All the lab-meat startups will have to use less of it—or eliminate it completely—to make their products cheap enough. Finless Foods (which aims to make a fish-free version of bluefin tuna) has reported that it's halved the amount of FBS it needs to grow its cells. And Schulze says the Memphis Meats team is working on ways of cutting it out entirely.

But there are other issues, says Datar, of New Harvest. She says we still don't understand the fundamental processes well enough. While we have quite a deep understanding of animals used in medical research, such as lab mice, our knowledge of agricultural animals at a cellular level is rather thin. "I'm seeing a lot of excitement and VCs investing but not seeing a lot in scientific, material advancements," she says. It's going to be tricky to scale up the technology if we're still learning how these complex biological systems react and grow.

Lab-grown meat has another—more tangible—problem. Growing muscle cells from scratch creates pure meat tissue, but the result lacks a vital component of any burger or steak: fat. Fat is what gives meat its flavor and moisture, and its texture is hard to replicate. Plant-based meats are already getting around the problem—to some extent—by using shear cell technology that forces the plant protein mixture into layers to produce a fibrous meat-like texture. But if you want to create a meat-free "steak" from scratch, some more work needs to be done. Cultured meat will need a way to grow fat cells and somehow mesh them with the muscle cells for the end result to be palatable.

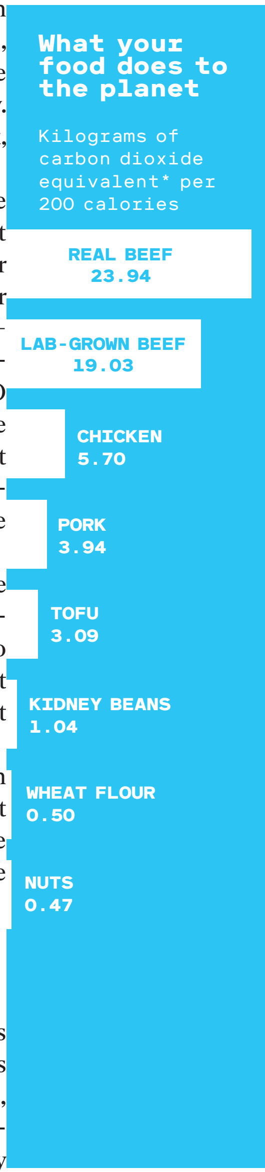
That has proved tricky so far, which is the main reason that first burger was so mouth-puckeringly dry.

The scientists at the Netherlands-based cultured-meat startup Meatable might have found a way. The team has piggybacked on medical stem-cell research to find a way of isolating pluripotent stem cells in cows by taking them from the blood in umbilical cords of newborn calves. Pluripotent cells, formed early in an embryo's development, have the ability to develop into any type of cell in the body. This means they can also be coaxed into forming fat, muscle, or even liver cells in lab-grown meat.

Meatable's work might mean that the cells can be tweaked to produce a steak-like product whose fat and muscle content depends on what the customer prefers: a rib-eye steak's characteristic marbling, for example. "We can add more fat, or make it leaner—we can do anything we want to. We have new control over how we feed the cells," says Meatable CTO Daan Luining, who is also a research director at the nonprofit Cellular Agriculture Society. "Pluripotent cells are like the hardware. The software you're running turns it into the cell you want. It's already in the cell—you just need to trigger it."

But the researchers' work is also interesting because they have found a way to get around the FBS problem: the pluripotent cells don't require the serum to grow. Luining is clearly proud of this. "To circumvent that using a different cell type was a very elegant solution," he says.

He concedes that Meatable is still years away from launching a commercial product, but he's confident about its eventual prospects. "I think there will be lines outside the store that are longer than for the next iPhone," he says.



IF YOU MAKE IT, WILL THEY EAT IT?

As it stands, lab-grown meat is not quite as virtuous as you might think. While its greenhouse emissions are below those associated with the biggest villain, beef, it is more polluting than chicken or the plant-based alternatives, because of the energy currently required to produce it. A World Economic Forum white paper on the impact of alternative meats found that lab-grown meat as it is made now would produce only about 7% less in greenhouse-gas emissions than beef. Other replacements, such as tofu or plants, produced reductions of up to 25%. "We will have to see if companies will really be able to offer low-emissions products at reasonable costs," says Oxford's Marco Springmann, one of the paper's coauthors.

It is also unclear how much better for you lab-grown meat would be than the real thing. One reason meat has been linked to a heightened cancer risk is that it contains heme, which could also be present in cultured meats.

And will people even want to eat it? Datar thinks so. The little research there has been on the subject backs that up. A 2017 study published in the journal PLoS One found that most consumers in the US would be willing to try lab-grown meat, and around a third were probably or definitely willing to eat it regularly.

Expecting the whole world to go vegan is unrealistic. But a report in Nature in October 2018 suggested that if everyone moved to the flexitarian lifestyle (eating mostly vegetarian but with a little poultry and fish and no more than one portion of red meat a week), we could halve the greenhouse-gas emissions from food production and also reduce other harmful effects of the meat industry, such as the overuse of fertilizers and the waste of fresh water and land. (It could also reduce premature mortality by about 20%, according to a study in The Lancet in October, thanks to fewer deaths from ailments such as coronary heart disease, stroke, and cancer.)

Some of the biggest players in the traditional meat industry recognize this and are subtly rebranding themselves as "protein producers" rather than meat companies. Like Big Tobacco firms buying vape startups, the meat giants are also buying stakes in this new industry. In 2016, Tyson Foods, the world's second biggest meat processor, launched a venture capital fund to support alternative-meat producers; it's also an investor in Beyond Meat. In 2017, the third biggest, Cargill, invested in cultured-meat startup Memphis Meats, and Tyson followed suit in 2018. Many other big food producers are doing the same; in December 2018, for example, Unilever bought a Dutch firm called the Vegetarian Butcher that makes a variety of non-meat products, including plant-based meat substitutes.

"A meat company doesn't do what they do because they want to degrade the environment and don't like animals," says Tetrick, the Just CEO. "They do it because they think it's the most efficient way. But if you give them a different way to grow the company that's more efficient, they'll do it."

At least some in the meat industry agree. In a profile last year for Bloomberg, Tom Hayes, then the CEO of Tyson, made it clear where he saw the company's eventual future. "If we can grow the meat without the animal," he said, "why wouldn't we?"

Niall Firth is MIT Technology Review's news editor.

Will genomic medicine cure my disease?

3

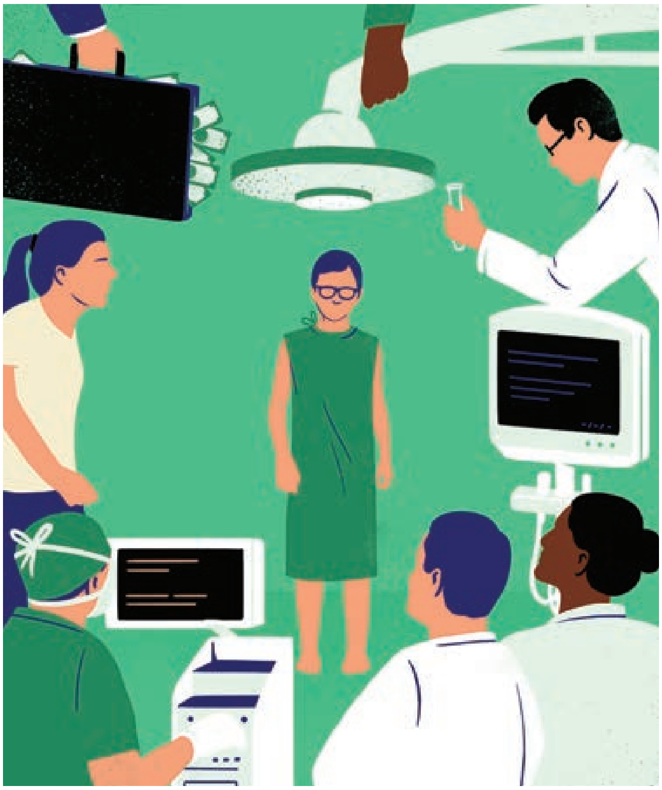
Most rare diseases have no treatment. Gene therapy could help, but given the lack of patients for each disease, there's little motivation for drug companies to find a cure. Now some desperate parents are funding the search themselves (page 42). Every cancer, we're finding, is a malady unto itself, and should be treated as such. Genome sequencing makes that possible (page 50), but can we turn that scientific insight into medical practice and change how we treat cancer?

A cure for one

By
Antonio Regalado

Illustrations by
Sébastien Thibault

One day, gene therapy may help with the rarest of diseases. Some parents aren't waiting.



Jennie and Gary Landsman launched an appeal to save their sons on Thanksgiving of 2017. By the end of the weekend the family, who live in Marine Park, Brooklyn, had raised $200,000.

In a moving three-minute video posted online, they sit on an overstuffed leather couch. Jennie glances away from the camera, betraying little emotion, as Gary talks. “We need your help, we really do,” Gary says, his voice breaking. The Landsmans’ two sons—Benny, then 18 months, and Josh, four months—both have a fatal genetic brain disorder called Canavan disease. Benny, limp on his mother’s lap, is already affected by nerve loss. Josh isn’t yet. But he will be if nothing is done.

Canavan is an “ultra-rare” disease. So rare, in fact, that there is no reliable understanding of how many children are born with it. Relatively few researchers study Canavan, and no drugs are approved to treat it. There isn’t even a single clinical trial open for some last-ditch remedy, the kind people battling cancer can turn to. Doctors told Jennie there was not much to be done. She should go home and make her boys comfortable until they died.

The Landsmans refused to accept that advice. Instead, Jennie hit Google and started e-mailing scientists. Here’s what she learned: there may be a way to fix the genetic error in the boys’ brains. But the family would have to pay for it themselves. And it would be expensive.

“We need one and a half million dollars, and our goal is to get it in the next six months,” Jennie says in the video.

The Landsmans had discovered gene therapy, technology that uses viruses to add healthy genes to cells with defective ones. After several decades caught in scientific backwaters, gene therapy has entered a golden age. During a span of four months, from August to December 2017, the US Food and Drug Administration (FDA) approved three such therapies, two for blood cancer and one for an inherited cause of blindness. Companies are investigating treatments for hemophilia and muscular dystrophy. “Once just a theory,” said the FDA’s chief, Scott Gottlieb, in July, gene therapy “may have the potential to treat and cure some of our most intractable and vexing diseases.”

The technology’s medical logic is especially irresistible for parents of children with the rarest diseases on earth. These are the 7,000 or so conditions that typically, like Canavan, are caused by errors in a single gene. Gene therapy suggests the ultimate bug fix—just give people working DNA instructions. The problem for the Canavan kids is that there have been too few patients for anyone to bring the research out of the lab and put dollars behind it. The same is true for countless other diseases you’ve never heard of, some of which are known to affect fewer than 50 people on the globe.

“The simple math is that there are a very limited number of patients. That is what created this crazy, crazy paradigm,” says Eric David, an executive with BridgeBio, a biotech in Palo Alto, California, that specializes in treatments for rare diseases. “Families are saying, ‘Oh my God, no one is going to pay for this. I have to fund it myself.’”

Gene therapy already has a reputation as medicine’s gnarliest economic case. The problem is who will pay. Even those few treatments approved for sale carry price tags as high as $1 million. Underlying the unheard-of prices is the cost of years of research, human tests, and paperwork to win the FDA’s sign-off, all in tiny markets with small pools of patients. Costly, too, is the still unwieldy process of manufacturing trillions of viruses, into each of which a gene is placed so it can be conveyed into people’s cells. The result? A growing gap between the list of diseases that could be treated with gene therapy and those that actually are.

I learned of six cases where parents financed clinical trials for gene therapy in which their own children were treated. These include Karen Aiach, who started a

“The simple math is that there are a very limited number of patients. That is what created this crazy, crazy paradigm.”

biotechnology company, Lysogene, based outside Paris; it funded the trial in which her daughter was treated for Sanfilippo syndrome. A connected Hollywood couple, the Grays, raised $7 million to pay for a trial that infused gene-carrying viruses into two of their daughters and several other children with a rare form of Batten disease. More than 20 other parent-financed trials are in the planning phase.

Other families are avoiding the rigors of formal studies and trying to secure untested gene therapies as emergency treatment. In Florida, a single boy was treated with a Canavan gene therapy in 2017 after his parents paid for the experiment. They did it under an exemption in federal rules called "expanded access," which can allow unapproved drugs to be offered to specific patients "whose life is immediately threatened."

That experiment fell into a gray zone, not quite research and not quite medicine. It is the same pathway the Landsman family is trying to follow, with the help of Paola Leone, a gene therapist in New Jersey, and Christopher Janson, a neurologist in Chicago. Leone and Janson asked the FDA last June to permit emergency use of their own Canavan gene therapy in up to five children they have designated in advance. The first two names on the waiting list: Benny and Josh Landsman.

According to the FDA, the strategy is not as unusual as it sounds. Of the approximately 700 gene-therapy trials it oversees, 77 fall into the desperate-case category, according to an agency spokesperson. It is not known in how many of these cases the families are covering the costs, but that is entirely legal, too. "We would love to do it in a broader, systematic fashion that would lead to a drug treatment, but we don't have the money," says Janson, a physician at the University of Illinois College of Medicine. "Until then, we are stuck on our own trying to help a couple of kids."

Some scientists who know of the Landsmans' plan fear it represents a new form of boutique medicine—a way to give those with fat checkbooks or a knack for viral fund-raising campaigns special access to cutting-edge breakthroughs. A different perspective is that it's just a preview of the personalized genetic medicine that will increasingly be available more generally.

In the future, health officials believe, it could become commonplace for scientists to detect a genetic mutation and whip up a custom DNA antidote for one person. "Those 7,000 diseases are ones where we know the molecular defect for most of them. We know exactly what the initial glitch was that has led to this outcome," Francis Collins, the director of the National Institutes of Health (NIH), said in a speech last year. "Shouldn't we think about ways to do that in a fashion that scales to hundreds or maybe thousands of diseases? So what would that take?"

Nobody really knows. And the Landsmans can't wait for Washington, DC, or drug companies to figure it out. At today's rate of new drug approvals for rare diseases—about 15 a year—it could take 1,000 years for companies to get around to all of them. With two sons slipping away at home, Jennie and Gary are measuring time in months instead. Josh has a big smile but never learned to crawl. He'll soon become like Benny, who moves his arms only weakly and communicates by glancing at pictures Velcroed to a felt pad. "He's never said 'mommy,'" Jennie told me. But he can still ask for her—one of the pictures pinned up there is hers.

Jennie says she hopes that all Canavan kids will someday benefit and that the researchers helping her "will become famous." But she did not raise all that money to fund an experiment or to become a philanthropist. "This is not a clinical trial," Jennie told me. "This is private. This is for Benny and Josh."

Perfect timing

Canavan disease is rare, but it's significantly more common among people of Ashkenazi Jewish descent, like the Landsmans. Like Tay-Sachs, it's enough of a threat that prospective parents in this population are tested to see if they are silent carriers of the gene error. About one in 40 are. A series of medical miscommunications, Jennie says, led her to mistakenly believe she had tested negative. Since it takes two mutated gene copies, one from each parent, to cause the illness, they saw no reason to test Gary.

Jennie and her pediatrician were slow to pick up on Benny's symptoms. Her sister said the toddler seemed "mushy," but the Landsmans' doctor said not to worry. By then she was pregnant with Josh. The disastrous diagnoses unfolded over a few days last summer. In late July, a blood test finally showed Benny had Canavan. Two weeks later, on Gary's birthday, they learned their newborn had it, too.

As Jennie remembers it, she spent weeks in depression, staring at sunbeams coming under the awning and trying to "live in the moment." But when I visited Leone, the gene therapist, at the Rowan University School of Osteopathic Medicine in New Jersey, she showed me e-mails Jennie had sent her between the two boys' diagnoses. "Can you help?" she had asked.

The idea of gene therapy traces back to 1970, but only recently have scientists mastered its components. In 2017, doctors at Nationwide Children's Hospital, in Ohio, described in The Lancet how they had prevented a group of infants from developing spinal muscular atrophy, a nerve disorder that, like Canavan, is fatal. The key elements: a virus that infects the right cells (nerves, in this case), immense doses, and timing. Give a one-month-old infant the missing gene, and the nerve damage doesn't begin. It now appears to scientists—and parents—that similar strategies must be capable of saving kids with other inherited nervous-system diseases.

Leone was a logical person for Jennie to approach. Between 2001 and 2005, Leone and Janson had, with government funding, treated 13 children with Canavan in one of the first attempts to change the genetic code inside a person's brain. At that time, scientists were unsure of the concept's potential, and their treatment, though it had some effect, was no cure.

Leone had been working toward a new Canavan gene therapy. But her last federal grant had run out in January 2018. In her lab, I saw a scientist curse at an old-model Mac that was slow to load an image. The

shoestring budget is nothing new. "When I started this work," she says, "people looked at me and said, 'You must be out of your mind to work on a rare disease—you are never going to find any money and no one is going to be interested.'"

Leone keeps pictures and memorials to Canavan kids she has known in her office. Over the years, she had told many of their parents there was no chance at a cure. But the Landsmans' timing was perfect. By the fall of 2017, Leone had given the new gene therapy to enough mice to see what she calls dramatic effects. The disease seemed to have greatly slowed, even reversed. "Then I was prepared to say 'Yes' to the family that came along," she says.

"There is a lot we can do"

Leone met the Landsmans in New York, near the 9/11 memorial, in September of 2017. Gary confessed that if he had a choice between fighting and fleeing, he wanted to flee. Many parents institutionalize children with Canavan. Gary wished he could take Jennie far away and never come back. "Excruciating pain," recalls Leone. "Eyes that had cried so much they were hard to see."

Jennie wanted to know what they could do. Leone told her: "There is a lot we can do, but the first thing is how much it will cost. I can tell you it's approximately $1.5 million."

"We can do it," Jennie said without blinking.

Leone tallied the costs. They would need to hire a company to chemically synthesize healthy copies of the gene that's broken in Canavan, set aside payments for neurosurgeons, and hire consultants to prepare a request to the FDA. The biggest single expenditure would be manufacturing. Making the viral particles—they're grown in thin sheets bathed in components of cow blood—remains a delicate craft, and there are long waiting lists at production centers. Leone believed it would cost at least $1 million just to make enough virus to treat Benny, Josh, and perhaps a few others.

The Landsmans didn't have the money. The family is squarely middle class. "But there's money everywhere, isn't there?" Jennie reasoned. She was right. Their video, posted to Facebook and later GoFundMe, a crowdfunding site, went viral. By now, they've been on TV and in People magazine. Eight thousand donors have already given more than $1.5 million. "This was all local people in a small Jewish community in Brooklyn," says Ilyce Randell, a Canavan patient advocate who has been in contact with the Landsmans and has funded Leone's work in the past. "It was a perfect storm—everyone rallied."

But if the Landsman children end up benefiting, she says, it will be because of research under way long before they were born. "To make it seem like they bought a cure for a million bucks—that is misleading," she says. "What is true is they came at the right time. Ten years ago you couldn't say, 'I'll raise money and get my kid treated.' Three years ago you couldn't do it. The science was not ready."

Unfair system

In August, many of the families and key researchers in the rare-disease world arrived in the security line at the NIH in Bethesda, Maryland. During a two-day meeting, cosponsored by the FDA, scientists gave talks whose topics teetered between remarkable results of tailored therapies and what the organizers called "unanswered questions" about how these could ever reach patients at affordable prices.

At today's rate of new drug approvals for rare diseases—about 15 a year—it could take 1,000 years for companies to get around to all of them.

The event attracted parents hoping to find gene-therapy specialists who would treat their children. One, Amber Freed, wore a name tag reading "*SLC6A1*," the scientific designation of a little-studied gene. Freed told a story that was by now becoming familiar. After months criss-crossing the country trying to diagnose her son's unexplained symptoms, she finally had his genome sequenced. In May, she learned he had a pathological *SLC6A1* mutation. Freed had been working as an equity analyst in Denver, Colorado, but quit the day of the diagnosis. "I stood up from my desk and never looked back," she says.

Until recently, many children with clusters of unusual symptoms would remain undiagnosed. Starting in 2010, genome sequencing became inexpensive enough to employ as a routine diagnostic tool. Now, more often than not, even mysterious inherited disorders can be linked to a genetic misspelling. "Now you can walk out of a hospital with a genetic cause," Freed told me. "I think pretty soon kids will walk out the door with a solution."

Without treatment, Freed's son will come to experience a violent form of seizure called a "drop attack." The victim remains conscious but frozen and can topple to the ground, unable to break the impact. "It's coming, but we are going to get the cure before it gets to that point," said Freed, who came to the meeting in a power suit and positioned herself near the stage. "We are going to find the cure for him. Our secondary mission is to help those who come after us."

That evening I spotted Freed perched on a stool at a Bethesda eatery, speaking to a researcher named Steven Gray. A soft-spoken southerner and gene-therapy specialist at the University of Texas Southwestern Medical Center, Gray has become the go-to scientist for parents like Freed. During the conference, he showed a slide listing 23 rare diseases for which he is trying to develop genetic treatments. Gray says he finds the kids' stories tragic and a powerful motivator.

Part of Gray's job is to reset parents' expectations. Gene therapy is not as simple as packaging a gene into a virus. Many diseases can be poor candidates—for instance, those in which a gene is overactive rather than broken. Often scientists have groundwork to do, such as engineering a mouse to mimic the condition. Bypassing these steps can be perilous. If a child's body has been missing a vital molecule since birth, for example, adding it may provoke a violent immune response. "We have gotten this wrong in the lab and we have killed mice," says Gray. "Gene therapy is not a pill you can stop taking."

Gray's best-known client is Lori Sames, whose daughter suffers from giant axonal neuropathy. The disease affects only about 80 people in the world. Sames managed to raise $6 million, which she funneled to Gray and into animal tests. In 2016, her daughter became the fifth child treated in a study of Gray's gene therapy at the NIH.

Gray told me that if a gene looks like a good candidate, and a family has money to support laboratory work, he will agree to take on their cause, no matter how rare the disease. "This is the most unfair system imaginable," he admitted. "If you don't have money, it won't happen."

To some bioethicists, when parents fund treatments it has the potential to create sharp ethical dilemmas. "There is a fairness issue if only the people who have the money get to be first in line," says Mildred Cho, a bioethicist at Stanford University, who has consulted on similar cases. "And there is a scientific integrity issue, because those with the money may not be the most appropriate or the best candidates. These decisions should be objective."

I asked Sames if she had created a conflict of interest by paying for research. The question makes "the hairs on my arms stand up," she said. "Anyone who suggests it's corrupt that parents privately fund development of a treatment for a child, in an attempt to save the child—well, I think it's irrational and rather insane. If the parents don't drive it, it's never going to happen. Wake up." Sames adds that the fund-raising she did never guaranteed her daughter, Hannah, a spot in the NIH trial. Hannah had to pass a lung function test like others to get in. "We were no different than any other candidate," she says. "I wept the day she passed the test." Since then the trial has been moving forward at a "glacial" government pace, according to Sames, and other parents are mad at her. "They are hurt—their child is failing before their eyes—and they are angry, angry their kid is not injected," she says. "But there is nothing I can do."

Some families are managing to move even faster to a treatment than Sames did. The Hollywood couple, film producer Gordon Gray and his wife, Kristen, were able to get two daughters treated at Nationwide Children's Hospital about one year after the girls were found to have Batten Cln6, an inherited nervous-system disease believed to affect just a few hundred kids. Kristen Gray says the couple paid for the trial in its entirety. They also formed a company to take commercial rights to the treatment.

Few parents, though, are able to raise millions or start a company. On GoFundMe, hundreds of appeals mention gene therapy, but most raise only a few thousand dollars. One woman from Texas appealed for funds because she has muscular dystrophy; she has gathered just $35. The medical possibilities are out there, "but I don't think there is the regulatory infrastructure or the funding infrastructure to really make it happen," says Steven Gray, the gene therapist from Texas.

Another obstacle is that most of the key components of gene therapy are patented—including the viruses, the production tricks, and engineered genes. That means parents, and the scientists who help them, are often working in a cloud of legal uncertainty. Leone says to treat the Landsman boys she will have to buy $250,000 worth of trial insurance. "I could have been stopped with a phone call, but I wasn't. People have been very kind," she says. "But I will tell you, there are so many pieces in the patent puzzle ... it's like a contemporary symphony, one that is atonal. It makes you want to scream."

Calling Bill Gates

Of the 7,000 rare diseases, around 90% currently have no treatment whatsoever. Gene therapy could potentially help with many, and in the future, new technologies like gene editing could, in theory, make it possible to fix nearly any genetic mutation. Christopher Austin, chief of an NIH branch responsible for new therapies, says eventually there may be as many different treatments as there are unique DNA flaws. To Austin, that means made-to-order, hyper-personalized medicine isn't some ethical mistake to avoid; it is the next step forward. "All of us need to think deeply that this is possible now," he says. It's something "that people have thought about for decades—and now it seems to be coming true."

Exactly who will pay to discover, develop, and deploy this Noah's ark of medicines is not clear. Lori Sames told me she sometimes fantasizes about approaching Bill Gates, whose foundation is trying to eradicate malaria and polio. Leone envisions a different solution: a global institute of cures, with access to manufacturing, hospital beds, and agreements in place to streamline the "biblical" work of dealing with insurers and regulators. "So any new disease, any new genetic mutation, we'd have everything set up," she says. "We would bring patients from all over the world for treatment."

Biotech companies have raced into gene therapy, but so far, much of their effort has been aimed at more common genetic conditions like hemophilia. The US government's clinical-trial website lists more than 20 open studies exploring gene treatments for that disease, which could be the technology's first blockbuster. The markets for ultra-rare diseases haven't drawn as much commercial interest. "Imagine a company with 75 employees that exists to treat 75 people. You can see the problem," says Eric David, the executive with BridgeBio.

In April 2018, however, something happened to make biotechnology executives take a fresh look. The Swiss drug company Novartis announced that it would buy the gene-therapy company AveXis for $8.7 billion. AveXis had just one drug in the clinic—it owned rights to the treatment for spinal muscular atrophy that had been tested at Nationwide Children's Hospital. The acquisition price was immense for a treatment used, at that time, on only about 15 kids, and for a disease that affects one in 10,000 births.

"My jaw hit the floor. I don't even know what $8 billion is," says Jerry Mendell, the doctor who led the trial. Mendell didn't hold shares in AveXis, but one of his center's former employees, Brian Kaspar, did. Kaspar, who joined the company, is now $400 million richer. "In my mind, the AveXis deal—there is a before and there is an after," says David. "After that, people who would not have looked at gene therapy for a disease quite that rare said, 'Wow—if I can get a trial going, maybe I can be worth a billion dollars too.'"

> **"All of us need to think deeply that this is possible now. It's something that people have thought about for decades—and now it seems to be coming true."**

One reason AveXis was worth so much is that the treatment seemed to be an outright cure. That could let Novartis charge $2 million per patient, and perhaps more. To Walter Kowtoniuk, a principal at the investment company Third Rock Ventures, in Boston, such medical successes mean diseases previously thought to affect too few people to attract companies are suddenly drawing intense interest. He says he has been "shocked" by the "massive competition" to gain control of gene-therapy programs.

That's created a situation in which desperate bids to treat children can rapidly turn profitable. In October 2018, the Gray family—which had helped form a virtual company around the Batten Cln6 treatment—sold the rights to another biotechnology company, Amicus, for $100 million. Some investors are starting to think Canavan looks pretty interesting too. It's widely known among Canavan parents that a couple in Florida spent more than $1 million to get their child treated in a one-person study organized by the University of Massachusetts and the University of Florida. I reached the boy's father, who asked to remain anonymous but did say his son seems to have benefited.

The Florida experiment helped launch Canavan out of the too-rare-to-care category. Early in 2018, David's company, BridgeBio, entered an agreement to license the treatment from the University of Massachusetts and created a subsidiary, Aspa Therapeutics, which he now leads. But Kowtoniuk says other investors have been angling to take over the project because the risk seems much lower now that one boy has been treated. "There is a battle, literally a battle, to license the technology," he says. "I think there is such a tidal-wave shift in what is going on right now."

The growing biotech interest could mean the end of the parent-led scrambles. David told me he doesn't think the epoch of parent-financed gene therapy will last very long. "It's transitional," he says. "I think it's going to be for a limited time."

A ticking clock

David says the formal clinical trial of his company's Canavan treatment, different in design from Leone's, won't begin for another year, maybe two. For his company it's important to plan carefully and not rush, since that would jeopardize its investments and its aim of getting a treatment approved.

Jennie Landsman's children, though, can't wait that long. A self-financed experiment is probably the only way her two kids can get gene therapy in time. When I visited the Landsman home, I stood behind Josh, who was belted into a high chair, as his mother showed him pictures of lunch foods: chicken, macaroni and cheese, corn. Jennie followed his gaze.

She had hoped the boys would be treated by now. The team submitted its proposal to the FDA in June 2018, but the agency responded with a notice, called a "clinical hold," delaying the experiment. At the time of writing, in October 2018, Jennie was counting on December at the latest. Janson, the doctor running the trial, thought sometime in 2019 was more likely. He and Leone have plans to submit a new request following a meeting with FDA officials. He has also started testing the treatment on monkeys, a costly safety step he predicts regulators may insist on.

Nerves are fraying. At Benny's age, Canavan patients often have a steep decline in brain function. Even gene therapy might not reverse it. "My blood pressure is really going up," Janson says. "We probably lost at least three to four months."

When I visited her, Jennie had the idea of going to the FDA meeting and bringing her kids. She wanted to know what I thought. If the regulators saw them, how could they say no? Janson doesn't think it's a good idea. "I think we have to go within the system," he says. "We aren't a drug company. We don't have unlimited resources to lobby the FDA."

I asked Janson if he thought it was fair that the Landsmans' kids could end up getting treated while some other family without a surprise GoFundMe success would not be. "Unfortunately, there are a lot of things in society that are not fair," he said. "There are parents who want to see me in my neurology clinic and can't because they don't have insurance. We have a problem in society."

Precision medicine, it seems, is just another example: "There is no easy answer to your question, because the system is not set up to deal with this."

Antonio Regalado is MIT Technology Review's senior editor covering biomedicine.


TUMOR SHAPE
TYPE OF CANCER
LUNG CANCER
METHOTREXATE
VINCRISTINE
DOXORUBICIN
CYCLOPHOSPHAMIDE
CISPLATIN
5-FLUOROURACIL
BLEOMYCIN
20%
28%
52%
DOSAGE
3
BLOOD TYPE
B+
AGE
54
GENDER
M
A T C
C A G
T G C
T G A
C A T
C T G
A G C
A T G
TREATMENT TIME
4-6 WEEKS
CANCER STAGE
1 2 3 4

One tumor at a time

Personalized cancer vaccines are a scientific breakthrough, but can they be a sustainable business?

by

Adam Piore

illustrations

Selman Design

The first time someone pitched Genentech's senior leadership on a personalized cancer vaccine, it did not go well. "I thought there was going to be a riot," Ira Mellman, then Genentech's head of research oncology, recalls.

From across the table, he watched the scientific review committee grimly shaking their heads as his team member and longtime collaborator Lélia Delamarre made her case. Then he overheard the head of clinical development turn to the person sitting next to him and mutter, "Over my dead body. A vaccine will never work."

That was in 2012. Cancer immunotherapy, which uses a person's own immune system to attack tumors, is now one of medicine's most promising fields, and one of the greatest breakthroughs in oncology in decades. But it took a long time to get there. Until the recent advent of a new class of blockbuster immunology drugs, the field was notorious for questionable science, hype, and spectacular disappointments.

And what Mellman and his team were proposing that day went further than turbocharging immune cells to make them better able to attack cancers. They were talking about a vaccine precisely tailored to stimulate the immune system to react to specific tumors. If it worked, the approach could, in some cases, be even more potent than other types of immunotherapy. But it faced a series of daunting hurdles. If Genentech, a San Francisco–based biotech company owned by the Swiss pharma giant Roche, were to attempt to develop a vaccine that could attack individual tumors, it wouldn't just have to accept new scientific advances; it would also have to embrace an entirely new and untested business model. That's because the vaccine Mellman and Delamarre envisioned could not be manufactured the traditional way, in large batches that could be packaged in bulk, warehoused, and dispensed off the shelf at your local pharmacy.

When Mellman and Delamarre said "personalized," they really meant it. The composition of each vaccine would be based on the characteristics of each patient's tumor DNA. The company would have to, in essence, make a separate treatment for every single patient.

Nor would this be the kind of drug you could order up with a prescription in hand and get in a few days, like Genentech's highly successful cancer drugs Herceptin and Avastin. To create this drug, the company would have to orchestrate a multistep process for each patient, performed at multiple sites. Each patient would need a biopsy, the tumor tissue would have to undergo full genome sequencing, the results would require complex computational analysis, and the individual vaccines would then need to be designed and queued up for manufacture. Theoretically, if the vaccines were to be produced on a large scale, this would have to happen hundreds of times a week. And it would have to happen fast.

If any single step in the process went awry, if a shipping mistake occurred or a batch was contaminated, it could prove deadly—because cancer doesn't wait.

No wonder the Genentech leadership was so skeptical.

After that calamitous first pitch meeting, Mellman and Delamarre retreated to their laboratories. They returned a few months later with more exciting data: they had identified specific targets on cancer cells, targets that would readily be attacked by immune cells. They also had fresh, convincing research from a growing number of other academic groups on the feasibility of their approach. And, critically, they had a preliminary plan for how Genentech itself might take the first tentative steps toward making tailor-made treatments an economically viable product.

This time the reception was different. The committee signed off on an exploration that would culminate in 2016 with a $310 million deal with BioNTech, a German company that has a technique for producing personalized vaccines to target tumors. In December 2017, the partners launched a massive round of human testing, targeting at least 10 cancers and enrolling upwards of 560 patients at sites around the globe.

At Genentech headquarters, Mellman and Delamarre's small team has grown by now into an army of hundreds, consisting not just of lonely lab workers but supply-chain specialists, regulatory experts, diagnosticians, and a whole host of consultants, all focused on the laborious task of figuring out how the production of their promising new product—should it continue to demonstrate the powerful effects seen so far—might be scaled up in a way that won't bankrupt the company.

"It's never been done, so we are learning as we go," says Sean Kelley, the project team leader overseeing the effort.

Nor are Genentech and BioNTech the only companies now pushing into this new territory. In late 2017, Moderna, a biotech based in Cambridge, Massachusetts, announced that, in partnership with pharmaceutical giant Merck, it intended to start human trials with a vaccine targeting solid tumors. Another company, Neon Therapeutics, founded by researchers at Dana Farber Cancer Institute and

The company would have to, in essence, make a separate treatment for every single patient.

Washington University, treated its first patient in phase 1 trials in May 2018 with a similar vaccine derived using a different method. It raised $100 million in an IPO this summer, driven largely by optimism over its approach.

The technology for the first truly personalized cancer vaccine is not yet proven. And these therapies are all likely to be expensive, Mellman acknowledged recently, sitting in a spacious conference room outside his office at Genentech's headquarters in South San Francisco. But he insists that if it's all done right, the extra costs and thinner margins will be more than offset by the sheer number of people who would use the treatment.

"You can imagine a scenario where every single cancer patient would benefit from this vaccine," he says. "That's unheard of."

Fighting against yourself

Scientists have been intrigued for decades by the possibility that cancer's greatest strength—its ability to mutate and evolve—might also be one of its greatest vulnerabilities.

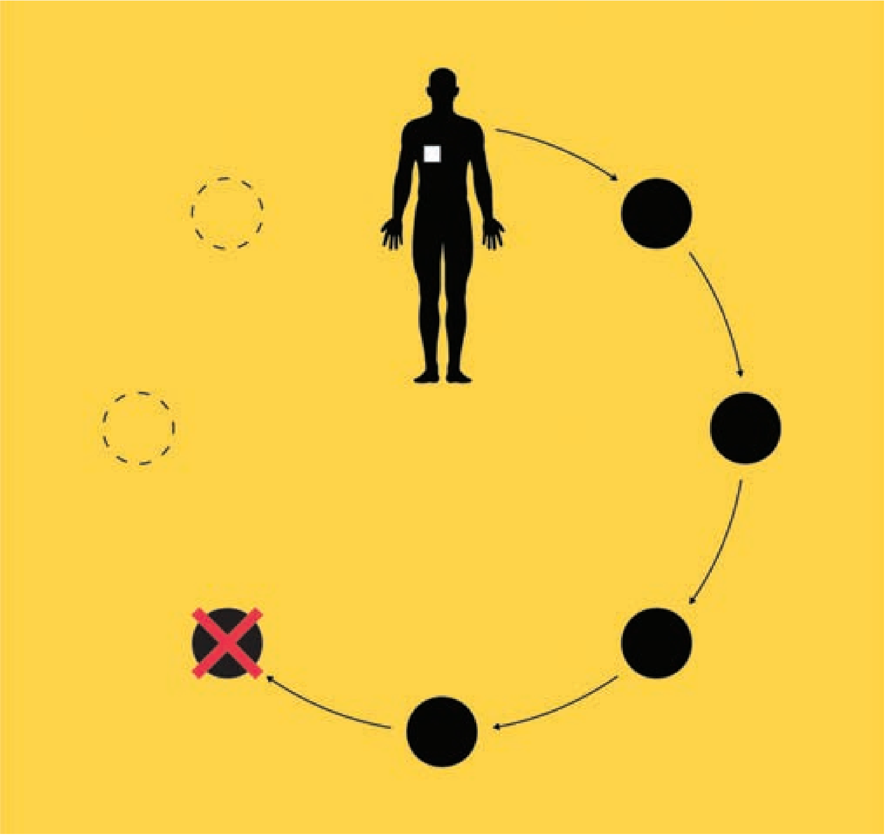
Mutations in cellular DNA are, after all, what cause cancer in the first place, by prompting the cells carrying them to grow and proliferate uncontrollably. As far back as the 1940s, some researchers were arguing that it might be possible to put the immune system's cellular bloodhounds onto the scent of a specific tumor by somehow priming them with a vaccine that helped it recognize the tumor's mutations. A number of researchers have experimented and continue to experiment with techniques that involve removing immune cells from the body, genetically engineering them, and then reinfusing them in the hopes of triggering a robust response. Other cancer immunologists have focused on developing drugs to turn off molecular switches on the immune system's T cells that can interfere with their ability to attack.

But until recently, the scientific tools simply didn't exist to take the sophisticated personalized approach Genentech is now pursuing—an approach that requires scientists to fully characterize an individual cancer tumor, identify the most attackable mutations, and then design a personalized vaccine that would provoke the immune system to target them.

The problem was identifying the right target molecules on the tumor cell, or—as researchers thought of them—the antigens that would catch the attention of the immune cells. "It was so much work to identify antigens in the past," says Robert D. Schreiber, director of immunotherapy at Washington University. "You could do all this work, and then you end up with one antigen from one individual that is not necessarily ever seen again in any other individual."

That all changed with the advent of cheap genetic sequencing. In 2008, five years after the Human Genome Project published the sequence of the first human genome, scientists published the first genome sequence of a cancerous cell. Soon after, scientists began to compare the DNA in tumor cells and healthy cells to characterize the myriad ways that they differed. These studies confirmed that all cancer cells contain hundreds—if not thousands—of mutations, most of which are unique to each tumor.

In 2012, a team of German researchers, led by scientists at BioNTech, sequenced a widely used mouse tumor cell line designed to mimic human melanoma cells. They identified 962 mutations and used RNA sequencing to identify 563 that were expressed in genes. The group then created vaccines made of protein fragments that contained 50 of the mutations and injected them into mice to see if this would prime the immune system to respond. About one third—16 of the mutations—were detected



by the immune system, and five of those generated an immune response designed specifically to attack any cell found to harbor such mutations.

It was concrete evidence suggesting that genome sequencing could be used to design an effective cancer vaccine capable of putting the immune system on the trail of multiple mutations at the same time—and that such a vaccine might indeed provoke the immune system to attack a tumor. The race was on to answer the next logical questions: Why is it that the human immune system can be stimulated to attack some mutations and not others? And how can we figure out which mutations are most likely to be vulnerable?

At the urging of Mellman, Delamarre took Genentech's own lab mice and sequenced their tumor cells, identifying 1,200 individual mutations not present in normal tissue. Then she measured how T cells naturally responded to them. Of those 1,200 mutations, she found, the mice's immune system had begun to mount attacks against only two.

To answer why only those two mutations appeared to attract an immune response, Delamarre took a closer look at the interaction between the cancer DNA and a key component of the mouse immune system known as major histocompatibility complex, which in humans is called the human leukocyte antigen system (HLA). The HLA complex comprises 200 different proteins that protrude from cellular surfaces like microscopic thumbtacks on a poster board. When passing immune cells detect the presence of a protein fragment that doesn't belong—a piece of an unwanted virus or bacterium, or a mutation—they sound the alarm and cause the body to attack it.

Delamarre had determined that roughly seven of the 1,200 tumor mutations she'd identified were displayed on the cellular surface by HLA. When she examined the structure of these seven protein fragments, something got her attention: in the two that the immune system had recognized, the mutations were prominent on the cellular surface, facing up toward passing immune cells. Those the immune system had ignored faced down and were hidden in grooves in the cellular surface or obscured on the edges of the HLA. The immune system attacked those two mutations because they were the easiest to detect. By injecting mice with a vaccine designed to target those two mutations, she could enhance their bodies' ability to fight the tumors.

Together, these findings were what helped her and Mellman convince Genentech's review committee that a cancer vaccine was worth pursuing.

Facing the music

Genentech's headquarters, in an industrial park just off California's Highway 101, is a sprawling campus of glass buildings, hulking warehouses, and grassy courtyards. On a sunny August morning, cheerful groups of men and women in shirtsleeves and T-shirts strolled casually through a courtyard outside the company cafeteria. A band was setting up, getting ready to regale the lunchtime crowd with some blues, while nearby some kitchen workers prepared outdoor grills to cook food for employees.

Much of this is paid for by cancer drugs. Genentech won approval for its first cancer treatments in 1997, and since then the company has fielded no fewer than 15 of them.

But a cancer *vaccine* is unknown territory. The initial human trials that Genentech and BioNTech launched last year are shaping up as a test not just of the vaccine's efficacy but of the two

If any single step in the process went awry, if a shipping mistake occurred or a batch was contaminated, it could prove deadly.

partners' ability to scale up the new technology. By design, the geographic scope and the number of conditions targeted in the trial are broad—so far Genentech and BioNTech have opened sites in the US, the UK, Belgium, Canada, and Germany, and they are likely to expand to other nations around the globe.

Producing the vaccines even for the small number of patients in early trials "was an extremely challenging process," says BioNTech CEO Ugur Sahin, a veteran cancer researcher who cofounded the company in 2008. "Everything was driven by pipetting and by people on the bench producing the vaccines," he says. "So we had a very small capacity."

BioNTech has been able to automate some functions and reduce the time it takes to manufacture each vaccine from three months to about six weeks. It is shooting to get that down to four weeks by the end of the year.

The company can now produce hundreds of vaccines in a year—it aims to reach 1,500 soon. But if Genentech and BioNTech are ever to bring the product to market, they will need to be able to produce between 10,000 and 20,000 a year, Sahin says.

In San Francisco, teams from Genentech and BioNTech track progress in a designated space, consisting of a suite of rooms. On the walls, there are huge charts spelling out the patient status, the manufacturing and supply chain, the duration and schedule for each activity. "The key thing is that on paper it can look like a very coordinated process, but if any of those steps break down, then you can be in a situation where you have to start over," Genentech's Sean Kelley notes.

A number of unanticipated challenges have arisen. Early on, the team was surprised to discover that workers at BioNTech were contractually prohibited from working on weekends—so there was no one to receive patient tissue samples arriving then.

Gregg Fine, a senior medical director who is overseeing the trials, says he has been surprised by how variable the turnaround time has been at clinics and labs where patient biopsies themselves are collected and analyzed—a problem, since individual vaccines can't be manufactured until the samples are received.

The issue, Fine believes, is that patients with metastatic cancer may have problems getting to the doctor in a timely manner because they are too sick. And many collection sites don't yet have a procedure for flagging their samples as urgent, which means they can get lost in the stack with other biopsies.

Getting the vaccines back to the patients themselves has also proved problematic. At least one vaccine has been held up at customs in New York City.

For now, the problems are manageable and informative because the number of patients is relatively small. But all these problems will have to be solved if the vaccines are ever to go mainstream. "You're not going to be able to wait six months for a vaccine if you have a patient with fast-progressing pancreatic cancer," says Kelley.

Genentech officials declined to speculate about the eventual price of the vaccine, insisting it was too early to know. "It's going to be more expensive," says Kelley. "This will cost us much more to make per person."

The cost of sequencing might come down, building out a manufacturing network would increase efficiencies, and new assays might be developed, or new technologies that allow the cheaper manufacture of the vaccines themselves. "We've done estimates, and we feel that right now it is viable, but we would like it to become, obviously, more and more viable," he says.

For now, though, one of the most promising advances in cancer research remains an experimental treatment. It might be a medical breakthrough, but it is facing a familiar logistical challenge: how to get the product cheaply and quickly where it needs to go.

Adam Piore is the author of *The Body Builders: Inside the Science of the Engineered Human*, about how bioengineering is changing modern medicine.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Does China own the future?

4

The knock on China has been that it hasn't been responsible for technological advances, but rather takes breakthroughs from other countries, copies them, and perfects them for a massive market. But that's changing, as China works to emerge as a quantum superpower (page 58) and leader in space rockets (page 62). It's also been trying for decades to leapfrog the US's semiconductor chip industry, and this time it might be about ready to do it (page 66).

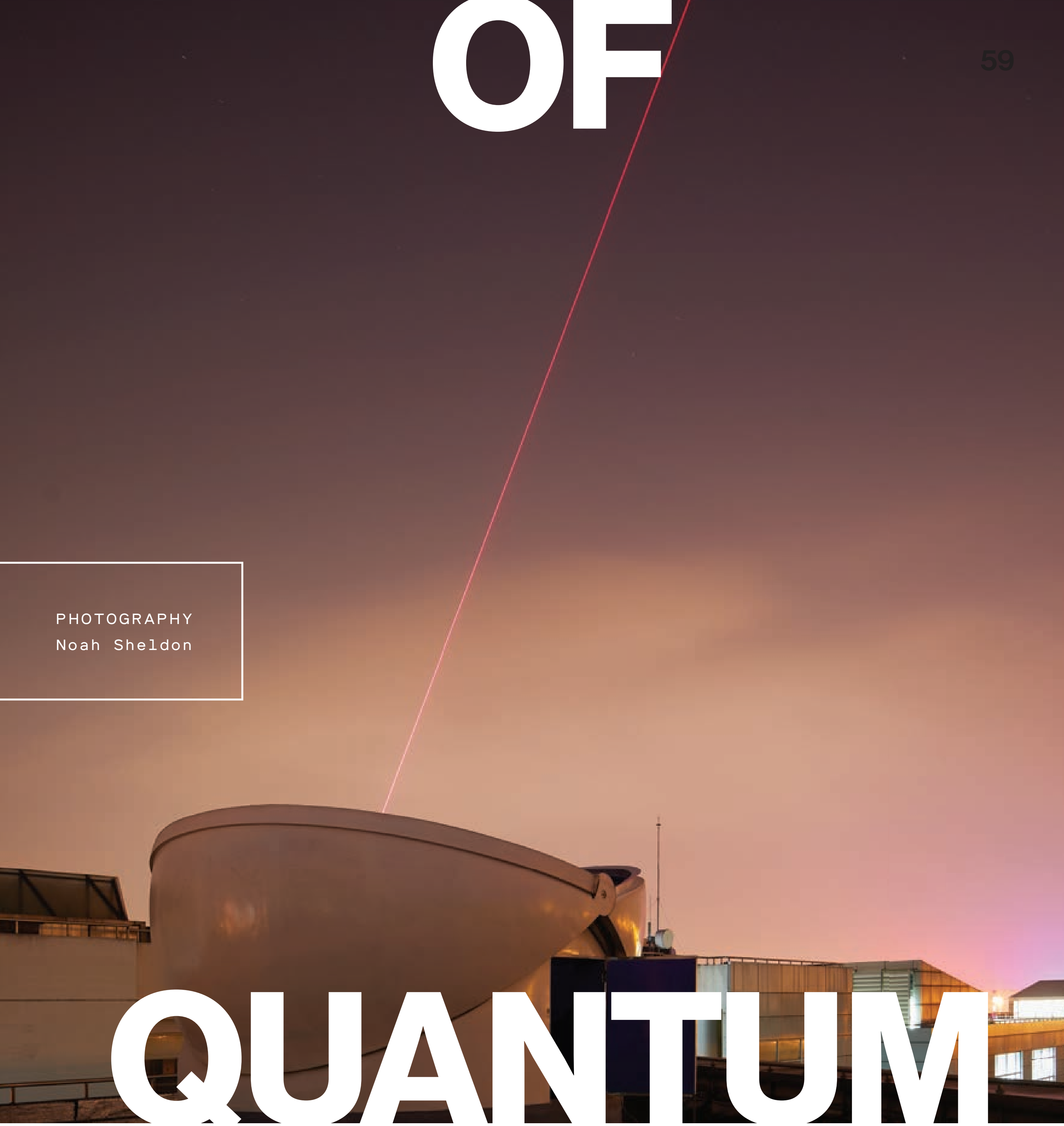
THE FATHER

BY
Martin Giles

Jian-Wei Pan is turning China into a quantum superpower, leading the way in technologies that could transform entire industries and change the way wars are fought.

On September 29, 2017, a Chinese satellite known as Micius made possible an unhackable videoconference between Vienna and Beijing, two cities half a world apart. As it whisked across the night sky at 18,000 miles (29,000 kilometers) per hour, the satellite beamed down a small data packet to a ground station in Xinglong, a couple of hours' drive to the northeast of Beijing. Less than an hour later, the satellite passed over Austria and dispatched another data packet to a station near the city of Graz.

The packets were encryption keys for securing data



OF QUANTUM

PHOTOGRAPHY
Noah Sheldon

transmissions. What made this event so special was that the keys distributed by the satellite were encoded in photons in a delicate quantum state. Any attempt to intercept them would have collapsed that state, destroying the information and signaling the presence of a hacker. This means they were far more secure than keys sent as classical bits—a stream of electrical or optical pulses representing *1*s and *0*s that can be read and copied.

The video encryption was conventional, not quantum, but because the quantum keys were required to decrypt it, its security was guaranteed. This made it the world's very first quantum-encrypted intercontinental video link.

The man behind this achievement is Jian-Wei Pan. A professor at the University of Science and Technology of China (USTC), sometimes known as "China's Caltech," the 48-year-old Pan has produced a series of breakthroughs that have propelled him to scientific stardom in the country. His work has won plaudits from President Xi Jinping, and he's often referred to in local media as "the father of quantum."

Quantum communications and computing are still nascent,

Jian-Wei Pan, standing in front of a receiver used in the transmission of ultra-secure signals from the Micius satellite, has helped lead China's quantum efforts. The picture of the receiver on the previous page shows a spotting laser used to help the satellite connect to the ground station.

but they are among the technological "megaprojects" on which China's government wants breakthroughs by 2030. It sees an opportunity to lead the dawning quantum era in much the same way that the US dominated the advent of computing and the information revolution that it sparked.

Pan, who in 2011 became the youngest-ever member of the Chinese Academy of Sciences, is central to this effort.

In an interview with MIT Technology Review, Pan talked about the importance of international collaboration, but he also made clear that China sees a unique window for it to shape the next meta-shift in the technology landscape. "We were only the follower and the learner at the birth of modern information science," he said. "Now we have a chance … to be a leader."

Pan's ambitions include a plan to create a globe-spanning constellation of satellites that constitute a super-secure quantum internet. Also on his checklist: helping China catch up with—and perhaps overtake—the US in building powerful quantum computers. The fundamental units of computation in these machines are qubits, which—unlike bits—can occupy a quantum state of *1* and *0* simultaneously. By linking qubits through an almost mystical phenomenon known as entanglement, quantum computers can generate exponential increases in processing power.

In the future, the machines could be used to discover new materials and drugs by running simulations of chemical reactions that are too much work for classical computers. They could also turbocharge artificial intelligence. Secure networks using quantum key distribution (QKD) could transmit sensitive data for things like financial transactions and provide utmost secrecy for military operations and communications. Researchers are also working on quantum sensors that would let submarines navigate without relying on satellite signals, and quantum radar that may be able to spot "stealth" aircraft.

JOINT EFFORTS

Despite the intense US-China competition in quantum technologies, the video call made possible by the Micius satellite—named for an ancient Chinese scientist and philosopher—is very much a result of international cooperation.

It came out of a collaboration between a team led by Pan and another led by Anton Zeilinger, a quantum physicist at the University of Austria. Zeilinger was Pan's doctoral supervisor in the 1990s, and he saw potential in the young Chinese student. "When he came here, he was one hundred percent focused on theoretical physics," recalls Zeilinger. "But I realized he could do more, so I suggested he switch to experiments, and he did that very successfully."

So successfully, in fact, that Zeilinger was only too happy when his former student proposed a collaboration on intercontinental QKD in 2011. Pan's team had already conducted experiments over a number of years to prove a space-based system could work, and it eventually got the Chinese government's green light to build a dedicated satellite, which was launched in 2016.

Making QKD work on the ground is hard enough. Doing it from a satellite meant solving a host of extra problems, from aligning the satellite's transmissions precisely with the ground stations to minimizing the number of photons lost in the atmosphere. Observers were impressed, says Hoi-Kwong Lo, a physics professor at the University of Toronto. He adds, "There's a huge amount of resources being devoted to quantum in China, which means they can do things other countries can't."

China's other achievements include building the world's longest terrestrial QKD network. The 2,032-kilometer (1,263-mile) ground link between Beijing and Shanghai was also masterminded by Pan and sends quantum-encrypted keys between way stations, offering an ultra-secure network for transmitting financial and other sensitive data. Some Chinese cities are also building municipal networks.

Gauging exactly how much China is investing in these and other quantum projects is hard because funding for government programs is opaque. But Pan says the money devoted to an upcoming national quantum plan for China will be "at least the same order of magnitude" as Europe's recently launched Quantum Technologies Flagship project, a 10-year, €1 billion ($1.1 billion) initiative.

While money matters, there's more to China's success than the bankrolling of satellites and other projects. The country also benefits from a decades-long strategy of sending young researchers abroad to learn from experts like Zeilinger and then enticing them home to continue their work.

China is producing plenty of high-quality quantum science papers, and the number of Chinese patents being registered in areas like quantum communications and quantum cryptography has also soared, far surpassing those being registered in the US and elsewhere.

To help develop future quantum researchers, the country is building a $1 billion National Laboratory for Quantum Information Sciences in Hefei that will open in 2020; it will bring together experts from a range of disciplines such as physics, electrical engineering, and materials science. Some of the money will be for a new USTC campus on the same site to train quantum researchers. "We are working hard to develop the workforce of the future in quantum technology," says Pan.

He's already created a center for quantum information and quantum physics at USTC. In June 2018 a team at the center announced it had set a world record for entangling qubits, linking 18 together. Advances like this will bring us closer to the point at which a quantum machine will finally be able to outstrip even the most powerful conventional supercomputer for certain tasks.

> Pan foresees a day when data centers on different continents will be connected via the quantum satellites he's planning.

There are also ambitious plans to scale up efforts in space. Pan says that over the next four to five years, China will launch four more low-orbit quantum satellites, and a high-orbit geostationary one will follow shortly thereafter. The long-term vision is to create a continent-spanning, quantum-secured internet that could eclipse today's version. Looking much further ahead, the technology could one day be used to secure everything from smartphones to laptops.

LEADER AND LAGGARD

So is China really set to dominate the emerging quantum era? And what will it do with that dominance if so?

The answer to the first of those questions is nuanced. While Micius and the ground-based QKD networks give China the edge—for now—in secure quantum communications, it still trails the US in quantum computing. However, as Pan's team's success with entangling qubits shows, it's making swift progress. Big Chinese tech companies like Alibaba and Baidu are investing heavily in quantum computing, too. Alibaba has launched a cloud computing service that lets people experiment on quantum processors, mirroring similar efforts by US companies such as IBM and Rigetti.

Isaac Chuang, an MIT professor and pioneer of quantum computing, notes that one of the reasons China has done so well in quantum science is the close coordination between its government research groups, the Chinese Academy of Sciences, and the country's universities. Europe now has its own quantum master plan to prompt such collaborations, but the US has been slow to produce a comprehensive strategy for developing the technologies and building a future quantum workforce.

Whatever happens elsewhere, China will press forward. Pan emphasizes commercial opportunities. Businesses are already using the Beijing-Shanghai network to ship information securely. And he foresees a day when data centers on different continents will be connected via the constellation of quantum satellites he's planning.

Those satellites, of course, could also be used for military purposes. Elsa Kania at the Center for a New American Security, a Washington, DC, think tank, says various parts of China's armed forces are funding research into quantum communications, sensors, and radar. Big companies like China Shipbuilding Industry Corporation, one of the country's largest builders of warships and submarines, are working with universities on quantum projects. If China thinks the technology could give it a military edge, it might pull back on international collaborations and keep innovations to itself.

A more optimistic view sees China remaining open to the kinds of interchanges that have helped turn it into a quantum superpower, and doing its utmost to profit from a new, quantum-inspired data economy. The notion that China could seize the lead here seems to inspire its top officials: Xi Jinping has even talked publicly of quantum science opening up "a new industrial revolution."

Whichever scenario ultimately plays out, China will be counting heavily on the father of quantum to steer it to success.

Martin Giles is MIT Technology Review's San Francisco bureau chief.

The rockets'

A Long March 2D rocket carrying a Chinese reconnaissance satellite blasts off from the Jiuquan Satellite Launch Center in 2008.

red glare

Will a cohort of new startups vault China to a lead in space?

by Joan Johnson-Freese

Late one afternoon in October 2018, from a remote and desolate launchpad in the Gobi desert, the Future soared into space.

The Future, a small satellite built for a China Central Television science show, was scarcely more capable than the very first Chinese satellite, launched from the same spot, the Jiuquan launch center, in 1970. And yet October's launch was historic: it was to be the first privately developed Chinese rocket to reach orbit.

Zhuque-1, the rocket carrying the Future to orbit, has three stages. The first stage fired smoothly. So did its second. A few minutes later, the third stage malfunctioned. The Future was lost.

Spaceflight is hard, and failure of new rockets common. SpaceX's first three launches failed: as its founder and head Elon Musk tells it, the fourth, successful launch came just before money ran out. SpaceX has changed the face of the US aerospace industry. After decades of domination by old-line companies, SpaceX is the most prominent of a new generation of firms that, by dramatically lowering launch costs, seek to revolutionize both human space travel and the satellite launch market.

Now that revolution is coming to China as well. Landspace, the firm that built the Zhuque-1, is not the only firm trying. At the time of this writing, in December 2018, another company, OneSpace, was also planning an orbital launch for later in the year while a third, iSpace, has ambitions for 2019.

Regardless of which company wins the race, two things are clear. Privately funded space startups are changing China's space industry. And even without their help, China is poised to become a space power on par with the United States.

As American and Russian space programs struggle with uncertain budgets, China is expanding its efforts on every front: communications and reconnaissance satellites; a navigation and positioning constellation to rival America's GPS; a human spaceflight program; and ambitious space-science and robotic exploration projects. All of these are enabled by a menagerie of new rockets with advanced capabilities.

Depending on how the weather at China's four spaceports compares with that in Florida and California, 2018 may be the first year in which more rockets reach Earth orbit from China than from any other country. As of early December, China was on pace for nearly 40 successful launches.

A planned December launch from the Xichang Satellite Launch Center in Sichuan (nearly a thousand miles southeast of the Jiuquan launch center) will send a robotic rover called Chang'e 4 to land on the far side of the moon. If it succeeds, it will be the first spacecraft to do so: China's space program is coming of age.

BY THE DAWN'S EARLY LIGHT

In 2014, the Chinese government decided to allow private investment in space-related industry. Landspace began with a few dozen people. It now has over 200 employees at a manufacturing base in Huzhou in eastern China and at assembly and testing facilities in X'ian, a central Chinese city. The company plans to work incrementally, beginning with nanosatellites—devices weighing between 1 and 10 kilograms (2 to 22 pounds)—then moving to larger cargoes and, eventually, into human spaceflight.

Landspace already has a contract with a Danish firm to launch a series of nanosize Earth observation and communications satellites into orbit around the equator. Having foreign contracts on the books is important not only because it brings in money, but also as a marker of confidence that China's space companies are for real.

In September 2018, iSpace launched three nanosatellites on a brief suborbital flight, becoming the first Chinese space startup to successfully get beyond Earth's atmosphere. Another company, LinkSpace, plans to launch a vertical takeoff, vertical landing rocket in 2020. Landspace, OneSpace, iSpace, LinkSpace, and ExPace (which fashions itself as a startup though it's a subsidiary of a state-owned enterprise) are the leaders of a bevy of lesser-known Chinese launch startups.

These launch companies are operating hand in hand with a number of new, privately funded Chinese companies that are focused on doing things *in* space, rather than on getting there. Spacety and Commsat, among others, are planning large constellations of small imagery and communication satellites.

Such constellations—whether Chinese or American—are transforming aspects of the way space is used. By making low-resolution satellite imagery much cheaper to gather (among other novel applications for small satellites), they are catalyzing an era of more nimble commercial, scientific, and military experimentation.

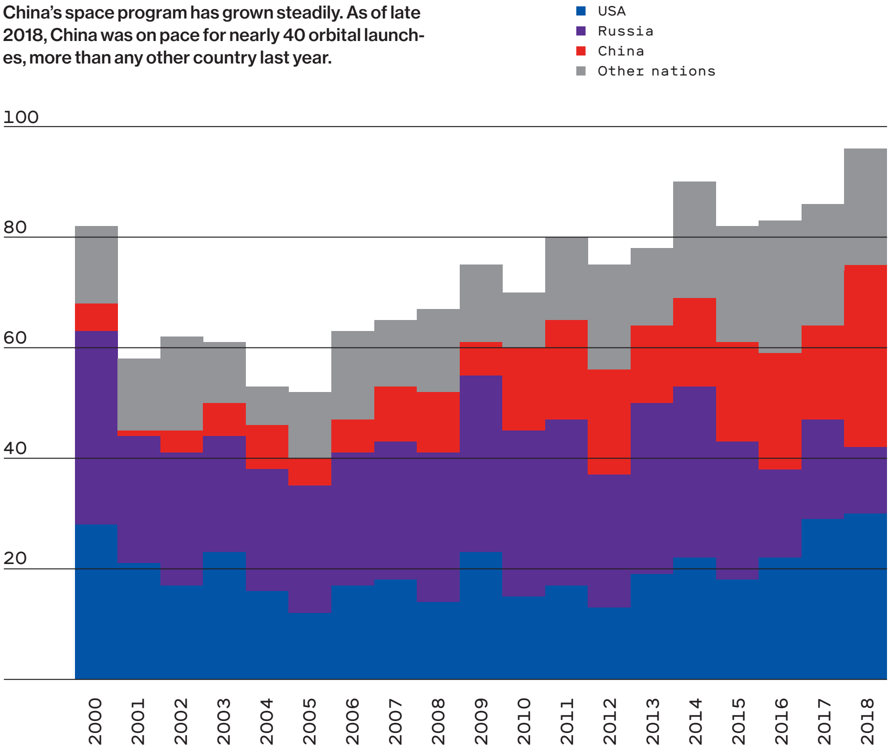
However, human space exploration requires heavy-lift rockets in order to launch space station modules, or to send people back to the moon or on to Mars. You also need heavy-lift rockets to put large communications satellites into geostationary orbit, where they can linger over a particular patch of ground. (Geostationary orbit is about 100 times farther away than low Earth orbit, and it takes a lot more energy to get there.) And you need them for sample-return missions that aim to bring chunks of the moon or Mars back to Earth.

Unlike SpaceX, none of the new Chinese space startups are developing such rockets. But China is.

China's established aerospace industry is an alphabet soup of state-owned enterprises that are the legacies of Russian-style numbered institutions and bureaus from Mao's days. The largest, Chinese Aerospace Science and Technology Corporation (CASC), is about as big as

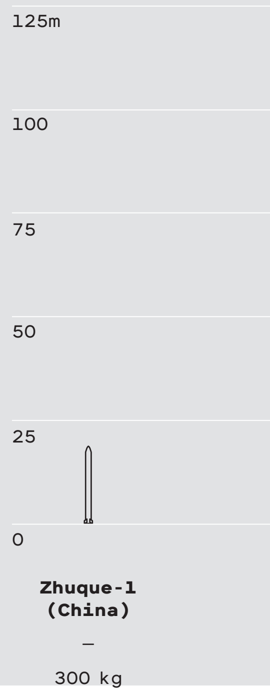
Orbital launches by nation 2000–2018 (as of November)

China's space program has grown steadily. As of late 2018, China was on pace for nearly 40 orbital launches, more than any other country last year.



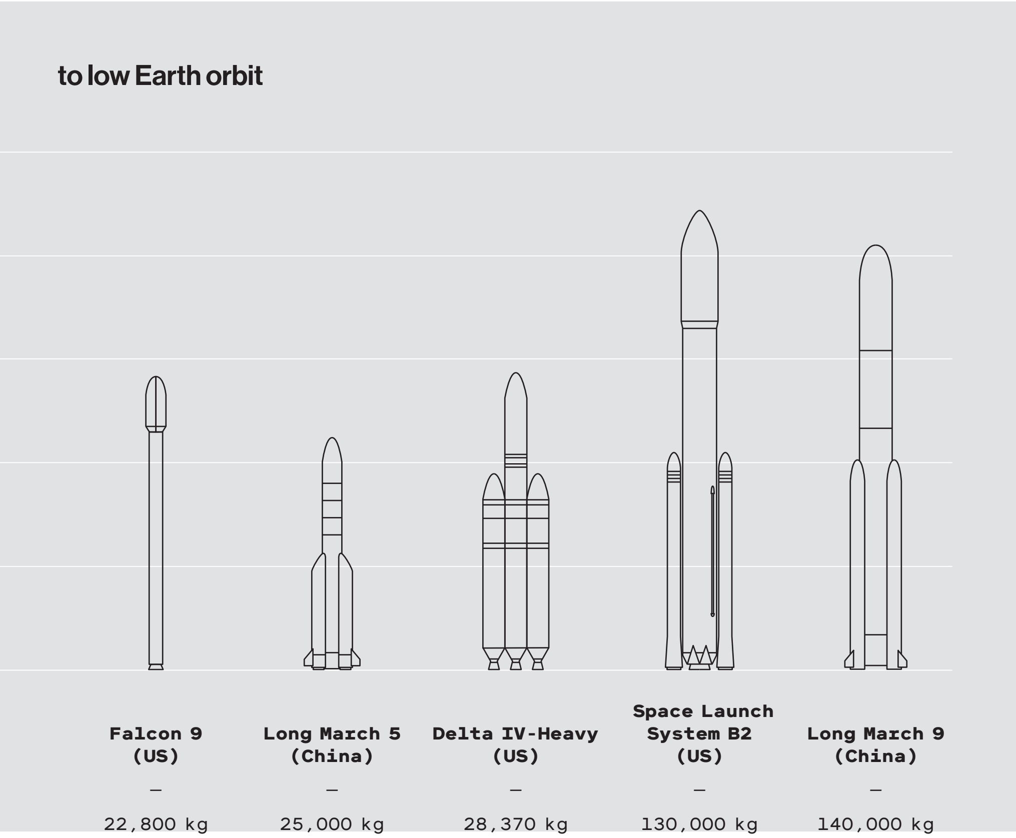
Space technology will provoke tensions regardless of who holds power. Missiles and satellites are launched the same way.

Payload capacity



China is also developing a space telescope that will have the same resolution as the Hubble—but a field of view 300 times larger.

PREVIOUS SPREAD: XU HAIHAN/GETTY IMAGES; SOURCE: PROJECT SPACE TRACK/US AIR FORCE



Boeing—it employs over 140,000 workers. A subsidiary called the China Academy of Launch Vehicle Technology (CALT) built the Long March 5, China's first heavy-lift rocket. CALT is also working on a super-heavy-lift rocket that, when completed in a few years, might become the most powerful ever built.

The Long March 5's first flight, in November 2016, was a success. But rocket science is, well, rocket science. More powerful rockets aren't just a matter of scaling things up: the complexity grows quickly. That first flight had been delayed for years as engineers worked out kinks in the cryogenic engines. Six minutes into the second flight, in July 2017, a turbo pump failed and the rocket crashed into the sea.

A number of China's ambitious plans are on hold until the Long March 5 starts flying again. If all goes according to plan, its next launch in July 2019 will carry a large, high-capacity communications satellite to geostationary orbit. The following launch, possibly later in 2019, will send Chang'e 5 to the moon—and back. If it succeeds, it will be the first such sample-return mission since the Soviet Union's Luna 24 brought 170 grams of lunar soil back to Earth in 1976.

China's next step in human spaceflight will be a large, permanently crewed space station. The launch of the station's core module by a Long March 5 is planned for 2020, the first step toward a complete station by 2022. Even when complete, China's space station will be only about a fifth the size of the International Space Station (ISS). But it will be entirely China's, while the ISS's future as a US-Russian collaboration (with some assistance from other countries) is in doubt.

China is also developing a space telescope that will have the same resolution as the Hubble—with a field of view 300 times larger. The telescope will be placed in orbit close to the space station, so that Chinese astronauts can quickly service the instrument should problems arise. CALT has learned from NASA's mistakes—it took over three years for NASA to fix Hubble's flawed mirror.

Assuming CALT works out the kinks, the Long March 5 will transform China's space capabilities. The successor CALT is developing, the Long March 9, whose first flight is penciled in for 2028, will be able to heave 140 metric tons into orbit, more than five times as much as the Long March 5. In capacity it will compare to the Saturn V—still the most powerful rocket ever built—and far exceed the most ambitious version of NASA's Space Launch System (SLS), which is also planned for 2028 (at the earliest). The Long March 9 would be capable of landing a man on the moon, and of launching a Mars sample-return mission.

The SLS and Long March 9 could both be delayed by technical setbacks. The difference is that where NASA's plans have shifted with each new administration and struggled to find support in Congress, CALT has had a steady mandate from the Chinese government.

The relationship between the US and China has deteriorated under the Trump administration. But the dual-use nature of space technology will provoke international tensions regardless of who holds power in either country. Missiles and peaceful satellites are launched the same way. Environmental monitoring satellites and military reconnaissance satellites are similar; communications satellites can transmit top-secret orders or provide Wi-Fi to airline passengers. Maneuverable satellites for refueling and repairing other satellites can also be used as weapons against an adversary's orbital platforms.

The US has spent considerable time trying to figure out how to stymie Chinese space plans. It blackballed China from the ISS; a widely criticized 2011 law prohibits bilateral contact between NASA and Chinese scientists. Such efforts are counterproductive. They isolate the US without acting as a meaningful check on Chinese ambitions. To stay ahead, the US will have to get its own house in order, rather than trying to hobble the competition.

Joan Johnson-Freese is a professor of national security affairs at the Naval War College.

ILLUSTRATIONS BY KYLE THOMAS HEMINGWAY

The Sophon AI chip is
designed by Bitmain,
a Beijing-based company.

The chip leap

forward

China has struggled for decades to build a competitive semiconductor industry. The era of artificial intelligence may offer an unprecedented opening.

By Will Knight

Donald Trump is speaking Mandarin.

This is happening in the city of Tianjin, about an hour's drive south of Beijing, within a gleaming office building that belongs to iFlytek, one of China's rapidly rising artificial-intelligence companies. Beyond guarded gates, inside a glitzy showroom, the US president is on a large TV screen heaping praise on the Chinese company. It's Trump's voice and face, but the recording is, of course, fake—a cheeky demonstration of the cutting-edge AI technology iFlytek is developing.

Jiang Tao chuckles and leads the way to some other examples of iFlytek's technology. Throughout the tour, Tao, one of the company's cofounders, uses another remarkable innovation: a hand-held device that converts his words from Mandarin into English almost instantly. At one point he speaks into the machine, and then grins as it translates: "I find that my device solves the communication problem."

iFlytek's translator shows off AI capabilities that rival those found anywhere in the world. But it also highlights a big hole in China's plan, unveiled in 2017, to be the world leader in AI by 2030. The algorithms inside were developed by iFlytek, but the hardware—the microchips that bring those algorithms to life—was designed and made elsewhere. While China manufactures most of the world's electronic gadgets, it has failed, time and again, to master the production of these tiny, impossibly intricate silicon structures. Its dependence on foreign integrated circuits could potentially cripple its AI ambitions.

However, AI itself could change all that. New types of chips are being invented to fully exploit advances in AI, by training and running deep neural networks for tasks such as voice recognition and image processing. These chips handle data in a fundamentally different way from the silicon logic circuits that have defined the cutting edge of hardware for decades. It means reinventing microchips for the first time in ages.

China won't be playing catch-up with these new chips, as it has done with more conventional chips for decades. Instead, its existing strength in AI and its unparalleled access to the quantities of data required to train AI algorithms could give it an edge in designing chips optimized to run them.

China's chip ambitions have geopolitical implications, too. Advanced chips are key to new weapons systems, better cryptography, and more powerful supercomputers. They are also central to the increasing trade tensions between the US and China. A successful chip industry would make China more economically competitive and independent. To many, in both Washington and Beijing, national strength and security are at stake.

> A more advanced chip industry will help China realize its dream of becoming a true technology superpower.

Silicon visions

On the outskirts of Wuhan, a sprawling city a few days' cruise up the Yangtze from Shanghai, stands a factory that would span several football fields. It belongs to Tsinghua Unigroup, a state-backed microchip manufacturer. By the end of 2019, the factory will be producing silicon wafers that will then be cut into advanced memory chips.

Tsinghua Unigroup aims to expand the Wuhan facility to three times its current size, at a total cost of $24 billion. It's developing two similar sites, one along the Yangtze in Nanjing and another further west in Chengdu, at similar cost. They will be the largest and most sophisticated chip factories ever built by a Chinese company.

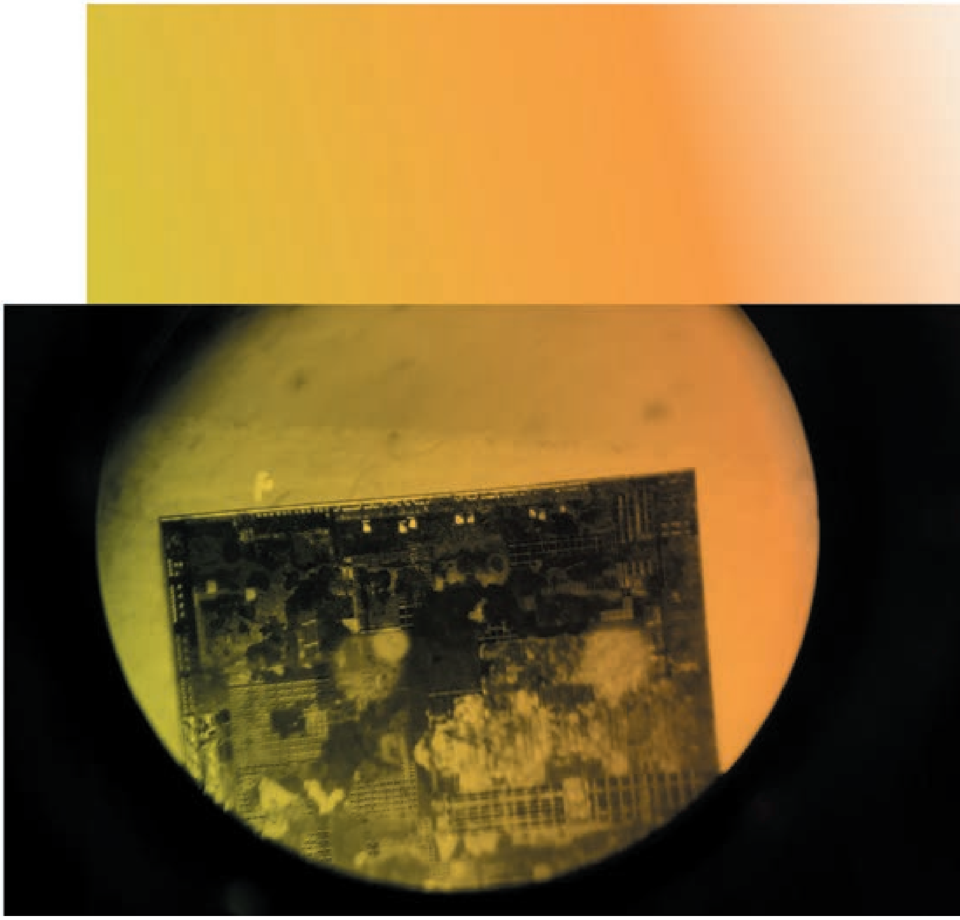
It's all part of an effort by China to drag its chipmaking industry forward. In 2014, the government established the National Integrated Circuits Industry Investment Fund, a subsidy program that plans to raise $180 billion from local-government-backed funds and state-owned enterprises. A year later, it released Made in China 2025, a sweeping blueprint for upgrading China's entire manufacturing industry. This set the hugely ambitious goal of producing $305 billion worth of chips per year and meeting 80% of domestic demand for chips by 2030, up from $65 billion and 33%, respectively, in 2016. Today global production stands at $412 billion.

There is still a long way to go. China is the world's largest and fastest-growing market for semiconductors, but no Chinese chipmaker has broken into the top 15 globally in terms of sales. Advanced chips are primarily made by companies from the US, Taiwan, Japan, South Korea, and Western Europe. China's big economic rival, the US, accounts for about half of global sales and half of China's chip imports.

Beijing has been trying to build a powerful microchip industry for a long time. Researchers developed China's first transistor not long after the device was invented in the US at the end of the 1950s. But the country fell behind as its universities and businesses went through the turmoil of the Cultural Revolution. In the 1960s, as the semiconductor industry began ramping up in Silicon Valley and Moore's Law was articulated, China's fledgling chip industry lay in ruins.

By the time the Chinese economy opened up in the 1980s, it was too late. Chipmakers partnered with foreign firms, but the manufacturing equipment they imported became outdated quickly, and they failed to produce even basic chips reliably or in sufficient volume. And even as China's electronics manufacturing took off in the 1990s, bureaucratic missteps and the ready availability of high-quality imported chips stymied further government pushes. No Chinese company could match the decades of expertise at foreign firms like Intel, Samsung, and Taiwan Semiconductor.

Mark Li, an analyst at Bernstein who tracks the chip industry in Asia, estimates that China's most advanced chipmakers are still at least five years behind. Since Moore's Law describes a doubling of chip performance every two years or so, that's a sizable gap. China does have numerous low-end fabs making the relatively simple chips used in smart cards, SIM cards, and even basic phones, but not the kinds of factories needed to produce advanced processors.



State-backed Tsinghua Unigroup showed off a microscope's view of a chip at a high-tech expo in Beijing.

Why does China still struggle to make advanced chips when it has become so good at so much else? Basically, because it's incredibly hard. The latest chips have billions of transistors, each with features only a few nanometers in size, crafted at the scale of individual atoms. They are so complex that it isn't possible to take one apart and copy its design, as Chinese entrepreneurs have done with many foreign products. And even if it were possible, it wouldn't provide the expertise required to design and fabricate the next generation.

"Manufacturing involves hundreds, even thousands, of technical challenges," says Yungang Bao, director of the Center for Advanced Computer Systems at the Chinese Academy of Sciences and an expert in microprocessor design. "It will take a long time to catch up."

PREVIOUS SPREAD: IMAGE COURTESY OF BITMAIN; NG HAN GUAN | AP IMAGES

Network effects

Artificial intelligence may change the game.

Deep learning is an AI technique that has proved its power in recent years to do useful things like spotting disease in medical images, teaching self-driving cars to stay on the road, and parsing spoken commands. It works in a fundamentally different way from most software.

Deep learning uses large networks that roughly resemble the multiple layers of neurons in a biological brain. As a network learns a task, a cascade of computations occur in successive layers. The results of each computation alter the connections between each layer and the next; essentially, the network reprograms itself as it runs. Its ability to recognize objects in images isn't the result of step-by-step logic operations, as in conventional programming, but gradually emerges as countless parameters inside the network are tweaked and re-tweaked through exhaustive training.

Researchers realized early on that the chips in game consoles, originally designed to be fast at rendering 3D imagery, are better for deep learning than general-purpose chips. And deep-learning algorithms are still mostly trained using scores of these graphics processing units (GPUs). One of the market leaders for GPUs is Nvidia, which built its business supplying hardware for gamers. But now Intel and others have designed powerful new chips for training deep learning. Even cloud software businesses like Google's and Amazon's are developing bespoke chips designed for their best algorithms.

Similar Chinese initiatives have been announced over the past year. In July 2018, search giant Baidu revealed that it is working on a chip called Kunlun for running deep-learning algorithms in its data centers. And in September, the e-commerce powerhouse Alibaba said it would spin out a new company dedicated to making AI chips. Tellingly, the new company's name is Pingtouge, a nickname for the honey badger, an African animal famed for fearlessness and tenacity.

The timing of the AI boom is fortuitous for China's chipmakers. The deep-learning revolution was gaining speed just as the government's latest chip push got under way. AI chip design is still in its early days, and in this technology—unlike memory and logic circuits—the country is not hopelessly behind.

Cambricon, one of the country's most valuable startups, is selling new chips specially designed for artificial-intelligence cloud applications.

CAMBRICON

Specialized hardware

Kai Yu has already played a significant role in China's AI revolution. A cheerful, bespectacled man who studied neural networks at college in China and Germany in the late 1990s and early 2000s, he founded Baidu's Institute of Deep Learning in 2013,

人工智能正在改变世界

"Artificial intelligence is transforming the world."

as the company became one of the first to bet heavily on AI.

Navigating Beijing's morning traffic in the backseat of a Didi, Yu says the importance of chip hardware quickly became apparent when Baidu started pouring resources into deep learning. In 2015, he says, he suggested that Baidu make a specialized AI chip. But it seemed costly and far outside of the company's expertise. So later that year, Yu left to found his own company, Horizon Robotics.

Horizon is focused on "application-specific" microchips that run pre-trained deep-learning algorithms. It's developing them for self-driving cars and smarter robots. But Yu thinks these chips will be everywhere before long. "If we look back in 10 years," he says, "more than half of the computations on a device will be AI related."

In August 2018, Huawei, China's biggest telecommunications and smartphone company, unveiled a mobile chip, the Kirin 980, that includes a "neural processing unit"—a section of logic designed for deep-learning tasks like image and voice recognition.

In one sense, the chip illustrates a lingering limitation of China's capabilities—it was manufactured by Taiwan's TSMC. But in another, it reflects China's striking progress and ambition. The chip is one of the country's first to include features as small as 7 nanometers. Smaller components make chips faster and more capable, but also a lot harder to design and manufacture, so this a significant coup for Huawei. Designs for the part of the chip optimized for deep learning come from a startup called Cambricon, founded in 2016 by researchers from the Chinese Academy of Sciences. Today Cambricon is valued at $2.5 billion, making it the industry's most valuable startup. In October, Huawei announced another AI chip, called Ascend, that is designed in-house.

Chip on the shoulder

China's chip ambitions have rattled other countries, especially the US. Partly that's because its efforts to gain access to technology have sometimes involved aggressive acquisitions, forced technology transfer, and, allegedly, industrial espionage. Chipmaking is key to military prowess, and the Obama administration sought to block Chinese attempts to acquire US chip technology long before Donald Trump arrived in the White House. It's one of the few issues that unite US politicians.

In April 2018 the US banned one of China's leading tech companies, ZTE, from using US chips because it had broken a ban on selling equipment containing US technology to Iran and North Korea. In October, the US said the memory-chip maker Fujian Jinhau, a company accused of stealing trade secrets, would need a special license to buy US-made components. These restrictions may partly be a response to property theft and unfair trade, but they also look like an effort to slow China's chipmaking progress.

Yet a trade war may only hasten China's ascent. "People in China realized that the US can easily stop their progress," says Bao at the Chinese Academy of Sciences. "It will probably speed things up."

However fast it happens, China's march to advanced chipmaking is all but unstoppable. No true superpower can afford to outsource technology that is so critical to both its economic growth and its military security. And after decades of playing catch-up, the country is finally seeing opportunities to establish mastery of the field.

In Tianjin, Tao is explaining that iFlytek is thinking about designing its own chips, to improve the performance of its electronic translators. Just then, the AI-generated version of Trump speaks up. 人工智能正在改变世界 (*Réngōng zhìnéng zhèngzài gǎibiàn shìjiè*), he says: "Artificial intelligence is transforming the world."

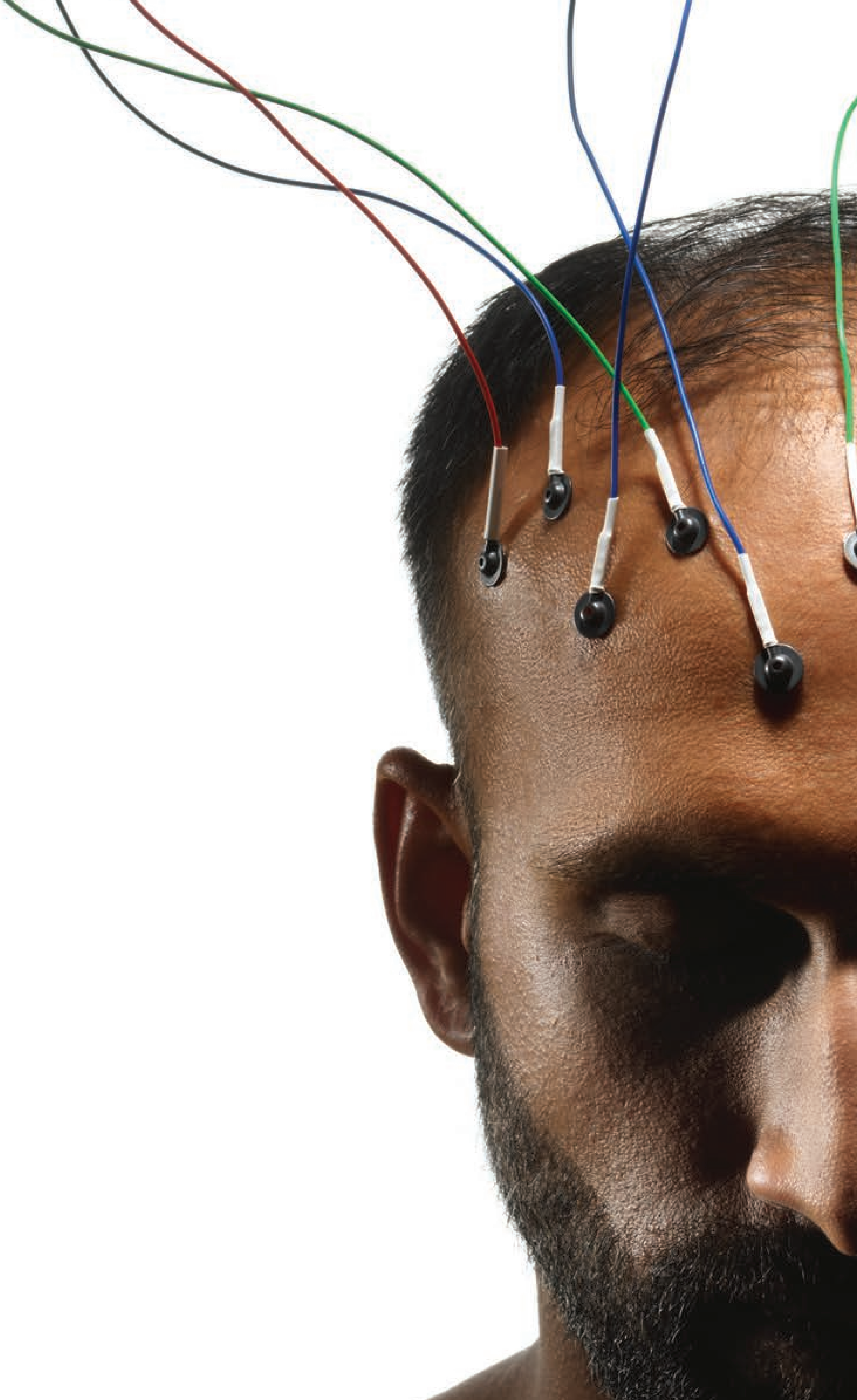
Will Knight is MIT Technology Review's senior editor covering AI.

How will technology change democracy?

5

Social media has made it easy for us to divvy ourselves up into opposing factions. But that's just the start. Now so-called "neuropolitical" consultants say they can intuit your feelings by observing your spontaneous responses—and then use that to manipulate your voting behavior (page 74). In a more positive vein, an experiment in Taiwan is employing technology to see if its citizens are ready for a bold new form of participatory government (page 80).

N E U R O P O L I T I C S



Meet the consultants who divine your political preferences by peering inside your brain.

BY ELIZABETH SVOBODA

PHOTO BY BRUCE PETERSON

Maria Pocovi slides her laptop over to me with the webcam switched on. My face stares back at me, overlaid with a grid of white lines that map the contours of my expression. Next to it is a shaded window that tracks six “core emotions”: happiness, surprise, disgust, fear, anger, and sadness. Each time my expression shifts, a measurement bar next to each emotion fluctuates, as if my feelings were an audio signal. After a few seconds, a bold green word flashes in the window: ANXIETY. When I look back at Pocovi, I get the sense she knows exactly what I’m thinking with one glance.

Petite with a welcoming smile, Pocovi, the founder of Emotion Research Lab in Valencia, Spain, is a global entrepreneur par excellence. When she comes to Silicon Valley, she doesn't even rent an office—she just grabs a table here at the Plug and Play coworking space in Sunnyvale, California. But the technology she's showing me is at the forefront of a quiet political revolution. Campaigns around the world are employing Emotion Research Lab and other marketers versed in neuroscience to penetrate voters' unspoken feelings.

This spring there was a widespread outcry when American Facebook users found out that information they had posted on the social network—including their likes, interests, and political preferences—had been mined by the voter-targeting firm Cambridge Analytica. While it's not clear how effective they were, the company's algorithms may have helped fuel Donald Trump's come-from-behind victory in 2016.

But to ambitious data scientists like Pocovi, who has worked with major political parties in Latin America in recent elections, Cambridge Analytica, which shut down in May 2018, was behind the curve. Where it gauged people's receptiveness to campaign messages by analyzing data they typed into Facebook, today's "neuropolitical" consultants say they can peg voters' feelings by observing their spontaneous responses: an electrical impulse from a key brain region, a split-second grimace, or a moment's hesitation as they ponder a question. The experts aim to divine voters' intent from signals they're not aware they're producing. A candidate's advisors can then attempt to use that biological data to influence voting decisions.

Political insiders say campaigns are buying into this prospect in increasing numbers, even if they're reluctant to acknowledge it. "It's rare that a campaign would admit to using neuromarketing techniques—though it's quite likely the well-funded campaigns are," says Roger Dooley, a consultant and author of *Brainfluence: 100 Ways to Persuade and Convince Consumers with Neuromarketing*. While it's not certain the Trump or Clinton campaigns used neuromarketing in 2016, SCL—the parent firm of Cambridge Analytica, which worked for Trump—has reportedly used facial analysis to assess whether what voters said they felt about candidates was genuine.

But even if US campaigns won't admit to using neuromarketing, "they should be interested in it, because politics is a blood sport," says Dan Hill, an American expert in facial-expression coding who advised Mexican president Enrique Peña Nieto's 2012 election campaign. Fred Davis, a Republican strategist whose clients have included George W. Bush, John McCain, and Elizabeth Dole, says that while uptake of these technologies is somewhat limited in the US, campaigns would use neuromarketing if they thought it would give them an edge. "There's nothing more important to a politician than winning," he says.

The trend raises a torrent of questions in the run-up to the 2018 midterms. How well can consultants like these use neurological data to target or sway voters? And if they are as good at it as they claim, can we trust that our political decisions are truly our own? Will democracy itself start to feel the squeeze?

Unspoken truths

Brain, eye, and face scans that tease out people's true desires might seem dystopian. But they're offshoots of a long-standing political tradition: hitting voters right in the feels. For more than a decade, campaigns have been scanning databases of consumer preferences—what music people listen to, what magazines they read—and, with the help of computer algorithms, using that information to target appeals to them. If an algorithm shows that middle-aged female SUV drivers are likely to vote Republican and care about education, chances are they'll receive campaign messages crafted explicitly to push those buttons.

Biometric practitioners say they can tap into truths that voters are unable to express.

Biometric technologies raise the stakes further. Practitioners say they can tap into truths that voters are often unwilling or unable to express. Neuroconsultants love to cite psychologist Daniel Kahneman, winner of the Nobel Prize in economics, who distinguishes between "System 1" and "System 2" thinking. System 1 "operates automatically and quickly, with little or no effort and no sense of voluntary control," he writes; System 2 involves conscious deliberation and takes longer.

"Before, everyone was focused on System 2," explains Rafal Ohme, a Polish psychologist who says his firm, Neurohm, has advised political campaigns in Europe and the United States. For the past decade, Ohme has devoted most of his efforts to probing consumers' and voters' System 1 leanings, which he thinks is as important as listening to what they say. It's been great for his business, he says, because his clients are impressed enough with the results to keep coming back for more.

Many neuroconsulting pioneers built their strategy around so-called "neurofocus groups." In these studies, involving anywhere from a dozen to a hundred people, technicians fit people's scalps with EEG electrodes and then show them video footage of a candidate or campaign ad. As subjects watch, scalp sensors pick up electrical impulses that reveal, second by second, which areas of the brain are activated.

ELIZABETH SVOBODA; PREVIOUS SPREAD: MODEL: SHAHJEHAN KAHN/MODEL CLUB INC; STYLIST: BRE WELCH

"One of the things we can analyze is the attentional process," says Mexico City neurophysiologist Jaime Romano Micha, whose former firm, Neuropolitka, was one of the top providers of brain-based services to political campaigns. Romano Micha would place electrodes on a subject's scalp to detect activity in the reticular formation, a part of the brain stem that tracks how engaged someone is. So if subjects are watching a political ad and activity in their reticular formation spikes, say, 15 seconds in, it means the message has truly caught their attention at that point.

> "There's nothing more important to a politician than winning."

Other brain areas provide important clues too, Romano Micha says. Electrical activity on the left side of the cerebral cortex suggests people are working hard to understand a political message; similar activity on the right side may reveal the precise moment the message's meaning clicks into place. With these kinds of insights, campaigns can refine a message to maximize its oomph: placing the most gripping moment at the beginning, for instance, or cutting the parts that cause people's attention to wander.

But while brain imaging remains part of the neuropolitical universe, most neuroconsultants say it's hardly sufficient by itself. "EEG gives us very general information about the decision process," Romano Micha says. "Some people are saying that through EEG we can go into the mind of people, and I think that's not possible yet." There are cheaper and more reliable tools, several consultants claim, for getting at a voter's true feelings and desires.

Electrodes everywhere

EEG scans, in fact, are now just one in a smorgasbord of biometric techniques. Romano Micha also uses near-infrared eye trackers and electrodes around the orbital bone to track "saccades," minuscule movements of the eye that indicate viewers' attentional focus as they watch a campaign spot. Other electrodes supply a rough gauge of arousal by measuring electrical activity on the surface of a person's skin.

Of course, you can't stick electrodes on every person watching TV and browsing Facebook. But you don't need to. The results from experiments on small neuro-focus groups can be used to influence voters who aren't being sampled themselves. If, for example, biodata reveals that liberal women over 50 are fearful when they see an ad about illegal immigration, campaigns that want to stoke such fear can broadcast that same message to millions of people with similar demographic and social profiles.

Pocovi's approach at Emotion Research Lab requires only a video player and a front-facing webcam. When volunteers enroll in her political focus groups online, she sends them videos of an ad spot or a candidate that they can watch on their laptop or phone. As they digest the content, she tracks their eye movements and subtle shifts in their facial expressions.

"We have developed algorithms to read the microexpressions in the face and translate in real time the emotions people are feeling," Pocovi says. "Many times, people tell you, 'I'm worried about the economy.' But what are really the things that move you? In my experience, it's not the biggest things. It's the small things that are close to you." Something as small as a candidate's inappropriately furrowed brow, she says, can color our perception without our realizing it.

Pocovi says her facial analysis software can detect and measure "six universal emotions, 101 secondary emotions, and eight moods," all of which interest campaigns anxious to learn how people are responding to a message or a candidate. She also offers a crowd-analytics service to track the emotional reactions of individual faces in a human sea, meaning that campaigns can take the temperature of a room as their candidate is speaking.

ERL's software is built around the facial action coding system (FACS) developed

The experts hope to discover voters' feelings via signals they're not even aware they're producing.

NEUROMARKETING S.A. DE C.V. AND DR. JAIME ROMANO MICHA

DMITRY KOSTYUKOV

"I measure hesitation," says Ohme. "I can change your mind only if you hesitate. If you are a firm believer, I cannot change anything."

by Paul Ekman, a famed American psychologist. Pocovi's algorithm deconstructs each facial image from the webcam into more than 50 "action units," movements of specific muscle groups. Distinct clusters of action units correspond to particular emotions: cheek and outer-lip muscles contracting at the same time reveal happiness, while lowered brows and raised upper eyelids betray anger. Pocovi trains her system to recognize each one by showing it many reference images from a large database of faces expressing that emotion.

Some critics of Ekman's system, such as neuroscientist Lisa Feldman Barrett, have argued that facial expressions don't necessarily correlate with emotional states. Still, a variety of studies have shown at least some correspondence. In a 2014 study at Ohio State University, cognitive scientists defined 21 "distinct emotions," based on the consistent ways most of us move our facial muscles.

Pocovi says her surveys also operate as an image-refining tool for candidates themselves. She analyzes video of candidates to pinpoint precise moments when their expressions make voters feel confused, disgusted, or angry. Politicians can then use this information to rehearse a different emotional approach, which can itself be vetted using Pocovi's survey platform until it produces the desired response in viewers. In one campaign Pocovi advised, a candidate was recording a TV ad spot with an uplifting, positive message, but it kept getting terrible reviews in test screenings. The spot's poor performance was a mystery—until Pocovi's analysis of the candidate's face showed he was unwittingly conveying anger and disgust. Once he realized what was going on, he was able to tweak his presentation and get a better response from the public.

Several onetime devotees of brain-scan analysis are also pursuing simpler and cheaper techniques these days. Before the 2008 financial crisis, Ohme says, international clients were more willing to fly five guys from Poland out to perform on-site brain studies. After the recession, though, that business mostly dried up.

That prompted Ohme to develop a different strategy, one untethered to time, space, or EEG electrodes. His updated approach stems from that used in unconscious-bias studies by social psychologist Anthony Greenwald, who became a mentor when Ohme visited the US on a Fulbright scholarship. Ohme says his smartphone-based test—which he calls iCode—reveals covert political leanings that would never surface in traditional questionnaires or focus groups.

Ohme's survey takers begin by answering calibration questions to assess their baseline reaction time. A habitually slower person, for instance, might have a "unit time" lasting 585 milliseconds, while someone quicker might take 387 milliseconds. Then images of politicians are shown on the screen, each paired with a single attribute, such as "trustworthy," "well-known," or "shares my values." Users tap "yes" or "no" to indicate whether they agree with each pairing. As the test proceeds, the app tracks not just how they answer but how quickly they touch the screen and what tapping rhythm they establish.

What's interesting, Ohme says, isn't how people respond to the questions per se, but how much they dither first. "When we measure the hesitation level, we can see that some answers are positive but with hesitation, and some are positive and instantaneous," he says. "We measure how much you deviated [from baseline]. This deviation is key."

Ohme declines to discuss his current political clients in much detail, citing confidentiality agreements. But he volunteers that in an iCode survey of nearly 900 people, he predicted Hillary Clinton's 2016 defeat before the election. Throughout the year, Clinton ran comfortably ahead of Trump in traditional polls. But when Ohme asked test subjects whether Clinton shared their values, they often hesitated for an unusually long time before responding that she did. Ohme knew a sense of shared values was a big factor motivating people to vote in 2016 (in previous elections "powerful" and "leader" were key), so the results of the test gave him serious doubts about a Clinton victory. He argues that if Clinton's campaign had run one of his studies before the election, she would have understood the depth of her vulnerability and could have made course corrections.

Ohme claims to have helped other candidates in similar straits. One of his tests revealed that while a certain European client had a good-sized base of supporters, many weren't motivated to get out and vote because they assumed their candidate would win. Armed with this knowledge, the campaign made a renewed push to get its loyal base to the polls. The client ended up winning in a squeaker.

The biggest lies in life

Does measuring people's spontaneous reactions to a TV ad or a stump speech tell you how they will ultimately vote, however? "On the applied side, it's pretty unclear, the hype from the reality," says Darren Schreiber, a professor in political science at the University of Exeter and author of *Your Brain Is Built for Politics*. "It's easy to over-believe the ability of these tools." So far cognitive tests have had mixed results. Contrasting studies have shown that implicit attitudes both do and don't predict how people vote.

When Ohme asked test subjects whether Hillary Clinton shared their values, they often hesitated for an unusually long time.

Still, Schreiber, who has conducted brain-scan tests of political attitudes, admits the technologies are worrisome. Democracy assumes the presence of rational actors, capable of digesting information from all quarters and coming to reasoned conclusions. If neuroconsultants are even half as good as they claim at probing people's innermost thoughts and shifting their voting intentions, it calls that assumption into question.

"We are susceptible in multiple ways, and not aware of our susceptibility," Schreiber says. "The fact that attitudes can be manipulated in ways we're not aware of has a lot of implications for political discourse." If campaigns are nudging voters toward their candidate without voters' knowledge, political discussions that were once exchanges of reasoned views will become knee-jerk skirmishes veering ever further from the democratic ideal. "I don't think it's time to run in panic," Schreiber says, "but I don't think we can be sanguine about it."

Ohme insists that voters can inoculate themselves against neuroconsultants' tactics if they're savvy enough. "I measure hesitation. I can change your mind only if you hesitate. If you are a firm believer, I cannot change anything," he says. "If you're scared to be manipulated, learn. The more you learn, the more firm and stable your attitudes are, and the more difficult it is for someone to convince you otherwise."

That's perfectly reasonable advice. But I wonder. After meeting Pocovi, I logged into Emotion Research Lab to let its software track my face while I watched a demo video. The video was of a laughing baby, and I felt the corners of my mouth quirking up. After, the computer asked me how I'd felt while watching. "Happy," I clicked. I'm a mom, right? I love babies. Yet when my emotion analysis arrived, it showed almost no trace of happiness on my face.

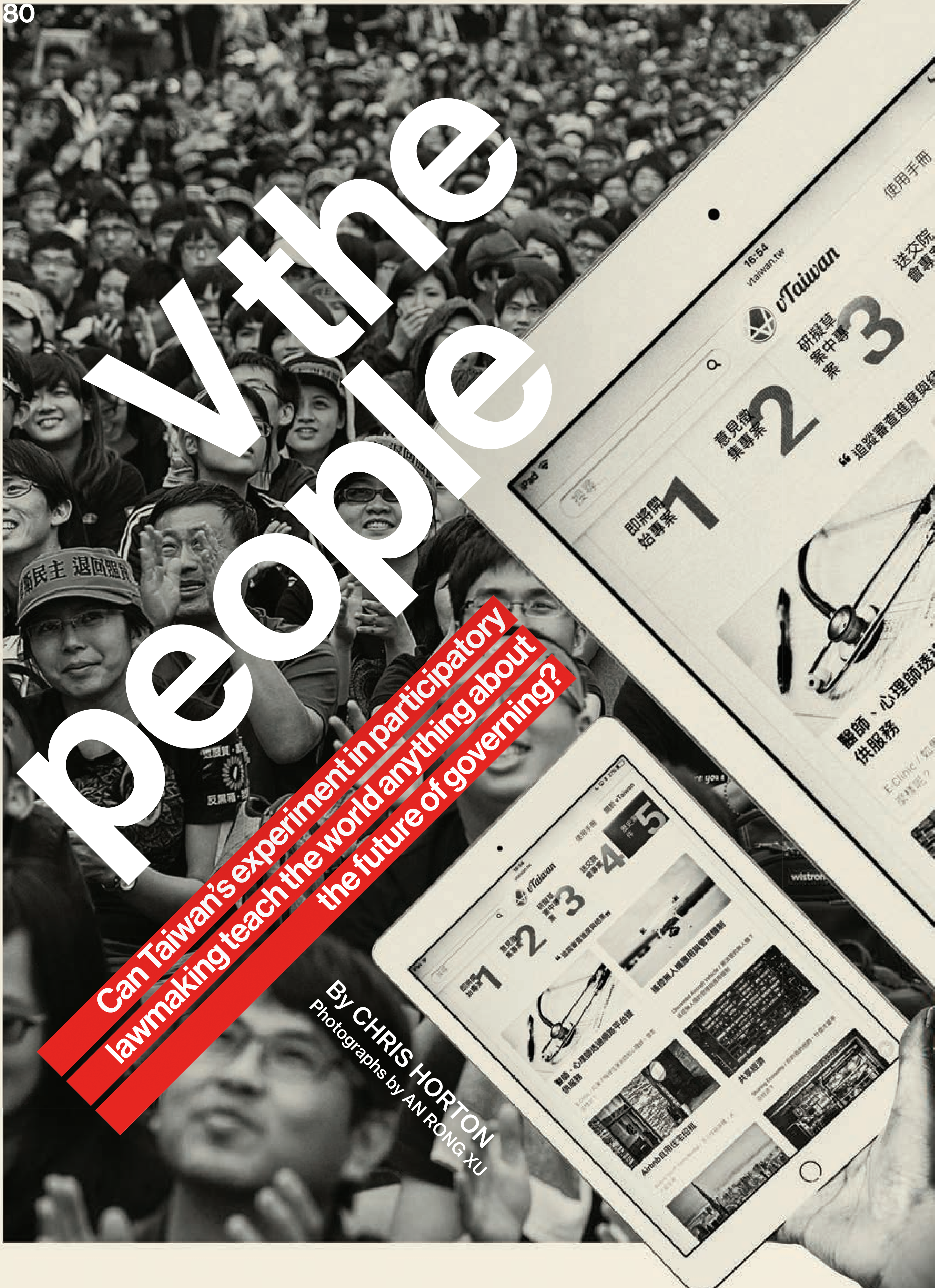
Thinking about the results, I realized the emotion software was right. I hadn't really been happy at all. I had taken the test late at night, and I had been exhausted. The computer had seen me in a way I wasn't used to seeing myself. I thought of something Dan Hill, the former advisor to the Mexican president's campaign, had told me. "The biggest lies in life," he'd said, "are the ones we tell ourselves."

Elizabeth Svoboda is a science writer in San Jose, California, and the author of What Makes a Hero?: The Surprising Science of Selflessness.

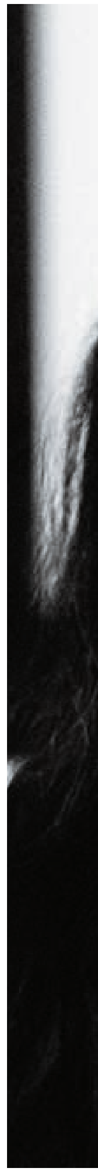
V the people

Can Taiwan's experiment in participatory lawmaking teach the world anything about the future of governing?

By CHRIS HORTON
Photographs by AN RONG XU




關於 vTaiwan
歷史案件
5
遙控無人機應用與管理機制
Uncrewed Aircraft Vehicle / 無法管的無人機？
遙控無人機的管理與應用機制
共享經濟
Sharing Economy / 你的我的他的，什麼才是平
臺經濟？
Airbnb自用住宅招租
vTaiwan



It was late in 2015, and things were at an impasse. Some four years earlier, Taiwan's finance ministry had decided to legalize online sales of alcohol. To help it shape the new rules, the ministry had kicked off talks with alcohol merchants, e-commerce platforms, and social groups worried that online sales would make it easy for children to buy liquor. But since then they had all been talking past each other. The regulation had gotten nowhere.

That was when a group of government officials and activists decided to take the question to a new online discussion platform called vTaiwan. Starting in early March 2016, about 450 citizens went to vtaiwan.tw, proposed solutions, and voted on them.

Within a matter of weeks, they had formulated a set of recommendations. Online alcohol sales would be limited to a handful of e-commerce platforms and distributors; transactions would be by credit card only; and purchases would be collected at convenience stores, making it nearly impossible for a child to surreptitiously get hold of booze. By late April the government had incorporated the suggestions into a draft bill that it sent to parliament.

The deadlock "resolved itself almost immediately," says Colin Megill, the CEO and cofounder of Pol.is, one of the digital platforms vTaiwan uses to host discussion. "The opposing sides had never had a chance to actually interact with each other's ideas. When they did, it became apparent that both sides were basically willing to give the opposing side what it wanted."

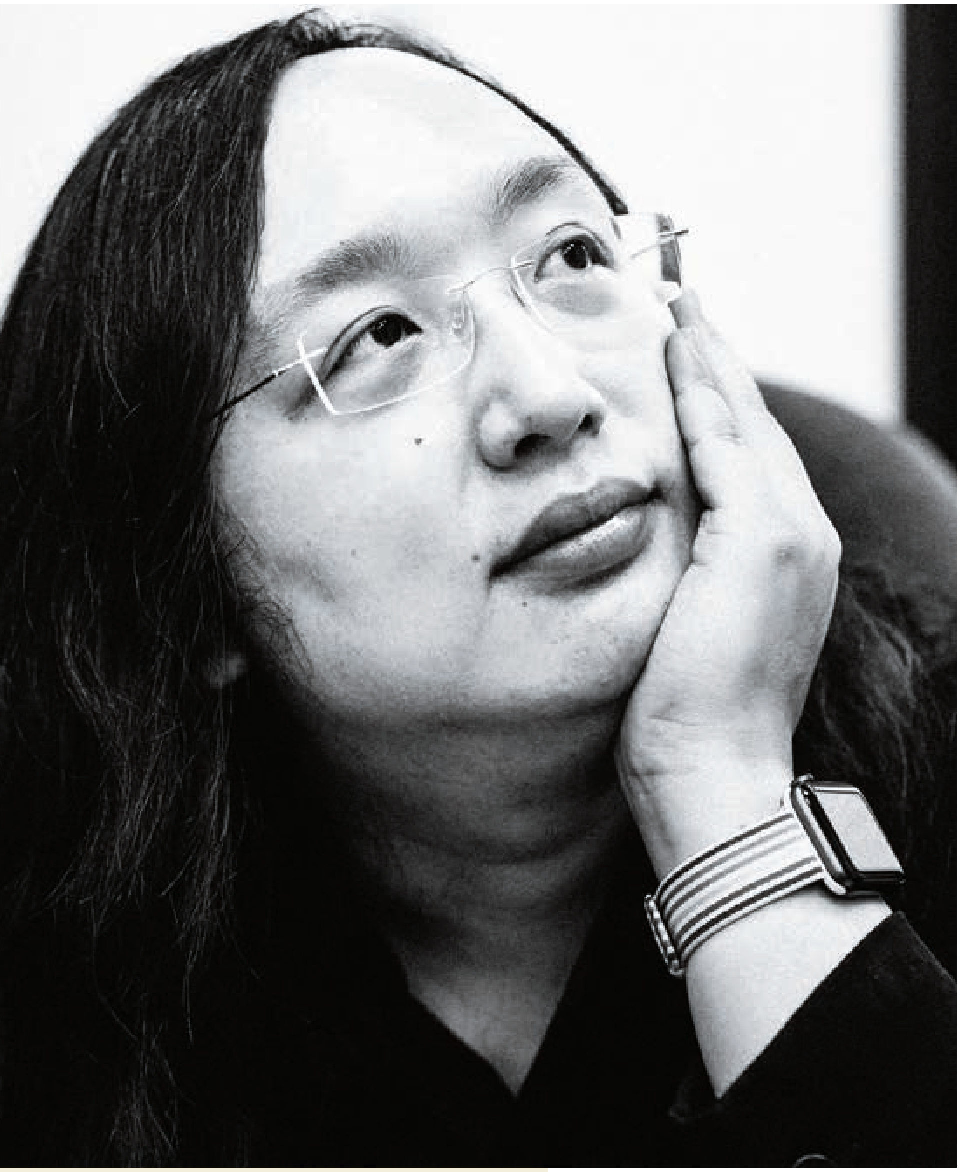
Three years after its founding, vTaiwan hasn't exactly taken Taiwanese politics by storm. It has been used to debate only a couple of dozen bills, and the government isn't required to heed the outcomes of those debates (though it may be if a new law passes later this year). But the system has proved useful in finding consensus on deadlocked issues such as the alcohol sales law, and its methods are now being applied to a larger consultation platform, called Join, that's being tried out in some local government settings. The question now is whether it can be used to settle bigger policy questions at a national level—and whether it could be a model for other countries.

"The opposing sides had never had a chance to actually interact with each other's ideas."

Taiwan might not seem like the most obvious place for a pioneering exercise in digital democracy. The island held its first direct presidential election only in 1996, after a century marked first by Japanese colonial rule and then by Chinese nationalist martial law. But that oppressive past has also meant that Taiwanese have a history of taking to the streets to push back against heavy-handed government. In Taiwan's democratic era, it was a protest four years ago that planted the seed for this innovative political experiment.

The 2014 Sunflower Movement, led by students and activists, derailed an attempt by President Ma Ying-jeou's government to ram through a trade agreement between Taiwan, which has been locally ruled since 1949, and China, which claims Taiwan as its territory. For more than three weeks the protesters occupied government buildings over the deal, which they felt would give China too much leverage over the Taiwanese economy.

In the aftermath, the Ma government invited Sunflower activists to create a platform through which it might better communicate with Taiwan's youth. A Taiwanese civic tech community known as g0v (pronounced "Gov Zero"), which had played a leading role in the Sunflower protests, built vTaiwan in 2015 and still runs it. The platform enables citizens, civil-society organizations, experts, and elected representatives to discuss proposed laws via its website as well as in face-to-face meetings and hackathons. Its goal is to help policymakers make decisions that gain legitimacy through consultation.



Wu Min Hsuan

Wu, an activist in the Sunflower Movement, says the government has missed out on chances to test vTaiwan on larger, non-digital issues such as pension reform. For vTaiwan to work, he says, "it needs real power."

Audrey Tang

Taiwan's digital minister was a leading hacker and Sunflower activist. She says that senior public servants need to see that people who comment online are "not protesters or mobs, but actually people with distinct expertise."

YIK FEI (PROTEST)

"I would say vTaiwan is about civil society learning the functions of the government and, to a degree, collaborating," Taiwan's digital minister, Audrey Tang, told me during a visit to her office. Tang, a famed hacker who helped the thousands of Sunflower protesters build and maintain their internal communications network, was appointed by the current president, Tsai Ing-wen, who won the 2016 election on a pledge of government transparency.

vTaiwan relies on a hodgepodge of open-source tools for soliciting proposals, sharing information, and holding polls, but one of the key parts is Pol.is, created by Megill and a couple of friends in Seattle after the events of Occupy Wall Street and the Arab Spring in 2011. On Pol.is, a topic is put up for debate. Anyone who creates an account can post comments on the topic, and can also upvote or downvote other people's comments.

That may sound much like any other online forum, but two things make Pol.is unusual. The first is that you cannot reply to comments. "If people can propose their ideas and comments but they cannot reply to each other, then it drastically reduces the motivation for trolls to troll," Tang says.

The second is that it uses the upvotes and downvotes to generate a kind of map of all the participants in the debate, clustering together people who have voted similarly. Although there may be hundreds or thousands of separate comments, like-minded groups rapidly emerge in this voting map, showing where there are divides and where there is consensus. People then naturally try to draft comments that will win votes from both sides of a divide, gradually eliminating the gaps.

"The visualization is very, very helpful," Tang says. "If you show people the face of the crowd, and if you take away the reply button, then people stop wasting time on the divisive statements."

In one of the platform's early successes, for example, the topic at issue was how to regulate the ride-hailing company Uber, which had—as in many places around the world—run into fierce opposition from local taxi drivers. As new people joined the online debate, they were shown and asked to vote on comments that ranged from calls to ban Uber or subject it to strict regulation, to calls to let the market decide, to more general statements such as "I think that Uber is a business model that can create flexible jobs."

Within a few days, the voting had coalesced to define two groups, one pro-Uber and one, about twice as large, anti-Uber. But then the magic happened: as the groups sought to attract more supporters, their members started posting comments on matters that everyone could agree were important, such as rider safety and liability insurance. Gradually, they refined them to garner more votes. The end result was a set of seven comments that enjoyed almost universal approval, containing such recommendations as "The government should set up a fair regulatory regime," "Private passenger vehicles should be registered," and "It should be permissible for a for-hire driver to join multiple fleets and platforms." The divide between pro- and anti-Uber camps had been replaced by consensus on how to create a level playing field for Uber and the taxi firms, protect consumers, and create more competition. Tang herself took those suggestions into face-to-face talks with Uber, the taxi drivers, and experts, which led the government to adopt new regulations along the lines vTaiwan had produced.

vTaiwan's website boasts that as of August 2018, it had been used in 26 cases, with 80% resulting in "decisive government action." As well as inspiring regulations for Uber and for online alcohol sales, it has led to an act that creates a "fintech sandbox," a space for small-scale technological experiments within Taiwan's otherwise tightly regulated financial system.

"It's all solving the same problem: essentially saying, 'What if we're talking about things that are emergent, [for which] there are only a handful of early adopters?'" Tang says. "That's the basic problem we were solving at the very beginning with vTaiwan."

But while vTaiwan can bridge gulfs in public opinion, what it can't always overcome is politics. After the Tsai administration took office in 2016, it withdrew all bills awaiting legislative approval. Observers chalked that up to the new president's desire to differentiate her agenda from her predecessor's. The online alcohol sales bill that the Ma government had drafted from the vTaiwan suggestions never saw the light of day.

That the government isn't required to heed discussions on vTaiwan is the system's biggest shortcoming. Jason Hsu, a former activist and now opposition legislator who helped bring vTaiwan into being during the Ma administration, calls it "a tiger without teeth."

Moreover, the Tsai administration has chosen to use it only for issues, such as regulating Uber, that have to do with the digital economy. That's because people who care about such issues are the ones most likely to be comfortable using a digital discussion platform. But some think it won't get serious traction with the public unless it is put to use on non-digital issues that matter to more people. C.L. Kao, one of the cofounders of g0v, argues that the

Jason Hsu

↓ A former activist, and now an opposition legislator, Hsu helped bring the vTaiwan platform into being. He says its big flaw is that the goverment is not required to heed its discusions.

Karen Yu

→ A lawmaker for the ruling party, Yu says that vTaiwan is "not a huge priority" for the government and has come "close to death" at times.

If vTaiwan's recommendations are ignored, the process runs the risk of being viewed as "openwashing."

government could have applied vTaiwan to two contentious recent issues, pension reform and labor reform, as a way to build its credibility.

In any case, Kao says, if vTaiwan's recommendations are ultimately ignored, as they were with the alcohol sales law, then the whole process runs the risk of being viewed as "openwashing"—something that creates the pretense of transparency. "The end goal is legislation," he says.

vTaiwan is one of dozens of participatory governance projects around the world listed on CrowdLaw, a site run by the Governance Lab at New York University. Most of them, says Beth Noveck, the lab's director, suffer from the same problem: they're not binding on governments, which means it's also hard for them to gain credibility with citizens. Still, she says, Taiwan's experiment is "a step in the right direction." It's "far more institutionalized" than what's been seen elsewhere, she adds.

The platform may be about to get a little more clout. This autumn legislators will debate and vote on a digital communications bill that, among other things, says that "digital-economy issues are to be deliberated in an open, multistakeholder process that the government has the duty to support," in Tang's words. But what "support" means—how much weight lawmakers or the government will have to give to vTaiwan's deliberations—is still up in the air.

Taiwan does have a newer participatory governance system that is getting more traction. Join, also overseen by Audrey Tang, is a platform for hosting and debating online petitions, again using Pol.is to create consensus. She describes it as a vTaiwan within the government—"basically the same … process, but with senior career public servants instead of g0v volunteers" at the heart of the platform.

Although petitions on Join still aren't legally binding, any government agency that agrees to participate in a deliberation must, if the petition gets more than 5,000 signatures, give a point-by-point response explaining why it agreed to or rejected the proposal. Five of Taiwan's cities or counties are testing Join; the aim is ultimately to roll it out nationwide, Tang says.

Join tends to attract a broader, older, and less tech-savvy range of users than vTaiwan. The advantage of this, says Tang, is that it doesn't tackle only digital-economy issues, as vTaiwan does, but a wide variety of questions, "like whether we should build a hospital in the southmost part of Taiwan, in Hengchun, or whether the first publicly open marine national park should ban fishing." The downside is that there's more resistance from the government bureaucracy. Senior public servants "need some hand-holding," she says, to be able to see people who comment online as "not protesters or mobs, but actually people with distinct expertise."

While only 200,000 people have so far taken part in a vTaiwan discussion, nearly five million of the country's 23 million inhabitants are already on Join. More than 10,000 voted on a recent proposal that advocated caning as a punishment for drunk driving, sexual assault, and child abuse.

Here too, the consensus-building tendencies of Pol.is can lead the discussion in unexpected directions. Initially, opinion on the caning issue was divided into three camps: besides the people who were for and against caning, a third group argued that it was too light a punishment for such offenses.

Eventually, however, the consensus opinions that emerged had nothing to do with caning at all, but were more focused on methods of preventing those crimes. At the time of this writing, proposals being considered for legislation included alcohol locks and confiscating drunk drivers' cars.

This suggests people had concluded that, in fact, "To cane or not to cane?" was the wrong question to ask. That kind of realization, and solution, wouldn't have emerged from a traditional online petition that only gives people the option of voting yes or no.

Karen Yu, a legislator in President Tsai's Democratic Progressive Party, says vTaiwan is "not a huge priority" for the administration and has come "close to death" at times. Join, she points out, at least benefits from the legitimacy of being managed by the government. Wu Min Hsuan, an activist who occupied Taiwan's Legislative Yuan during the Sunflower Movement protests, says Join has already proved itself much more productive than vTaiwan. The obstacle, he believes, is political will. "The experiment is important and has value," he says. "But the platform has its limits. It needs real power."

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Will gene editing alter the human race?

6

Late last year MIT Technology Review was first to report that Chinese scientist He Jiankui had edited human embryos to make them HIV-resistant and implanted them into women—one of who ultimately gave birth to twin girls. The act was condemned worldwide as a violation of ethics, but that's hardly likely to stop continued experiments (page 88). As another Chinese researcher put it, "The development of science and technology is unavoidable."

The man who crossed the ger

Three years ago an unknown Chinese scientist edited the DNA of human embryos. It was a step on an inexorable path to designer babies.

By Antonio Regalado

mline

It could have been anyone. It was so easy. But it was him. Junjiu Huang.

In 2015, Huang, a stem-cell researcher at Sun Yat-Sen University in Guangzhou, first reported using the gene-editing tool CRISPR on human embryos. His paper was rejected by top Western journals on the grounds that it didn't follow ethics rules and presented scant science, but that April it found its way into print in an obscure English-language publication in Beijing.

The result was, in Chinese, *xuān rán dà bō* (轩然大波), or "towering waves"—a sensational controversy.

Huang had only carried out a lab experiment, in which he'd tried to fix a gene error that causes a blood disease. His test subjects were abnormal IVF embryos, about the size of the period at the end of this sentence, and they were soon destroyed. No attempt was made to create a child.

Still, Huang had broken a taboo: altering the DNA of so-called germline cells, those that affect heredity.

The implication was clear. Genetically edited people could one day be born. And those changes would be passed on to future generations.

The reaction to Huang's work was instant, visceral, and global. Humankind could drive its own evolution, but the person holding the wheel was a youthful-looking biologist from southern China whom no one had ever heard of. His scientific effort was called "totally premature" and a "dreaded" experiment. The dean of Harvard Medical School ascribed to Huang potentially "deranged motivations."

I wrote about Huang's research in 2015, so it was with a sense of déjà vu that I watched the international reaction this November when He Jiankui, a scientist at the Southern University of Science and Technology in Shenzhen, announced he'd changed the DNA of human embryos to make them HIV-resistant and implanted them into women—one of whom, He claimed, gave birth to twin girls. Once again, an ambitious Chinese scientist had crossed into unknown territory to score a controversial first. Once again, his papers were rejected and attacked by furious Western scientists.

These events have made it apparent that the scientific community is deeply uncertain and conflicted about how to roll out a technology that will affect humanity's shared gene pool. He's shocking baby announcement came just before a major international summit in Hong Kong whose purpose had been to discuss gene-editing technology and its implications for reproduction—that is, to determine whether there should be CRISPR babies at all. Despite the wave of anger at He's news, the summit leaders did not conclude that humankind isn't responsible enough to engineer its own heredity or should enact a moratorium while we learn a bit more. Rather, it ended with the clearest call yet by science leaders to move the technology toward medical use in IVF clinics.

The dream is that future generations will benefit from longer and healthier lives because their bodies possess genetic vaccines against heart disease, Alzheimer's, and more. The nightmare, though, may be pretty close to what He was allowed to present on stage in Hong Kong: children whose genomes were clumsily and needlessly mutated as part of an international science race.

The dream is that future generations will benefit from longer and healthier lives. The nightmare, though, is children whose genomes are clumsily and needlessly mutated as part of an international science race.

It could still be that China's government cracks down on the gene-editing efforts: at the time of writing, He was under investigation by everyone from the local health board to China's ministry of science and technology, and he had vanished from view. In the US, starting pregnancies with gene-edited embryos was blocked by Congress in 2015. But American researchers have been prowling labs in China, looking to set up shop there and push CRISPR babies forward in ways they can't at home.

Once gene editing was developed, the pace of technological exploration made it inevitable that someone would create a birth, and someone will again. Even if the technology doesn't move forward in China, it will just happen somewhere else.

THE SPARK

I had traveled to China in October 2018, a full month before the announcement of the CRISPR babies, to understand the country's intentions for embryo engineering, an area in which its scientists had taken a notable lead: of the 10 papers I could locate describing lab-edited embryos, eight were from China, and one each from the US and the UK. Whatever was happening, China would be the place to learn about it. If there was a secret project to make a baby, perhaps I could unearth it. I began with Huang, who had dropped off the media radar entirely in 2015.

Huang told me that our interview, in a tea house in Guangzhou, was the first he'd given since his paper was published. Even now, he did not want to recall the international censure his first embryo-editing report had generated, nor the towering pile of inquiries that flowed into his in-box. "I don't remember," he said.

Huang was ready to speak because passions had cooled and embryo editing had become an accepted, if limited, line of research. (When US scientists edited embryos in 2017, it was heralded as a "breakthrough.") Many had begun to see the procedure as a potential new way to prune risks of genetic disease from tomorrow's children. Huang slowly relaxed his guard. He told me he was married and played volleyball. The means to edit embryos and alter heredity? "A necessity of history," he said.

Yet Huang appeared to have no inkling of the news He would soon reveal. When I asked him what advice he would have for anyone in a rush to start a clinical trial in an IVF clinic, he said he thought it was unlikely anyone was trying. "We are far from the proper timing for this," he said.

Huang's life story would be familiar to many Chinese scientists—"just normal," he said. He grew up on a farm, but his family moved to a town so his parents could work in a factory building boat parts and send him to school, where he was singled out for his high grades.

Even as a boy, he says, he found the embryo a source of fascination. He mated purple, white, and green corn to make hybrids, and during the 1990s he followed popular reports of a Chinese effort to clone a panda. "I thought the embryo was a very mysterious type of cell," he says. "It has all the information needed to form something, but how does the process work?"

So Huang noticed when, in 2012, US, European, and South Korean scientists developed a versatile new way to alter the DNA information inside living cells. Called by its acronym, CRISPR allows scientists to easily cut open the double helix at any location so they can add or remove genetic instructions. A few hundred dollars' worth of supplies and chemicals is all that's needed.

By May 2013, a team at MIT, led by Rudolf Jaenisch, had injected CRISPR into mouse embryos, leading to the birth of the first CRISPR-modified mammals. But China, with its loose rules on animal research and its ambitions to become a worldwide leader in the technology, rapidly claimed the rest of the animal zoo. "We lost the mouse. But we won the sheep, the goat, and the monkey," says Huang Xingxu (no relation), a professor of biology at Shanghai Tech University.

The birth of two edited monkeys in Yunnan province, announced in January 2014, led some observers to realize that edited humans might be next. But who would take such a step? What kind of social understanding or global agreement might be needed? There was none.

Huang says he had "no idea what the reaction would be" to his research.

XUEXUN ZHOU

Junjiu Huang says he first introduced CRISPR into human embryos just three months after the monkey report. It was, as some feared, very simple to do. "We spent about half a year to finish the project, because it's not a very complex experiment," he says.

Huang was well positioned to do it. Guangzhou has large, well-established IVF clinics interested in research. And Huang also perceived the need for a new form of treatment. About 10% of the population in the growing city of 13 million carries a genetic error that creates a risk for beta thalassemia, a blood disease. What if CRISPR could be used to replace the broken gene with a working copy in embryos? That, he imagined, would be a "new technique" to eradicate the disease in newborn children. In his tests, Huang worked with abnormal embryos rejected by the IVF lab.

"I was doing basic research … to test the feasibility," he says. He admits he had "no idea what the reaction would be."

"IRRESPONSIBLE" FOR NOW

It wouldn't take long to find out. Huang's effort to install a normal beta thalassemia gene in embryos did work sometimes, but there were serious problems. CRISPR is error prone and can make unwanted edits, called "off targets." It meant the chance of introducing new and potentially harmful mutations. Also, the process wasn't efficient. Often the embryo ended up with a mixture of corrected and uncorrected cells, a so-called mosaic—a problem that was to end up afflicting most of He's embryos as well.

To many scientists, the risk of unwanted and undetected errors is what makes it so unwise to create a CRISPR baby. "It's clearly not ready," says Zheng-Yi Chen, a Harvard University scientist who works with CRISPR in pigs in China. "You don't know the consequences to develop a whole human being. Any subtle difference could be magnified by a billion- or trillion-fold. It could change the landscape."

Gestation period

Since the invention of the gene-editing tool CRISPR, its use to modify human beings has proved inexorable.

2012

US and European scientists develop powerful and easily programmed molecules for cutting DNA. The gene-editing tool is named CRISPR-Cas9.

The first gene-edited monkeys are born in southern China. Scientists deleted two genes from their bodies.

2013

2014

Chinese researchers begin altering human embryos with CRISPR. They aim to correct the mutation causing the blood disorder beta thalassemia.

Huang's lab results alarmed top Western biologists who reviewed them starting in late 2014. They claimed the work was sloppy and made sure his submission was rejected by both Science and Nature, the world's premier science journals. But in truth, the experts were shocked by how advanced the Chinese work was. Before Huang could publish his report elsewhere, American biotech executives who had seen his text called for an immediate moratorium on all embryo editing. Their editorial, published by Nature, was titled "Don't edit the human germline."

It would be the first, and last, organized call from gene-editing experts to shut down the lab research. Days later, a broader group of specialists, writing in Science and including Jennifer Doudna, a co-discoverer of CRISPR, took the position that lab studies should be encouraged but called for an urgent international meeting to "explore responsible uses of this technology." That meeting, eventually held at the National Academy of Sciences in Washington, DC, in December 2015, drew top biologists and ethicists from around the world, including China.

Biologists have struggled to understand their own power and to contain the risk that governments could step in with regulatory restrictions on CRISPR. Seeing how quickly the technology was moving, David Baltimore, the former president of Caltech, speaking for the conference organizers, hit the pause button: he stated that making a baby would be "irresponsible" for now. Such an undertaking needed to wait until the technology was better studied and until there was a "broad societal consensus" about why we'd want to change the gene pool at all.

That summit statement after the meeting in Washington was agreed to by the scientific academies of the US, the United Kingdom, and China—the last of these an arm of the central government. Huang, the junior researcher who started it all, wasn't at the historic forum. "I was not invited," he says.

WHEN "NO" MEANS "MAYBE"

A year later, in February 2017, the US National Academy of Sciences published a detailed set of recommendations written by a cadre of mostly American senior scientists. It found that no country was yet in a position to safely create a human whose genes were altered with CRISPR. But the technology was not in itself impermissible, the scientists said. So long as such a project was aimed at preventing serious disease, was preceded by safety studies, and met other—somewhat undefined—conditions, it might be acceptable to try for a live birth.

In Shenzhen, He Jiankui was listening. A biophysicist and expert in DNA sequencing, he had studied at Rice and Stanford but had returned to China. He had a professorship, funding, and, it appears, the ambition of being the first in the world to produce a child genetically engineered with CRISPR. That March, according to documents, he came to an ethics committee at a South China hospital with a proposal for a clinical trial of a treatment

MONKEYS: CELL, NIU ET AL. / EMBRYO: RWJMS IVF PROGRAM | WIKIMEDIA COMMONS

2015

Science leaders from China, the UK, and the US warn it would be "irresponsible" to create a child from edited embryos.

The US Congress forbids the Food and Drug Administration to allow the creation of genetically modified children.

2016

US intelligence agencies classify CRISPR as a potential weapon of mass destruction.

2017

The US National Academy of Sciences says it is permissible to genetically engineer humans, but only under extraordinary conditions.

2018

A researcher in China announces the birth of twin girls whose genomes were altered with CRISPR to make them resist HIV.

HUMAN GENOME EDITING SUMMIT

intended to make children immune to HIV. He believed he could win the Nobel Prize. In those documents, He cited the US academy's report, telling others the Americans had "approved" the idea of germline editing—which, in some sense, they had.

In Shenzhen, He quickly began assembling the data that would let him meet the academy's standard—or something resembling it. He focused on two genes whose deletion from a person's genome can have a health benefit. One was CCR5, without which people can't usually get HIV. Deleting the other, PCSK9, leads to extraordinarily low levels of "bad" cholesterol and a much reduced chance of heart disease.

The ideas were ambitious—closer to an enhancement than a cure, since they'd prevent diseases in the future rather than correcting a DNA defect in the embryo. But they also met one of the American report's criteria—that CRISPR not be used to modify children if there were "reasonable" alternatives.

In most cases where parents carry a risk gene for an inherited disease, like cystic fibrosis, they will pass it on to only half their children—so the genetic error can be weeded out during IVF procedures by testing embryos and picking those that didn't inherit the faulty gene. Many scientists believe gene-editing embryos will never be necessary, for that reason. Only CRISPR, though, can endow a child with a trait—such as HIV immunity—that the parents didn't have. That's why He considered his approach to be fair game.

He's students began working on what turned into tests on more than 300 human embryos, plus countless mouse and monkey cells. The work was enabled by the Western CRISPR industry that had grown up to distribute the technology's components and, often, collect profits. For instance, in 2016 He had e-mailed the Broad Institute, in Cambridge, Massachusetts, seeking a license to its important CRISPR patent and rights to use the gene-editing tool in human beings. Broad declined, since it had already sold rights for human therapeutics to its own spinout company, Editas Medicine. Broad did, however, sell He a license to market CRISPR's key ingredients. (An official with Broad noted that all its legal agreements prohibit "any human germline modification" and that making babies is "a clear and flagrant violation.")

The He team also reached out to the scientific community on issues of science and ethics. Kiran Musunuru, a gene-editing scientist at the Perelman School of Medicine in Pennsylvania, recalls getting peppered with questions from a graduate student in He's lab: "Do you think these are reasonable and feasible?" wondered Feifei Cheng about some mouse experiments. The Chinese scientists didn't exactly hide their purpose, either. In one e-mail, Cheng said, "I think our research will illustrate whether … genome editing in embryos, not in adult, is efficient and safe for the first time."

The focus on safety was the giveaway clue. Safe or not safe doesn't matter for a research embryo; they are all destroyed after a few days of growth in a laboratory. Safety would only matter if you intended to create a pregnancy.

He Jiankui even took part in meetings and ethics symposia meant to determine whether babies should be made. “He spoke, but he didn’t seem to listen,” says Stuart Newman, a biologist at New York Medical College, who attended a January 2017 workshop at Berkeley organized by Doudna, where He was among those present. Doudna had always worried about how CRISPR could be misused and told a gathering of journalists that August that the sudden announcement of a CRISPR baby could be a “worst-case scenario.” Now, He was headed back to China to do exactly that.

He was not dissuaded even by his own data. After he gene-zapped test embryos, his detailed DNA-sequencing studies of the outcome convinced him that the problem of unwanted, off-target edits was minimal and he would be able to see any that did occur. But he was not so easily able to control mosaicism—a result of the fact that CRISPR didn’t always edit every cell in the embryo, or ended up editing cells in different ways. His data on test embryos found that the majority were mosaics, according to a 2017 presentation.

He: CRISPR babies are here.

ASSOCIATED PRESS

GENE SUPERPOWER

Chinese scientists are working in an atmosphere of loose regulations and great ambitions. China’s government wants to lead the world in biotechnology. At an institute in Shanghai, I heard a speech by Zhou Qi, a prominent stem-cell scientist who was among a group that met last March in Beijing to map out a new government strategy for achieving that goal. “China,” he said in the speech, “will put biotechnology as a very high, very important priority.”

To achieve that, China has paid special attention to both gene editing and stem-cell research—the corner of biology dealing with the Promethean capacity of certain cells (including the fertilized egg) to form hearts, lungs, and any other body part. In October 2018, Zhou led a team that—through a complex series of steps involving stem cells, gene editing, and cloning—had shown that two male mice could have offspring together. And I heard him tick off a list of unpublished results that sounded scientifically important and, I thought, were also all likely to cause sensational headlines.

In the Chinese-language literature, I found scattered boasting and calls to move forward quickly. “In the area of human germline editing technology, we have already stepped to the forefront,” researcher Liu Jian-Qiao wrote a few months ago. Liu said that research should be “bounded” by international norms established in 2015, but that China should also influence those standards: “We should … strive for more of a right to have our voices heard, and for greater authority to take initiative in the area of clinical applications research.”

In China, there wasn’t the same reluctance as in the US to think about the technology’s benefits. The embryo-editing teams I interviewed were all clearly preparing the technology for eventual use in humans. Some of them, for instance, were attempting to locate cases where—in line with the US National Academy of Sciences’ criteria for using CRISPR—germline gene editing might be the only answer. One such scientist was Fan Yong, who like Huang is based in Guangzhou. “We are currently mainly selecting diseases that can only be cured by using embryonic gene editing treatments,” he wrote in an e-mail. One candidate group Fan was exploring is deaf men and women who marry, a common occurrence in a country as large as China. If both parents’ hearing loss has the same genetic cause, it can mean they can’t have a hearing child. Fan told me he thinks correcting deafness in embryos “is a natural choice for public health in China.”

Still, none of the Chinese scientists I spoke to said they thought a baby was coming anytime soon. They noted that under a 2003 government guideline, no IVF clinic was supposed to take a genetically modified embryo and start a pregnancy. "From the perspective of technology as well as how society would accept it, I don't think we're at that point yet," Huang told me when I visited with him. Maybe one day, he said, when the technology was more advanced.

TOO LATE

In Shenzhen, He wasn't waiting.

It appears that by about February 2018, He's team had transferred edited embryos into the uterus of a woman (who remains unidentified). They continued to monitor the pregnancy, taking blood draws and peering at the twins' genomes that way. It remains unclear what authorities—if any—in China signed off on the trial. He's own university now claims it knew nothing about the study, which was carried out quietly if not secretly.

He may have planned to make his big reveal of the CRISPR babies in November during the Second International Summit on Human Genome Editing in Hong Kong, a meeting whose purpose was to debate the prospect of making such babies, and where he was among some 70 scheduled speakers. "I suspect he was planning to pull a Steve Jobs–style 'one last thing' during his talk," says Musunuru, referring to the Apple founder's trick of saving the biggest news for last. It would be the ultimate fait accompli—a "bombshell" set off before the world. Instead, reports of He's undertaking leaked just before the meeting, and the scientist rushed to post a series of recorded statements to YouTube. The twins were named Lulu and Nana. "We hope you have mercy for them," He said. "I believe families need this technology."

Oversight? It's unclear if there was much. A daring cure? Not really. HIV can be treated or prevented with other, cheaper methods and still affects less than 0.1% of the population in China. As David Liu, a Harvard biologist, asked He in Hong Kong: "What is the unmet medical need?" The question cut to the quick—in medicine, risky interventions for healthy people are unacceptable. The embryos He chose to edit were normal.

"When I realized what had happened, I screamed—literally," says Musunuru, who has seen the genetic readouts on the embryos that had turned into the twin girls. There had been "a mess of different edits"—that is, cells were changed in different ways. The girls may prove to be made up of a mosaic of differently edited cells as well. "The first gene-edited baby was going to be a disturbing event, no matter what," he says. "The fact that it happened this way, with flawed embryos, by researchers who were either clueless about the problem or simply couldn't care less, made it 100 times worse."

The criticisms after He announced the births were unrelenting. "Beyond belief," said Feng Zhang, of the Broad Institute, another of CRISPR's co-inventors. Huang weighed in with a statement that what his counterpart had done was "against the law, regulation, and medical ethics of China."

Some scientists, it turns out, were in the know about He's work. One can only guess why they remained silent. But we know how the He affair ended in Hong Kong. George Daley, the dean of Harvard Medical School and the same person who implied a few years back that Huang wasn't right in the head, took the stage and, though he called He's work a "misstep," did not condemn it. Instead, Daley spoke in favor of using CRISPR in IVF clinics in the future, saying it was time to move past the question of "ethical permissibility" and on to the question of how to do it correctly.

In their final statement, summit leaders gave no mention to a criterion they had once agreed was paramount before moving into clinical applications: "broad societal consensus." There is no consensus yet about whether we should engineer human beings—and there may never be. But He's claim helped make the question moot. We already have.

It's unclear what will happen to He. His clinical trial was halted, and the government seems about equally likely to block any further babies as to endorse them. He left the Hong Kong conference early, saying he would "remain in China, my home country, and cooperate fully with all inquiries about my work."

Huang, meanwhile, went back to Guangzhou and is continuing his research. In our interview, which occurred before the announcement of the CRISPR babies, I had asked him whether he would do anything differently if he could go back in time. Would he put CRISPR in a human embryo? "I would do it again," he said. "The development of science and technology is unavoidable."

> **"The first gene-edited baby was going to be a disturbing event, no matter what. The fact that it happened this way, with flawed embryos, by researchers who were either clueless about the problem or simply couldn't care less, made it 100 times worse."**

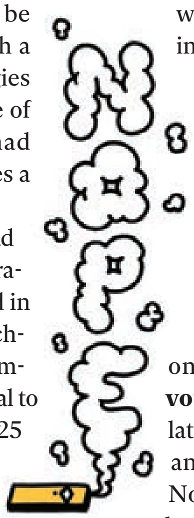
Antonio Regalado is a senior editor at MIT Technology Review.

The 10 worst technologies of the 21st century

No issue on the best ideas in tech would be complete without a list of the worst.

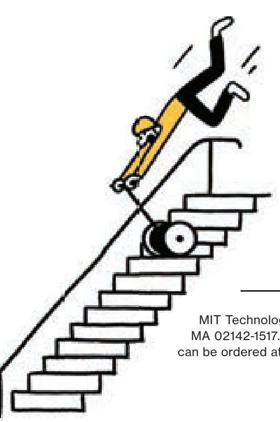
By the editors
Illustrations by Daniel Savage

You'd think it would be easy to come up with a list of bad technologies from the past couple of decades. But we had a hard time agreeing: What makes a "bad" technology?

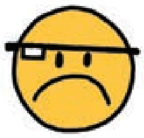


After all, technologies can be bad because they fail to achieve admirable aims, or because they succeed in wicked ones. The most useful technologies can also be the most harmful—think of cars, which are crucial to the modern world yet kill over 1.25 million people a year. And when well-intentioned technologies fail, is it because they are fundamentally flawed or just ahead of their time?

Take the **Segway**. Inventor Dean Kamen hyped it as a device that would transform cities and transportation. It turned out to be an expensive scooter that makes you look silly. Hoverboards were similarly all the rage until their batteries started exploding. But now (smaller) scooters and (safer) powered skateboards are increasingly popular.



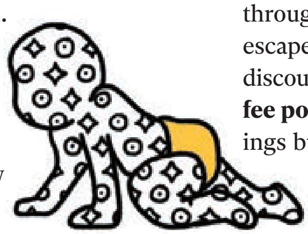
If **Google Glass** had been developed by a lesser company, we probably wouldn't pick on it so much. But Google should have known better. It made the wearer appear elitist and invasive. Then again, like Segways and hoverboards, this was a failed product, not a failed technology; augmented-reality glasses and heads-up displays are finding their public.



Some technologies are well-intentioned but solve no real problems and create new ones. Before **electronic voting**, automated tabulating of paper ballots left an auditable paper trail. Now elections are more vulnerable to hacking.

Some failures apply a technological fix to what is really a social or political problem. Take **One Laptop per Child**, which set out to solve inequality in education with a new gadget. But was it simply too early? Commercial laptops, tablets, and—above all—smartphones have since inundated the developing world.

Indiscriminate uses of technology worry us. Sometimes this is because regulations are flouted. Gene-editing techniques like CRISPR may one day cure all manner of diseases, but right now we don't know if CRISPR is safe to use in humans. That's why the **CRISPR babies** born in 2018 make our list.



Other times, it's because technology has outpaced regulation. **Data trafficking**, the sharing and remixing of people's data without their control or awareness, has contributed to the undermining of personal liberty and democracy itself.

Some technologies are just misapplied. So far **cryptocurrency** looks mainly like a way for a handful of speculators to get very rich while a lot of other people end up poorer. But the technology underlying it, blockchain, could yet be transformative in other areas.

Still, there are a few inventions we could agree have no redeeming features. Juul and other **e-cigarettes** are addicting a new generation to nicotine, through a loophole that allowed them to escape public health regulations meant to discourage cigarette smoking. **Plastic coffee pods** save half a minute in the mornings but produce tons of hard-to-recycle waste. And as for **selfie sticks** … need we say more?

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