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HACKING THE HUMAN OS

How Big Data Will Transform Medicine and Health

SPECIAL REPORT

IEEE

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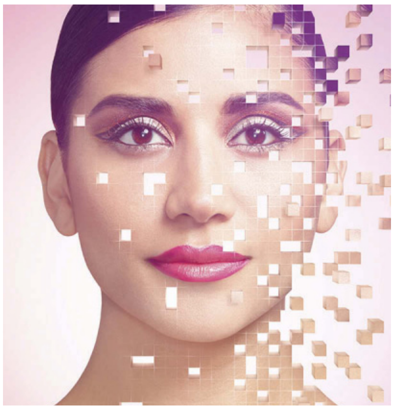
Hacking the Human OS

SPECIAL REPORT Medicine has always sought to understand the human body's operating system. Now, with biometric sensors and big-data analytics, we're learning how to fix the bugs **P. 23**



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The Institute

Available on 5 June 2015

NEXT WAVE OF WEARABLES This special issue of *The Institute* describes what's needed to make wearable fitness and health trackers more accurate, seamless, and better equipped to monitor vital signs—not to mention more enjoyable to use. This issue also explores some of the many career opportunities available for engineers in the life sciences.

MEET THE CANDIDATES We interviewed the 2016 IEEE president-elect candidates, Senior Member Karen Bartleson and Life Fellow Frederick "Fred" Mintzer, about why they volunteer for the organization and their goals for its future.

GUIDING INTERNET POLICY Learn about IEEE's new Internet Initiative, a platform dedicated to bringing together the technical community with policymakers to discuss Internet governance, cybersecurity, and privacy.

FROM LEFT: OMAR HAVANA/GETTY IMAGES; MIKE McGREGOR; EVAN ACKERMAN

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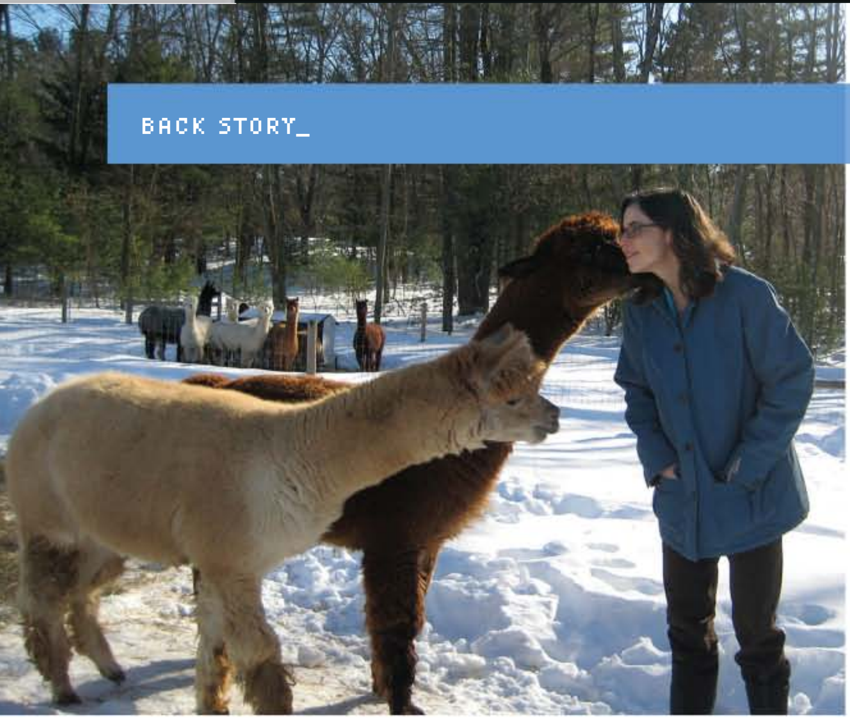

Tech Reporting in Muck Boots

USUALLY, WHEN *IEEE Spectrum*'s biomedical editor, Eliza Strickland, heads out into the field to report on cutting-edge technologies, she doesn't have to borrow a pair of muck boots. For her article in this issue about a remarkable couple on the forefront of the personalized medicine revolution, however, extreme measures were necessary.

John Halamka, chief information officer of Boston's Beth Israel Deaconess Medical Center, lives with his wife, Kathy, on a farm in Sherborn, Mass. The vegetarian duo nominally raise alpacas for wool and poultry for eggs, but really they do it for sheer joy. "Watching the chickens chase the fireflies at dusk makes every day a bit better," John has written on his "geek doctor" blog.

Strickland visited the farm in February to learn about John's pioneering work on query tools that mine hospitals' databases of electronic health records, finding medical wisdom in troves of big data. These tools became vital to the Halamkas when Kathy was diagnosed with breast cancer in 2011. After a long interview at the kitchen table, John announced that it was time for Strickland to meet the animals. He outfitted her with boots and a barn coat, and they headed outside into the snowy fields. "Remember," said John, "the alpacas are friendly, but they're not exactly huggable. We just hang with them." Strickland did her best to follow instructions.

John, who trained as an emergency-room physician before turning toward engineering, says his hands are those of a farmer now, not a doctor. Both of his skill sets are put to the test, though, for one of the trickier farm tasks: the biannual trimming of the alpacas' toenails. ■

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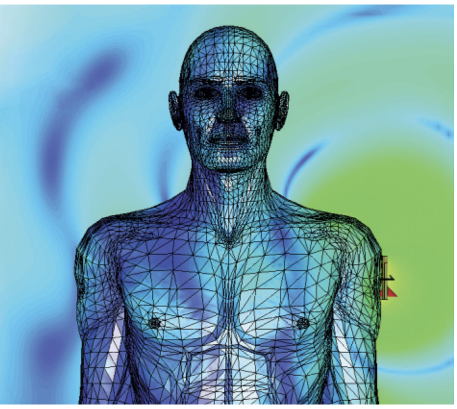

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Ariel Bleicher

Bleicher is a senior editor at *Nautilus*. In "100,000 People, 250 Biomarkers, and the Quest for Good Health" [p. 48], she writes about a new project that aims to track and also improve the health of ordinary Americans. "It's a tantalizing idea—being able to monitor your body so intensely that you know you're getting sick way before you actually feel sick," Bleicher says. "The billion-dollar question is: Could that knowledge help you avoid sickness altogether?"

David Brown

For "Computer Modelers vs. Ebola" [p. 54], freelance journalist Brown spent several days at the Virginia Bioinformatics Institute with the diverse team of computer scientists, biologists, and mathematicians who tried to predict the course of the West African Ebola outbreak. Brown himself combines several fields of expertise: He's a physician who signed on with *The Washington Post* in 1991 for what he thought would be a short stint as a medical reporter. "That stretched on for 22 years," he says.

Elie Dolgin

Dolgin, a journalist based in Somerville, Mass., observed scientists examining sewage in their quest to understand the health of entire cities, which he reports on in "Smart Sewers for Public Health" [p. 12]. "This microbial world around us and within us, we're discovering, is one of the most important mediators of health," Dolgin says. The job wasn't quite as dirty as he'd expected. "The sewage was surprisingly clear," he says. "I wouldn't drink it, but it wasn't as bad as I'd imagined."

Dave Levitan

Levitan is the science writer for FactCheck.org, where he investigates the false and misleading claims about science that U.S. politicians occasionally make. For this issue, he traveled to Iceland to interview Kári Stefánsson of Decode Genetics [p. 47], who would like to capture the DNA of Iceland's entire population. Although Stefánsson is a neurologist by training, he has the charisma of a successful politician, Levitan notes. "A big chunk of that population seemed to describe Stefánsson as a 'character'—affectionately, of course."

Emily Waltz

Waltz is a freelance journalist based in Nashville. In "The Quantified Olympian" [p. 36], she surveys some electronic aids that athletes are using to guard against injury and boost performance. "I've played tennis since I was 5, and by the time I was a senior on my high school team, the spine-bending motion of my serve had done a number on my lower back," says Waltz. "Keeping an eye on a kid's mechanics using wearable sensors might help coaches and parents prevent such injuries."

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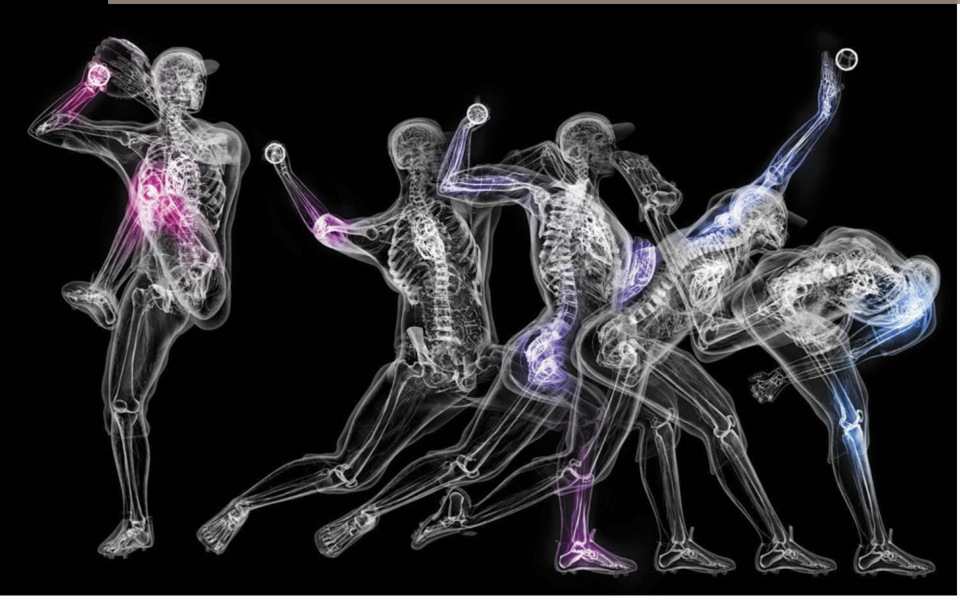


Homing In On Health Care's Sweet Spots

Sweeping changes are coming as we turn into medical information nodes, sending and receiving data about ourselves

IN HIS CLASSIC *The Sweet Spot in Time*, John Jerome detailed the pursuit of the athletic sweet spot, of excellent execution over time. How do superb athletes, or teams of athletes, achieve peak performance over and over again? To the study of the biomechanics of movement and the biochemical breakdown of glucose, we now add the study of big data.

Major league baseball, to give one sports example, has relied on algorithmic data crunching to create models of the best possible combinations of players and field positions for more than a decade. Now baseball geeks can get jobs in team systems development, building the proprietary databases and machine learning software that supply the ingredients for the team's secret playoff sauce.

Professional sports was among the first "people" industries to embrace big data. In this issue, we describe how medicine is now mining big data to cure illness and possibly prevent it. And, eventually, we may try to make our exquisite biology even better than it is upon our arrival on terra firma. What hubris!

Before big data becomes big data–a mass of unruly bits that need to be tamed by combinatorial brute force–it is little data, our own personal data. *New York Times* reporter Steve Lohr calls the trend toward working with aggregated personal data "data-ism," which he describes as "a point of view, or philosophy, about how decisions will be–and perhaps should be–made in the future."

The ability to collect large amounts of little data via wearables (and soon ear-mounted hearables and even implanted disappearables) fuels health care's "quantified self" movement, a term coined by Kevin Kelly and Gary Wolf in 2007. In 2013, a Pew Research Center study revealed that 69 percent of Americans were already tracking their diet, exercise, or a health indicator such as blood pressure, although only 21 percent were using technology to do so. Change is coming quickly: The consulting company IHS projects that more than 230 million wearable devices will be sold in 2019.

It's useful to remember that we are, in our unadulterated biological forms, awash in self-monitoring systems, such as proprioceptors and mechanoreceptors that track body position and sensory receptors that tell us what's going on in the world around us. In most cases we process this data effortlessly. Biometric devices make our internal monitoring systems transparent, so we can use the information that these systems are continually gathering to better effect.

Self-monitoring allows us to take an active role in maintaining and improving our health, to find our daily sweet spots. We don't have to wait for doctors to see us: We can see what to do ourselves, in real time.

That's the good news. But big data's transformation of medicine also comes with big challenges. Data ownership and privacy will be prime among them. Where do all these data reside, how are they collected, curated, retrieved? Once they leave your device or your doctor's office, where do they go and who gets to use them?

Even harder questions lie ahead. Clearly only a fraction of humanity will benefit from these early efforts. What happens to the rest? Will "all natural" human beings become the disabled among us? And how are we defining mental and physical excellence? Would Stephen Hawking have been a better physicist if his ALS had been repaired, or Beethoven a better musician with his hearing restored?

In baseball, when a pitcher is throwing well he's said to be throwing seeds; the hitter can't even see the ball coming. We'll need to step up our game as the seeds of big-data changes in medicine start flying at us, fast and furious. –SUSAN HASSLER

Special thanks to **Eliza Strickland**, the lead editor for this issue.

BRYAN CHRISTIE DESIGN

NEWS

4

NUMBER OF PEOPLE RESCUED WHEN MICROWAVE RADAR WAS USED TO DETECT THEIR HEARTBEATS AFTER THE NEPAL EARTHQUAKE

BULENT DORUK/ANADOLU AGENCY/GETTY IMAGES

CHEAP EARTHQUAKE-WARNING SYSTEMS

Crowdsourced networks of low-cost sensors and cellphones could have provided life-saving seconds in Nepal

While predicting earthquakes remains a dream, scientists have developed early-warning systems that give people precious seconds to run out of buildings or take cover. Such systems are in place in Japan and Mexico. The U.S. Geological Survey (USGS) is testing a system that gave a 5- to 10-second warning when a temblor hit California's Napa Valley in 2014. That kind of warning might have saved hundreds of lives when a 7.8-magnitude earthquake devastated Nepal on 25 April.

Earthquake-warning systems come at a high price, though, too high for countries like Nepal and others in quake-prone zones in South Asia, the Caribbean, and Central and South America. But researchers are now working on more affordable, crowdsourced warning systems based on low-cost sensors and cellphone electronics.

Today's alert systems deploy networks of hundreds of expensive, extremely sensitive seismic sensors that detect energy »

WARNING IN NEED: Emergency rescue workers carry a victim of the Dharahara Tower collapse in Kathmandu, Nepal. Engineers are developing more affordable earthquake warning systems.

waves, along with GPS sensors to detect permanent ground movement due to the motion of the geological fault that triggers the earthquake.

Battalgazi Yildirim, founder of Zizmos, based in Palo Alto, Calif., thinks he can get as good—or in some cases even better—earthquake data from a network of cheap sensor packages. These are made up of microelectromechanical accelerometers attached to inexpensive, off-the-shelf cellphone equipment that manages data gathering and communication. "The sensor packages used by the USGS cost about [US] $30,000 each," he says. "We're putting out sensors that cost $100 each to build."

The network should have virtually no installation or maintenance costs, because Yildirim plans to rely on the kindness of the crowd. Zizmos asks for volunteers to donate a tiny bit of interior wall space and a power outlet to host a sensor package, which is about the size of a deck of cards.

With a $150,000 research grant from the National Science Foundation, the company was to launch a trial this May, after this issue went to press, involving 268 sensors distributed in California. When a sensor detects a rumble, it will send information about the time of the event and the magnitude of the shaking to a cloud-based server; algorithms will check reports from neighboring sensors to determine whether the vibration was local—say, from a truck going by—or felt elsewhere. If the latter, the system will calculate a hypothetical epicenter for the earthquake, the original time of the event, and an estimated magnitude. For earthquakes with magnitudes greater than 4.0, it will issue an alert.

Benjamin Brooks, a geophysicist with the USGS, has a different crowdsourcing approach in mind. Why not tap into the GPS sensors in people's phones and navigation systems, he says. GPS-equipped cellphones are ubiquitous in developing countries, and such a crowdsourced system would offer early warning at practically no cost. "A country like Nepal, with high earthquake hazards and minimal resources, is where a crowdsourcing approach would be most effective," Brooks says.

In research presented in the journal *Science Advances* two weeks before the Nepal quake hit, Brooks and his colleagues tested the ability of consumer-grade GPS devices to detect earthquakes. They subjected a Google Nexus smartphone and a commercial GPS module to displacements ranging from 10 centimeters to 2 meters. Both GPS sensors picked up the smallest motion.

Next, the researchers performed simulations using data from a hypothetical magnitude-7 earthquake in northern California and from the real 2011 magnitude-9 earthquake that hit Tohoku-oki, Japan. They simulated smartphone responses based on census data around the earthquake epicenters and recorded a phone as triggered if it and its four nearest neighbors measured more than 5 cm of movement. If at least 100 phones were triggered, the system declared an earthquake.

It took fewer than 5,000 smartphones to detect the simulated California earthquake within 5 seconds, giving enough time to warn San Francisco and San Jose. For the Japan quake, which had an offshore epicenter, detection occurred at just over 80 seconds, too slow for the closest onshore towns but in enough time to issue a warning to Tokyo.

"Sadly, on the Wednesday before the Nepal earthquake I had a discussion with a Nepalese colleague about proposing precisely such an approach," Brooks says. "There would be challenges in terms of cellphone service in such a mountainous region, but we think it would be doable there eventually."
—PRACHI PATEL & TEKLA S. PERRY

OMAR HAVANA/GETTY IMAGES

GETTY IMAGES

FULL-HD VOICE IS NEARLY HERE

Combining codecs for voice and music will yield perfectly clear calls

HD Voice, the first major upgrade to telephone sound quality since the vacuum-tube era, has finally become widely available—just in time for a new generation of phone service called Full-HD Voice to take its place.

At the Mobile World Congress in Barcelona earlier this year, Fraunhofer IIS (Institute for Integrated Circuits) demonstrated a system based on a combination of powerful standard algorithms that can encode and decode in real time the full audio spectrum to 20 kilohertz in stereo. Switching to Full HD, which could be done in many devices as early as next year, would also mark the complete merging of voice into the mobile data stream, a goal long in the making.

Full-HD Voice converts speech into packets that can flow through the Internet along with data traffic, incorporating algorithms that can recover from packet loss, which turns today's Voice over Internet Protocol (VoIP) calls into choppy, unintelligible hash. The technology includes algorithms that encode music and other nonspeech audio, sounds that are typically mangled by codes optimized to squeeze many voice calls into narrow slices of the spectrum. Because Full-HD Voice carries the whole audio spectrum, calls sound as if everybody's in the same room; you can even hear soft background sounds, like the faint clatter of fingers on a keyboard. And the powerful coding-decoding (codec) software can run as a smartphone app.

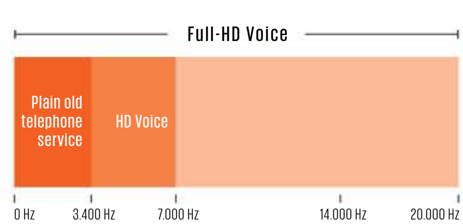
"We want to bring telephony into the 21st century," just as HD television has done for video, says H.P. Baumeister, director of Fraunhofer IIS's U.S. branch, in San Jose, Calif.

There's no doubt that voice telephony still has a foot in the 20th century. Modern landline phones have a frequency range of 300 to 3,400 hertz, a standard based on Bell Labs studies of the requirements for intelligible speech dating back to the 1920s. That range cuts off high frequencies needed to discriminate between consonants such as *f* and *s*, but it fit the limited bandwidth of old analog copper phone lines.

In 1988, the International Telecommunication Union approved the G.722 standard for HD Voice, which allows digital phone lines to carry 50 to 7,000 Hz. But it was little used because it would have required upgrading the landline phone network. The first three generations of cellular phones instead retained the 3,400-Hz narrowband landline audio, but they often sounded worse because of the way they compressed speech to squeeze more calls into the limited mobile spectrum. [See "Why Mobile Voice Quality Still Stinks—and How to Fix It," *IEEE Spectrum*, October 2014.]

The broader bandwidth of the Internet allowed Skype and some other VoIP services to carry 7,000-Hz HD Voice, but VoIP calls into the phone network have been limited to 3,400 Hz. Most 4G smartphones include dedicated circuits running algorithms to code and decode 7,000-Hz HD Voice, but they can connect at that rate only if both phones and every link between them can handle the signals. In practice, that means it works only between 4G phones on the same carrier.

Full HD will be able to bridge the audio gap regardless of the network or the device connected to it. The technological heart of Full-HD Voice is a standard called the Enhanced Voice Services (EVS) codec. Its speech compression algorithms are more complex and powerful »



SOURCE: FRAUNHOFER IIS

EASY LISTENING: Unlike earlier systems, Full-HD Voice will cover the whole range of human hearing.

NEWS

than those used for the decade-old HD Voice system, and it can squeeze stereo speech spanning the whole audible range into data rates as low as 9.6 kilobits per second. The codec also includes other algorithms developed to compress music.

The separate algorithms are vital because speech and music are compressed in different ways. Voice compression typically relies on algorithms called code-excited linear prediction (CELP), which is built on the physics underlying the human vocal system. CELP can reduce the data rate of voice signals by about a factor of 10. "That coding did a good job on speech but was terrible on everything else," says Richard Stern, an electrical and computer engineering professor at Carnegie Mellon University, in Pittsburgh.

Music-compression algorithms, such as the MP3 and AAC codecs used for streaming audio, are optimized for human auditory perception. For example, the algorithms don't bother to accurately reproduce the soft components of sounds likely to be masked by louder sounds at other frequencies and times. That method can represent a wider range of sound, but it requires more bits per second than a speech-based codec, Stern says.

The new EVS codec is a hybrid, containing algorithms for both voice and music, and it switches between them as needed. The new voice algorithms are substantially more complex than those of the decade-old 7,000-Hz codec. Rather than being developed around characteristics of specific languages, as earlier codecs were, these are nearly language independent. The music part is the latest low-latency version of the AAC algorithm, developed for real-time streamed communications. Called AAC-ELDv2, it delivers CD-quality stereo sound in a stream of only 32 kb/s by transmitting one stereo channel plus a lower-data-rate signal that represents the difference between that channel and the other stereo channel.

An important feature of the combined package, says Baumeister, is that EVS is the first codec designed to compensate for packet loss. Such losses degrade voice quality and are inevitable on IP networks such as 4G LTE.

To verify performance of the codec and its loss tolerance, Fraunhofer IIS and 11 partners—including Ericsson, Huawei, Qualcomm, and Samsung—spent millions of euros on human listening tests. Full-HD Voice quality was possible even at data rates as low as 9.6 kb/s.

The processing power of modern smartphone chips is a key enabler for the new codecs. They can be implemented in digital signal processing chips as the 7,000-Hz codecs in 4G smartphones are, or as apps running on a smartphone's applications processor. The EVS codec "is not complex compared to the apps in a smartphone," says Baumeister.

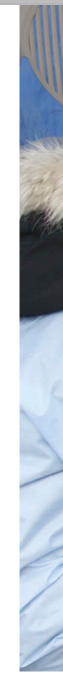
Because Full-HD Voice can tolerate packet losses, it could feed compressed data directly into the Internet data stream for routing directly to other equipped devices, like a Skype-to-Skype call between computers or smartphones. Fraunhofer's Mobile World demonstration did that using apps on Google Nexus 5 phones. With no need for network upgrades, Baumeister says, "you could conceptually roll out service this year, but next year is more realistic."

You can hear samples at http://www.full-hd-voice.com, but be sure to use good headphones in a quiet environment. Stern compares the difference to the shift from standard resolution to HD television. "It's going to be subtle, not a huge difference in intelligibility, but it will sound better and more natural, like a high-quality speaker system," he says.

—JEFF HECHT

SMART SEWERS FOR PUBLIC HEALTH

With robotic samplers, public-health officials will study cities' microbiomes



Newsha Ghaeli reached down an open manhole one morning in April and grabbed a hose dangling in the rushing streams of the sewer below. As she pulled up the hose, she spotted a wad of toilet paper clinging to its end and recoiled in disgust, accidentally splashing a few drops of dirty water on strands of exposed hair sticking out from her face mask. A Cambridge, Mass., sanitation worker offered comfort: "A little caca won't hurt you," he said.

Ghaeli is an architect and research fellow at MIT who recently helped coordinate a 24-hour effort to collect water samples from the sewer beneath an East Cambridge neighborhood. Every hour, the team pulled up half a liter of precious sludge. Ghaeli and her colleagues were doing the groundwork for an ambitious project that aims to understand the well-being of a city by tracking its residents' biological and chemical waste. Eventually, with robotic samplers placed below the streets, Cambridge may have a "smart sewer" that will let public-health officials study the city's collective microbiome—the communities of microorganisms that live in humans' guts.

"The idea is to look at patterns of sewage relative to how we live our daily lives," says Yaniv Jacob Turgeman, who until recently was the research director of the project. "We want this to be something that has actionable insights that enable public health in a meaningful way."

The project—dubbed Underworlds and supported by a US $4 million grant through the Kuwait-MIT Center for Natural Resources and the Environment—is one of a few with that goal, and it has been embraced by the city that the research team calls home. "If you get information closer to real time, you can rally resources to try to address a problem before it becomes a much bigger problem," says Sam Lipson, director of environmental health for Cambridge. "Those kinds of metrics are generally not available in public health."

Until recently, this type of "sewage epidemiology" was used mostly to monitor population-level trends in illicit drug use. In Europe, for example, a recent study of sewage from 42 cities throughout the continent revealed that cocaine and ecstasy use was greatest in large metropolises on weekends, whereas cannabis and methamphetamine use was

THE QUANTIFIED SEWER: Scientists sample sewage in Cambridge, Mass., to prepare for a large experiment that will seek to track the city's health by examining its waste.

ELIE DOLGIN

more evenly distributed throughout the week in towns of all sizes.

The MIT team will also test for drugs–both illicit and pharmaceutical–but it plans to go much further, albeit in a research capacity. (Lipson stresses that a community review process would need to be completed before any comprehensive monitoring program commences in Cambridge.) Led by Eric Alm, a computational microbiologist, and Carlo Ratti, an architect and engineer, the Underworlders will screen for viruses, such as influenza and norovirus, to detect incipient outbreaks in Cambridge. They will sequence the DNA of bacteria to identify food-borne pathogens. And they will search for biochemical indicators of various aspects of human health and disease.

"The MIT project is extremely ambitious and pioneering," says Christian Daughton, a chemist with the U.S. Environmental Protection Agency who spearheaded the idea of using sewage to track community health. "If this project proves successful in demonstrating some sort of proof of principle, it could represent a significant, seminal advancement in the prospects for quickly and inexpensively monitoring public health in real time."

That next level will be far more automated. Ratti and his team at the MIT SENSEable City Laboratory are currently designing manhole-width, 30-centimeter-tall robots that will be suspended on cables to allow them to move up and down vertically in the sewer. Using a custom-made smartphone app and a Bluetooth connection, the researchers will be able to control the robots remotely to collect samples and feed data into a detailed sewage sampling information system. The robots will serve mostly as collection vehicles, although the researchers hope to embed sensors to measure temperature, flow, and other parameters.

The plan is to start testing the robots in the sewers in the coming months as the researchers ramp up to 10 sites throughout Cambridge. In this way, they hope to gain a sense of the geographic diversity of sewage signals across the city. Later this year, they will also begin to set up a similar platform in Kuwait, a country that's almost 1,000 times the size of Cambridge. "The scale of what they're trying to do is impressive," says Ryan Newton, a microbial ecologist at the University of Wisconsin-Milwaukee who has worked with wastewater samples. "They should be able to get a really, really good handle on the variability in that population."

More than one-third of Kuwaiti children are overweight or obese. With enough long-term data from Kuwait, sewage analysis could theoretically reveal whether public health campaigns, such as a recent effort to curb the amount of sodium in bread, are having an impact on people's metabolic well-being.

Similar efforts are gearing up around the world. New York University biologist Jane Carlton will report at the Microbes in the City meeting this month that she and her colleagues are halfway through a two-year project to characterize bacteria and other single-celled organisms as well as viruses living in raw sewage flowing though New York City. Carlton is also in discussions about establishing a comparable sewer sampling initiative in Shanghai.

Meanwhile, a team from the Argonne National Laboratory, in Illinois, has begun a seven-year project to test for metabolites and microbial life from the sewer overflow pipes and rivers of Chicago. As in the Underworlds project, much of the data collection remains manual for now. But Jack Gilbert, a microbial ecologist who is leading the Chicago initiative, is working on a battery-powered sensor that runs DNA amplification reactions to search for any of 385 different organisms in a single sample of wastewater. The microfluidic device is currently housed in a box about the size of a suitcase and transmits data via Bluetooth.

"We hope to have these sensors in-line from the sewage water treatment plants," says Gilbert. "The technology is still in a prototype form, but theoretically the microbiome and virulence factors associated with any potential threats could be automatically detected and relayed to a central system."

The possibilities are near endless, says Underworlds' Alm. The challenge is to determine what's feasible. "There are so many things you can do with the platform," he says. "Let's build it and then see what works." –ELIE DOLGIN

NEWS

NEWS

GIVING SUPERCOMPUTERS A SECOND WIND

Laser links help old computers learn new tricks

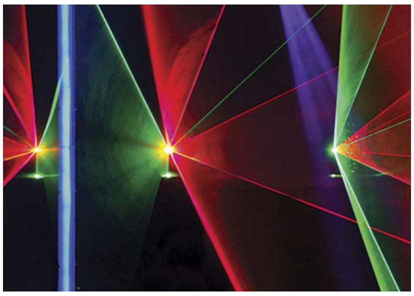
The speed of high-performance computing has soared from around 100 gigaflops in 1993 to over 50 petaflops today and is on course to hit the long-sought exascale (10^{18} floating-point operations per second) mark in the 2020s. Yet this remarkable supercomputing progress can be something of a super nightmare for the institutes and government agencies asked to invest the hundreds of millions, even billions of dollars that leading systems can cost.

"We are achieving a 1,000[-fold] improvement over 10 years, so after just 5 years a conventional supercomputer is no longer able to perform (at the necessary standard) and has to be trashed," says Michihiro Koibuchi, a systems architect at Japan's National Institute of Informatics, in Tokyo. Koibuchi and his colleagues think they have a solution that will let users get more out of older machines: free-space optics, lasers that link supercomputer nodes through the air.

Typically, the thousands of processing nodes that make up a high-end supercomputer are clustered into several popular network topologies depending on the computer's primary use. The topologies are implemented as cable-connected switches that link a select group of server-stuffed cabinets. With multiple users running different jobs at the same time, mapping a program's communications needs to the most suitable topology for a particular job is essential for efficient processing. But such mapping becomes problematic when the same system must serve very different types of applications at the same time.

"Day by day, fragmentation occurs as tasks end at different times and others are added, causing mapping to break down," says Koibuchi. Consequently, some applications end up performing inefficiently—for instance, when their data is forced to hop between a number of switches, or when an ordered parallel application is forced to adapt to a random topology used for irregular applications.

Koibuchi and his colleagues from several universities believe that free-space optics (FSO) can mitigate this breakdown and improve performance and resource use. FSO uses laser light to transmit data through the air from one terminal to another in its line of sight. With its wide, gigabit-scale bandwidth, it is used outdoors in interbuilding links and in aerospace and satellite communications. So handling the 40-gigabit-per-second transfer rates of high-performance computers indoors shouldn't be a problem.



"Rather than relying on a few fixed topologies, we propose using FSO terminals mounted on the cabinets to provide line-of-sight communications between almost any two cabinets," says Koibuchi. "Network topologies can then be reconfigured dynamically. This will help applications better maintain their topologies, reduce fragmentation and latency, and also cut the amount of cable used."

The idea gets support from Erik D'Hollander, a parallel computing expert at Ghent University, in Belgium. "Because FSO terminals can be readily adjusted for any type of topology, they have a huge potential to replace the data-communication fixed backbone between... supercomputer cabinets," he says.

FSO terminals suitable for supercomputer use are not yet available, however, so Koibuchi and his colleagues simulated several terminal layouts in software. What they found was a reduction in latency of up to 9 percent and a 36 percent reduction in fiber-optic cable length. That's a significant savings, considering that a system might have thousands of kilometers of cables and they are discarded when machines become obsolete.

To confirm these results physically, the researchers constructed four small prototype bidirectional FSO terminals from off-the-shelf components. These included optical transceivers rated at both 10 and 40 Gb/s, commodity infrared lasers, and collimator lenses used to direct the beam, as well as motors and gears to aim the terminals in any direction with a margin of error of just 0.003 degrees at 40 meters. At this distance, the tests confirmed the simulation results and achieved a data rate of 38 Gb/s.

Despite the tests' success, Koibuchi admits that commercializing the technology is not likely to happen anytime soon. "There is only one real hurdle left to overcome, but it's severe. At present there are no mass-produced high-bandwidth FSO terminals."

D'Hollander, too, sees the economics of FSO as a problem. "I'm less optimistic about the cost effectiveness of FSO terminals employing accurate steering and tracking equipment," he says. "Perhaps fixed FSO terminals without a steering mechanism would be a viable alternative."

Koibuchi says his team is studying the high-bandwidth FSO problem with NEC Green Platforms Research Laboratories, a unit of the Japanese maker of electronics and supercomputers. —JOHN BOYD

ISTOCKPHOTO

RESOURCES

PHOTOGRAPH BY Mike McGregor

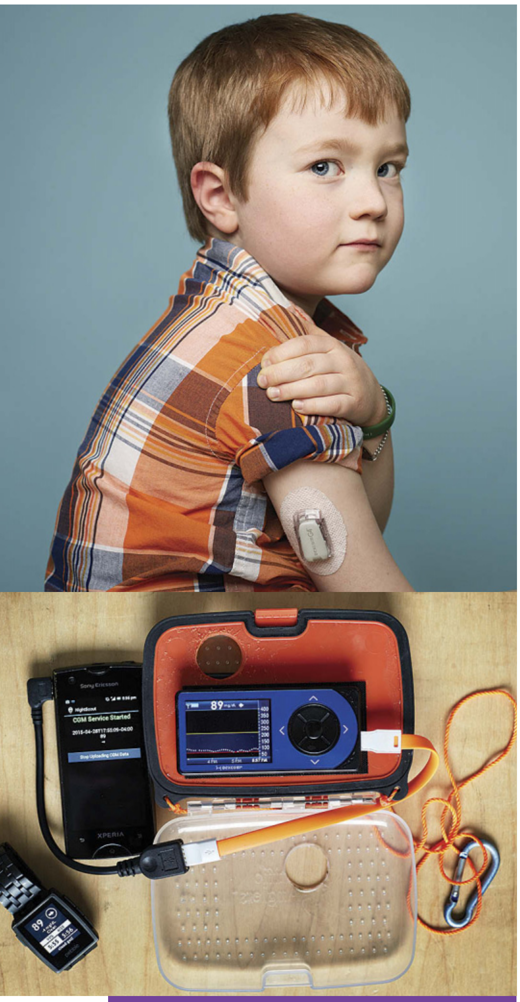
78,000

THE APPROXIMATE NUMBER OF CHILDREN DIAGNOSED ANNUALLY WORLDWIDE WITH TYPE 1 DIABETES

DIY DIABETES REMOTE MONITORING

CONNECTING A SMART WATCH TO A GLUCOSE SENSOR LETS PARENTS KEEP TABS ON DIABETIC CHILDREN

My son, Evan, was diagnosed with type 1 diabetes in August 2012. Type 1 diabetes is an autoimmune disease that attacks the pancreas and prevents insulin production. The body needs insulin to transport glucose from the blood to the cells. Synthetic insulin is used to manage type 1 diabetes, but it doesn't work as quickly as human insulin. Determining the right dose of insulin for a given meal's carbohydrate content becomes an all-consuming balancing act. Too little insulin and blood sugar skyrockets, causing potentially life-threatening complications. Too much insulin and blood sugar plunges to dangerous levels.



PEACE OF MIND: Evan wears a blood-sugar sensor and transmitter [top]. A box contains the receiver and a smartphone, and a Pebble watch lets his parents monitor his sugar levels.

The shock of the diagnosis continued to set in over the next few months, as my wife, Laura, and I attempted to figure out how to keep a 4-year-old alive and happy. Eight to 12 finger-prick checks to measure blood glucose and 4 to 8 shots of insulin a day—these became the course of our days and nights. It was the most painful and dark period in my life, and we needed to find a better solution. So began a technological journey that allowed us to improve Evan's quality of life—and ultimately the lives of many others.

I was soon drawn to continuous glucose monitors (CGMs). These report blood glucose levels every 5 minutes, thanks to a small radio transmitter attached to a fine sensor wire that runs under the skin (the wire is replaced weekly, the transmitter every six months). Finger checks can't give you the information that a CGM can, such as the rate of change of glucose levels. This data could be vital, not only to Evan's immediate care but also his long-term health.

We purchased a Dexcom G4 CGM in February 2013 and immediately loved it. (The receiver costs US $400, and it's another $400 for each transmitter. Sensor wires cost $99.) We were no longer flying blind between finger checks. We could merge the data from the G4 with reams of nutrition data we had been collecting and thus fine-tune Evan's insulin dosing.

But dropping Evan off at day care triggered a wave of panic: We were once again in the dark. I wanted us—Laura, the school nurse, and me—to be able to see his glucose level at any moment and get alerts when it was headed out of range.

At the time, Dexcom didn't provide remote access, but I knew that the Dexcom G4 receiver could furnish glucose data via its USB port. Dexcom's own Windows software was pulling data in this way, and fortunately, Dexcom supplied an API (application programming interface) library as part of its software installation. It took about 3 hours to code a C# program that polled the receiver and uploaded the data to a Google spreadsheet. We sent Evan to day care with a small laptop equipped with the receiver. While he was in his classroom, we could see his blood glucose via either a simple website or an iOS app I threw together. It was life changing, as it allowed Evan some freedom from the typical type 1 diabetes regimen at day care. Still, when Evan went out for recess or long walks, putting him out of range of the laptop's receiver, we were blind again. Thus began my work on a truly ambulatory solution, based on a smartphone rather than a laptop.

My family primarily uses iOS devices, but power limitations and closed frameworks made hooking up the receiver to an iPhone far more difficult than to an Android phone. I got a Motorola Droid Razr M phone, and once I had the basic USB enumeration down—so my phone could "see" the receiver when it was plugged in—I started decoding the G4's communication protocol. Using the same C# program as before, I ran commands and captured the USB traffic as it flowed between my computer and the receiver. With this data, I wrote an Android app to extract glucose data and upload it to our Google spreadsheet via the cellular network. In my excitement, I tweeted my discovery. What happened next was incredible.

Another "diabetes dad," Lane Desborough, contacted me. He wanted to build a similar system for his son. I shared my C# program with him and continued to refine the Android app over the summer, in preparation for Evan's return to school. Lane created Nightscout, a Web app with predictive alerts. These alerts are based on glucose levels uploaded to a database built using the open-source MongoDB platform. Lane transformed my system into a tool that anyone could use.

While Dexcom has subsequently released Share, a proprietary remote-monitoring system, it works only with iOS devices. By having reverse engineered the G4's communication protocol and created an open online database system, we can access the data on a wider range of equipment. For example, I picked up a Pebble smartwatch the first day they were available at retailers, and within a few hours, I had written software that lets me see Evan's glucose level at a glance.

Lane and I (along with Ross Naylor) continued to collaborate, and in early 2014, we made the C# uploader, Android app, Pebble watch, and Nightscout code open source. Subsequently, better software engineers than I have improved the code and made it easier to use; a Facebook group for Nightscout, set up by Jason Adams, now has nearly 12,000 members, and our code made the semifinal round for the 2014 Hackaday Prize.

While remote monitoring may seem invasive, it is in fact liberating. Evan can play more, learn more, and simply do more, because his life is far less disrupted by the demands of diabetes. We can mitigate most hyper- and hypoglycemic events without interrupting his day. I am proud to have taken back some of what we lost that day in August 2012 and blessed to know that my little boy's diabetes has helped so many others. —**JOHN COSTIK**

PHOTOGRAPHS BY **Mike McGregor**

RESOURCES_REVIEW

A MAN AND HIS MOUSE

A MUSICAL RE-CREATES THE DEMO THAT FORESHADOWED MODERN COMPUTING

HIGH-TECH THEATER: Mikel Rouse [right] re-creates Douglas Engelbart's famous introduction of the computer mouse in 1968.

VALERIE OLIVEIRO

In 1968, at the Fall Joint Computer Conference in San Francisco, Douglas Engelbart blew an audience away by showcasing a set of computing technologies then under development at the Stanford Research Institute (now SRI International) in Menlo Park, Calif. His demonstration was the first time the wider computing community had seen a mouse, word processing, dynamic links, shared-screen collaboration, and many other elements of what is now considered modern computing.

This April, in Stanford University's Bing Conference Hall, Stanford Live presented the world premiere of *The Demo*, a multimedia theatrical performance. *The Demo* intersperses video of Engelbart's original demo with a variety of other videos, still images, abstract lighting effects, live and recorded music, a chorus of half a dozen people, and actors portraying Engelbart and Bill English. (English managed the operations behind the scenes during Engelbart's original demo.)

But while a crowd of longtime Silicon Valley innovators was happy to have an occasion to gather together and honor a pioneering moment, this time the show left the audience less than wowed. In fact, the real-life English, who was a guest of honor for opening night, got the most enthusiastic applause of the evening.

It started out strong—with a video of Engelbart on a central screen and Mikel Rouse (who cowrote the show with Ben Neill) playing the role of Engelbart, lip-synching and mimicking Engelbart's hand and body motions. A driving techno beat joined in, giving an energy to the video beyond Engelbart's calm, steady delivery. But the music, with lyrics based on lines of computer code and phrases that appeared onscreen in the original demo (like "word word word word word," "hardware design hardware design," and "apples bananas carrots soup") soon became repetitive, and the constantly changing images and light patterns that were at first fascinating eventually became exhausting.

As one audience member put it during a postshow talkback, it was "long, really long." And I had to agree. In fact, my companion felt she'd gotten the gist of it by intermission and skipped the second half.

The length, Neill says, was an intentional attempt to replicate the original 100-minute demo; at 90 minutes, this performance was actually a little shorter. The steady chanting of a choir of voices—some live, some prerecorded—was intended to emphasize Engelbart's somewhat hypnotic delivery, a dreamy quality that Neill says attracted him to the video of the original presentation. He had also found it fascinating that Engelbart's demo was very much a performance and, perhaps, the first computer event to be so theatrical.

Neill explains that the intent of this piece of theater was not to give a narrative history of Engelbart's work—although it does bring in chunks of text and images from his life before the demo and the progress of technology after it. Instead, his aim was to echo the original demo by demonstrating an advanced system of networked technology.

And in that aspect, it was a success. The computer music, the strange "mutantrumpet"—an electrified combination of three trumpets and a trombone—the light shows, and the video projections on screens covering the walls and ceiling of the hall were perfectly synced with the live performers. Rouse's fingers flying on a chorded keypad, an exact replica of the one Engelbart used but here configured as a musical instrument digital interface, or MIDI, was the most fascinating part of the live performance; for a long time I thought he was simply keeping time with the music, but I was awed when I figured out that he was actually controlling many of the effects.

The piece was commissioned and developed by the Krannert Center for the Performing Arts and the eDream Institute, both at the University of Illinois at Urbana-Champaign, and it was developed during a number of residencies and workshops. The creators admitted that it was very much a work in progress, so it's likely to evolve before it comes to the stage again. **—TEKLA S. PERRY**

RESOURCES_TOOLS

BABY BY THE NUMBERS

KEEP TABS ON YOUR NEWBORN WITH A SMART ANKLE BRACELET

Wearable technology is currently primarily associated with two product categories—fitness trackers and smart watches. But wearables are beginning to show their potential in other areas as well. Ultimately, they are likely to enter into many facets of our daily existence. This article is the first in a series that will look at exemplars of wearables targeted at different stages of our lives.

We start at the beginning: infancy. Babies born this year could conceivably spend their entire lifetimes wearing an array of wireless sensors on their bodies, the minutiae of their daily lives measured, recorded, and analyzed. And the Sproutling baby monitor could be the first in that long line of devices.

As new fathers, Chris Bruce and Mathew Spolin each had that moment of anxiety common to many parents: standing at the door of the nursery, worrying if the baby was breathing and wondering whether to go inside and check, just in case. In Bruce and Spolin's case it helped inspire the founding of their San Francisco startup, Sproutling, and its eponymous product. In development for two years, Sproutling's US $299 baby wearable was unveiled last August. (Spolin left the company this April.) A band worn on the ankle and encapsulated in medical-grade silicone, the wearable uses an optical heart-rate sensor to monitor the baby's pulse, shining a light onto the skin and measuring the wavelength of returning light. A contactless sensor gauges the baby's temperature. An accelerometer tracks the baby's position and motion and can alert parents if the baby rolls over.

DA DA DATA: The Sproutling baby monitor measures heart rate, temperature, and movement. The monitor's docking station can recharge it wirelessly.

A base station doubles as a wireless charger, using magnetic resonance (the Alliance for Wireless Power's Rezence wireless charging standard), to provide enough power to run the band for one to two days at a time. The base station is also equipped with additional sensors that audit the room's temperature, humidity, light, and noise levels. Together, the wearable and base station gather up to 16 measurements a second, which are processed and used to advise the parent, who may be wondering: Is it too noisy? Has the temperature risen, making it uncomfortable for the baby?

Unlike with many fitness wearables, the actual numbers—how many decibels of noise, the baby's temperature, and so on—are not displayed or charted for parents (although a ring of light on the base station does pulse at the rate of the baby's heartbeat, as does an animated heart on the smartphone app). Instead, Sproutling's algorithms convert the data into alerts for the parents only as needed, sending a push notification on a smartphone, say, if the baby's temperature has suddenly spiked. "It's not designed to give you graphs and numbers," Spolin says. "It's really to let you know when things are okay or when you should check on your child."

Taking into account factors such as how much the baby slept earlier in the day, as well as the baby's age and historical temperament, Sproutling's machine learning algorithms can also predict how long the baby should sleep and when the baby might wake up. How accurate its predictions are is yet to be proved; Sproutling won't start shipping until late July or August. "The more and more it's used, and the more we learn about your child, the better it gets over time," Bruce says. "We want to help parents get that sixth sense of what's going on, to quantify patterns that parents can't do themselves."

The overarching objective is to reduce parental anxiety. "I'm building the stuff I wanted as a parent," says Bruce, whose children are now 4 and 6. "We were looking at that antiquated baby monitor and trying to see: 'Is she breathing? Did she roll over?' Now we can tell you that yes, the baby's heart is beating, and you can go to sleep." **—ELLEN LEE**

SPROUTLING

RESOURCES_CAREERS

KIRA RADINSKY
USING MACHINE INTELLIGENCE AND DATA MINING, THIS ENTREPRENEUR PREDICTS THE FUTURE

KIRA RADINSKY

KIRA RADINSKY IS A RISING STAR IN PREDICTIVE analytics. She combines the use of artificial intelligence and online data mining to predict likely futures for individuals, societies, and businesses. Radinsky made headlines two years ago for developing a series of algorithms that dissect words and phrases in traditional and social media, Web activity, and search trends to warn of possible disasters, geopolitical events, and disease outbreaks. Her system predicted Cuba's first cholera epidemic in decades and early Arab Spring riots. ● The algorithm—which grew out of Radinsky's Ph.D. work at Technion–Israel Institute of Technology, in Haifa—looks for clues and historical patterns inferred from online behavior and news articles. "During an event, people search [for related topics] much more than usual," she says. "The system looks for other times we saw a spike in that same topic and analyzes what was going on in the places that had this same spike."

With the 2012 Cuba cholera outbreak, for example, the system "learned," by perusing news items, that cholera outbreaks occurred after droughts in Angola in 2006 and large storms in Africa in 2007. The algorithm also noted other factors, such as location, water coverage, population density, and economy. When Cuba presented similar conditions, the system warned of an outbreak, and a few weeks later, cholera was reported.

Radinsky has parlayed her research into a 3-year-old startup, SalesPredict, with 20 people on staff and offices near Tel Aviv and in San Francisco. SalesPredict focuses on helping businesses, including several Fortune 100 companies, find new opportunities for sales or retain existing customers and clients. The company has raised US $4 million from venture funding and has been doubling its revenue every quarter—except the first quarter of 2015, when it tripled.

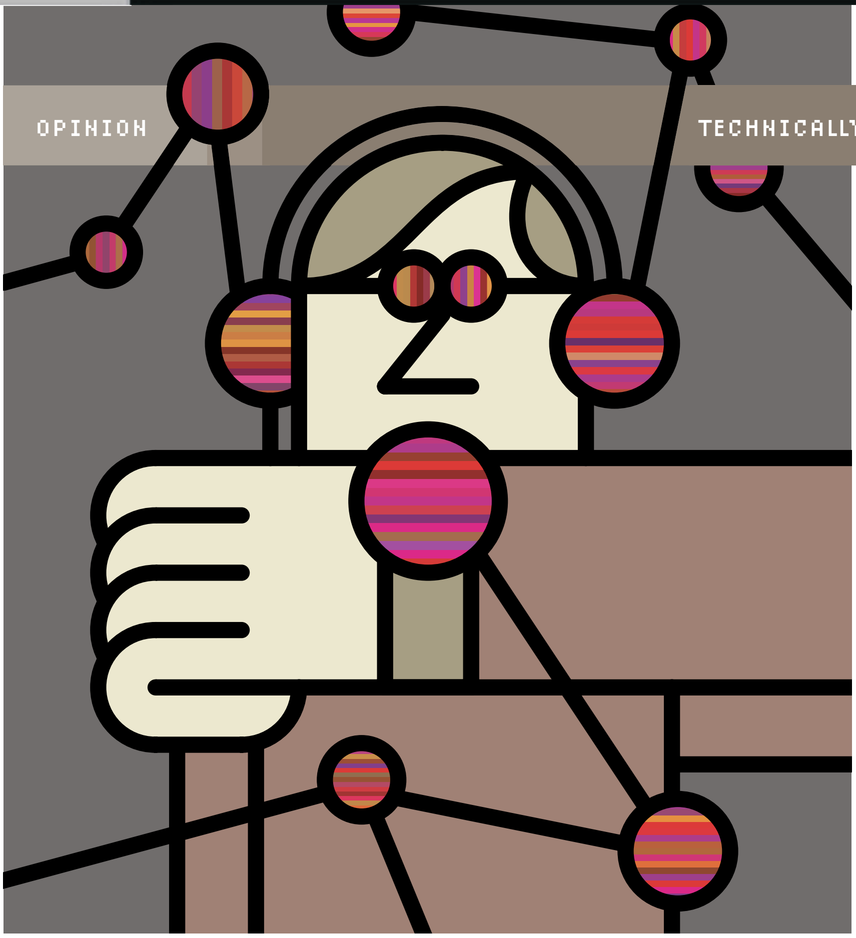
"It's big data meets game theory," Radinsky says. "There was so much data at each company about their historical sales, but very few actions were taken to scientifically analyze it."

As a youth, Radinsky wanted to be a scientist. But the summer before high school, she botched a research project at a science camp. "It was biology and computers together. I was in charge of feeding the cells. I was not good at that, and I killed those cells by mistake. After that, they had me process the data instead—and it turned out to be something I enjoyed."

Radinsky enrolled at Technion in 2002 at just 15, earning extra cash by programming websites on the side. At 18, she did her mandatory Israel Defense Forces duty as a computer scientist in its intelligence division. She completed bachelor's and master's degrees in computer science in 2009, and a Ph.D. in machine learning and artificial intelligence in 2012, at 26.

Since graduating, she's served full-time as SalesPredict's chief technical officer. "Getting into predictive analytics usually requires master's and Ph.D. degrees in data mining and machine learning. Data scientists have strong math and statistical backgrounds. It's a very academically oriented field," she says. "For my company, it helps if you've worked for a company like Google or have strong engineering skills on how to scale machine learning systems."

Radinsky believes in developing this technology to benefit not only business but also society. "Mining patterns in data can lead humanity to a new era of faster scientific discoveries. We are working on several pro bono activities in the medical domain to apply learning machine algorithms to predict cancers and find the driving causes of diseases." **—SUSAN KARLIN**



EVER CLOSER TO THE MACHINE

We do not ride on the railroad; it rides upon us.
—*Henry David Thoreau,* Walden

THOREAU'S WARNING ABOUT the effects of technology seems more relevant than ever in this era of boisterous technological innovation—an era that seems particularly determined to bring computers and other "smart" devices ever closer to the people using them, and to generate new words and phrases that reflect this increased proximity. • The starting point here is the **wearable**, a computer designed to be worn, either as an item of clothing or as an accessory. The most promising wearable of recent years was Google Glass, which popularized the **smart glasses** (or **eyeables**) industry and brought **glasseslike** devices into the mainstream. (An earlier invention was **memory glasses**, which included a tiny video camera attached to a wearable that used the video feed to recognize people as they came into view.) Glass failed mostly because it became too easy to crack jokes about users being **glassed out** (that is, having a vacant look and an obliviousness to their surroundings) and to see Glass as an example of **jerktech**, technology that encourages antisocial behavior (such as surreptitiously photographing or recording people). • If wearing a computer on your face was a step too far for most people, wearing one on your wrist seems more reasonable, hence the generally positive reception accorded **smart watches** (particularly the Apple Watch), **smart bracelets** (such as the Microsoft Band), and **smart trackers** (such as the Fitbit **fitness tracker**, the Jawbone UP 24 **activity tracker**, and the Trax **GPS tracker**). There are also fitness and GPS trackers that attach to bicycles, turning the devices into **rideables**. In fact, we seem to have a fascination for tracking our every move, a mania that has now extended into **family wearables**, particularly the ultimate gadget for helicopter parents: the **baby wearable**.

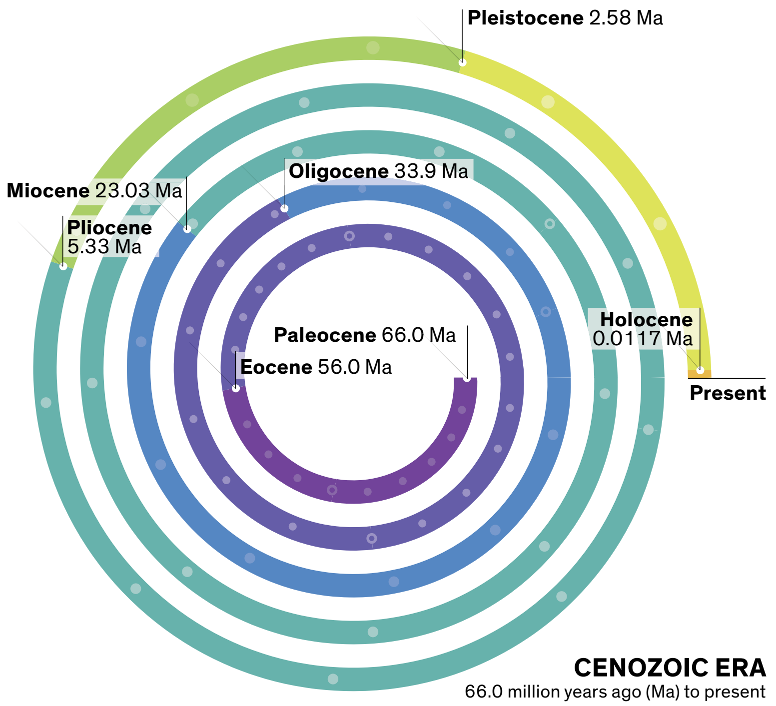
We've all gotten used to slipping earbuds into place, so would it be such a leap to upgrade them to something smarter? Enter the **hearable**, an in-ear computer that's also known as an **earable** or a **smart ear device**. Not intimate enough for you? Then how about the **embeddable**, a device inserted under the skin, or an **ingestible**, a device that you swallow (such as a **smart pill** that reports how the body is reacting to its medication). I should also mention **nearables**, which become smart only when a mobile computer comes into range; **awareables**, which sense their surroundings; and **there-ables,** which are present in the spaces we move through during the day. (I'm indebted to Hugo van Kemenade for uncovering many of these terms.)

Many wearables startups are focused on devices that augment the stuff we wear every day, especially clothes and shoes. Hence the buzz around **tech togs**, particularly **smart clothes**. These include **smart shirts**, which monitor your heart rate, and **smart shoes**, which count your steps. In some cases, the actual materials have electronic properties, making them so-called **e-textiles** (or **smart textiles**).

A while back I read an interview with a wearables researcher. This person has a doctorate from MIT, so you have to assume she's pretty smart. However, when asked about the future applications of wearables, she mentioned "jackets that tell you what the temperature, barometric pressure, or smog level is" and "a baseball hat that tells you the score of the game." These ideas are so comically useless that I had to double-check that I wasn't reading the latest issue of *The Onion*. If we are on our way to becoming **citizen-terminals**, bristling with body-mounted gadgetry, if we are becoming *that* close to the machine, then let's hope it's for better reasons than these. ■

ILLUSTRATION BY Greg Mably

IT'S TOO SOON TO CALL THIS THE ANTHROPOCENE



MANY HISTORIANS AND EVEN SOME SCIENTISTS argue that we are living in the Anthropocene, a new epoch characterized by the human control of the biosphere. Next year the International Geological Congress will consider recognizing this name as the latest addition to the standard geological time scales. • My reaction, echoing the Romans: *Festina lente*. Make haste slowly. • To be quite clear: There is no doubt about the pervasiveness of our interference in global biogeochemical cycles, the loss of biodiversity attributable to human actions—the mass dumping of our wastes; the large-scale deforestation and accelerated erosion of soils; the global extent of pollution generated by farming, cities, industries, and transportation. In combination, these man-made impacts are unprecedented and of a scale that may well imperil the future of our species. • But is our control of the planet's fate really so complete? There is plenty of counterevidence. Fundamental variables that make life on Earth possible—the thermonuclear reactions that power the sun, suffusing the planet with radiation; the planet's shape, rotation, tilt, the eccentricity of its orbital path (the "pacemaker" of the ice ages), and the circulation of its atmosphere—are all beyond any human interference. Nor can we ever hope to control the enormous terraforming processes, the Earth's plate tectonics driven by internal heat and resulting in slow but constant creation of new ocean floor, forming, reshaping, and elevating landmasses whose distributions and altitudes are key determinants of climate variability and habitability.

Similarly, we are mere bystanders watching volcanic eruptions, earthquakes, and tsunamis, the three most violent consequences of plate tectonics. We can live with their frequent, moderate displays, but the very survival of some of the world's largest cities—notably Tokyo, Los Angeles, and Beijing—depends on the absence of megaearthquakes, and the very existence of modern civilization could be cut short by megavolcanic eruptions. Even when measuring time not in geological but in civilizational terms we also face far from negligible threats from Earth-busting asteroids whose path we might be able to predict but not to alter.

In any given year these events have very low probabilities, but because of their enormous destructivity their effects are outside the historic human experience. We have no good way to deal with them, but we cannot pretend that, in the long run, they are less relevant than the loss of forest species or combustion of fossil fuels.

Besides, why rush to elevate ourselves into the creators of a new geological era instead of waiting a bit to see how long the experiment conducted by *Homo sapiens* can last? Each of the six elapsed epochs of the Cenozoic era—from the beginning of the Paleocene 66 million years ago to the beginning of the Holocene 11,700 years ago—lasted at least 2.5 million years, including the last two (the Pliocene and the Pleistocene), and we are now less than 12,000 years into the Holocene. If there is in fact an Anthropocene, it may date no further back than 8,000 years (counting since the beginning of settled agriculture) or 150 years (counting from the takeoff of fossil fuel combustion).

Should we manage to be around for another 10,000 years—a trivial spell for science fiction readers, an eternity for modern, high-energy civilization—we should congratulate ourselves by naming the era shaped by our actions. But in the meantime, let us wait before we determine that our mark on the planet is anything more than a modest microlayer in the geologic record. ■

INFOGRAPHIC BY Erik Vrielink

Hacking the Human OS

How Big Data Will Revolutionize Medicine

IF YOU WEAR A FITNESS TRACKER, you're already generating scads of health-related data. It's the start of a grand experiment. In coming years, doctors will try to answer a vital question: Can they use your data to keep you stronger, healthier, and happier? § We begin our three-part report with "Reading the Code," which goes beyond today's wearables to consider the future of biodata-gathering hardware. Soon you'll be able to slap sensors on your skin as if they were temporary tattoos, and eventually doctors may implant them in your body. In fact, a baby could be instrumented at birth to provide a continuous stream of data. § Your information will go to the cloud–a link that companies such as Apple are already facilitating–where analytics software will let specialists study *your* body, and what treatments are likely to work on it. Doctors' recommendations will be backed by analysis of countless other people's bodies and treatments. We explore the possibilities of digitized medicine in "Analyzing the Code." § The point of all this effort is to keep you healthy or cure what ails you, and that's the subject of our third section, "Changing the Code." Technological interventions, informed by vast amounts of data about how your body works, can usher in the most fundamental revolution in medicine since the advent of surgery. It won't happen without surmounting daunting obstacles, including doctors' skepticism and privacy concerns. But it's going to happen. In the pages that follow, we'll show you how and why. ▶▶▶

PHOTO-ILLUSTRATION BY Dan Saelinger

SPECIAL REPORT

Hacking the Human OS

PART 1

Reading the Code

THE BODY IS A FANTASTICALLY sophisticated machine. Most of the time, it runs just fine on its own. But, inevitably, things go wrong, and early detection of warning signs can be the key to preventing a total breakdown. § We are on the verge of being able to monitor your physiological indicators day and night, at minimal cost, and with technologies so unobtrusive that you'll forget their presence. Flexible skin patches, for example, can keep tabs on body temperature, heartbeat, and hydration. If you have diabetes, new implants can track your blood-glucose levels and feed the data to a responsive system worn on the body. Yes, an artificial pancreas is finally within reach. A pocket-size general diagnostic tool—named after the "Star Trek" tricorder—is also close to reality. With hospital-grade hardware appearing in consumer gadgets, medicine is increasingly in your own hands. ►►►

INSIDE

PHOTO-ILLUSTRATION BY Dan Saelinger

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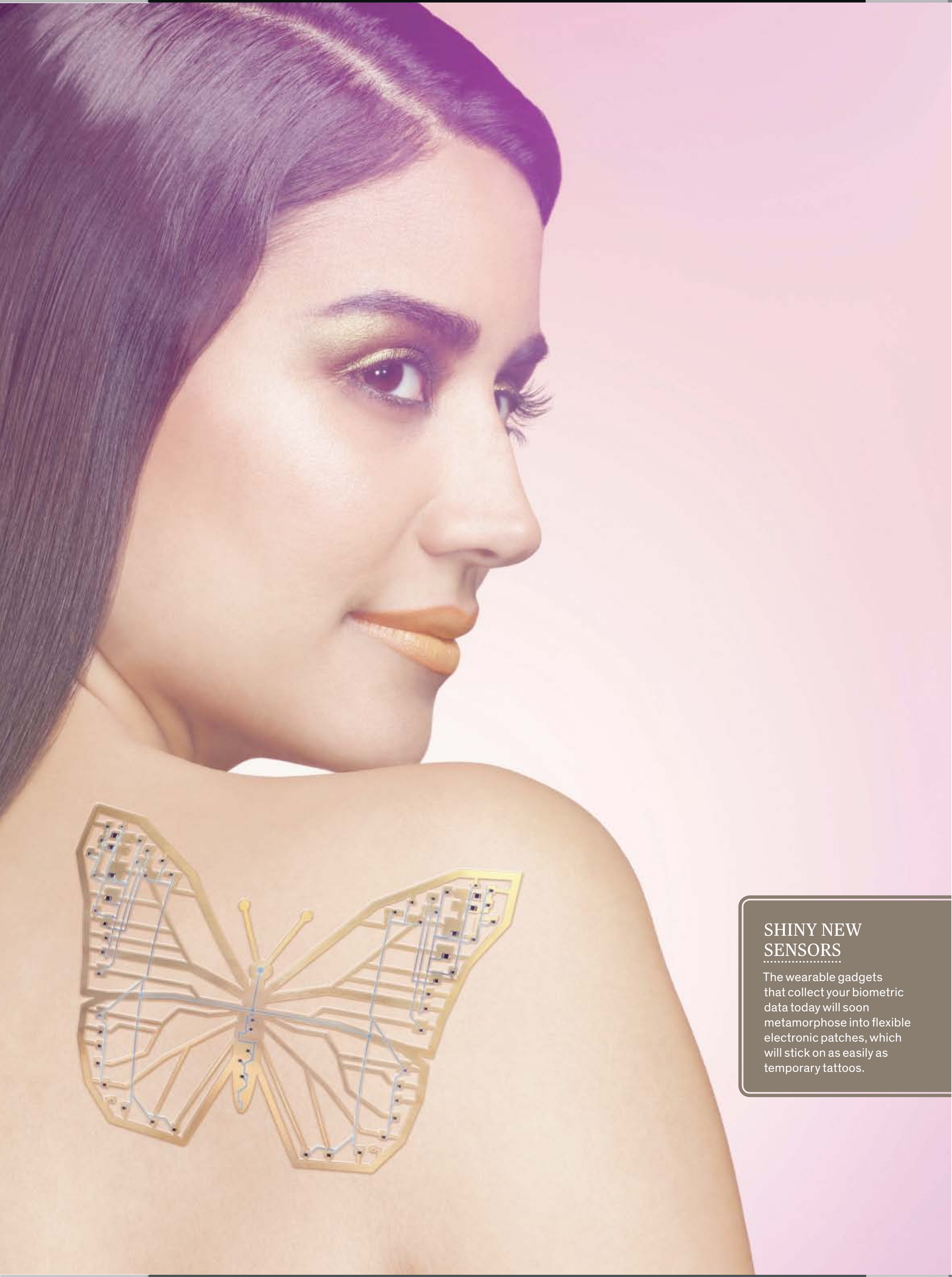


SHINY NEW SENSORS

The wearable gadgets that collect your biometric data today will soon metamorphose into flexible electronic patches, which will stick on as easily as temporary tattoos.

Giving Your Body a "Check Engine" Light

TEMPORARY TATTOOS CAN REPLACE TODAY'S CLUNKY BIOMEDICAL SENSORS

By **Tekla S. Perry**

I TURN THE KEY TO START THE LITTLE Ford SUV I've rented for my visit to the University of Illinois at Urbana-Champaign, and a message flashes briefly on the dash: "Tire pressure low." I ignore it. My own car is 12 years old; I'm not accustomed to a car that monitors its own health. Turns out, though, that the little Ford wasn't kidding. The next morning I find the car has a flat tire.

Modern cars are laden with sensors that constantly monitor the vehicle's vitals and indicate, for example, when a filter needs replacing or whether the air bag is working. Electronics diagnose failures after they happen and even predict problems that are imminent. Wouldn't it be great if we could monitor our bodies in much the same way?

That very idea, ironically enough, is what has brought me to Illinois. I'm here to see John Rogers, a materials science professor at the University of Illinois with a bold vision: Someday, he believes, we will all have sensors on our bodies that send information to a mobile phone, similar to the way a car's sensors feed the vehicle's computer.

We've already taken the first steps in this direction. Many of us now wear fitness bands that track our activity and heart rate and assume we're sleeping if we don't move for a while. But most of these bands aren't exactly chic or unobtrusive, so even the more die-hard among us take them off sometimes. And the information they dispense is interesting but hardly vital: They can't detect signs that you're getting sick or tell your doctors anything they need to know, much less replace an office visit.

But there's no reason why they can't, says Rogers. Think about your last medical exam. Your doctor checked your pulse, your temperature, your blood pressure, and maybe your blood oxygen. If any anomalies showed up, you may have been sent for further tests—perhaps an electrocardiogram for your heart, a blood test to check for diabetes, electromyography if you were having muscle weakness, or possibly even a polysomnogram at a sleep lab to check for apnea. All of these tests require specialized and costly equipment, trained medical technicians, or invasive pokes.

BY THE NUMBERS

1 billion

Number of visits to U.S. doctors' offices in 2010

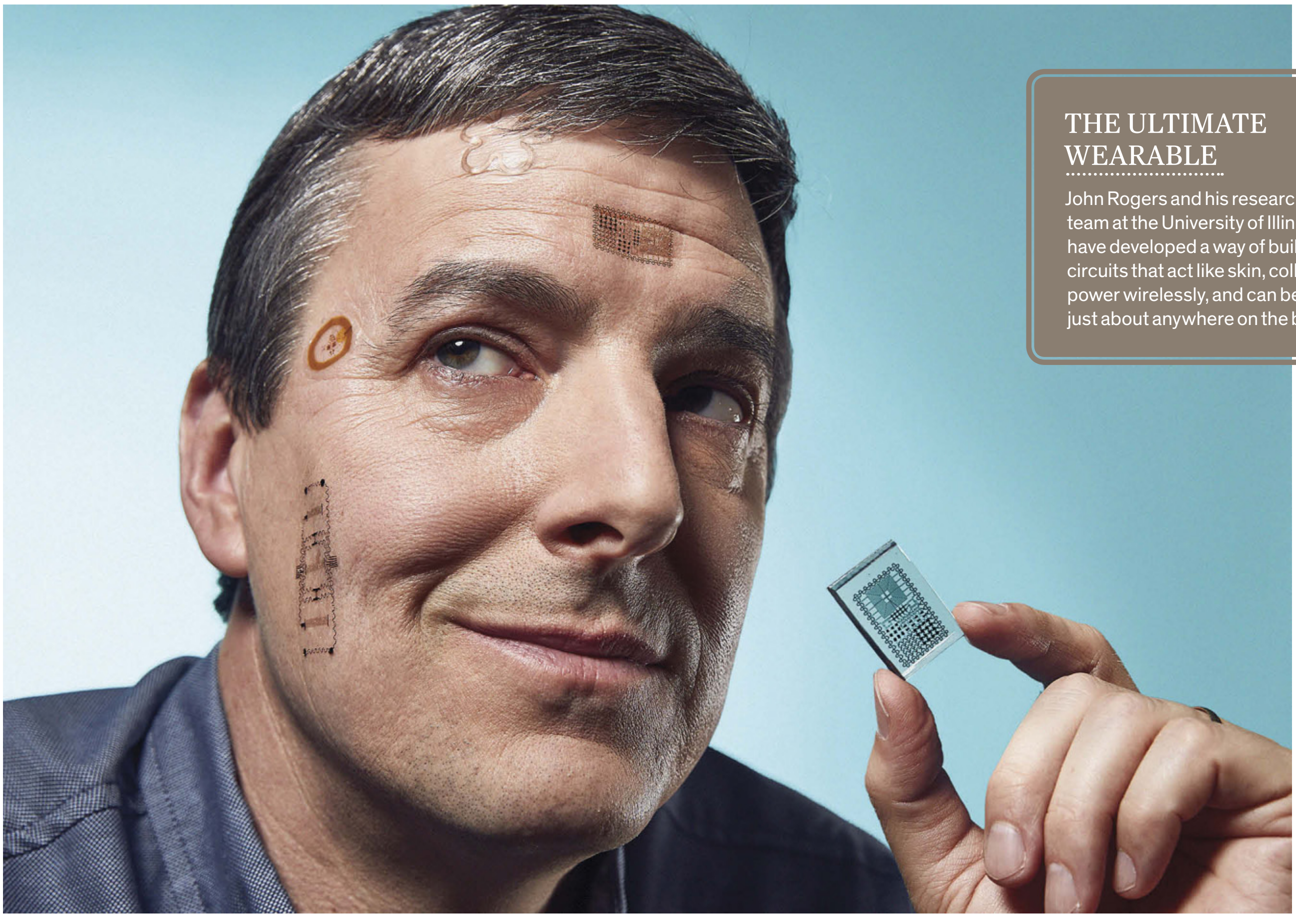
These tests—and more—could be accomplished by means of sensors so light, durable, and comfortable that you could wear them on your body for weeks at a time. It's no distant dream: At press time, several sensors developed by members of Rogers's research team had entered or were about to enter clinical trials in the United States and Europe, and the first commercial versions were expected to become available by the end of this year.

Rogers says these sensors are so much like skin that you don't notice you're wearing them—and I didn't have to take his word for it. I wore one on my inner forearm for more than a week. This version was a test unit that simply transmitted a greeting when triggered by an Android smartphone; units with biosensors haven't yet been made available to journalists.

Simple though it was, my sensor delighted me. It clung unobtrusively and tenaciously to my arm as I went about my life—showering, sleeping, and exercising. It also got me thinking about how future versions of these sensors are going to make our lives better—not a decade from now but within a couple of years, Rogers promises.

THE ILLINOIS TEAM ISN'T THE ONLY one trying to make skinlike electronics. Takao Someya is leading a group at the University of Tokyo that's working to develop electronic skin made of organic semiconductors and

PREVIOUS PAGE: CGI: SIMON DANAHER; STATISTIC SOURCE: 2010 NATIONAL AMBULATORY MEDICAL CARE SURVEY, CDC



THE ULTIMATE WEARABLE

John Rogers and his research team at the University of Illinois have developed a way of building circuits that act like skin, collect power wirelessly, and can be worn just about anywhere on the body.

carbon nanotubes. Zhenan Bao at Stanford is also working with organic semiconductors to develop an electronic film that would be as sensitive as human skin and could be applied over robotic limbs. And researchers at the University of California, San Diego, are developing inks that would allow scientists to draw sensors directly onto the skin.

But Rogers's skinlike sensors are poised to be the first to get out of the lab and onto our bodies. In 2008, Rogers teamed with Roozbeh Ghaffari to start a company called MC10, in Cambridge, Mass., to turn his group's research on stretchable electronics into commercial health care products. MC10 today has about 60 full-time employees, US $60 million in venture capital and corporate investment, and one product on the market: the Checklight, a skullcap for precisely measuring accelerations during athletes' head impacts. It's not a skinlike sensor patch, but it does bend to conform to the shape of a body part. (Rogers serves on the board of MC10 and helps plan the company's research and technology efforts with Ghaffari, who is now MC10's chief technology officer.)

MC10 started making the first skin patches—the company calls them Biostamps—in late 2012. Most of these early units were used for internal development or codevelopment efforts with partners. MC10 began developing a new generation of the technology in late 2014; most of these Biostamps are now going to medical researchers for use in clinical trials. Consumer-wellness Biostamps are also being developed for companies targeting their own special niches. A cosmetics company may package a sun-monitoring Biostamp with sunscreen, for example, or a pharmaceutical company could include motion- and temperature-monitoring Biostamps with a package of medication.

The basic Biostamp is a thin sticker about the size of a British ten pence or an American quarter. It looks like a temporary tattoo a child might get at a birthday party, but because it has been designed to be mechanically similar to skin, it can't really be felt by the wearer

PHOTOGRAPH BY Saverio Truglia

once it's applied. A Biostamp can contain hundreds of thousands of transistors, as well as resistors, LEDs, and a radio-frequency antenna. It's waterproof and breathable, and it costs just tens of cents when manufactured in quantity. It can be worn for a week or so, before the normal shedding of skin cells begins to force the thin substrate to peel from the skin, like an early-season sunburn.

A Biostamp is built out of stretchable circuits supported by an extremely thin sheet of rubber. To make these circuits, Rogers and his colleagues in Illinois start by fabricating their transistors, diodes, capacitors, and other electronic devices on wafers of any common semiconductor material. They typically use silicon but could also use gallium arsenide or gallium nitride. These are not ordinary semiconductor wafers; they're kind of like the Oreo cookie of semiconductor wafers. They have a thin top layer of semiconductor material, a thicker bottom layer of the same material that acts as a rigid support during manufacture, and a sacrificial layer of a different material in between. In the case of a silicon wafer, this sacrificial layer is silicon dioxide. After the device manufacture is complete, a chemical bath eats away that central layer and frees the thin top layer.

Then a stamp made of soft silicone presses onto the wafer. Raised areas on the stamp lift away selected electronic devices in the same way a rubber stamp picks up ink from a stamp pad. After picking up the devices, the silicone stamp deposits them onto a temporary substrate, usually a plastic-coated glass plate. This plate then goes through a standard photolithography process that connects the devices with copper conductors in the form of serpentine coils, which make the connections stretchable.

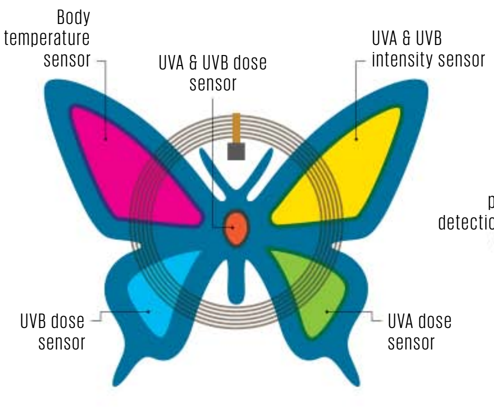
The next step is to transfer the interconnected devices from the plastic-coated glass onto what will go to the consumer–a thin sheet of rubber already attached to a plastic backing sheet, with a layer of adhesive in between. To do this, a machine pushes the rubber against the array of devices and coils that are still clinging to the plastic-coated glass. A final chemical bath dissolves the plastic between the electronic circuits and the glass, leaving the circuits attached to the rubber. And the last step happens when the Biostamp gets into the hands of the user–who exposes the adhesive and sticks the rubber-backed electronics onto the skin.

In many Biostamps, all the electronics are created using this process. In some cases, however, a Biostamp design incorporates a microprocessor without packaging, which the researchers thin down to 5 to 10 micrometers. A few more micro-

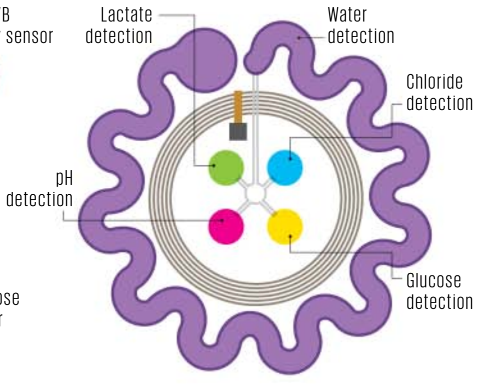
HOW IT WORKS

Inside the Biostamp

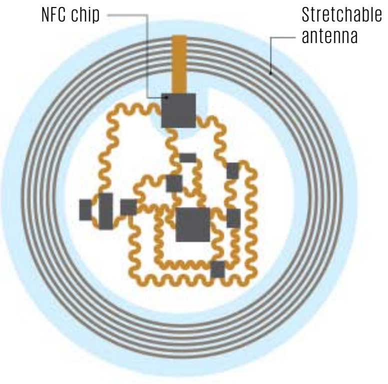
WHILE ALL BIOSTAMPS have a few common characteristics—they stretch like skin, include flexible circuits, and can be powered wirelessly—different functions require different sensors. The butterfly sensor on the left is designed to monitor exposure to the sun's ultraviolet (UV) rays, the center sensor uses sensitive dyes to detect chemicals in sweat, and the sensor at the right uses electronic circuitry to measure blood pressure.



UV EXPOSURE & TEMPERATURE



PERSPIRATION & BIOCHEMISTRY



BLOOD PRESSURE

ILLUSTRATION BY James Provost

meters of flexible resin cover the circuitry to protect it from water. For now, though, most Biostamps don't have full-blown microprocessors on board. Most of those now being tested simply gather data and transmit it; analysis happens elsewhere, generally on a smartphone or tablet.

A Biostamp powers itself by harvesting energy from near-field communication (NFC) radio signals, typically from the wearer's cellphone. It communicates with the phone the same way. NFC, which sends data at 13.56 megahertz, is a feature of almost all current-model smartphones, which use it for wireless-payment schemes. At the moment the stamps work only with Android phones, but the hardware is compatible with the type of NFC technology on the newer iPhones.

The stamp converts the RF energy picked up by an antenna to electrical energy by means of an inductive coil. A Biostamp can generate tens of milliwatts of power when within a meter or so of a phone transmitting an NFC signal. For longer-distance power gathering, a Biostamp can be built to receive radio signals at frequencies between 1 and 2.5 gigahertz from a transmitter up to several meters away.

The current tattoo-like versions of the technology don't store energy, although Rogers's group and MC10 have already built and tested stretchable batteries and supercapacitors. But in a hospital room, say, with an NFC transmitter under the bed or a longer-distance RF transmitter in a corner, Biostamps can operate continuously and indefinitely.

Right now, Rogers and his students are evaluating stretchable sensors that measure body temperature, monitor exposure to ultraviolet light, and check pulse and blood-oxygen levels. They're also developing sensors that can track changes in blood pressure, analyze sweat, and obtain signals from the brain or heart for use in electroencephalograms and electrocardiograms. All of these sensors, Rogers says, are intended to make measurements with enough accuracy to be useful in medical settings–a much higher standard than that needed to build a typical consumer wearable.

ACHIEVING THAT STANDARD IN A THIN and stretchable device has compelled Rogers and his team to rethink how medical measurements are done. Consider blood pressure: It's usually measured by placing a cuff around a patient's arm and inflating the cuff until it cuts off blood flow. Then the cuff gradually deflates until blood

THE ARGUMENT | **B.J. FOGG**

CAN TECHNOLOGY CHANGE BEHAVIOR?

HUNDREDS OF APPS and consumer gadgets help count your calories, track your workouts, and monitor your progress toward your health goals. But studies show that most people stop using these tools within six months. B.J. Fogg, a Stanford professor and industry consultant who studies "persuasive technology," explores whether technology can in fact change human behavior for the better.

***IEEE SPECTRUM*: An app can tell me that a large McDonald's chocolate shake contains 850 calories, and that I'll have to jog for 2 hours to burn it off. How helpful is that?**

B.J. FOGG: There are two types of informational prompts: the "why" information that's supposed to motivate you and the "how-to." I don't encourage the approach that uses constant nagging with the "why" motivation cues. A "how-to" prompt might say: "Here's how to eat healthy when you're in this airport."

Why not focus on motivation?

In general, what you can do with technology is help people do what they already want to do. If you create a technology that prompts people at the right moment, and if it's something they already want to do, you can change behavior. It's that simple to say, but it's hard to accomplish.

How do technologies get these prompts wrong?

When done poorly, triggers will either frustrate or annoy us. They'll frustrate us if we have the motivation but not the ability to carry out the action. They'll annoy us if they keep prompting us to do a behavior, but we don't want to do it—we have the ability without motivation.

You run "boot camps" on designing for behavior change. What's the message you're drilling into your recruits?

Pick a behavior you want to do and be very specific, make it really easy to do the behavior, and figure out what's going to prompt you to do it. If you want to drink a kale drink every morning, you don't need to work on motivation. You need to figure out how to make it really easy to do and what will remind you to do it. It's really a design problem.

—Interview by Eliza Strickland

ILLUSTRATION BY Jacob Thomas

starts flowing through the vessels in the arm again; that gives the systolic reading, a measure of the pressure during the contraction of the heart. The cuff continues to deflate until the doctor can no longer detect the sound of the blood flowing. This produces the diastolic reading, the pressure when the heart muscle is relaxed, between beats.

A tiny Biostamp can't cut off blood flow. It can, however, measure the pulse at two points, just a centimeter or so apart. With this information, a smartphone can calculate a physiological indicator called pulse-wave velocity, which varies as blood pressure changes. So researchers Tony Banks, SeungMin Lee, and Matt Pharr in Rogers's group are developing two types of Biostamp pulse detectors.

BY THE NUMBERS

56 percent

Visits to primary care physicians, as a percentage of all doctors' visits

One uses light; it alternately flashes a red and an infrared LED and uses a photodetector to pick up the light reflected from the skin beneath the Biostamp. Because deoxygenated blood absorbs more red light and oxygenated blood absorbs more of the infrared, fluctuations in those levels create a waveform that represents the heartbeat. That's basically how the newest fitness bands detect a pulse, though the Biostamp version can get a more stable signal because the skin doesn't shift under it. The other type of pulse detector under development uses piezoelectric strain sensors to monitor the stretching and relaxing of the patch as it reacts to the blood coursing through the vessels under it. In this scheme, greater stretch translates to higher pressure.

In either case, these measurements of pulse converted to pulse-wave velocity tell the wearer only how blood pressure is changing–they don't give the baseline blood pressure reading. But for patients whose blood pressure needs to be monitored closely, simply keeping track of variations is vital.

BIOSTAMP BRIGADE: These stamps include a variety of ultrathin unpackaged electronics, flexible circuits, and sensitive dyes. They harvest energy and communicate wirelessly and can support a variety of sensors to allow the monitoring of different bodily functions.

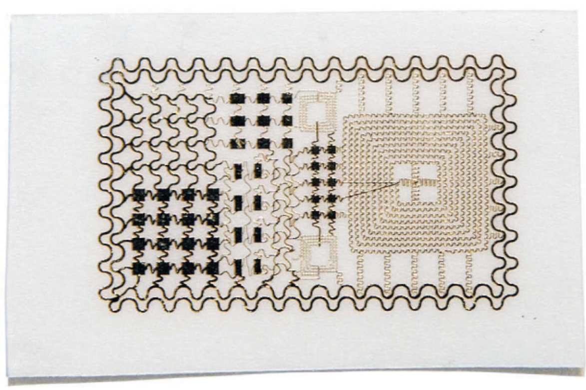
Instead of seeing a nurse daily for a blood pressure check or using bulky home monitoring equipment, the patient would put on a new Biostamp every week or two, get it calibrated, and just scan the stamp with a phone to take a reading that could be sent automatically to the doctor.

Another promising Biostamp version will monitor sweat. Daeshik Kang and Aheyon Koh, postdocs in Rogers's group who are working with research staff member Banks, have built a Biostamp with microfluidic channels that wick sweat along a calibrated path. Chemically sensitive dye on the path changes color as the sweat hits it, while other dyes on the patch change color in response to glucose, lactic acid, chloride, and sodium. When scanned with a smartphone, circuitry on the patch activates a phone app that analyzes the color changes and offers

STATISTIC SOURCE: 2010 NATIONAL AMBULATORY MEDICAL CARE SURVEY, CDC suggestions, such as "Time to hydrate," or, for a woman being monitored for pregnancy-onset diabetes, "Time to visit the doctor." MC10 researchers, in collaboration with Rogers's group, are also investigating possible ways to use this sweat-derived data for monitoring cardiac health.

These chemically sensitive Biostamps, unlike fully electronic wearable sweat monitors being developed elsewhere, aren't reusable; at the end of your workout, race, or stress test, when you've stopped sweating, you won't be able to reset the patch, so you'll have to throw it out. They'll be so cheap, though, that you won't care.

Rogers is confident that Biostamps will become staples in hospitals. An initial trial began this year in the neonatal intensive care unit at Carle Foundation Hospital, in Urbana, Ill., where doctors are using Biostamps to monitor temperature and other vital signs of newborns. The doctors stick Biostamps on an arm, a leg, the forehead, and the chest of each infant, while an NFC antenna under each incubator powers the devices.



THIN AND STRETCHY: This Biostamp is a test bed for a variety of stretchable devices; it includes arrays of transistors, diodes, capacitors, inductors, LC oscillators, temperature sensors, strain gauges, an LED, an inductive coil, and a simple antenna.

AS WORD OF HIS BIOSTAMPS GETS out, Rogers and MC10 have been fielding requests not just from doctors and trainers but also from government officials and business executives. Many discover his work by reading one of the hundred-plus papers that have appeared in scientific journals in recent years.

"I read his paper in *Science* four years ago," says Guive Balooch, global vice president in charge of new technologies for L'Oréal, the hair-care and cosmetics giant. "We went to him because measuring the skin and understanding changes over time can help us identify and test products."

L'Oréal is now working with a Biostamp group on a skin hydration sensor that monitors how heat travels across the skin under the patch. A device on the patch creates a tiny burst of heat that is detected by a temperature sensor on the same patch. L'Oréal is hoping to eventually use this information to test the efficacy of its products; the patch could track changes in hydration as people use its products over time and more general changes as the skin ages. Researchers at the company have already done one trial with 20 subjects, each wearing six Biostamps. The initial study simply established correlations among hydration, temperature, skin thickness, and the travel of heat through the skin. Within 5 to 10 years, Balooch expects, the technology will do more. "I would love to see a beauty patch on someone's body give them skin-care recommendations," he says. L'Oréal is also funding research on Biostamps that measure UV exposure and signal when it's time to reapply sunscreen.

In my week-plus of wearing a stripped-down Biostamp, I found myself eager to roll up my sleeve and show it off. After seeing countless demos in Rogers's lab of potential applications, and recalling the L'Oréal research in particular, I even became annoyed about having to do things the usual way. Sitting in the sun one hot afternoon, I debated whether to reapply sunscreen and, looking at the patch on my wrist, I thought, "You could tell me this, you know."

Later that same week, feeling like I was coming down with a cold, I went hunting for a thermometer. Again I glared at my Biostamp and wished it were the temperature-sensor one I'd seen demonstrated in Illinois. And the Fitbit Flex I've been wearing for more than a year and once thought was so sleek? It looks huge and clunky to me now.

OTHER RESEARCHERS ARE studying the possibility of using temperature-sensing Biostamps to measure mental stress in air traffic controllers (the tougher the mental task, the cooler the temperature of the hand) and using heat-generating Biostamps to push drugs through the skin. In a clinical trial at Northwestern University's medical school, in Chicago, research teams have tested Biostamps that measure both temperature and heat flow in tissue to monitor wound healing. And Biostamps that adhere behind the ear to measure the electrical activity of the brain for sleep studies were to go into clinical trials this spring at Carle Foundation Hospital. This method would be far less cumbersome than the wired sensors typically used now.

Of course, any device that gathers health data must ensure patient privacy, so any | CONTINUED ON PAGE 75

RANDI KLETT (2)

PART 1: Reading the Code | MONITORING

Diabetes Has a New Enemy: Robo-Pancreas

SENSORS, ACTUATORS, AND ALGORITHMS CAN AUTOMATICALLY CONTROL BLOOD SUGAR

By **Philip E. Ross**

THE FIRST GREAT WONDER DRUG was insulin, the blood-sugar-regulating hormone that was isolated in Canada nearly a century ago. The before-and-after pictures still astound: a skeletal wraith on the left, a rosy-cheeked child on the right.

But the promise of insulin has yet to be fulfilled. Normally, the pancreas, an organ near the liver, secretes insulin to control the concentration of glucose in the blood. In patients with type 1 diabetes—once known as juvenile diabetes because it's usually diagnosed in children—the pancreas makes no insulin of its own, so those with the disease must work hard to mimic that organ's function. If blood sugar goes too low, the patient faints; if it goes too high, it poses long-term risks to the eyes, nerves, and arteries. So several times a day the patient must prick a finger to test blood sugar, make a calculation based on planned meals and exercise, and adjust the injection of insulin to account for it all. The burden of self-management goes on night and day.

Now, after half a century of work, a solution at last is in the offing: the artificial pancreas. It links data from an implanted blood-sugar sensor to a computer, which then controls how a pump worn on the hip dribbles insulin under the skin through a pipette. In its fully realized form, the machine would take the patient out of the decision-making loop, which is why it is often called a closed-loop system.

"It is a classic problem in control technology, which is the methodology used in process control," says Ahmad Haidar, an electrical engineer working on the problem at the Institut de Recherches Cliniques de Montréal (IRCM). Such technology is used, for instance, to guide a spacecraft or to govern the processing of crude oil in a refinery. Haidar's group is one of a number of academic and corporate teams vying to create a closed-loop system for an artificial pancreas.

"Each patient is represented by a set of differential equations," Haidar says, "parameterized based on physical information—body weight and total daily insulin dose, for instance." Then the algorithm figures out how to administer that dose from one minute to the next to keep the glucose levels within safe bounds. Partial versions of the closed loop are being rolled out now, and more advanced versions are in clinical trials.

The work of Haidar's group and others is finally promising to complete a vision that began more than a half-century ago and always seemed just around the corner. In 1978, in fact, an engineer at Sandia National Laboratories, in New Mexico, wrote in these pages of an "electronic pancreas" that would come in three to five years' time. This time, though, is different: Actual products are hitting the market, and closed-loop systems that take over more of the diabetes management are in trials. Finally, everybody in the field agrees that a solution is nigh.

A SLEW OF IMPROVEMENTS IN sensors, actuators, algorithms, and insulin are coming together to create the artificial pancreas. Brian Herrick, diagnosed with type 1 at age 3, got to see the latest results for himself last November, during a trial in New York City of a system devised at the University of Virginia.

"The thing that was cool about it was that it works," says Herrick, 27, who directs strategic communications at the Juvenile Diabetes Research Foundation (JDRF). Together with a colleague, he spent several days and nights in a controlled setting, surrounded by doctors and engineers.

"We used a Dexcom continuous glucose sensor, hooked through a cellphone with an algorithm and to a Roche pump, linked to it by a Bluetooth signal," says Herrick, recalling each detail as if the trial had just happened. "One night my blood sugar was 80 [milligrams of glucose per deciliter of blood], with an arrow point-

is supposed to recheck the numbers with a finger stick before an injection).

It's not completely automated, like the trial system was, but such continuous monitoring is itself a huge advance over 10 years ago, and one that lends itself to remote monitoring through the cloud. Last year, Dexcom got FDA approval for its Dexcom G4 Platinum System with Share, which parents can use to keep tabs on their kids' blood sugar.

"Sure, it gives peace of mind to a mom or dad whose child goes to a first sleepover," says Jorge A. Valdes, chief technical officer of Dexcom, in San Diego. "But consider: Once the data is in the servers, there's a lot we can do to affect disease management." For instance, doctors could mine the data for patterns in which patients suffer from low blood sugar, then adjust diet or insulin dosage accordingly.

The information can also be used to prove to insurers that the money they spend on health care is productive

BLOOD SUGAR, ONLINE

Brian Herrick tracks the ups and downs of glucose in his bloodstream with a Dexcom system—a skin-hugging sensor that communicates via Bluetooth with a handheld monitor.

ing downward–it was dropping at 2 milligrams of glucose per deciliter per minute. The system shut off insulin, the blood sugar cruised down to 78, sat there, rose to 110, and then, no more movement. It was level." Normal fasting blood glucose ranges from 70 to 100 mg/dl.

The trial mainly looked at nighttime control, which is critical, because the patient may not wake in time to handle a bout of low blood sugar. "My mother is still fearful of my sleeping at night, even though I've got my fiancée sleeping next to me," says Herrick.

For now he is back to his old routine, making all the decisions himself, but with some help from a Dexcom glucose sensor that he applies to his upper arm, under his sleeve; it beams data to the screen of a pager-size reader. He uses the information to help decide what to eat and how much insulin to administer (although technically he

ing results. "Health care providers are more and more being paid for outcomes," Valdes says. "Payers want patients to stay on the system; now they can make sure that patients do."

THE DEVELOPMENT OF THE TECHnology has proceeded by measured steps, much like the progress toward the driverless car–first antilock brakes, next GPS navigation, then adaptive cruise control and self-

PHOTOGRAPH BY David Yellen

parking. Finally, at the end of the rainbow, the Google self-driving car. The first step toward a robotic pancreas came in 1964, when a hospital-based experiment proved, in principle, that it was possible to achieve near-normal blood-sugar control. In the 1970s, Dean Kamen invented the insulin pump, making it possible for patients to administer insulin to themselves in a continuous fashion, rather than through frequent injections. Soon after, a hospital system called Biostator GCIIS was released in Germany; it combined a pump with a large, complex continuous glucose monitor.

In recent years, pumps have become smaller, more reliable, more programmable, and more comfortable, using ever-finer pipettes, which the patient inserts through a slightly larger needle. Continuous glucose monitors were first approved a decade ago, and they are beginning to replace the finger-prick method, now that improved coatings and other engineering details have allowed patients to keep their superthin electrochemical sensors under the skin for seven days. "I've had this one in for eight," says Herrick.

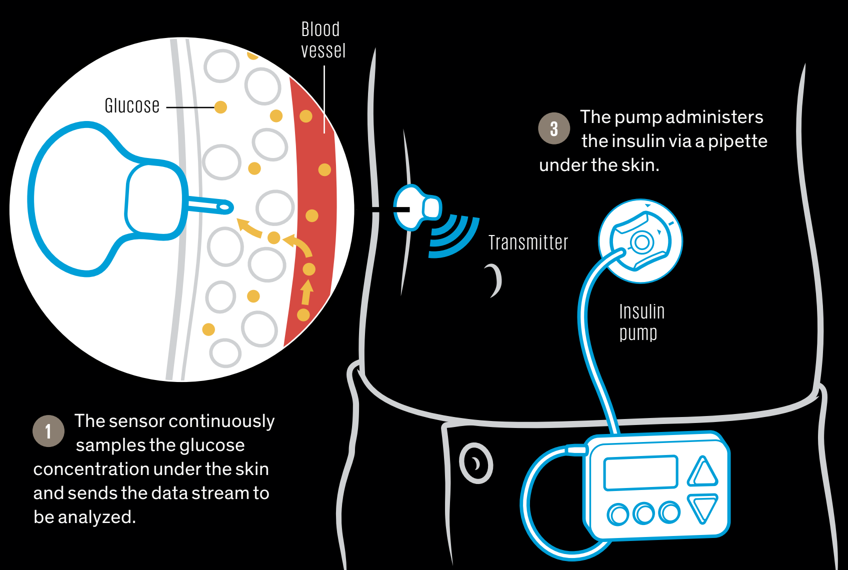
The first machine worthy of the name of artificial pancreas was Medtronic's Minimed 530G, which went on sale in the United States in 2014. It stops the flow of insulin when the patient's blood glucose falls below a set point. Then, in January, Medtronic began selling the 640T; like the system Herrick tested, this system stops the insulin when its algorithm merely predicts that the patient's blood sugar will drop. It's on the market in Australia and is set to sell in Europe later this year. In the United States, the clinical trials are just getting under way.

Medtronic's first clinical tests of what became the 640T began about a decade ago, says Francine R. Kaufmann, the company's chief medical officer and a practicing endocrinologist. Why the long delay between the proof of concept and routine use? "There's a big difference when you take someone who goes out and lives daily life, exercises, gets drunk, and other stuff," Kaufmann says.

Much can go wrong. Pumps clog, algorithms misfire, sensors get walled off by scar tissue. Some of the recent technical advances are proprietary and still under wraps, but it's known that Medtronic and Dexcom have developed biocompatible coatings as well as sensors with multiple electrochemical sites that can be polled to see which ones no longer work properly.

One of the biggest challenges is lag. In a feedback-control system with too much lag, your efforts to lower the upswings and raise the downswings can make those variations worse. Glucose sensors typically show you where your blood sugar was 10 minutes ago, but because they also track changes over time, they can give you a pretty good idea of where you stand now. The real problem is the insulin. Today's

HOW IT WORKS



Copying the Pancreas

SOON AFTER A RISE IN GLUCOSE in the bloodstream, a parallel rise in the intercellular fluid of the skin occurs. Sensors inserted into the skin detect that rise and beam the data to a computer, which directs a pump to send pulses of insulin under the skin. From there the insulin moves on to the bloodstream and throughout the body, lowering the glucose to safe levels.

ILLUSTRATION BY James Provost

bioengineered insulins, called analogues, reach their peak effect in 60 to 90 minutes. Even faster-acting analogues, now in the lab, may shave off another 15 minutes, but even that's not good enough.

"To get a meaningful improvement, enough to have a fully closed loop, you need insulin to act in 10 to 15 minutes–total," says Roman Hovorka, a specialist in mathematical informatics at the University of Cambridge, in England. "Two analogues in development are about 15 minutes faster than today's–and that's nowhere close enough."

Your body responds to a meal as a sprinter does to a starter's commands. When you just contemplate eating, nerves signal the pancreas to start synthesizing insulin: *On your mark*. When you swallow, insulin-making cells get ready for release: *Get set*. When your digestive tract has broken starch down into sugar and dumped it into the bloodstream, the pancreatic cells directly sense this change and dump their pent-up insulin: *Go*. In a heartbeat, the hormone reaches the liver, just a few centimeters away, where much of it is absorbed immediately. The liver then soaks up sugar, blood-sugar concentration falls, and the pancreas steps down its activity.

That level of control is far beyond what lag-plagued pumps can reasonably hope to achieve. The only way to match it is by growing or implanting new insulin-secreting cells in the patient's body. Efforts in that direction have achieved scattered successes since the development, in the 1970s, of ways of controlling tissue rejection. But progress has been slow.

For now at least, the closed-loop robo-pancreas is ahead of such biological approaches, says IRCM's Haidar, even though it will never duplicate the human body. "We know an airplane isn't better than a bird," he says. "We're not replicating a pancreas–we can never beat how the body works."

One way to speed the insulin's effects is to implant a pump right inside the abdominal cavity, so the insulin can get to the liver more quickly. "But you're talking about surgery," Haidar says. "If you have a 2-year-old daughter, which would you prefer?"

BESIDES THE SENSOR AND THE pump are the algorithms, the secret sauce that allows the artificial pancreas to analyze, learn, and control. One of the first algorithmic techniques looked at the rate of change of blood sugar. Another one, sometimes called an expert system, sets up a table that pairs | CONTINUED ON PAGE 76

THE ARGUMENT | **ERIC TOPOL**

CAN HEALTH CARE BE DEMOCRATIZED?

CARDIOLOGIST ERIC TOPOL envisions a world in which everyone controls their own health care, collecting huge quantities of personal data with the help of smartphones, gadgets, and apps. The technology exists now, he says, to make the health care system truly democratic.

***IEEE SPECTRUM*: In your latest book, *The Patient Will See You Now*, you stress that the patient is the unrecognized expert in health care. Are most people ready to take on such a role?**
ERIC TOPOL: Consumer surveys show that about 80 percent really want to take control of their health care. I've seen patients, once they start seeing their data on their smartphone screen—they're really into it. So I'm pretty optimistic we're talking about the majority of people.

What about people who just don't want to know that much about themselves?
My advice is, just give it a try. It's really not that difficult or expensive to be actively engaged in your own health care. Think of your data freely flowing to your own devices: You'll know much more about yourself, what's working, what's off track.

You argue for evidence-based medicine—for example, approval of drugs based on clear indications that they benefit patients. That seems like a no-brainer.
We don't have much good evidence for the vast majority of what we do. Instead we have "eminence-based" guidelines, handed down like the Ten Commandments. In the future we'll have millions of people giving their data, in the wild, in the real world, and not in a contrived clinical trial. When [Apple's] ResearchKit announced mPower for Parkinson's disease, which is a smartphone app that tracks a person's voice tremor and gait, 10,000 patients enrolled in a matter of days.

When will all this happen?
Medicine is not a profession that changes too readily. It took 110 years to fix the hospital gown, and it's still not fixed. But I've been a physician for 30 years, and I've never seen anything like this. The technology is here, and we've got a whole better way of doing things. I just hope we can get consumers and employers to demand it.

—Interview by Jean Kumagai

ILLUSTRATION BY Jacob Thomas

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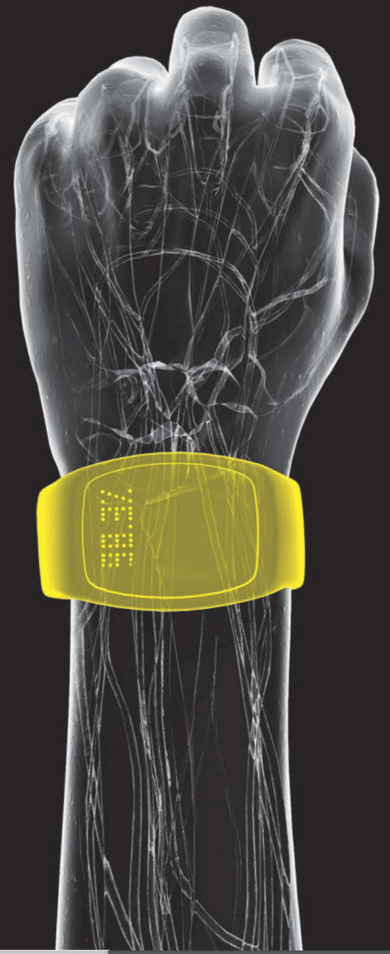
PART 1: Reading the Code | **SPORTS**

The Quantified Olympian

BIOMETRIC GADGETS are transforming the way the world's elite athletes are trained. These wearable sensors provide on-the-go physiological measurements, which previously required bulky and costly lab equipment. Just as weight-training regimens became popular 40 years ago to build more resilient athletes, wearables are now helping players both improve performance and ward off injury. • "I definitely see them as becoming part of everyday training," says Marko Yrjovuori, a biomechanics specialist who trains the Los Angeles Lakers basketball team. Here are some state-of-the-art systems that are changing the game for elite athletes, including a few within reach of dedicated amateurs. —*Emily Waltz*



READIBAND

WHAT IT IS: This electronic wristband measures sleep quality and quantity, which can help predict a player's reaction time for the next day. Coaches can use an associated online tool to monitor the sleep patterns and fatigue of professional athletes.

HOW IT WORKS: The band's accelerometer senses tiny movements of the wearer's wrist, which reveal whether the wearer is asleep or awake. To predict fatigue, the results are fed through the SAFTE (Sleep, Activity, Fatigue, Task, and Effectiveness) model, which was developed by the U.S. Army. An "effectiveness score" rates the quality of the wearer's slumber.

WHO'S USING IT: Vancouver Canucks, Seattle Sounders, and Dallas Mavericks

PRICE: US $22,800 per year for 20 Readibands, including analytics software (individual wristbands are not sold)

MOTUS SLEEVE

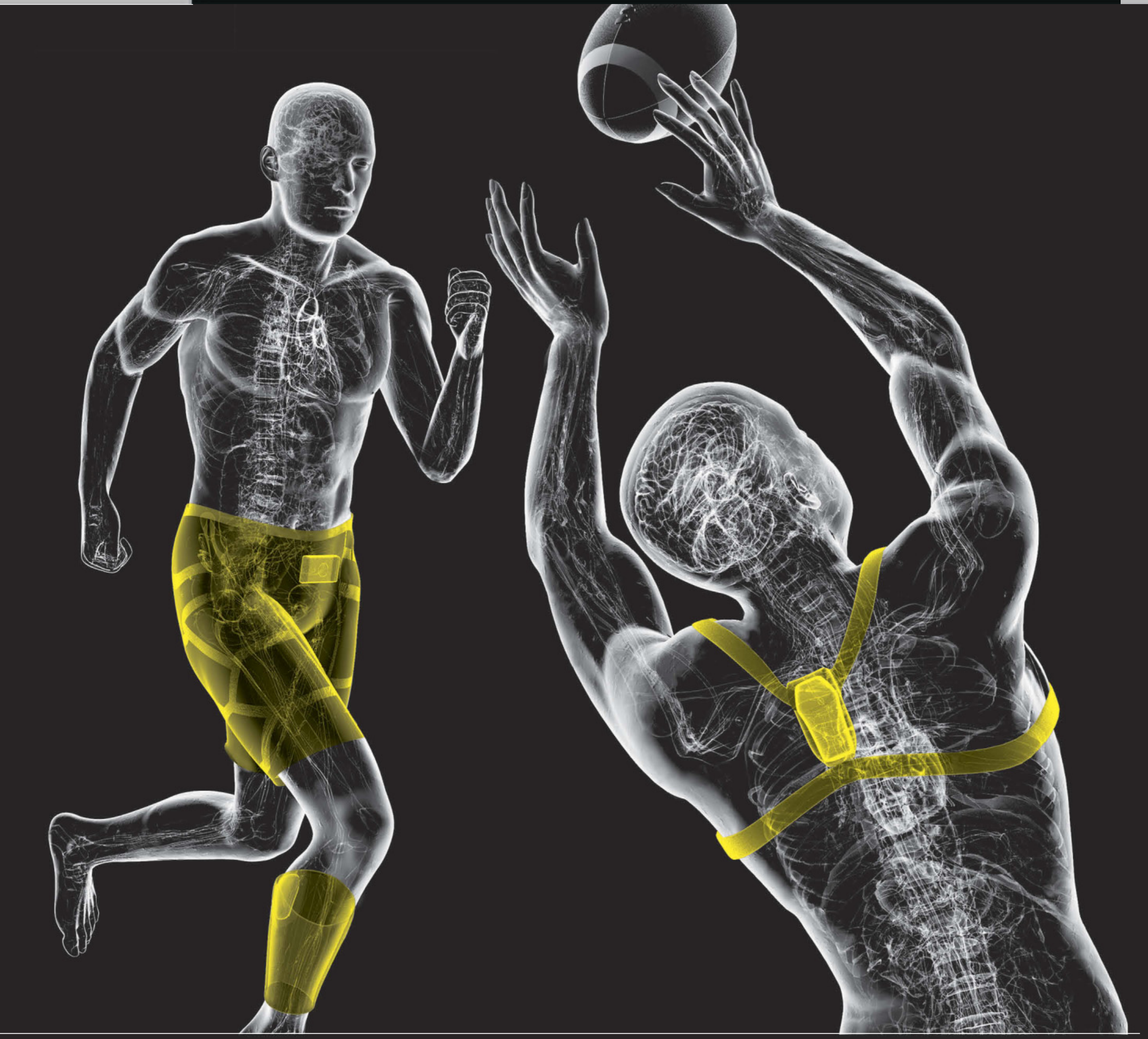
WHAT IT IS: A compression sleeve with sensors tracks a baseball player's throwing motions. Pitchers who use the sleeves to correct their technique may be able to prevent ulnar collateral ligament (UCL) injuries, which have resulted in an epidemic of reconstructive procedures known as Tommy John surgeries. Previously, quantifying ballplayers' throwing motions required motion-capture imaging.

HOW IT WORKS: The sleeve tracks arm movements with accelerometers and gyroscopes and sends data via Bluetooth to a smartphone. Based on an estimate of the player's arm motions and basic biomechanical principles, the Motus app calculates elbow torque—the stress a pitcher puts on his UCL. It also tracks metrics such as arm speed, maximum shoulder rotation, and elbow height at ball release.

WHO'S USING IT: Pitchers with more than two dozen professional baseball teams during spring training this year

PRICE: US $150

ILLUSTRATIONS BY Bryan Christie Design



MYONTEC MBODY PRO

WHAT IT IS: Compression shorts with sensors measure muscle imbalances in the legs. The garment can determine, for example, whether athletes are favoring one leg or are using their quadriceps disproportionately compared with their hamstrings. The feedback can help athletes improve their technique and possibly forestall cramps or injuries.

HOW IT WORKS: The shorts combine electromyography (EMG) measurements of muscle activity with accelerometer and heart-rate data. The high-end version, Mbody Pro, provides a more detailed analysis of EMG data than the consumer versions, Mbody Bike&Run and Mbody AllSports.

WHO'S USING IT: Los Angeles Lakers, Pittsburgh Penguins, professional boxers, Olympic snowboarders and ice skaters, and more than 20 sports institutes and training centers around the world

PRICE: €4,000–€6,800 (€770 for the consumer-version starter kit)

BSX INSIGHT

WHAT IT IS: A compression sleeve worn on the calf measures lactate threshold—the level of exercise intensity above which lactic acid builds up in the bloodstream, causing discomfort and forcing the athlete to slow down. Normally, monitoring lactate threshold requires multiple finger-prick blood samples, which must be sent to a lab. This noninvasive sensor, however, can be worn while working out.

HOW IT WORKS: The device uses near-infrared spectroscopy to estimate lactic-acid concentration. Lights of different wavelengths shine through arteries in the calf, and sensors measure the reflections to reveal changes in blood oxygenation and other parameters.

WHO'S USING IT: Many professional cyclists, runners, and triathletes, as well as a British soccer team and an NBA team

PRICE: US $420 (multisport version)

OPTIMEYE S5

WHAT IT IS: This device's sensors precisely record a player's movement on the field or court. The device, which sits over the upper back inside a compression garment, monitors acceleration, deceleration, change of direction, jump height, and distance traveled, among other metrics. Coaches use the data to keep tabs on how hard players are working and to prevent injuries resulting from overtraining.

HOW IT WORKS: Accelerometers, magnetometers, gyroscopes, and a GPS receiver record as many as 100 data points per second. Algorithms determine what the athlete is doing based on the software's sport- and position-specific analytics. The data is accessible in real time on the sidelines through a wireless link.

WHO'S USING IT: Nearly half of the NFL, a third of the NBA, more than 100 NCAA teams, half the English Premier League, and dozens of other professional hockey, soccer, rugby, and rowing teams around the world

PRICE: About US $175 per athlete per month, depending on the number of devices purchased

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PART 1: Reading the Code | DIAGNOSTICS

The Race to Build a Real-Life Tricorder

CAN THE "STAR TREK" HEALTH SCANNER BECOME A REALITY?

By **Evan Ackerman**

TATIANA RYPINSKI IS MAYBE TWO bites into her salad when she realizes it's time for her next meeting. She gets to her feet and heads to the Biomedical Engineering Design Studio, a hybrid of prototyping space, wet lab, and machine shop at the Johns Hopkins University's Homewood campus, in Baltimore. Rypinski and a few of her colleagues gather near some worktables with power outlets dangling from the ceiling. A tool cart is in one corner, a microscope in another. Two 3-D printers sit idle along a wall. The students have agreed to meet me here to discuss their work on a project whose goal is not just inspired by science fiction–it actually comes straight out of "Star Trek." They want to build a medical tricorder.

BY THE NUMBERS

20.8 minutes

Average time a U.S. doctor spends with a patient in a consultation

In 1966, "Star Trek" introduced the tricorder as, in essence, a plot device. Like the transporter, which could "beam" people between starships and planets without asking the audience to sit through lengthy landing sequences, the tricorder could rapidly diagnose medical conditions and suggest treatments, keeping the story moving. With a wave of this fictional device, a Starfleet crew member could get a comprehensive medical analysis without having to be admitted to the ship's sick bay.

Here in the real world, though, if you have a nonemergency situation, you may wait days–weeks, in some places–to see a physician. And if you need laboratory tests, receiving a diagnosis can take even longer. A lot of waiting is involved, and waiting is the last thing you want to do when you're sick. It's even worse in the developing world, where a shortage of medical facilities and personnel means that seeing a doctor may not be an option at all. What we need is a tricorder. A real one.

Rypinski is the leader of Aezon, one of the teams participating in the Qualcomm Tricorder XPrize. The competition launched in 2012, when the XPrize Foundation and U.S. chipmaker Qualcomm challenged innovators from around the world to develop a portable, consumer-friendly device capable of diagnosing a comprehensive set of medical conditions. More than 300 teams registered, and after a series of reviews, the organizers selected 10 finalists, announced last August.

This month, the final phase of the competition starts. Each finalist team was expected to deliver 30 working prototypes, which will now undergo a battery of tests with real patients. Prizes totaling US $10 million will go to the winner and two runners-up, to be announced early next year, when "Star Trek" will be celebrating its 50th anniversary.

AEZON IS THE YOUNGEST FINALIST team: All of its members are undergraduates at Hopkins. Some have never even seen the original "Star Trek" episodes. "My dad is a huge fan, though," one student tells me. For her part, Rypinski is unfazed. "This is something we're doing because we love it," she says, "and I think that sets us apart."

The other finalists include high-profile startups like Scanadu, in Silicon Valley, and well-funded medical companies like DNA Medicine Institute, in Cambridge, Mass., which has a partnership with NASA. Four teams are based in the United States, and the other six are from Canada, England, India, Northern Ireland, Slovenia, and Taiwan.

Their tricorders won't be all-powerful portable scanners like those in "Star Trek," but they still must demonstrate some impressive capabilities. They'll have to diagnose 13 medical conditions, including anemia, diabetes, hepatitis A, leukocytosis, pneumo-

STATISTIC SOURCE: 2010 NATIONAL AMBULATORY MEDICAL CARE SURVEY, CDC

XPRIZE

nia, stroke, tuberculosis, and urinary tract infections. In addition, teams choose three additional conditions from a list that includes food-borne illness, melanoma, osteoporosis, whooping cough, shingles, mononucleosis, strep throat, and HIV. And their systems must be able to monitor vital signs like temperature, blood pressure and oxygen saturation, heart rate, and respiratory rate—not only in real time but for periods of several days as well.

The goals may seem impossibly difficult, but XPrize believes they can be achieved, thanks to a host of relatively recent technological advances. These include sophisticated machine-learning methods applied to medical data, cost-effective microfluidic and other lab-on-a-chip systems, and faster and cheaper laboratory tests such as rapid polymerase chain reaction (PCR) for DNA analysis. Just as important, there's the popularization of personal genomics services and fitness-tracking gear, exemplifying people's desire to learn more about their bodies and health.

Because the enabling technologies already exist in some form today, much of the challenge is about integrating them into a compelling system, says Grant Campany, senior director of the Qualcomm Tricorder XPrize. A tricorder isn't intended to keep you out of your doctor's office: It won't be able to treat any of the conditions it can identify. But it will be able to give you a fast and detailed picture of what may be the matter with you—which is much better than googling your symptoms and sorting through dubious medical websites, as many people do today.

Campany says the diseases chosen for the challenge are often not diagnosed early enough and therefore lead to a significant number of deaths and hospitalizations: "The goal here is to try to identify things as soon as possible so that people don't wait and get sicker."

IT'S LATE FEBRUARY, AND AEZON IS reaching a critical phase of its project. Rypinski tells me the team has a number of working components but now needs to combine them into a complete system that can be delivered to the organizers in just three months. There's a limited amount that she's willing to share with me about her team's tricorder; Aezon, like most other XPrize competitors, is keeping its technologies heavily under wraps.

Still, it's safe to say the various systems will likely work in a similar fashion. How? Say you're feeling ill. Most tricorders will probably include

TECH FROM "STAR TREK"

Dressed in a Starfleet uniform, Tatiana Rypinski holds a replica tricorder during a photo shoot for the Qualcomm Tricorder XPrize. She leads one of the finalist teams in the competition.

an application running on a phone or tablet as the main user interface. The app–a kind of AI doctor–will start by asking you a series of questions: Do you have a headache? Are you feeling dizzy? Did you vomit? It may also ask you about your age, weight, height, and medical history.

Next, it will collect your vitals, measured by a sensing device you wear on your body–a fitness tracker-style wristband, or maybe an electronic necklace. (The competition calls for this monitor to be able to gather data for 72 hours, even while you sleep.) Depending on your answers and vital signs, the app may ask you to perform some additional tests. These you will do using yet another piece of hardware, a kind of "lab in a box" unit, which will be able to perform certain diagnostic tests using samples of saliva, urine, or blood.

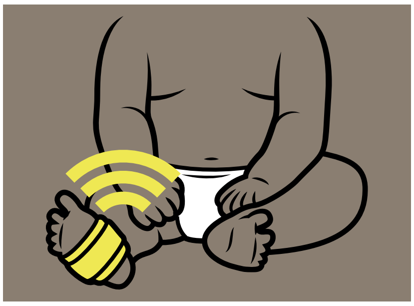
Finally, after receiving the test results and crunching all the other data, the app will give you a diagnosis and direct you to more information such as reliable medical resources or support groups for people with that disease. It may also include a "call your doctor" button, or it may even dial an emergency number.

Some teams are building devices that you could mistake for a "Star Trek" prop. Scanadu, before it joined the XPrize competition, ran a highly successful crowdfunding campaign to develop Scout, a sleek white disc you place against your forehead. Packed with sensors, the little device measures heart rate, skin and core body temperature, respiration rate, blood pressure and oxygen saturation, and electrocardiogram (ECG) data. For the XPrize, it's unclear whether the company will use the

TRICORDER STAND-IN

Your Smartphone

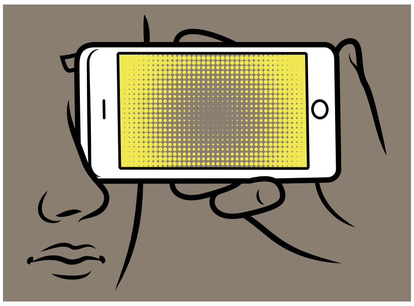
CAN A SMARTPHONE tricked out with gizmos and apps replace a doctor's traditional diagnostic tools? We'll soon find out. Capitalizing on the impressive sensors and processing power in today's smartphones, startups are turning them into mobile diagnostic and monitoring instruments for both consumers and health care workers. As capable as some of these innovations already are, it's unclear whether they will pass muster with government regulators, which is why many of their makers are not yet touting them as bona fide medical devices. *—Sarah Lewin*



PEDIATRICS

Baby Vital-Signs Checker

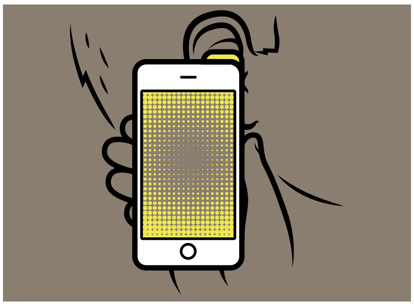
The **OWLET SMART SOCK** keeps tabs on an infant's heart rate and blood-oxygen levels. LEDs shine red and infrared light through the foot, and sensors measure how that light is absorbed by oxygen-carrying hemoglobin molecules in arterial blood. The sock transmits this data over Bluetooth to a base station and to the smartphone of the nearby (and presumably anxious) parent.
PRICE: US $250 (available for preorder)



OPHTHALMOLOGY

Eye Examiner

The **PORTABLE EYE EXAMINATION KIT (PEEK)** adds a lens adapter to the smartphone's camera. Health care workers in remote locations can then use the phone to scan a patient's retina for disease and to check for cataracts. Associated smartphone apps can be used to test the patient's vision.
PRICE: £70 (available for preorder; not available in the United States)



OTOLOGY

Eardrum Inspector

The **OTO** turns an iPhone into an otoscope that uses the phone's camera to view the eardrum at high magnification. With the home version, parents can send images of their children's eardrums to on-call clinicians to diagnose middle-ear infections. A pro version allows doctors to share images with their patients.
PRICE: US $79 for the Oto Home (currently available only in California); $299 for the Oto Clinic

ILLUSTRATIONS BY James Provost

same device or enhance it, perhaps coupling it with a wearable accessory that can gather data over longer periods.

Canadian team Cloud DX has designed a futuristic-looking plastic collar to measure vital signs. The U-shaped device wraps around your neck, and its extremities have electrodes that sit over your chest to record your heart's electrical activity. Its tricorder also includes a lipstick-size scanning wand for skin and ear exams that its creators say "Dr. McCoy would be proud of," referring to the USS *Enterprise*'s chief medical officer.

SITTING IN THE BIOMEDICAL ENGIneering Design Studio, Rypinski and her colleagues look absolutely exhausted, and it seems like they're running on little more than determined enthusiasm. She tells me that after reading about the tricorder competition in 2012, she sent e-mails to different departments at Johns Hopkins–known for its strong biomedical engineering program–to see if anyone was interested in forming a team. A lot of people showed up for the first few meetings. The hard part was finding people who would come back. "Over time, the people who were really interested in the project stuck with it," she says, "and here we are."

For the competition, Aezon adopted a divide-and-conquer approach. The 30 or so team members formed small groups to investigate individual diseases and determine which data they needed to successfully diagnose each of them.

Two of Rypinski's colleagues–Alex Kearns, a mechanical engineering student, and Akshay Srivatsan, a computer science student–tell me they have designed a smartphone-based diagnostic app that works "the way a doctor thinks." To do that, the app relies on a machine-learning technique known as a naive Bayes classifier, which is commonly used by researchers building such medical-diagnostic applications. The idea is to adjust the probability of a given diagnosis every time the system receives a new piece of information, which may include symptoms, vitals, or lab results.

BY THE NUMBERS

23.1 seconds

Average time a U.S. doctor spends listening to a patient's initial concerns

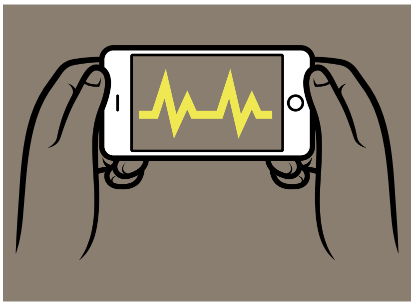
STATISTIC SOURCE: THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

To gather vital signs from patients, some Aezon team members developed a monitoring device to be worn around the neck. Its creators decided to form an independent company, Aegle, to raise funds and market the monitor separately after the competition.

For some of its tests, Aezon has partnered with the Johns Hopkins BioMEMS & Single Molecule Dynamics Lab. The team is hoping that some micro- and nanoscale molecular analysis methods recently developed at the lab could be used in a fast and cheap diagnostic test of blood samples.

For other tests, though, the team is turning to simpler technologies. Cyrus Zhou, a biophysics major, and Ned Samson, a mechanical engineering student, are working on a test for leukocytosis, which is an elevated white blood cell count. "Initially, we were going to make a microfluidic device," says Samson. "But from the people we talked to, it's like a Ph.D. to do that."

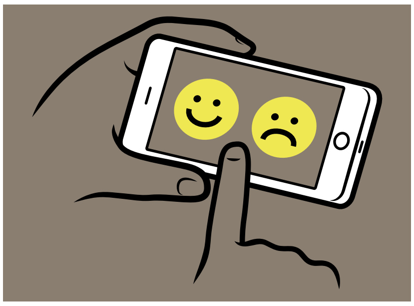
The students found a commercially available chip that causes blood cells to spread out, making them easier to see. They're now trying to combine the chip with a set of lenses that can act as a simple and inexpensive optical microscope. Their plan is to use the camera | CONTINUED ON PAGE 77



CARDIOLOGY

An ECG in Your Phone

With the **ALIVECOR HEART MONITOR**, a patient with a heart condition can collect a personal electrocardiogram, a record of the heart's electrical activity. While the patient touches electrode-carrying sensors attached to the phone's case, an associated app displays the patient's heart rate and flags irregular rhythms known as atrial fibrillations. The app also transmits data to the patient's doctor. **PRICE:** US $75



PSYCHOLOGY

Something to Watch Over You

Mental-health clinicians can use the **MOBILE THERAPY** app to keep tabs on patients between sessions. The app uses self-reports, linguistic analysis, and smartphone sensors to gather information about the patient's feelings, behaviors, movements, and interactions with other people. It then relays this information to the clinician, who can look for trends and spot trouble signs. **PRICE:** US $480 per year for a clinician

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SPECIAL REPORT

Hacking the Human OS

PART 2

Analyzing the Code

AS SENSORS AND INTERNET-CONNECTED health gadgets proliferate, your biometric data will become more medically valuable and a lot more voluminous. But what will you do with all this information? Will you send it to your doctors? What will *they* do with it? § Medical researchers are now building analytic tools that can turn raw data into actionable intelligence. Some are conducting vast surveys of vital statistics; others are mining existing databases of medical treatments and outcomes. They're looking for patterns, and they hope to find the best treatments for your specific case of your specific ailment. Tech giants such as Apple and Samsung are vying to be a part of this new medical-data industry, but arrayed against them are many doctors and an entrenched, highly bureaucratic system. It will take years for the necessary institutions to adapt or come into existence. Hopefully, in the end, the system that's better at saving lives will win. ►►►

INSIDE

PHOTO-ILLUSTRATION BY Dan Saelinger

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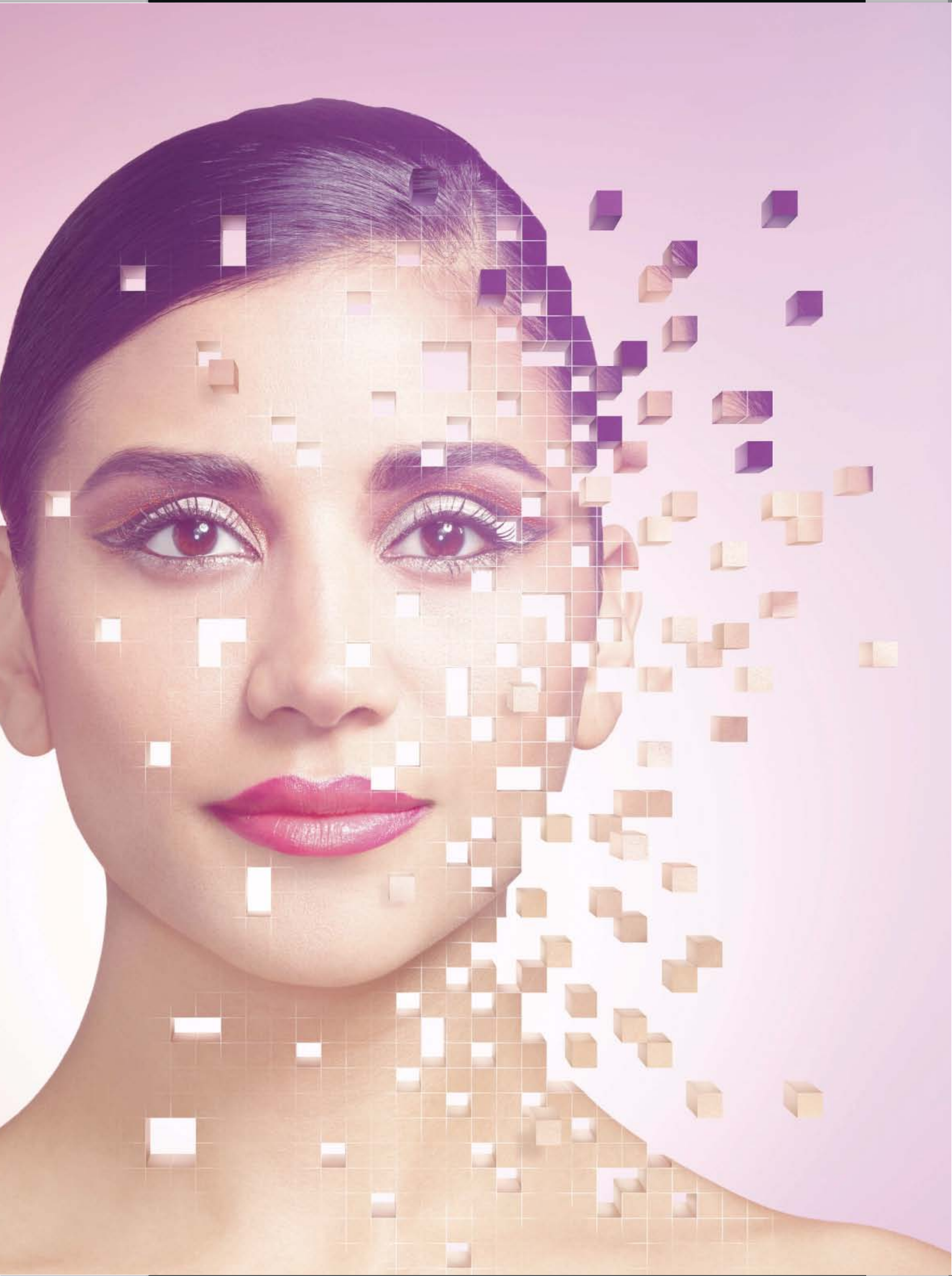


PART 2: Analyzing the Code | **BUSINESS**

Tech Giants Bet on Biometrics

APPLE AND ITS RIVALS WANT TO CAPITALIZE ON YOUR PERSONAL HEALTH DATA. BUT IS THERE REALLY MONEY IN IT?

By **Lee Gomes**

THE CONSUMER TECHNOLOGY COMpanies that own desktop software, Web search, and mobile phones have set themselves a new goal. They're aiming to carve themselves a slice of health care, the US $3 trillion industry that represents nearly a fifth of the U.S. economy.

There's a lot at stake here, and not just financially. Pundits have described a future in which your body is minutely and continuously monitored. Your wearables and assorted wireless-enabled gadgets–your bathroom scale, perhaps a blood-glucose monitor–would gather torrents of physiological data. Someday, the data might even come from biosensors worn on the body, like tattoos, or ultimately, from implanted devices. This flood of info would sluice to your smartphone before streaming off to the cloud. Apps could continuously monitor the data and, if it took an alarming turn, bring it to the attention of a medical professional. Although the quantities of data might well be huge, this vision could be realized with technologies available now or anticipated soon.

The heavyweight corporate muscle behind the vision comes from Apple, Google, Microsoft, and Samsung, which have all launched e-health initiatives, mostly based around smartphones and wearables. Indeed, the fast-growing health care business would seem a natural next step for the tech giants. Technology, including the sort of high-volume digital technology inside smartphones, is playing an increasingly important role in health care. And billions of dollars are now being spent converting the paper-based charts that doctors have long used into modern digital records. Devices, digital data–that's what these tech giants do. Why shouldn't they do it in health care, too?

Well, start with the fact that Google's, Microsoft's, and Samsung's initiatives have all been around for a couple of years, without any discernible impact on the market. Nevertheless, they're now being joined by Apple. In connection with its new Apple Watch, the company has announced HealthKit, its own approach to aggregating information from various fitness devices. Apple is pushing HealthKit with a stylish, full-glitz marketing campaign, and its top executives are extolling it in high-profile forums. "We believe we're just at the beginning of amazing new health and wellness solutions for our customers,"

ILLUSTRATION BY Tavis Coburn

Apple CEO Tim Cook told investors during a recent conference call.

Can Apple succeed where its cohorts have–so far–struggled? It's common in Silicon Valley these days to hear about the many ways that these new technologies are going to "disrupt" the world of health care. The problem is that most medical professionals aren't buying in, arguing that there's scant evidence that these consumer technologies will be of much use.

Many experts argue that the significant challenges facing the U.S. health care system, such as obesity, can't be solved with apps and trackers. For all the excitement inside the technology world about wearable digital devices and personalized health data, many doctors regard these gadgets as toys for the well-off and fit.

"Every new technology goes through a period of initial enthusiasm," says Steven Ommen, a professor of medicine at the Mayo Clinic. "And then the daunting realities set in."

The tech giants' only hope would seem to be to find an entrée that enables them to gain a footing amid the harsh realities of the slow-moving health-data business, as well as the skepticism of doctors. In fact, and despite those obstacles, experiments on chronically ill people, notably patients with diabetes, have already shown that there are benefits from smartphone-based health monitoring. It's a niche, at least, and it raises the question of whether the tech giants will stay interested long enough to try to parlay it into something larger.

CONSUMER INDIFFERENCE WILL BE yet another hurdle. "All the companies are looking to be the aggregators of consumer health data," notes Lynne Dunbrack, who covers personal monitoring devices and related areas as research vice president for IDC Health Insights. The problem, though, is that with a few exceptions, "consumers just aren't that interested in managing their health or reviewing their health records that closely," she says, adding that providers find it challenging to get patients to use their patient portals, through which users can enter their own health data.

As with any movement there are true believers: "Self quantification" enthusiasts believe so strongly in better living through gadgetry that they routinely post their personal fitness data online for all to see. But that kind of zeal is unusual, and for many who buy a fitness tracker, the typical usage pattern mimics closely the ones for diets, gym memberships, and other efforts to get in shape: It starts strong and then fizzles out. A third of the people who buy a wearable fitness device stop using it within six months, according to market researchers Endeavour Partners of Cambridge, Mass. Many other studies have reached the same conclusion.

Although Google, Microsoft, and Samsung haven't officially abandoned their health efforts, Roeen Roashan, a medical technology analyst at IHS Technology, said their projects appear to be on the back burner.

But Apple's media department forwarded a barrage of stories and press releases involving HealthKit, including announcements involving partnerships with prestigious medical institutions like the Mayo Clinic. Still, Apple is likely to face the same challenges that vexed its predecessors.

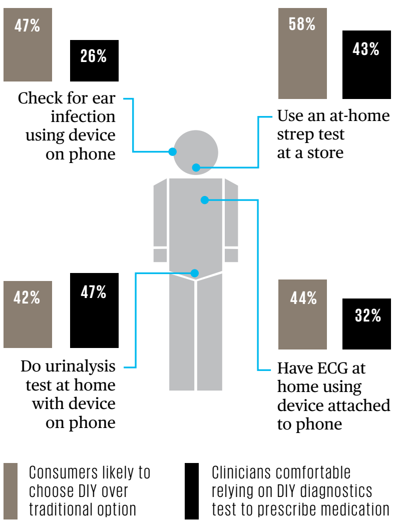
One challenge is demographic. The kinds of people who are attracted to digital health products tend to be upscale and educated–the "worried well" who least need medical attention. Those with chronic medical problems, especially ones associated with obesity, are likelier to be poor and uneducated. "The average type 2 diabetic is not going out and buying a $600 mobile phone and a

BY THE NUMBERS

100,000

Mobile health apps available for iOS and Android in 2014

STATISTIC SOURCE: RESEARCH2GUIDANCE, 2014



***DO* TRY THIS AT HOME:** Smartphone health apps tend to appeal more to patients than to doctors (and perhaps more to both than to regulatory agencies).

$300 Apple watch," says Sean Wieland, who follows stocks in the health information industry for the brokerage firm Piper Jaffrey.

A second issue is that doctors don't share the tech industry's "more is better" approach to data. "There is a big concern that health care providers will be getting a huge amount of new information that they don't want," says Bill Hanson, chief medical information officer for the health care system at the University of Pennsylvania. This would include, he said, hour-by-hour readouts of weight, pulse, blood pressure, and the like.

One of the problems with at-home data, Hanson adds, is that doctors have no context for the information. "When I have a patient in front of me, I can look and see that blood pressure has increased because the patient is nervous. But I don't have that sort of knowledge about data from outside a medical setting. Someone might have had a weight gain simply because they ate food with a lot of salt and retained fluids."

Another problem with data-hungry diagnostics is that they're based on the assumptions of preventive medicine, some of which have recently been upended. The conventional wisdom used to be that frequent screenings for diseases allowed doctors to catch and treat pathologies like prostate and breast cancer while they were still nascent. Instead, medical researchers have discovered that overscreening can cause more trouble than it solves by inflicting risky procedures on "false positives"–patients who test positive for an ailment they don't have.

There's also a liability issue, Hanson says. Plaintiff's attorneys in medical malpractice suits routinely subpoena all of a patient's health records. Should those records include copious real-time data involving heart rate, for example, a lawyer could zero in on a single anomalous reading and attempt to blow it out of proportion. "They're getting increasingly sophisticated about using medical records," says Hanson.

COMPANIES LIKE SAMSUNG AND Apple may also struggle with the software technologies used in connection with electronic medical records (EMR), which are produced with different corporate cultures and customer relationships than those that consumer companies are used to.

An EMR system replaces the racks of bulging charts that were once a familiar sight in doctors' offices; each patient's record contains clinical notes, lab results, and other information. The EMR market is highly regulated, not only for privacy reasons but also because the U.S. federal government is now spending billions of dollars subsidizing what it hopes will be an industry-wide transition to EMR-based record keeping and is trying to make sure the money is well spent.

The EMR market, at least for big hospitals and health clinics, is highly concentrated, with a few companies controlling most of the business. These big EMR providers tend to maintain a much lower profile than the Apples and Googles of the world. Ever heard of Epic Systems Corp., of Verona, Wis.? It's the biggest of the lot, and it's not even a public company.

When they discuss their coming role in health care, Apple and the others tend to talk of complementing the technology provided by big EMR vendors rather than replacing it. Consider what Apple is doing with the Mayo Clinic, one of HealthKit's premier customers.

Mayo designed a smartphone app based on software from Epic, of which Mayo is a customer. Patients use the app to e-mail their doctors, schedule appointments, and check on test results. When Mayo patients first sign up for the app, they can allow Mayo to access their Apple HealthKit data–if they have it–and present it alongside their Epic data. As the app is still in its early days, few people have signed up, according to Ommen, the Mayo medical professor.

Analysts who follow the multibillion-dollar-a-year EMR market say the consumer companies have little chance of making a major impact on it. "Health care requires a tremendous amount of domain expertise," said Wieland, of Piper Jaffrey. While consumer companies tend to be closely followed in the media, meaning their health care announcements usually get a great deal of coverage in the general interest press, "they actually don't have a very strong track record. It's still the Epics of the world that end up the winners."

The final issue is regulatory. The U.S. Food and Drug Administration recently clarified the extent to which it will regulate digital devices. It said that, in general, fitness-oriented devices that record

STATISTICS SOURCE: PWC'S HEALTH RESEARCH INSTITUTE straightforward information, like how much a wearer walks in a given day, won't be in its purview.

But "medical grade" devices–for example, sleep-apnea technologies that regulate breathing–must get FDA approval and typically require a doctor's prescription. And if these devices collect information that might play a significant role in how a doctor treats a patient, a prescription would usually be required for those too. But the companies that make such systems don't seem interested in using a consumer-oriented platform, such as a smartphone, for handling the data they gather.

One example is iRhythm Technologies of San Francisco, which makes a patch that heart patients wear for two weeks to help cardiologists detect arrhythmias. Although the data could be stored in, say, Apple's iCloud, iRhythm instead uses Amazon.com's servers because of the regulatory compliance they offer, says Kevin King, the company's president and CEO.

Although medical professionals have doubts about using consumer-grade health monitors in the general population, they believe that patients with chronic conditions might benefit enormously from them. Such patients often get admitted to hospitals as a result of an avoidable development. Often, the patient's relapse is preceded by an easily detectable signal, like a surge in blood sugar or blood pressure–one that no one notices because the patient is at home. Wearable digital devices would take the surprise out of such episodes, doctors say, enabling them to track these patients after discharge and to intervene with a phone call. In many–if not most–cases, patients could be kept out of the hospital with a relatively simple step, like an increase in medication.

U.S. hospitals are under great pressure to reduce readmissions, because of changing federal reimbursement policies that penalize hospitals when patients are readmitted too quickly after a discharge. "There is a lot of potential promise in using digital home monitoring in these cases to catch these things while they're happening," says Penn's Hanson. "And being able to intervene early is a holy grail."

Monitoring a select group of chronically ill patients to prevent their early readmission to the hospital isn't quite the same as turning every sensor suite and smartphone into a fitness coach, let alone a sophisticated and continuous health monitor. But its usefulness can be clinically proved, and tens of billions of health care dollars could be saved. That's a worthy goal in itself. And if it's the start of something more ambitious, so much the better. ■

POST YOUR COMMENTS at http://spectrum.ieee.org/techgiants0615

THE ARGUMENT | **KÁRI STEFÁNSSON**

IS PRIVACY OVERRATED?

ICELAND'S DECODE GENETICS wants to sequence the DNA of the country's small population—about 320,000 people—and match it with a rich genealogical record and national health databases. But not everyone is keen on giving up their genetic secrets. Decode's founder and CEO, Kári Stefánsson, thinks people should stop worrying about privacy and start thinking about curing disease.

***IEEE SPECTRUM*: What's the main challenge to gathering massive amounts of genetic and personal data to make medical discoveries?**
KÁRI STEFÁNSSON: The biggest problem has to do with privacy. The probability that anyone will use data like these to hurt people is extraordinarily small. It is just the perception that is somewhat troubling. When you go to the hospital or to your doctor, the probability that the health care system can help you is based upon the fact that those who came before allowed information about themselves to be used to make discoveries. I think it is completely unacceptable that you could demand service from the health care system at the same time as you refuse to have your information used to make discoveries.

So privacy concerns get in the way of medical breakthroughs?
Our queasiness when it comes to use of data is making discoveries more difficult [and] more costly. We have to find a way of convincing people that this is one of their duties in society, to allow information about themselves to be used in the context of medical research.

In an ideal world, would Decode have unfettered access to all Icelanders' genomes? All humanity's?
We don't have unfettered access to anything. All of our access is controlled by our National Bioethics Committee and our Data Protection Authority. We are tightly controlled, and we should be. Over the past 18 years, not a single data point has ever leaked out of this building. No one has ever been hurt by the data we have gathered. The only thing we have done is to make discoveries that shed light on the nature of disease, on the nature of the human condition in general. So when you are weighing the risks against the benefits, this experience is extraordinarily valuable.

—Interview by Dave Levitan

ILLUSTRATION BY Jacob Thomas

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PART 2: Analyzing the Code | DEMOGRAPHICS

100,000 People, 250 Biomarkers, and the Quest for Good Health

RESEARCHERS SEEK THE KEYS TO WELLNESS IN A PROJECT OF STAGGERING AMBITION

By **Ariel Bleicher**

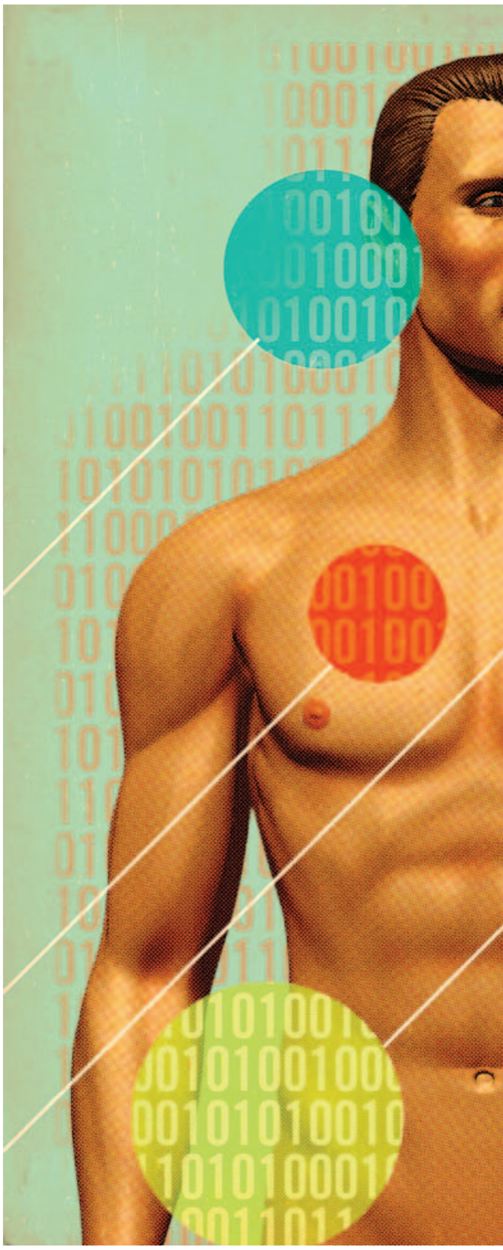
WHEN A FRIEND ASKED ED Lazowska to join a study in which researchers would obsessively monitor his body and then give him tips on improving his health, he was wary. "My wife and I really enjoy drinking wine," confesses Lazowska, a computer scientist at the University of Washington. What if the data told him he had to cut back?

But curiosity got the better of him, and he enrolled. On the researchers' dime, he got his genome sequenced. He let a local lab technician draw 14 vials of his blood every three months. And he collected his own spit, urine, and stool samples, which he shipped from a FedEx store.

Using these specimens, investigators measured concentrations of more than 250 proteins, fats, sugars, vitamins, minerals, hormones, and other molecules circulating in Lazowska's bloodstream. They cataloged dozens of species of microbes living in his gut. Through the Fitbit band on his wrist, they tracked his physical activity and sleep.

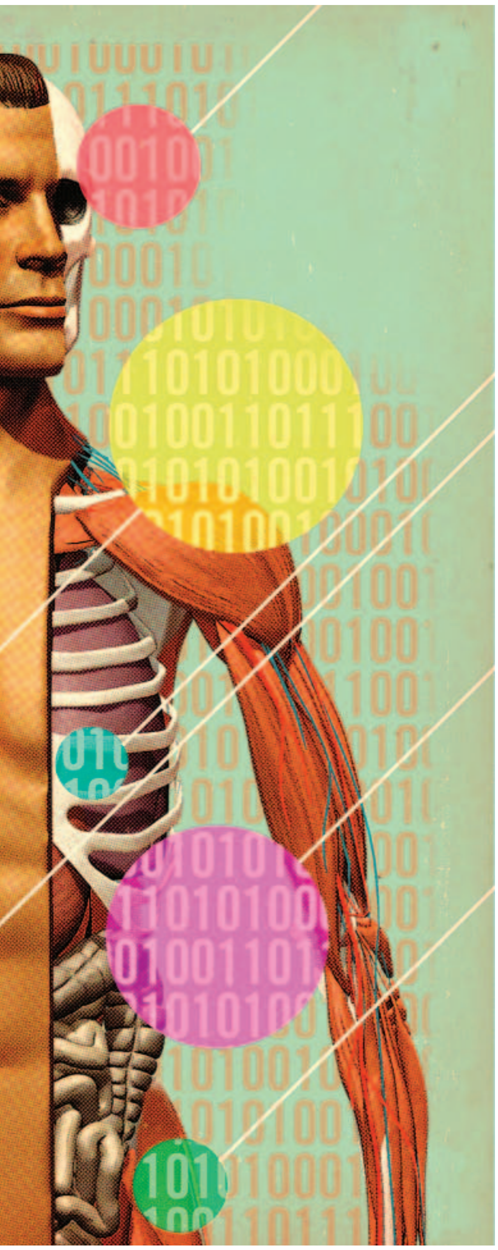
All this information went into the computers of the Institute for Systems Biology, a nonprofit research outfit in Seattle, where scientists, led by president and cofounder Leroy Hood, are now analyzing data from 105 volunteers. These brave self-samplers receive medical advice in return for their efforts. But Hood also considers them the first cohort in an experiment of vast ambition.

For his 100K Wellness Project, Hood hopes to recruit 100,000 healthy people like Lazowska and scrupulously observe their physiology for 25 years, waiting for the healthy to turn sick. No one has ever scrutinized so many able-bodied people in such detail before. Only recently have genome sequencing and other bioanalytic methods become fast and affordable enough for someone to propose such a venture and not get laughed out of the room. (The institute will likely rely on philanthropic foundations to fund the project's next stage—an expansion to 1,000 subjects—and may seek government grants or industry partners to scale up.)



Hood believes this data-intensive probe of human biology will reveal the earliest harbingers of such killers as cancer and heart disease, and change

ILLUSTRATION BY Tavis Coburn



health care in the process. Modern medicine, he laments, focuses on sickness, not wellness. Doctors treat symptoms after they emerge rather than trying to prevent them. But what if doctors could track thousands of minute changes in their patients' bodies and make sense of that data? Could they stave off disease much longer?

Hood calls his approach *P4 medicine*—medicine that is predictive, preventive, personalized, and participatory. Expounding on it, he can sound more like an evangelist than an empiricist. He's free with phrases like "profound revolution" and "paradigm shift." And he will do his darndest to convince you that a health care system based on "optimizing wellness" would "save enormous amounts of money." But not everyone is convinced.

ALL 105 PARTICIPANTS WHO completed the pilot study got results they could act on. Lazowska learned that his mercury levels were distressingly high. "So I switched from tuna sushi to salmon sushi, and my blood mercury dropped in half," he says. He also had elevated levels of a blood biomarker called homocysteine, which may increase risk of heart disease and stroke. That spike might have been a mystery if not for a second data point: Lazowska's genome scan showed a gene variant that made it difficult for his body to absorb the B vitamin folate, which keeps homocysteine in check. After he tweaked his vitamin regimen, his homocysteine levels settled down to normal.

Yet some researchers caution that the project's ability to predict and prevent illness isn't yet proved. There isn't clear evidence, for example, that taking B vitamins to lower homocysteine levels actually reduces risk for heart problems. And it's tough to ferret out the origins of disease while simultaneously trying to avert it. "Active intervention changes the thing you want to study," says Vasan Ramachandran, principal investigator of the Framingham Heart Study, which began in 1948.

Hood and his colleagues are confident that big-data analytics will enable scientists to sort through that complexity. By observing a large population over time, his team expects to identify many smaller cohorts that can be compared. "Not everyone will follow the advice they get," says Joel Dudley, director of biomedical informatics at the Icahn School of Medicine at Mount Sinai, in New York City. For example, some people with high mercury will keep eating tuna. Some will switch to salmon. Does that menu revision alter well-being? "You can see in real time what little interventions send one group one way and another group another way," says Dudley, who plans to collaborate with Hood's team.

Another concern: Intensely monitoring healthy individuals could make them less well, not more. Take today's screenings for prostate cancer, which often flag benign lesions and slow-growing tumors that will never become life threatening. Worried that patients were undergoing unnecessary surgeries, medical groups recently scaled back screening recommendations. The more measurements you take, the more likely you are to find something wrong. "As my internist friend likes to say, 'Nobody's healthy—they just haven't been tested enough,'" says Nigel Paneth, a professor of epidemiology and biostatistics at Michigan State University.

Hood disagrees. By tracking a variety of biomarkers, he contends, health professionals will gain a deeper understanding of disease and ultimately produce smarter diagnoses. But even if doctors have better information, will people make better health choices? Even the fanciest genetic sequencers, chemical assays, and data analytics may simply state the obvious: Eat better, quit smoking, reduce stress. As for Lazowska, he's still enjoying his wine. ■

POST YOUR COMMENTS at http://spectrum.ieee.org/wellnessproject0615

PART 2: Analyzing the Code | TREATMENTS

Their Prescription: Big Data

HOW ONE COUPLE FOUGHT CANCER IN THE NEW ERA OF PRECISION MEDICINE

By **Eliza Strickland**

JOHN AND KATHY HALAMKA MET ON their first day in their freshman dorm at Stanford. They decided almost instantly that they made the perfect team: With his science background and her artistic sensibility, they'd be able to handle anything that college, or life, could throw at them.

They proved their point three decades later, when Kathy was diagnosed with stage III breast cancer at the age of 49. John, as chief information officer of a Boston hospital renowned for its technological innovations, made sure that his other half got the most cutting-edge treatment.

BY THE NUMBERS

1.7 million

Breast cancer diagnoses worldwide in 2012

That didn't mean exotic new drugs or experimental surgery. Rather, her doctors planned her treatment with the help of big-data tools that John himself, along with his colleagues, had only recently brought into existence.

On a bright midwinter day in Sherborn, Mass., the couple are telling their story in the kitchen of their snug farmhouse. Outside the window, their alpacas walk in a neat line down a freshly shoveled path between towering snow banks. Inside, for lunch, Kathy is serving a frittata made from their own chicken eggs, and John is cracking open two varieties of hard apple cider that he'd lovingly brewed with fruit from their orchard. Jars of jam and honey, products of their blueberry bushes and beehives, are glowing, jewel-like, on the kitchen counter.

It was in the middle of Kathy's grueling chemotherapy treatment that the Halamkas moved to this 15-acre farm. Planning the new homestead "gave us something positive to look forward to," she says.

Kathy received her diagnosis in December 2011. The fast-growing tumor had already launched a few malignant cells into her lymph nodes, but the cancer hadn't spread any further. The conservative treatment option would have been a mastectomy, removing either one breast or possibly both, followed by chemotherapy. "That would have been the basic standard of care," Kathy says. But human beings are far from standard. Doctors have long talked of the promise of precision medicine, in which tailored treatment matches the patient's exact case. That's what Kathy got.

John, as CIO of Beth Israel Deaconess Medical Center and a professor at Harvard Medical School, had been instrumental in creating an open-source platform called Informatics for Integrating Biology and the Bedside, or i2b2. Several Boston hospitals began building that platform in 2004 to enable researchers to query vast databases of patients' electronic health records, letting them study treatment outcomes and find subjects for clinical trials. A few years later, five Harvard-affiliated hospitals used i2b2 to create a powerful search tool they named the Shared Health Research Information Network (SHRINE), which linked the five institutions' databases.

In 2008 the tool was just a proof of concept. But by the time of Kathy's diagnosis, her doctors could use SHRINE to sift the records of 6.1 million patients for valuable information. What they found made a world of difference for Kathy.

John explains that SHRINE allows physicians to search for patients who have certain characteristics, returning "de-identified" results that don't violate patient privacy rules. When Kathy's care team at Beth Israel Deaconess was planning her treatment, they searched for precedents. "We could say, 'I'm looking for age-50 Asian females who were treated with stage III breast cancer,' " John remembers. "What were their medications, what were their outcomes?"

This big-data tactic led to a somewhat unusual treatment for Kathy. She

STATISTIC SOURCE: CANCER RESEARCH UK, 2014

WIFE, PATIENT, SURVIVOR

To find the best treatment for Kathy Halamka's stage III breast cancer, her husband, John, deployed the big-data query tools he'd developed with a network of Harvard-affiliated hospitals.

PHOTOGRAPH BY David Yellen

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THE ARGUMENT | LESLIE SAXON

SHOULD YOU GET PAID FOR YOUR DATA?

IN EXCHANGE FOR FREE SERVICES, online consumers have gotten used to giving up personal information, such as what they google and what they write in e-mails. Should that same model apply to the biometric data collected by fitness trackers and apps? Leslie Saxon, executive director and founder of the Center for Body Computing at the University of Southern California, says there's value in all those heartbeats and step counts and thinks consumers should profit from it.

***IEEE SPECTRUM*: Are people already inured to giving up biometric data in exchange for a service?**

LESLIE SAXON: No, I think there will be a backlash as people realize they're being exploited for their data. It's a bad back-end model: Your data is sold five ways to Tuesday. There should be ways to get revenue out of biometric data streams that benefit the people who are providing it.

Who would buy this biometric data?

The life insurance company John Hancock just announced that it will provide Fitbits to its customers: If you use your Fitbit, you get a discount. Or imagine a teenage driver: If you use a Breathalyzer on your iPhone, you could get a discount on your car insurance. And a discount is the same as being paid. It's money in your pocket.

Will some individuals have particularly valuable data?

Because I do a lot of work with elite athletes, I have thought about this as a way to extend their brands. The same way a TV broadcast can show their speed on the field, it could also show their biometrics. Fantasy football is almost as big as real football; imagine having this additional data to help with your fantasy team. It's another insight. Or what if you were able to compare your data with theirs? People often continue to follow elite athletes of their era, so this could potentially be a revenue stream for athletes long after they retire. That could be more positive than selling a shoe brand to people who can't afford it.

—Interview by Eliza Strickland

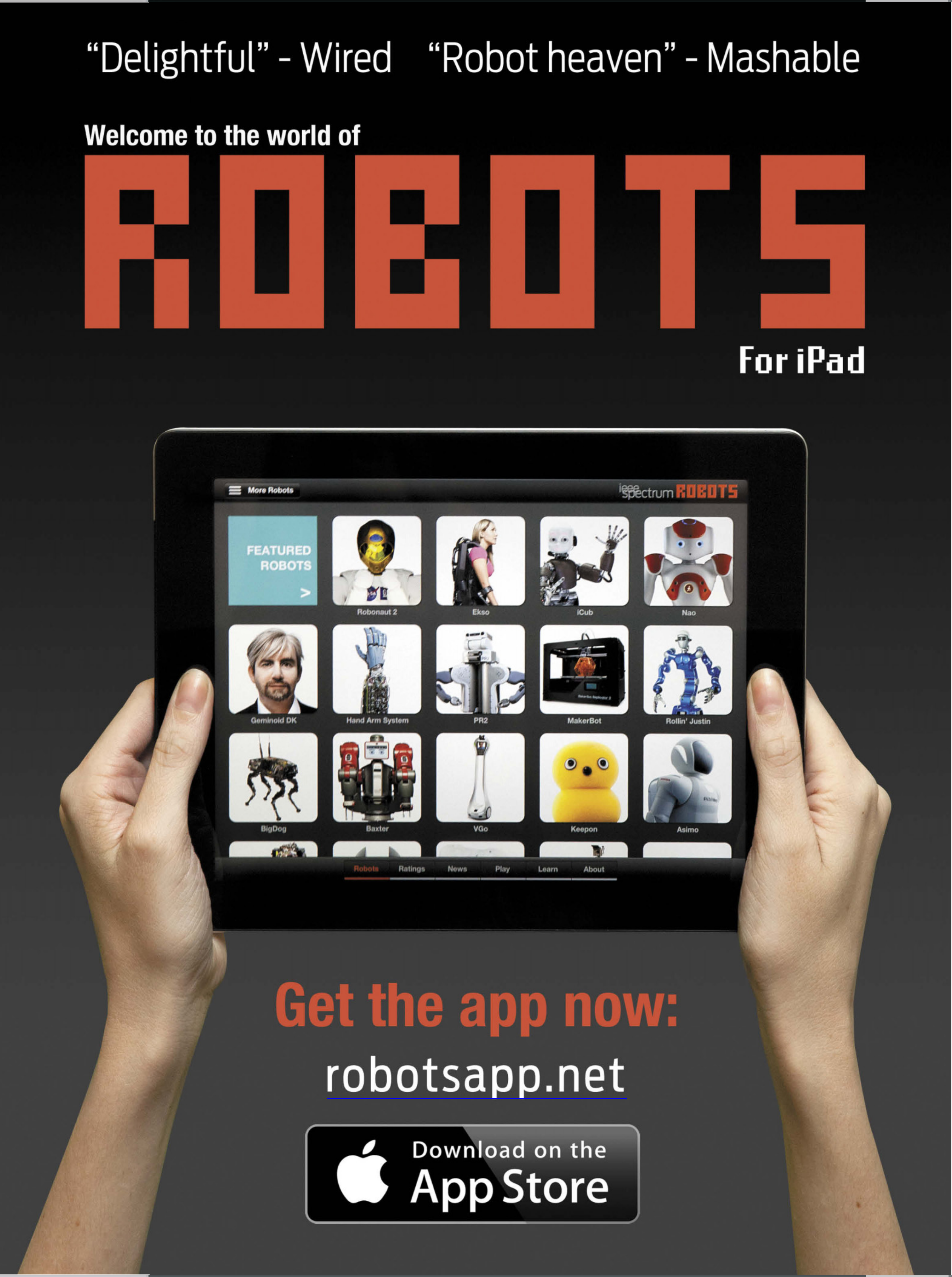
and her doctors decided to hold off on surgery and instead start by targeting her estrogen-sensitive tumor cells with chemotherapy drugs. "By the third chemotherapy session, the doctors almost couldn't feel the tumor anymore with palpation," Kathy says. "By the time I was completely done with the chemotherapy regimen, the people in radiology thought they were being punked." The radiologists simply didn't see the tumor on her scans, she explains with a gentle little smile. Kathy got a lumpectomy in May 2012, and she's still on drugs that block the production of estrogen. But it's hard to imagine how her outcome could have been better.

At last count, the i2b2 platform had been adopted by more than 100 medical institutions worldwide. A 2014 case study called it "arguably the most widely used clinical research data infrastructure based on [electronic health records] in the world." The open-source SHRINE search tool has also proved popular, with researchers in the United States and Europe deploying it to monitor public health in real time, detect the harmful side effects of certain medications, and investigate other medical topics. The U.S. government is now funding research on using SHRINE to find participants for clinical trials.

And yet, just a couple of years ago, hospitals were deeply reluctant to get involved with the development of SHRINE and similar tools. Not only did John and his colleagues have to deal with hospitals' concerns over patient privacy, they also had to convince competing medical institutions to share their databases–considered valuable intellectual property–with one another. The pioneers also grappled with the technical challenge of searching across databases with different structures and health records in different formats. All these problems prompted the SHRINE developers to use a peer-to-peer architecture rather than collecting information in a central repository. With a P2P system, each institution retained control over its records and translated queries into a format that matched its database.

Now that the search tools have proved their value, John expects many more institutions to recognize them as the natural next step in digitized medicine. Over the last decade, he says, hospitals have simply been doing the preliminary work of putting patient information into electronic formats. These electronic health records "have been dumb databases for many years, but now they can become decision-support tools and care-management tools," he says. "That's really where we're headed." | CONTINUED ON PAGE 77

ILLUSTRATION BY Jacob Thomas



"Delightful" - Wired "Robot heaven" - Mashable
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PART 2: Analyzing the Code | MODELING

Computer Modelers vs. Ebola

DID REAL-TIME EPIDEMIC MODELING SAVE LIVES IN WEST AFRICA?

By **David Brown**

HERE'S WHAT WE KNOW FOR SURE. On the afternoon of Friday, 3 October 2014, Pyrros A. Telionis got a telephone call from the U.S. government's Defense Threat Reduction Agency (DTRA). He was sitting in a featureless cubicle in Blacksburg, Va., that would have made the cartoon office drudge Dilbert feel right at home. The voice on the phone was brisk and professional. And highly specific. Could Telionis provide, by 8 o'clock Monday morning, a list of the best places to build Ebola treatment centers in Liberia's six southernmost counties?

There may or may not have been a U.S. Air Force cargo plane on a tarmac somewhere, loaded with construction materials, awaiting Telionis's list of locations. *IEEE Spectrum* couldn't confirm that part of the story.

At first glance Telionis, a Ph.D. student in computational biology at Virginia Tech, might not seem the obvious person to advise the Department of Defense, which was preparing to send about 3,000 people to West Africa to help combat the worst outbreak of Ebola virus the world has ever seen. The military personnel planned to build Ebola treatment centers, mobile labs, and a hospital for infected health care workers.

Telionis did, however, bring hidden strengths to the Defense Department's urgent assignment. Behind him was the expertise and computing power of the Network Dynamics and Simulation Science Laboratory, which is part of the 250-person Virginia Bioinformatics Institute. Split between Virginia Tech's Blacksburg campus in rural southwest Virginia and an office building near Washington, D.C., the lab has done epidemic modeling for the Pentagon for nine years. Just that week, Telionis had run an experimental program he'd written to determine the best locations for Ebola treatment centers in a few Liberian counties. DTRA was impressed by the exercise, and now the agency wanted him to do it for real.

First, Telionis had a decision to make. It was the last day to drop classes at Virginia Tech without penalty. He abandoned Advanced Methods of Regression Analysis and spent the next 64 hours working for DTRA.

His research was part of the lab's ambitious efforts to represent, through mathematical equations, the evolution of a deadly epidemic. Ideally, such models should be able to predict how quickly a disease will spread, who is most at risk, and where the hot spots will be, enabling public health authorities to take steps that diminish or shorten the epidemic. Those calculations require vast amounts of information, not only about a disease's behavior but also about a population's.

To find the optimal locations for six Ebola treatment centers, Telionis's computer model sought to minimize the distance an infected person anywhere in the six-county area would have to travel for treatment. Each center had to be on a road confirmed to exist–not easy information to come by in poorly mapped Liberia. But Telionis, working with a fellow grad student, James Schlitt, had found a list of such roads on the Web the week before. He was less certain about the distribution of the six counties' populations, so he used two estimates: one from Oak Ridge National Laboratory (LandScan), the other from a consortium of European and American universities (WorldPop). He was also

THE PATHOGEN

EBOLA IS CAUSED by a virus and spreads between humans through direct contact with bodily fluids. Infected people can suffer from diarrhea, vomiting, and both internal and external bleeding, making them very contagious. Doctors have neither a vaccine nor an effective medication to treat the disease.

ERIK VRIELINK

AT THE EPIDEMIC'S EPICENTER

A Liberian child sits in an Ebola isolation ward housing people who might have contracted the contagious disease.

JOHN MOORE/GETTY IMAGES

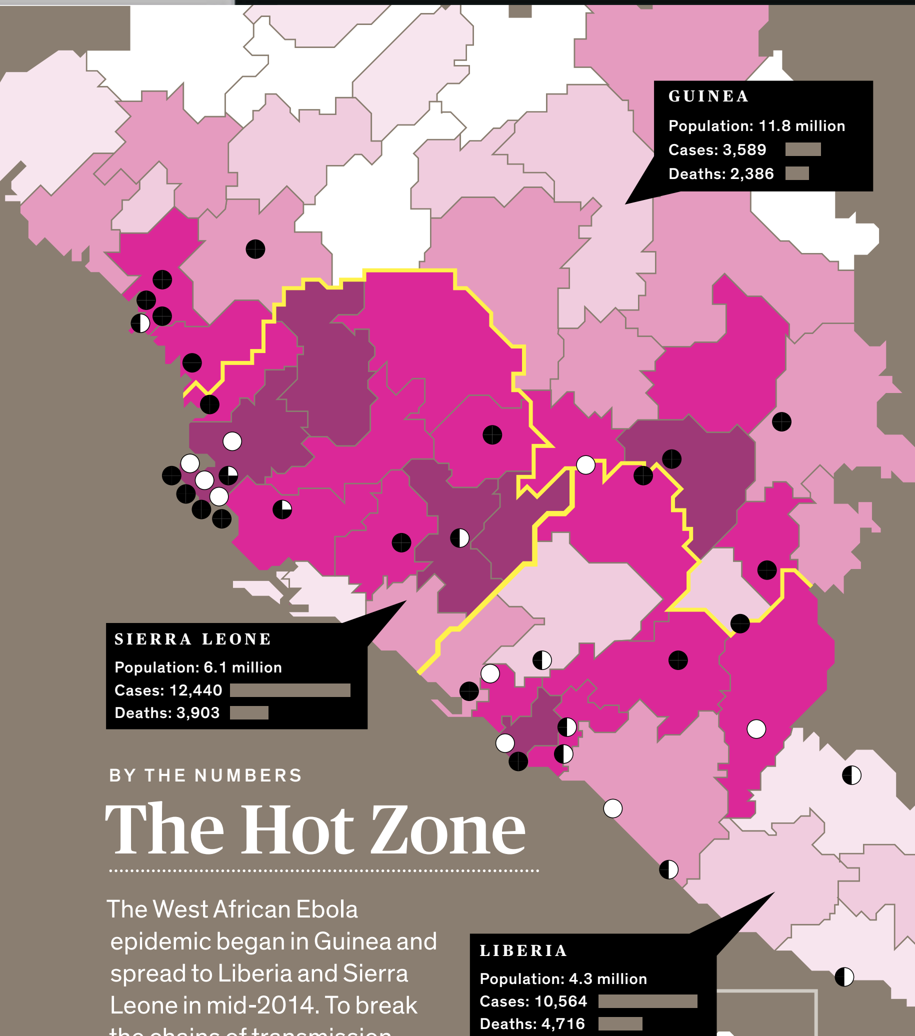
terrified that the program he'd written for the earlier exercise might have an overlooked bug. So he asked Schlitt to write an entirely new one, in a few hours, using different software. "People's lives were on the line," Telionis recalls months later. "We were actually pretty nervous the whole weekend."

The two students barely slept, but they delivered their 19-page product–including maps, tables, and animations–at 6:26 a.m. on Monday. They beat their deadline by an hour and a half.

DID THE VIRGINIA TECH MODELS make a difference to the Ebola response? We may never know for sure. The map of the treatment centers that the Defense Department built certainly looks a lot like the one that Telionis and Schlitt turned in. Beyond that, it's impossible to say, because Defense Department officials won't comment.

The same uncertainty surrounds the weekly forecasts other Virginia Tech modelers gave to the DTRA from August 2014 through February 2015, which included predictions of the epidemic's likely course and estimates of how various interventions might change it. DTRA officials say the work was "actually useful," but they won't provide details. People at the Pentagon, the U.S. Centers for Disease Control and Prevention (CDC), and the U.S. Department of Health and Human Services will speak of the modeling's utility only in general terms.

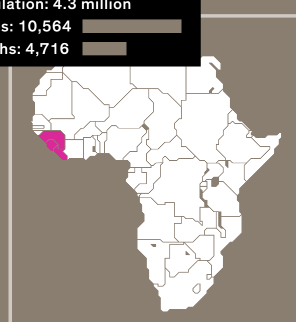
The researchers who were desperately crunching the numbers during the outbreak say that real-time epidemic modeling, done for policymakers since the 2003 SARS outbreak, got its harshest test with Ebola. For the most affected countries–Guinea, Liberia, and Sierra Leone–much of the data used to generate epidemic models was missing, old, or unreliable. That included information on population, household size, daily activities, travel patterns, and the condition and even the existence of roads. Data on key disease-specific variables, such as new cases per week and time from symptom onset to hospitalization, was also spotty for much of the



BY THE NUMBERS

The Hot Zone

The West African Ebola epidemic began in Guinea and spread to Liberia and Sierra Leone in mid-2014. To break the chains of transmission, health workers isolated the sick in specialized Ebola treatment centers, traced their contacts, and emphasized safe burial practices. The epidemic is now ebbing: In the last week of April 2015, only 18 new cases were reported.



EBOLA TREATMENT CENTERS

Maintained · Closing · Scaled down · Closed

CONFIRMED CASES

501–4000 · 101–500 · 21–100 · 6–20 · 1–5 · 0

Source: World Health Organization, situation report, 29 April 2015

outbreak. There was also a complicating factor not seen in most epidemics: Traditional West African burial practices, in which untrained people often wash and touch the dead, could act as "superspreader" events.

As a consequence, modelers had a hard time answering the most important question: How bad will this get? Some wildly inaccurate forecasts prompted media criticism, which in turn drew defensive responses. A letter in November 2014 to the journal *Nature* signed by 24 workers from various modeling teams was headlined "Ebola: Models Do More Than Forecast."

Now, with the Ebola gone from Liberia and tamped down in the other two countries, the global health community is taking stock of the role of epidemic modeling in its response. In late March of this year, the National Institutes of Health held a closed-door meeting of modelers to discuss why so many predictions were off. Christopher Dye, director of strategy for the World Health Organization (WHO) and an epidemiologist, said recently, "If you take modeling out of the response to this epidemic, would it have made any difference? I would say very little."

Others were more sanguine. Modeling "had a substantial effect," says Matthew Hepburn, an infectious diseases physician at the Defense Advanced Research Projects Agency. "It really set off alarm bells." Richard Hatchett, chief medical officer of the U.S. government's Biomedical Advanced Research and Development Authority, thinks modeling's usefulness lies in its ability to help organize thinking. His office hosted a weekly teleconference of modelers, which sometimes involved 100 people from two dozen institutions. "What decision makers are most interested in is what risks they're facing," he said. "They turn to modeling to help them understand risk–the high side and the low side–and the likely impact of a set of interventions."

In their mathematical struggle against a highly infectious virus that tore through West Africa, modelers were up against a challenge the likes of which they had never seen. But it's worth asking: In the fray, did they learn enough to make such tools a realistic hope for the next epidemic?

THE MOST RECENT EBOLA OUTBREAK began in Guinea in December 2013. By March it had spread to neighboring Liberia and soon entered crowded cities that had never before experienced Ebola's ravages. Yet it wasn't until 8 August 2014 that the

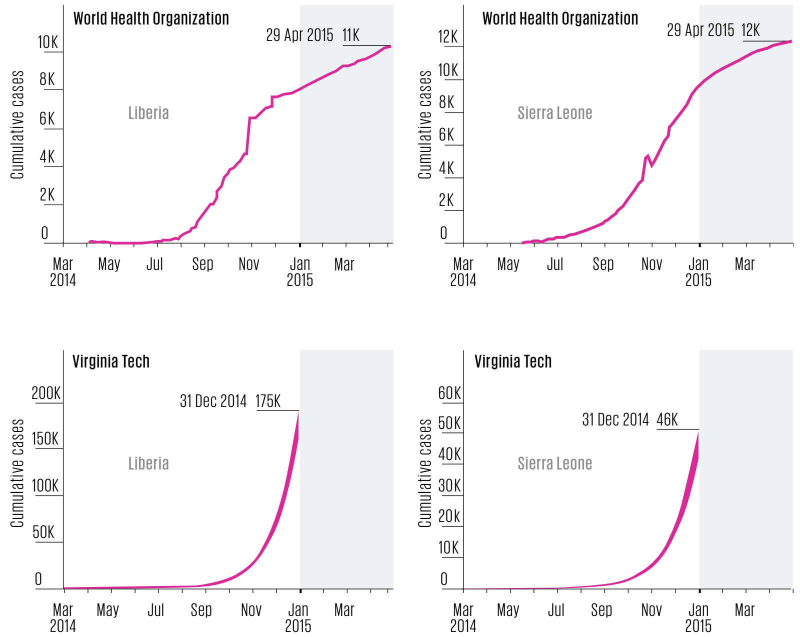
INFOGRAPHIC BY Erik Vrielink

WHO declared a "public health emergency of international concern." The world was playing catch-up from the start, and so were the modelers.

Virginia Tech graduate student Caitlin Rivers, who was finishing her doctorate in computational epidemiology, was one of those running the race. When her advisor, Bryan Lewis, asked her to turn her attention to Ebola in July, she started with a model built from the data of a 1995 outbreak in Central Africa and published by a French scientist in 2007.

That model partitioned the population into categories: susceptible, exposed, infectious, hospitalized, dead but not yet buried, and those no longer capable of virus transmission because of burial or recovery. It considered everyone, from infants to the elderly, to be at equal risk of infection and assumed the disease would move through a population in a homogeneous fashion. In other words, it was a gross oversimplification, especially for a complex pathogen like the Ebola virus. But it was better than nothing.

To sharpen her model, Rivers knew she needed this outbreak's case counts per day or week. These are essential for building an epidemic curve, which visually depicts the growth of an outbreak over time. Rivers searched the Web and found that the Liberia and Sierra Leone governments published reports (sporadically, but sometimes twice a day) listing the numbers of new cases, cases in treatment, contacts being sought, and contacts found. The data was in PDF form, so she did the "very unglamorous work" of transcribing it onto a machine-readable spreadsheet. She knew other researchers would be interested, so she posted it on GitHub, a website for open-source data. By October, her database was getting 2,000 visits a day.



The Problem With Prophecy

The Virginia Tech modelers produced their forecasts [bottom row] for the Ebola epidemic's course in Liberia and Sierra Leone in October 2014 based on data from preceding months, when the number of people infected by the virus was growing exponentially. Their forecasts, and those of many other modelers, vastly overpredicted the actual toll of the disease. As of May 2015, the World Health Organization's record [top row] put the cumulative total of Ebola cases at 10,564 for Liberia and 12,440 for Sierra Leone.

DATA SOURCES: WORLD HEALTH ORGANIZATION; VIRGINIA BIOINFORMATICS INSTITUTE, VIRGINIA TECH

Once Rivers and Lewis had four weeks of data in hand, they cranked the first curve out of the model. "It showed exponential growth," Rivers recalls. "Which is really the last thing you want to see in an outbreak."

The data Rivers compiled didn't include some information essential for forecasting, such as the length of time from exposure to infectiousness and the duration of infectiousness. Some modelers used values measured in previous Ebola outbreaks, but Rivers doubted that historical data would apply to the current scenario. So she had her computer program estimate those values based on what the epidemic curve was showing. It was a good strategy; her values turned out to be close to the actual ones the WHO eventually published. Her model also did well in calculating a key variable called the "basic reproduction number," which is the number of secondary infections caused by each primary infection in the early phase of an epidemic. Rivers's model came up with the number 2.2, not far from the WHO's final figure of 1.8.

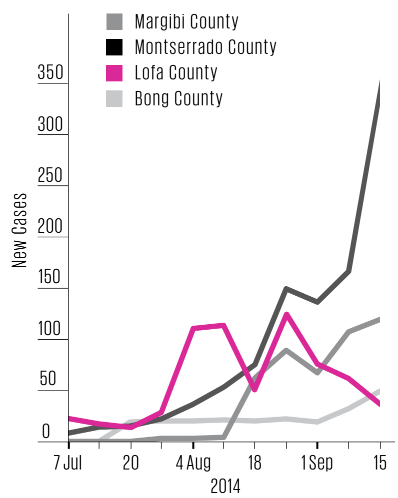
What wasn't close was Virginia Tech's crucial forecast of how big the epidemic might get. On 16 October 2014, the team published a paper saying there could be 175,000 cumulative cases in Liberia by the end of the year. It was a startling figure, especially in light of the fact that at the time of publication, there had been just 4,665 cases in that country. The prediction assumed that the length of time infected people stayed in the community and the fraction of them who were eventually hospitalized wouldn't change. But even when the modelers ran the numbers with a radically different scenario–with all infected people hospitalized, and the length of time they spent in the community cut by one quarter–they still predicted that West Africa's Ebola epidemic would be raging on New Year's Day. "These results...suggest that the epidemic has progressed beyond the point wherein it will be readily and swiftly addressed by conventional public health strategies," they wrote.

Virginia Tech's forecast wasn't the only troubling one. A team from Yale projected that Monrovia, Liberia's biggest city, might see a total of 171,000 cases by Christmas if the epidemic-fighting efforts in place in September didn't improve. Researchers at the CDC built a model that assumed more than half of cases were unreported and said Liberia and Sierra Leone might see an astounding 1.4 million Ebola cases by the end of January.

When 2015 dawned, however, the tally was nowhere near those predictions. The total was 20,712 cases in Guinea, Liberia, and Sierra Leone combined. And in all three countries, the epidemic had begun to ebb.

In a sense, the high forecasts were really worst-case scenarios. They assumed that additional treatment centers wouldn't open up, contact tracing wouldn't improve, and burial practices wouldn't get safer. But all of those improvements were in fact taking place. The forecasting teams were also brave (or foolhardy) enough to make forecasts early, which required projecting months into the future. Other forecasters waited, built more sophisticated models, and used them to project just a few weeks ahead. A team led by a researcher at Northeastern University, in Boston, incorporated steadily improving infection control into its model. It predicted Liberia's year-end total would be 11,806 cases, which was close to the WHO's final tally of 8,157. But that forecast was released on 7 January–after the end-of-year forecasting time frame.

In any case, the lack of accuracy should not be interpreted as an indication of the pointlessness of forecasting, modelers argued. Even inaccurate forecasts helped to quantify how interventions–singly or in combination, immediate or delayed–could change an epidemic's trajectory. In so doing, they helped decision makers establish priorities.



A SUBTLE SIGNAL: Many Liberian counties reported alarming numbers of new cases in late August and September 2014—but in Lofa county [shown in pink], the numbers were dropping. Almost nobody noticed.

And then there was the rhetorical utility of modeling. "Your assertion that models of the Ebola epidemic have failed to project its course misrepresents their aims," Rivers wrote in the November 2014 letter to *Nature*. "They helped to inspire and inform the strong international response that may at last be slowing the epidemic." Martin Meltzer, CDC's head modeler, says: "I like to think we in a small way contributed to that 'Go big, go quick' response." He makes no apology for the high-side estimate of 1.4 million cases.

THE EPIDEMIC PEAKED IN LIBERIA in the first week of September 2014–ironically, just about the time many overshooting modelers were preparing their forecasts. In hindsight, that peak might have been predicted if modelers had recognized the importance of what was happening in one particular part of the country.

Ebola entered Liberia through Lofa County, which borders on both Guinea and Sierra Leone, so its outbreak was the most "mature" one in the country. Lofa's epidemic curve flattened out in August, and by early September case counts had fallen slightly for several weeks in a row. Analysts weren't sure whether this decline was a blip or a real indicator of change. If the latter, it was evidence that public health campaigns in Lofa had finally convinced people to alter their behavior: to go to the hospital if they developed symptoms, to isolate exposed family members, and to consign the dead to "safe burial" teams. As the epidemic matured elsewhere and public awareness reached a critical threshold, all of Liberia might soon follow Lofa's trend.

"Staring at the data, I saw inflection coming in the curve," recalls Ira Longini, a modeler at the University of Florida who participated in the government-sponsored conference calls of epidemic modelers. "We had these weekly Ebola calls, and I pointed that out. Nobody seemed to pay any attention to it."

As it happens, Virginia Tech's Bryan Lewis had also noticed the data from

DATA SOURCE: VIRGINIA BIOINFORMATICS INSTITUTE, VIRGINIA TECH

Lofa. On 23 September, he put three slides labeled "Learning from Lofa" in his weekly presentation to the Defense Department, showing what Liberia's epidemic curve would look like if it followed Lofa's trend. The forecast was far less frightening than prior ones he'd presented to defense officials, but it wasn't well received. "I got harshly criticized," he recalls. "They thought it was a stupid experiment: 'How do you know that Liberia is going to start acting like Lofa?'"

In hindsight it's easy to recognize Lofa as a bellwether. It's also easy to say now that researchers erred in calibrating their Ebola models while the outbreak was growing exponentially and in assuming the exponential growth would continue. Such projections were unlikely to produce accurate forecasts, because the virus's transmission depends so heavily on changeable human behaviors.

The experts swear their models will work better next time. The Virginia Tech group is now creating an epidemic model that will represent the entire world and its complicated human occupants. Every country will have a "synthetic" population that stands in for the real one. There will be the right number of elementary school students per square mile, the right number of women in workplaces with more than 50 employees, the right number of households with fewer than five people, and myriad other demographic data slices. The model will also attempt to capture, at least roughly, what people do each day–the probability of leaving the home, going to a farm, getting on a bus or an airplane. Researchers don't have those details for many places and will often have to infer them. For example, in estimating how many people labor in Liberia's various types of workplaces, the Virginia Tech modelers are using data from Mexico. In other cases, an available database can give analysts a good approximation of unavailable information. Tracking the locations from which cellphone calls are made, for instance, gives a good moment-by-moment view of how people are moving in a region.

These "agent-based" models will give a more nuanced picture of how pathogens affect and sicken a population. "This is the wave of the future," says Stephen Eubank, deputy director of the Virginia Tech lab. "It's going to take a concerted effort to gather the data and the expertise. But it's going to happen."

And so, too, will another Ebola outbreak. ■

POST YOUR COMMENTS at http://spectrum.ieee.org/ebola0615

THE ARGUMENT | **THERESA MacPHAIL**

WILL OUR DATA DROWN US?

ONE PERSON, properly motivated and equipped, can generate terabytes of personal data. While all that fine-grained information could prove invaluable, it also threatens to overwhelm the health care system. Medical anthropologist Theresa MacPhail spent several months during the H1N1 flu pandemic observing researchers with the Centers for Disease Control and Prevention (CDC) as they struggled to make sense of all that big data.

***IEEE SPECTRUM:* What did you see at the CDC on a typical day?**
THERESA MacPHAIL: During the first wave of the pandemic, the analysts were getting 1,000 to 1,200 e-mails a day—spreadsheets, lab reports, surveillance alerts, direct answers to their own questions. They had multiple conference calls and at least two or three in-person meetings every day. It was intense.

Your CDC sources told you "the data were crap." What did they mean?
That the data was divorced from any context—information needed to interpret the data, like what lab did it come from, how were they running their assays. "Good" information came from sources they knew and trusted. There are some older CDC analysts I think of as "context repositories"—they can instantly provide the context for a new piece of information.

Is that something a machine can do?
The CDC, WHO [World Health Organization], and other institutions are trying to design better surveillance algorithms. When you're identifying a new outbreak, it's important to look at tweets, blogs, news reports—all that unstructured data that's so hard to handle. These massive computer programs like Google Flu Trends are designed to scan for certain keywords and spit out reports. But a human still has to go through it.

I think we're looking at big data wrong. The real usefulness of big data is to show gaps in our thinking. In the Medicare system, for instance, many people weren't opting for drug coverage, even though it would save them money. So they redesigned the enrollment campaign to get more people signed up. Big data didn't say why those people didn't sign up, and it didn't solve the problem, but it showed us we had a problem.

—Interview by Jean Kumagai

ILLUSTRATION BY Jacob Thomas

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SPECIAL REPORT

Hacking the Human OS

PART 3

Changing the Code

GATHERING AND ANALYZING all this health-related data will require enormous technical and institutional efforts, which will be undertaken with a noble goal: improving the lot of humanity. But to do that, doctors must be able to turn analyzed data into treatments. § These treatments will be many and varied. Some are obvious. If physiological indicators suggest you have arterial plaque, analysis of your specific situation may produce a new diet and medication regimen tailored to your needs. But more exotic possibilities are coming into view. Imagine microrobots that swarm over a tumor delivering chemotherapy drugs that target your genetic subtype of cancer. Consider, too, the researchers who are learning the electric language of your nervous system and building stimulators to treat such varied conditions as epilepsy, asthma, and depression. § There's a long road from today's fitness gadgets to such sophisticated medical interventions. The path won't be straight or easy. But it will be worth the trouble. ▶▶▶

INSIDE

PHOTO-ILLUSTRATION BY Dan Saelinger

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PART 3: Changing the Code | ROBOTICS

Microbots on a Fantastic Voyage

ENGINEERS ARE BRINGING MEDICAL ROBOTS TO THE LIMITS OF SIZE AND FUNCTION

By **Rachel Courtland**

IN THE 1966 FILM *FANTASTIC VOYAGE*, scientists at a U.S. laboratory shrink a submarine called *Proteus* and its human crew to microscopic size and then inject the vessel into an ailing scientist. Once inside, *Proteus* motors its way through the bloodstream and into the brain, where members of the crew don scuba gear and use a laser gun to perform delicate surgery.

From our comfortable 21st-century perch, there is a lot in *Fantastic Voyage* to smile about. But the notion of performing medical procedures at microscopic scales is now slowly sneaking out of the realm of science fiction. Thanks to developments in microfabrication and other areas, researchers are pushing the limits on the size and capabilities of objects small enough to move through the human body.

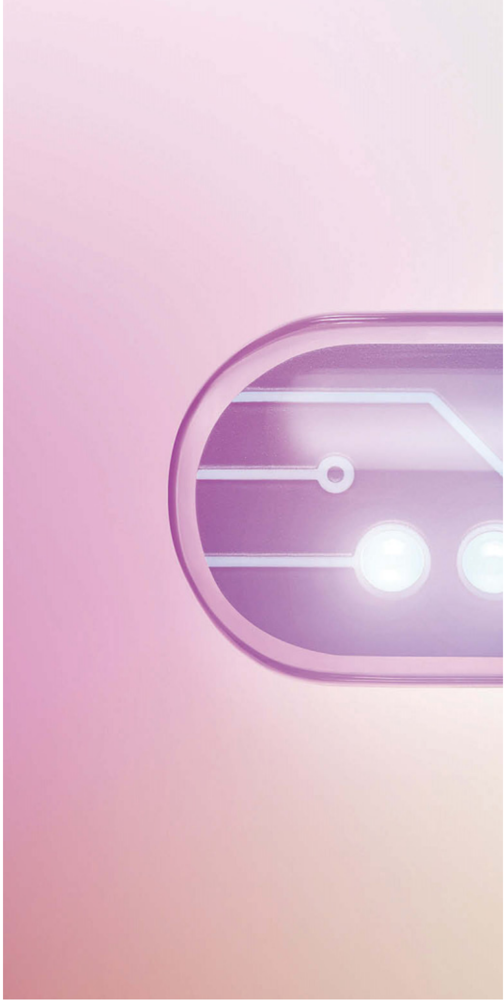
In the past 10 years or so, a menagerie of whimsical-sounding designs has emerged: microrobots driven by bull sperm and bacteria, starfishlike microgrippers that can close their arms around tissue as they get warm, spinning magnetic helices that can deliver DNA to cells, steerable magnetic spheres packed with drugs, micromotors powered by gastric acid, and microscallops that can flap their way through the vitreous humor of the eye.

Many of these devices are still little more than laboratory curiosities, but others are being tested in animals. And some engineers are confident that tiny, untethered instruments will one day be used in medicine. "Our biggest impact will be in health care," says microroboticist Metin Sitti, who leads the Physical Intelligence Department of the Max Planck Institute for Intelligent Systems, in Stuttgart, Germany. He coauthored a recent survey of the field for *Proceedings of the IEEE*.

BY THE NUMBERS

>2.5 million

The number of swallowable PillCam SB capsules, designed to image the small bowel, that have been sold since its debut in 2001



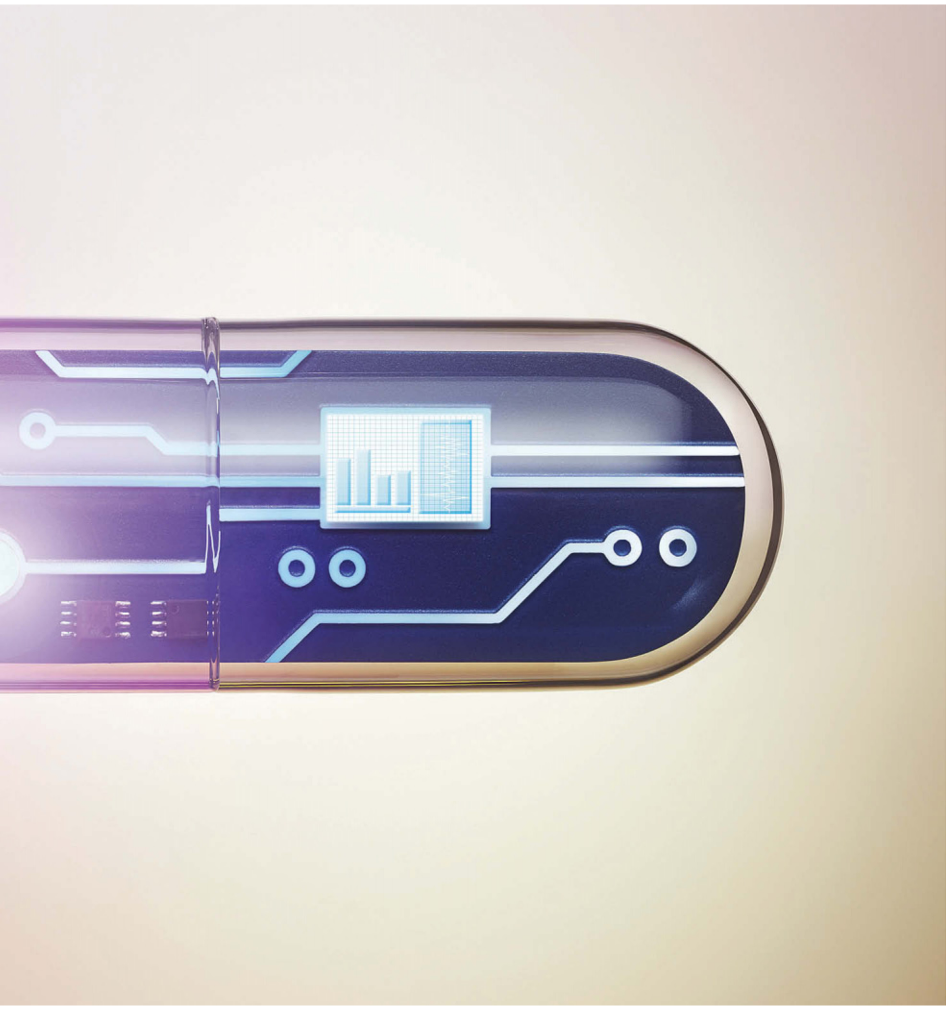
With the right design, researchers say, a microrobot–or a swarm of them–could deliver a highly targeted dose of drugs or radioactive seeds, clear a blood clot, perform a tissue biopsy, or even build a scaffold on which new cells could grow.

These sorts of activities could help extend two current trends in medicine: diagnosing diseases earlier and targeting therapies more precisely, says Bradley Nelson, a professor of robotics and intelligent systems at ETH Zurich. "The dream is the *Fantastic Voyage*," he says.

Realizing that dream will mean overcoming a range of engineer-

PREVIOUS PAGE AND THIS PAGE: PROP PILL: SWELL; STATISTIC SOURCE: COVIDIEN

PHOTO-ILLUSTRATION BY Dan Saelinger



ing obstacles. At microscopic scales, nearly every aspect of robotic operation needs to be rethought; power and movement become especially tricky. And working in the human body applies extra constraints: You need to be able to keep track of where an object is, make sure it isn't toxic and won't injure tissue, and design it to degrade safely or leave the body once its mission is complete.

"It's just been in the last few years that I think the community has started to get a handle on these fundamental problems," Nelson says. Now, he adds, the focus has turned to what can be done with the technologies researchers have in hand.

MEDICINE IS ALREADY EMBRACING miniaturization, and some technology now makes its way through the human body without any tether to the outside world. There are, for example, battery-powered gadgets about the size of a large vitamin pill that can snap images of the esophagus, intestine, and colon as they move along.

And in 2012, the U.S. Food and Drug Administration gave Proteus Digital Health, headquartered in Redwood City, Calif., the green light to market a much smaller swallowable technology: a single-square-millimeter silicon circuit that can be embedded inside a pharmaceutical pill.

"It's the smallest ingestible computer in the world," says Markus Christen, a senior vice president at Proteus. He is quick to note that its capabilities as a computer are limited. The Proteus chip carries neither an antenna nor a power source. Instead, it contains two electrode materials that are electrically connected when the pill surrounding the chip dissolves and the circuitry comes into contact with the stomach's gastric juice. For 5 or 10 minutes, the chip has enough power–between 1 and 10 milliwatts–to modulate a current, transmitting a unique identifier code that can be picked up by an external skin patch.

Sizewise, the Proteus chip is just at the upper end of what might be considered a microrobot. The chip is more than sufficient, Christen says, to help patients keep track of drug consumption and help pharmaceutical companies monitor how closely subjects in clinical trials follow a regimen when they're testing a new drug.

Making objects smaller yet more capable will require creative solutions. One of the biggest hurdles is power. Miniaturization doesn't favor traditional chemical battery technology, says Max Planck's Sitti. Shrink an object down below 1 millimeter, he says, and "the battery's capacity will go down drastically."

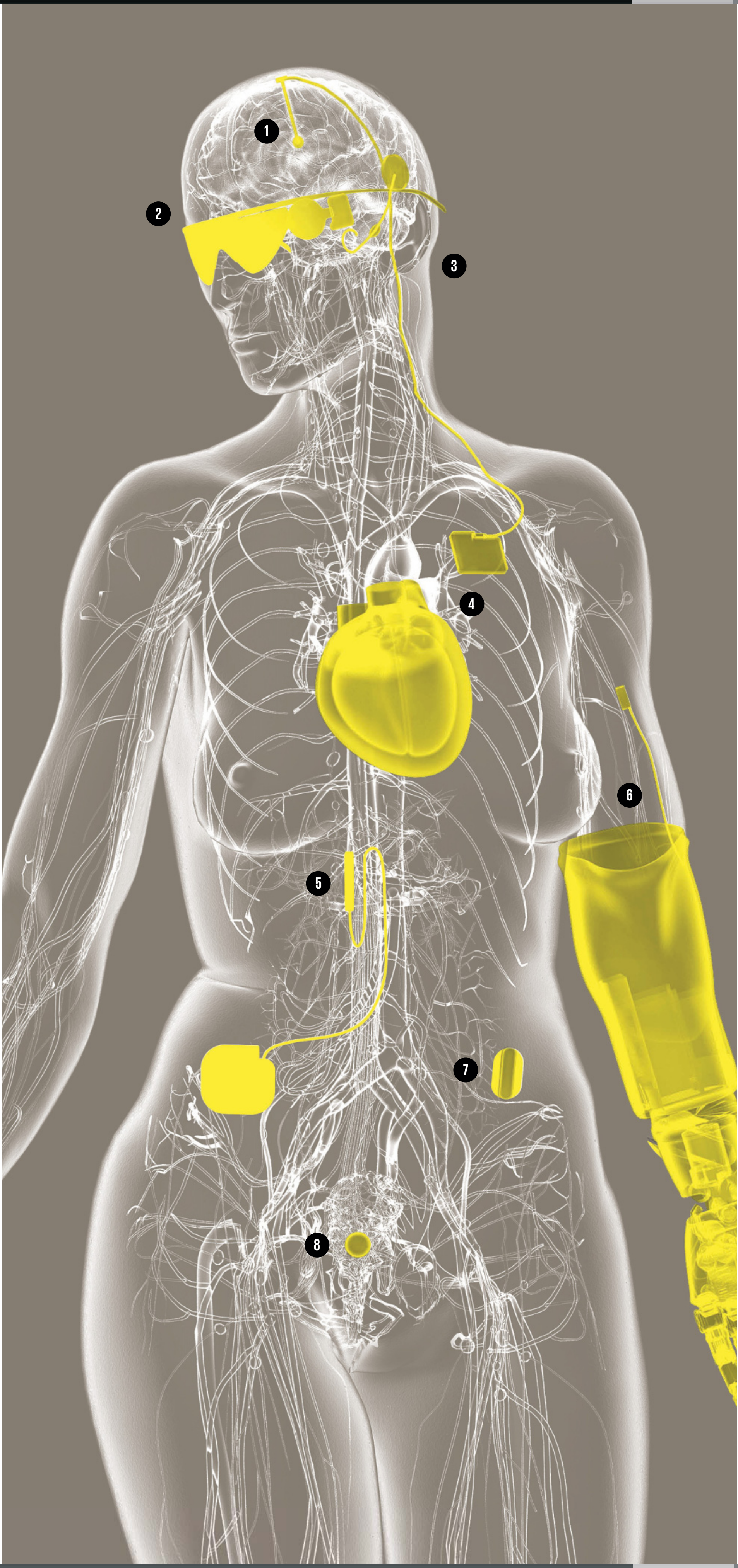
One alternative is wireless power transfer–piping in radio waves, for example, from outside the body to generate electricity. But this approach also becomes difficult at small scales. To harvest the energy, a microrobot would need some sort of antenna, and that antenna can't be too small if it's to collect a meaningful amount of energy. It must also stay fairly close to the source.

Given these limitations, engineers are looking at new ways to gather power for activities such as propulsion. One option is to create what are essentially small chemical rockets—objects that can react with substances in the body, such as gastric acid, to move around. Researchers are also exploring what can be done with biohybrids, in which bacteria are harnessed to do the swimming and perhaps even pursue a target based on signals, such as the change in concentration of a particular molecule.

In some cases, it may even be possible to do without any onboard source of energy. At Johns Hopkins University, in Baltimore, David Gracias and his colleagues have developed microgrippers—star-shaped devices that can measure less than 500 micrometers from tip to tip. The grippers can be made of materials that respond to environmental factors such as temperature, pH, and even enzymes. A temperature-sensitive gripper's arms will close when exposed to the body's heat. If placed well, the arms will close around tissue, performing a miniature biopsy.

Such grippers might provide a less invasive way to screen for colon cancer in patients who suffer from chronic inflammatory bowel diseases. Today, Gracias says, such screening can involve taking dozens of samples with forceps, in an effort to get good statistical coverage of the interior surface of the colon. Instead, a doctor could insert hundreds or thousands of microgrippers into the colon through a tube and then retrieve them using a magnet or, later, by sifting through the patient's stool.

Based on tests in live pigs, Gracias's team estimates that about one-third of the grippers capture tissue. Others may come up empty-handed because they have the wrong orientation or close before reaching anything. But



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PART 3: Changing the Code | IMPLANTS

The Ultimate Cyborg Patient

MODERN MEDICINE offers a multitude of ways to go bionic: Today's implanted electrical devices can stimulate the nervous system, restore the senses, deliver drugs, and may soon replace entire organs. Here's a sampling of cyborg technologies that benefit from advances in processing power, batteries, and sensors, which allow these devices to adapt therapies on the fly. *—Sarah Lewin*

1 BRAIN

DOCTORS already use deep brain stimulators to quiet Parkinson's tremors and are investigating their application for depression and other disorders. A new implant from Medtronic, the Activa PC+S, may yield fresh insights. When not generating impulses, this implant records brain signals, providing information that may help doctors understand how neurological diseases arise.
STATUS: In testing, approved in Europe

2 EYES

TO RESTORE SIGHT to the blind, the Argus II from Second Sight captures images with a video camera and stimulates the retina with 60 tiny electrodes, allowing patients to discern shapes and movement. It's intended for people with diseases that cause photoreceptor cells to degenerate.
STATUS: On the market

3 EARS

THE NEXT-GENERATION cochlear implant may be the fully implantable device from MIT's Microsystems Technology Laboratory, which does away with external microphones and power sources. It captures sound with a piezoelectric sensor that detects the middle ear's natural vibrations, then stimulates the auditory nerve.
STATUS: Experimental

4 HEART

UNTIL NOW, virtually all artificial hearts have been used to pump blood only while patients with heart failure wait in the hospital for transplants. But soon, patients could go home with the new heart from Carmat, which is intended to last for years and uses a microprocessor and sensors.
STATUS: In testing

5 SPINE

ST. JUDE MEDICAL'S latest neurostimulator, the Protégé, sends electric pulses to the spinal cord to interrupt signals that cause chronic pain. It's the first such device built for upgrades, so new software can be added as researchers develop new therapies.
STATUS: On the market

6 LIMBS

WITH CUFF ELECTRODES around nerve bundles in their arms, amputees gain feeling from sensors in their prosthetic hands. Researchers at Case Western Reserve University and the Louis Stokes Cleveland Veterans Affairs Medical Center are developing a system that turns sensor information into stimulation patterns, which travel up the nerves to the brain.
STATUS: Experimental

7 BLADDER

ON-THE-MARKET implants treat incontinence by stimulating the sacral nerve to improve bladder control. At the U.S. Department of Veterans Affairs' Advanced Platform Technology Center, researchers are developing an implanted pressure sensor for the bladder that will trigger the stimulator.
STATUS: Experimental

8 OVARIES

MICROCHIPS BIOTECH'S drug-delivery chip will release tiny amounts of a birth-control hormone every day for up to 16 years when implanted under a woman's skin—and can be turned off via remote control if she wants to get pregnant.
STATUS: In testing

ILLUSTRATION BY Bryan Christie Design

he says this approach, which minimizes the cost and maximizes the ease of manufacturing, could be powerful.

"The typical idea has been that you have one device that you guide precisely [to perform a] surgical procedure," Gracias says. His strategy borrows a page from the imperfect world of biology: "If you have a large number of not-perfect devices, you may be able to achieve the same functionality as one perfect one."

THE GASTROINTESTINAL TRACT IS a fairly forgiving place to work inside the human body. It's relatively large and easy to access externally, and it automatically funnels objects through the body. Exploring trickier locations, such as the eye, the brain, and the bloodstream, will likely require more sophisticated microrobot designs.

One significant hurdle is the machines' potential to trigger clots. "When you talk to clinicians, one thing that makes them go white and never want to talk to you again is any kind of notion of putting something solid in the bloodstream," says John Rogers, a pioneer of soft electronics for the body at the University of Illinois at Urbana-Champaign. "There are just really serious consequences of any kind of structure that's free-floating and just traveling around." [For more about Rogers and his work, see "Giving Your Body a 'Check Engine' Light," in this issue.]

Precise placement of microbots is therefore crucial. Even the most sophisticated microswimmers, ones capable of following a change in pH or temperature, might not be able to combat the powerful currents in the bloodstream. "The reality is, these things are not going to swim for long distances in your body," says ETH Zurich's Nelson. An autonomous swimmer might be able to muster only

THE ARGUMENT | KEVIN FU

WILL BIONIC BODIES GET HACKED?

AS PATIENTS WELCOME neurostimulators, medical microbots, and other hardware into their bodies, they're welcoming potential security flaws too. Kevin Fu, an associate professor of electrical engineering and computer science at the University of Michigan, says the medical device industry needs to get serious about cybersecurity now to ensure that life-saving technologies remain safe and trusted in the future.

***IEEE SPECTRUM:* Are medical device manufacturers considering security early enough in the design process?**
KEVIN FU: Yes and no. Some manufacturers show up to meetings about improving medical device security and participate in good faith. The real problem is that some manufacturers still aren't showing up.

Yet you and others have shown how medical devices can be compromised.
I don't see any maliciousness. If you're a manufacturer and some hacker comes and says the sky is falling, you'd probably laugh it off. The sensationalism has a negative impact. It distracts from the serious engineering.

The U.S. Food and Drug Administration issued the first cybersecurity guidelines for medical devices. What's in them?
They're the equivalent of hand washing in medicine—they're the basics. Cybersecurity hand washing means you enumerate the risks, put in place technical controls to mitigate the risks you've identified, and make sure you have the ability to determine if those controls are working effectively. To security professionals this isn't surprising, but to a biomedical engineer it really is groundbreaking.

What's the biggest security threat to medical devices today?
The main risk is conventional malware that accidentally breaks into a medical device. That is not your sinister hacking plot. For example, the FDA got a report that a pharmaceutical compounder [a machine that makes liquid drugs] had Conficker, a rather old worm. It turns out the compounder was running Windows XP Embedded, a 10-year-old operating system. It was completely susceptible. This is classic hand washing: Imagine you haven't washed your hands for 10 years and then you decide to pick your nose.

—Interview by Eliza Strickland

20 µm or so of fast, directed motion, he says, so it's likely that external guidance will be needed to get the device most of the way to its destination.

One of Nelson's targets is the retina. Today, drugs designed to treat the retina can be injected into the eye, where they slowly diffuse, but only a fraction of such a dose may reach its target. Microbots laden with drugs, Nelson says, could potentially deliver them in a more targeted manner, reducing doses as well as side effects.

One obvious strategy for guiding a robot to the right spot is to build it out of magnetic materials and then steer it externally with magnets. Researchers have used MRI machines to do this in animals. But Nelson, Sitti, and others are pursuing less powerful electromagnet configurations capable of even greater control.

Moving a microrobot with magnetic fields turns out to be surprisingly tricky. "We're still learning about the mathematics and physics of that," Nelson says. To move an object with a robotic arm in any arbitrary way, he explains, you need six actuators for a full six degrees of freedom: movement in the *x*, *y*, and *z* directions, and rotation around each of those axes. When he and his colleagues worked out a way to finely control a simple magnetic microrobot with five degrees of freedom, they found that eight separate external magnetic coils were needed. Adding in the sixth degree, Nelson says, requires that the microrobot have a more complex magnetic profile than a simple bar magnet.

Nelson's team can use its magnets to control a helical microrobot with magnetic fields of less than 10 millitesla, a fraction of what's created in an MRI. "We can twist these helices and cause them to corkscrew and move forward," he says, much in the same way that *E. coli* bacteria propel themselves by rotating their flagella. Earlier this year, his team reported that it had successfully used coated versions of these artificial bacterial flagella in the laboratory to deliver genetic material to human cells.

In the near term, Nelson is looking to see how his magnetic control technology could be used by doctors in a tethered fashion, as a way of finely guiding the tips of catheters through the cardiovascular system. But in the long term, he's exploring what might be done once this physical connection to the outside world is severed. For him and many other researchers, the possibilities seem vast—as big as the human body itself weighed against the complex, ever-moving world of the microscale. ■

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ILLUSTRATION BY Jacob Thomas

PART 3: Changing the Code | COMPUTING

Dr. Watson Will See You... Someday

IBM'S GAME-SHOW-WINNING AI STRUGGLES TO FIND THE ANSWERS IN HEALTH CARE

By **Brandon Keim**

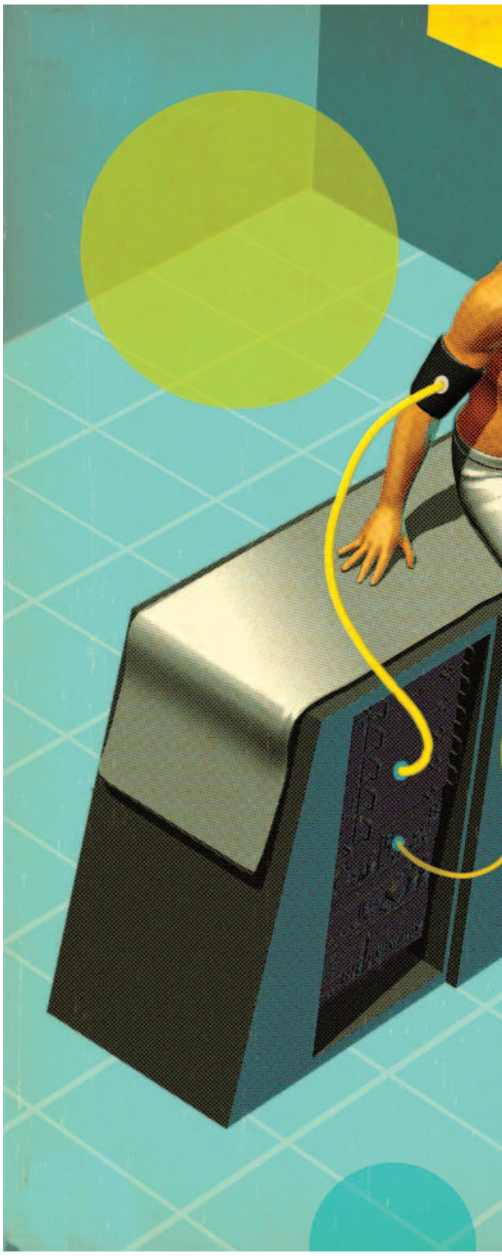
FOUR YEARS AGO, NEIL MEHTA WAS among the 15 million people who watched Ken Jennings and Brad Rutter—the world's greatest "Jeopardy!" players—lose to an IBM-designed collection of circuits and algorithms called Watson.

Mehta, a physician and professor at the world-renowned Cleveland Clinic, wondered what might be possible if Watson's powers were turned to medicine: "I knew that the world was changing. And if not Watson, then something like it, with artificial intelligence, was needed to help us."

Mehta wasn't the first doctor to dream of a computer coming to his rescue. There's a rich history of medical AIs, from Internist-1—a 1970s-era program that encoded the expertise of internal-medicine guru Jack Myers and gave rise to the popular Quick Medical Reference program—to contemporary software like Isabel and DXplain, which can outperform human doctors in making diagnoses. Even taken-for-granted ubiquities like PubMed literature searches and automated patient-alert systems demonstrate forms of intelligence.

So it's no wonder that shortly after Watson's "Jeopardy!" triumph, IBM announced that it would make Watson available for medical applications. The tech press buzzed in anticipation of "Dr. Watson." What is medicine, after all, but a series of logical inferences based on data? Four years later, however, the predicted revolution has yet to occur. "They are making some headway," says Robert Wachter, a specialist in hospital medicine at the University of California, San Francisco, and author of *The Digital Doctor: Hope, Hype, and Harm at the Dawn of Medicine's Computer Age* (McGraw-Hill, 2015). "But in terms of a transformative technology that is changing the world, I don't think anyone would say Watson is doing that today."

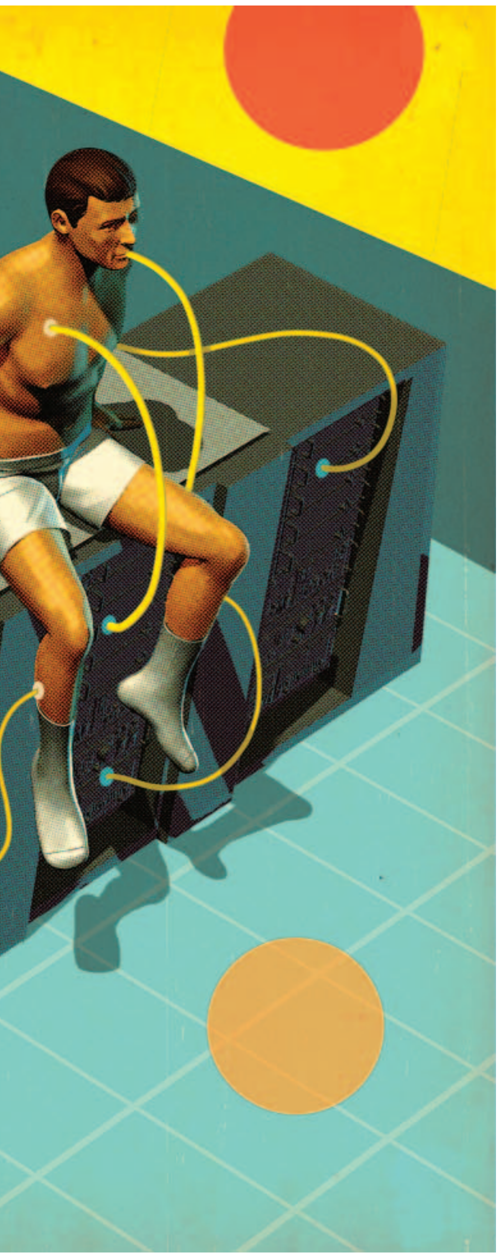
Where's the delay? It's in our own minds, mostly. IBM's extraordinary AI has matured in powerful ways, and the appearance that things are going slowly reflects largely on our own unrealistic expectations of instant disruption in a world of Uber and Airbnb.



IMPRESSIVE AS THAT ORIGINAL "Jeopardy!"-blitzing Watson was, in medical contexts such an automaton is not really useful. After all, that version of Watson was fine-tuned specifically for one trivia game.

Watson's engine needed to be adapted for medicine and, within

ILLUSTRATION BY Tavis Coburn



that broad field, to specific disciplines and tasks. Efforts to do so have spawned many different medical Watsons. Some of the first could be found at the Cleveland Clinic, Memorial Sloan Kettering Cancer Center, MD Anderson Cancer Center, and insurance company WellPoint (now called Anthem), each of which started working with IBM to develop its own health-care-adapted version of Watson about three years ago. Two years later, as the hardware shrank from room-size to small enough for a server rack, another round of companies signed on to collaborate with IBM. Among these are Welltok, makers of personal health advisory software; @Point of Care, which is trying to customize treatments for multiple sclerosis; and Modernizing Medicine, which uses Watson to analyze hundreds of thousands of patient records and build treatment models so doctors can see how similar cases have been handled.

Watson's training has been slow going, especially as each iteration needs to be tested with new questions. And Watson's text-processing powers, which might seem to make it an ideal tool for handling the rapid growth of medical literature, have proved to be of limited value. In many cases, as when modeling the decisions of top lung-cancer specialists at Memorial Sloan Kettering, there aren't yet journal articles or clinical guidelines with the right answers.

Another issue is data quality. WatsonPaths, which Mehta has been developing at the Cleveland Clinic, is the closest thing yet to that archetypal Dr. Watson, but it can work only if the AI can make sense of a patient's records. As of now, electronic medical records are often an arcane collection of error-riddled data originally structured with hospital administration in mind rather than patient care.

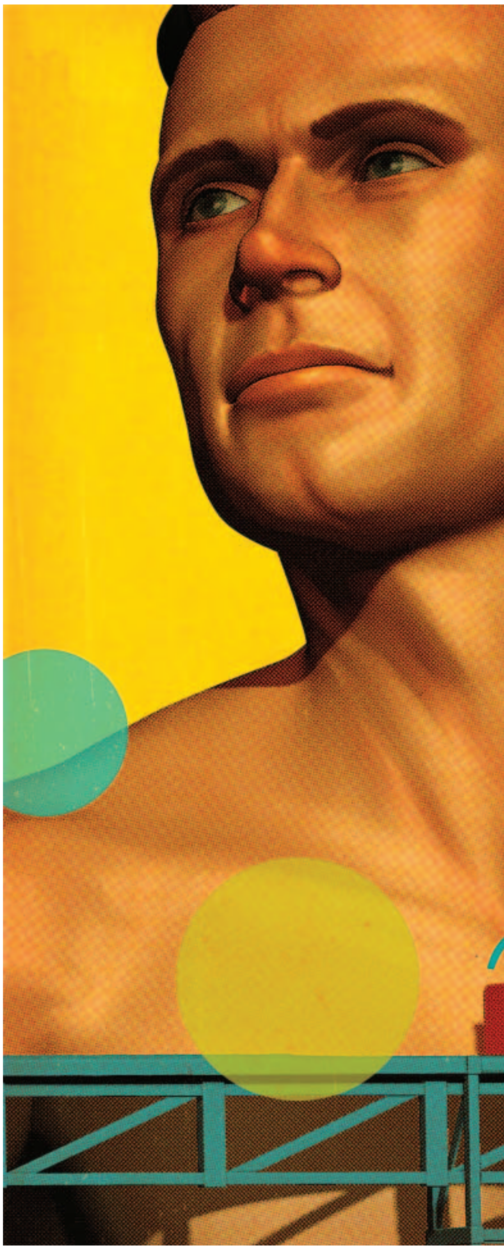
WHILE ITS "JEOPARDY!" TRIUMPH was "a great shot in the arm" for the field, says Mark Musen, a professor of medical informatics at Stanford, IBM is just one of many companies and institutions in the medical-AI space. Take the AI that Massachusetts General Hospital developed called QPID (Queriable Patient Inference Dossier), which analyzes medical records and was used in more than 3.5 million patient encounters last year. Diagnostic programs like DXplain and Isabel are already endorsed by the American Medical Association, and startup company Enlitic is working on its own diagnostics. The American Society of Clinical Oncology built its big-data-informed CancerLinQ program as a demonstration of what the Institute of Medicine, part of the U.S. National Academies, called a "learning health system." Former Watson developer Marty Kohn is now at Sentrian, designing programs to analyze data generated from home-based health-monitoring apps.

Meanwhile, IBM is making its own improvements. In addition to refinements in learning techniques, Watson's programmers have recently added speech recognition and visual-pattern analysis to their toolbox. Future versions might, like the fictional HAL 9000 of sci-fi fame, see and hear. They might also collaborate if innovations in individual deployments are eventually shared.

How will all this shake out? When will AI transform medicine, or at least help improve it in significant ways? It's too soon to say. Medical AI is about where personal computers were in the 1970s, when IBM was just beginning to work on desktop computers, Bill Gates was writing Altair BASIC, and a couple of guys named Steve were messing around in a California garage. The application of artificial intelligence to health care will, similarly, take years to mature. But it could blossom into something big. ■

FOR AN EXTENDED VERSION of this article or to post your comments, go to http://spectrum.ieee.org/drwatson0615

Follow the Wandering Nerve



DOCTORS STIMULATE THE VAGUS NERVE TO TREAT EPILEPSY, HEART FAILURE, STROKE, ARTHRITIS, AND HALF A DOZEN OTHER AILMENTS

By **Samuel K. Moore**

"THIS IS A BOTTLE OF PILLS," SAYS J.P. Errico, showing me something that's obviously not a bottle of pills.

Errico, who is cofounder and CEO of ElectroCore Medical, is holding the GammaCore, a noninvasive vagus nerve stimulator. If ElectroCore's R&D work holds up, this device is about to turn decades of evidence about the importance of a single nerve into a new kind of medicine: an electrical therapy as benign as a morning swim and as straightforward as popping a pill with your coffee.

Look at an anatomy chart and the importance of the vagus nerve jumps out at you. *Vagus* means "wandering" in Latin, and true to its name, the nerve meanders around the chest and abdomen, connecting most of the key organs–heart and lungs included–to the brain stem. It's like a back door built into the human physiology, allowing you to hack the body's systems.

Vagus nerve stimulation, or VNS, got its start in the 1990s, when Cyberonics, of Houston, developed an implanted stimulator to treat particularly tough cases of epilepsy. That application was just the beginning. Researchers soon found that stimulation had the potential to treat a variety of ailments, including painful neurological conditions such as migraine headaches and fibromyalgia, inflammatory problems such as Crohn's disease and asthma, and psychiatric ailments such as depression and obsessive-compulsive disorder.

Scientific enthusiasm notwithstanding, the clinical history of VNS has been mixed. Trials with patients suffering from treatment-resistant depression produced good results–but not quite good enough to convince U.S. government-run insurance programs to pay for its use. This past August, a stimulator produced by Boston Scientific performed poorly in a major trial with heart-failure patients. Cyberonics and its competitors are still figuring out what signals are best to send along the vagus nerve to tap into the brain's systems and fix what ails us.

Progress has been excruciatingly slow. Treatments typically require implanting a pocket-watch-size pulse generator in a patient's chest, which is wired to a pair of electrodes encircling

ILLUSTRATION BY Tavis Coburn

the vagus nerve in the neck. These trials involve patients for whom all other options have either failed or been ruled out and who are willing to undergo an invasive "treatment of last resort."

But what if VNS could be the first thing your doctor prescribed? What if, as ElectroCore promises, it really was as easy as taking a pill? That's what the New Jersey-based startup is aiming for. ElectroCore has developed the first vagus nerve stimulator that isn't implanted: It's a handheld device you simply press against your neck. If that's all it takes to hack into the brain and treat some of the most troubling conditions around, medicine might look very different a decade from now.

THE IDEA THAT THIS SINGLE NERVE can have such a profound effect on so many different organs and ailments might seem far-fetched. To understand the underlying logic of this treatment, consider the anatomy of the vagus nerve and where it connects to the brain.

The nerve terminates in the brain stem at a structure called the nucleus tractus solitarius. "The NTS is a junction in the brain," explains Milton Morris, who until recently was senior vice president of R&D at Cyberonics. From there, the vagus nerve's signals travel to other important brain structures with bewildering Latin names, such as the locus coeruleus and the dorsal raphe nuclei. Most of these structures produce neurotransmitters–the chemicals brain cells use to communicate–that have an inhibitory effect, decreasing a neuron's excitability.

That anatomical perspective clarifies how VNS produces its therapeutic benefits. An epileptic seizure, for example, is the result of waves of excitation sweeping through the brain. Deploying the brain's natural dampers should–and apparently does–cause these waves to peter out. Many of the ailments now being investigated by vagus nerve researchers likely involve similar overexcitation, or oversensitivity. "Epilepsy might be just one end of a spectrum," Errico says.

Some connections along this spectrum have been known for a long time: About 2,400 years ago, Hippocrates noted an association between epilepsy and depression, two ailments now treated with VNS. Researchers have stumbled upon other links more recently: Errico and scientists at Columbia University discovered that asthmatics they successfully treated with stimulation reported fewer headaches.

ElectroCore found further hints of relationships between maladies by delving into patient complaints collected by the United Kingdom's National Health Service. Sorting through the data helped the company identify its first clinical targets–migraines and cluster headaches–but also suggested future research directions. The data showed that care for patients with headaches is surprisingly expensive, as they consult doctors up to three times as often as average and take up to four times as much medication. But all this extra health care isn't necessarily to address their headaches; these patients tend to have other chronic conditions such as fibromyalgia, anxiety, and asthma that may be treatable through VNS. The data suggest that these conditions may have a common root, at least in some patients.

Today these problems are served by a multibillion-dollar pharmaceuticals market. But those drugs don't always work, and they can have troubling side effects. So instead of trying to squash these electronic upstarts, some big pharma companies are getting in on the game.

BY THE NUMBERS

11 percent

Fraction of adults worldwide who experience migraines

STATISTIC SOURCE: EUROPEAN BRAIN COUNCIL, 2011

British drug giant GlaxoSmithKline has been the most public with its support, even coining the term "electroceuticals" to describe the emerging therapies. "Our goal, basically, is to speak the electrical language of the nerves to achieve a higher treatment effect," said Kristoffer Famm, head of bioelectronics research at GSK, in a recent interview. In 2013, GSK created a US $50 million venture capital arm, Action Potential Venture Capital, to fund electroceutical startups. It's first pick was the vagus nerve implant company SetPoint Medical.

SetPoint was cofounded by Kevin Tracey, a neurosurgeon and immunologist. Motivated by the mysterious death of an infant burn patient under his care, Tracey went on to prove the existence of the "inflammatory reflex"–a pathway through which the brain can quell inflammation by sending signals through the vagus nerve to the spleen. SetPoint Medical is dedicated to manipulating that reflex to treat rheumatoid arthritis and Crohn's disease, among other inflammatory afflictions. Though its therapy requires an implanted stimulator, the small device fits entirely in the patient's neck, greatly reducing the extent of surgery. The company has always aimed to make the device as much like a drug therapy as possible, explains SetPoint chief technical officer Mike Faltys. "We didn't get pharmaceutical funding until recently," he says, "but we had the pharmaceutical idea from the start."

BY THE NUMBERS

€27 billion

Estimated annual cost of migraines in Europe

THINK ABOUT PILLS FOR A MOMENT: You take them either on a schedule or in response to a symptom. They're portable, and their number can be limited by prescription.

ElectroCore's device shares all these attributes, says Errico. A typical regimen is two or three 2-minute doses twice a day, but if you sense a migraine coming on, you can use the stimulator to head off a full-blown attack. ElectroCore's device is smaller than an iPhone 6, so it's easy to tote around. (The company's engineers recently built a stimulator into the case of a Samsung smartphone just to show it could be done.) And it can be programmed by your doctor to deliver a set number of doses.

Making the world's first noninvasive nerve stimulator was quite an engineering challenge. Consider the signaling problem: The vagus nerve is made up of many individual nerve fibers of several different types, some transmitting signals up into the brain and some signaling down to the organs. Some do helpful things such as calming overexcitation in the brain or signaling the spleen to reduce inflammation, but others do things that could be dangerous such as slowing your heart rate. The signal must be able to activate the "good" fibers while leaving the "bad" ones unchanged.

Adding to the difficulty is that to reach the nerve, the stimulator has to transmit its signal through several centimeters of flesh without causing excessive muscle contractions. The signal must also pass through a layer of skin that's both electrically resistive and chock-full of pain receptors.

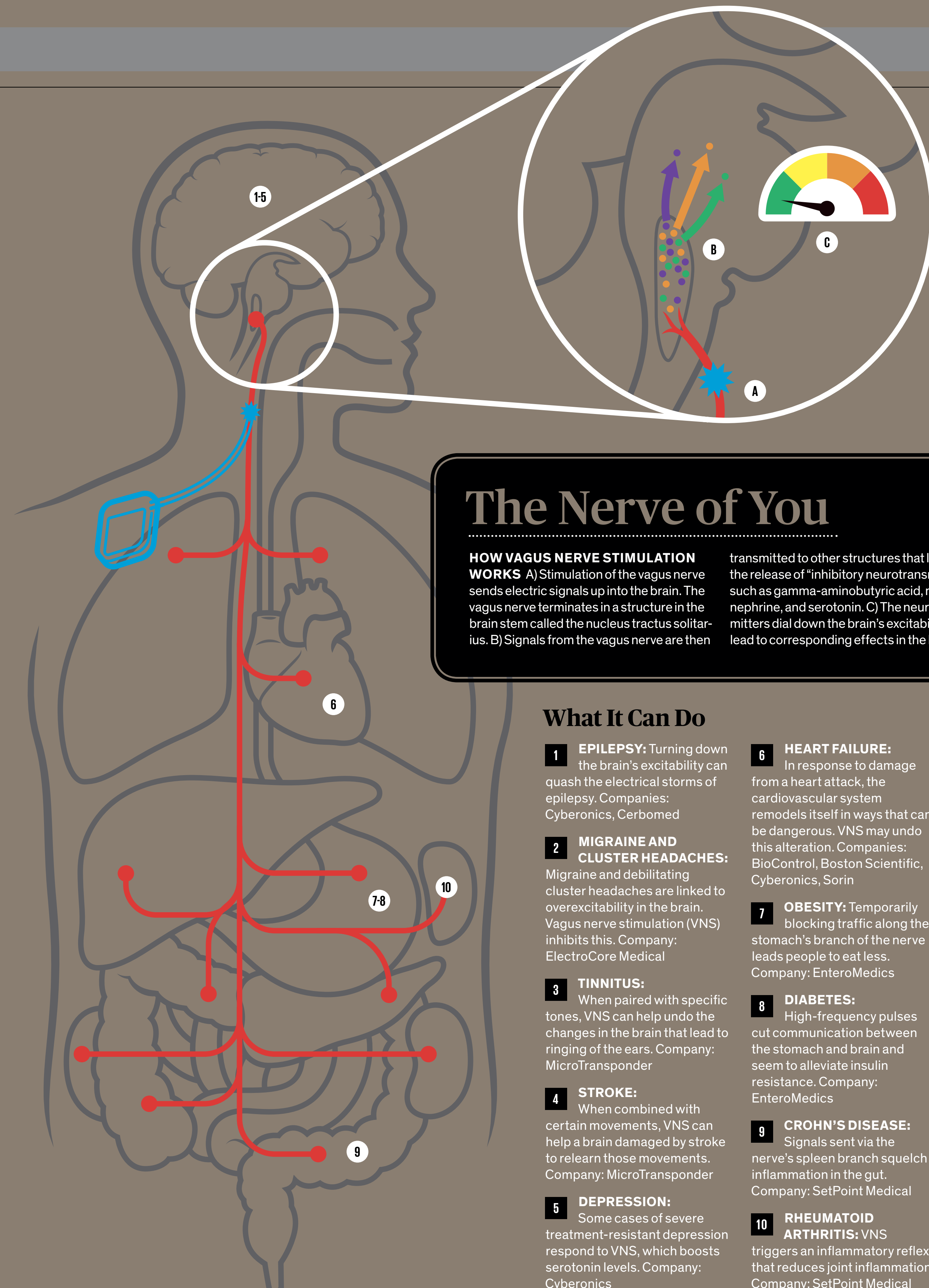
ElectroCore's researchers knew that directing the signal through the good fibers instead of the bad ones is just a matter of hitting a sweet spot of signal strength. Their real innovation was sending that signal painlessly through the skin, explains vice president of research Bruce J. Simon. The key, he says, is to understand that the skin acts the way a capacitor in a filter circuit does: It blocks direct current and low frequencies, but a high enough frequency signal will pass through it. But brain responses to VNS are frequency dependent. ElectroCore's brain-hacking code needs 25 one-millisecond pulses per second–but this low a frequency would trigger pain receptors while passing through the skin. So the stimulator forms each of the 25 pulses from a burst of 5,000 hertz. The high-frequency signals slip painlessly past the skin, losing only about half their strength along the way. The nerve fibers themselves do the rest of the job, modifying the signal that reaches them so that only the train of 25 pulses remains to propagate up into the brain.

The handheld stimulator can produce pulses at a range of voltages; because people's necks and nerves vary anatomically, the voltage is adjustable for each patient–though it always remains below the level that would trigger the bad nerves. ElectroCore's researchers found that the optimum voltage is about equal to the level that causes a person's lower lip to twitch.

"My number is 28 [volts]," says company chief operating officer Frank Amato, as he demonstrates the device. You get the sense that everyone at ElectroCore knows his or her number. I tried it as well, though on my arm and with the goal of causing my hand to contract. My number was 12.

ElectroCore isn't alone in seeking a noninvasive way to access the vagus nerve. Germany-based Cerbomed has developed a stimulator that hangs

STATISTIC SOURCE: EUROPEAN BRAIN COUNCIL, 2011



The Nerve of You

HOW VAGUS NERVE STIMULATION WORKS A) Stimulation of the vagus nerve sends electric signals up into the brain. The vagus nerve terminates in a structure in the brain stem called the nucleus tractus solitarius. B) Signals from the vagus nerve are then transmitted to other structures that lead to the release of "inhibitory neurotransmitters" such as gamma-aminobutyric acid, norepinephrine, and serotonin. C) The neurotransmitters dial down the brain's excitability and lead to corresponding effects in the body.

What It Can Do

1 **EPILEPSY:** Turning down the brain's excitability can quash the electrical storms of epilepsy. Companies: Cyberonics, Cerbomed

2 **MIGRAINE AND CLUSTER HEADACHES:** Migraine and debilitating cluster headaches are linked to overexcitability in the brain. Vagus nerve stimulation (VNS) inhibits this. Company: ElectroCore Medical

3 **TINNITUS:** When paired with specific tones, VNS can help undo the changes in the brain that lead to ringing of the ears. Company: MicroTransponder

4 **STROKE:** When combined with certain movements, VNS can help a brain damaged by stroke to relearn those movements. Company: MicroTransponder

5 **DEPRESSION:** Some cases of severe treatment-resistant depression respond to VNS, which boosts serotonin levels. Company: Cyberonics

6 **HEART FAILURE:** In response to damage from a heart attack, the cardiovascular system remodels itself in ways that can be dangerous. VNS may undo this alteration. Companies: BioControl, Boston Scientific, Cyberonics, Sorin

7 **OBESITY:** Temporarily blocking traffic along the stomach's branch of the nerve leads people to eat less. Company: EnteroMedics

8 **DIABETES:** High-frequency pulses cut communication between the stomach and brain and seem to alleviate insulin resistance. Company: EnteroMedics

9 **CROHN'S DISEASE:** Signals sent via the nerve's spleen branch squelch inflammation in the gut. Company: SetPoint Medical

10 **RHEUMATOID ARTHRITIS:** VNS triggers an inflammatory reflex that reduces joint inflammation. Company: SetPoint Medical

ILLUSTRATION BY James Provost

on a part of the ear where a minor branch of the vagus nerve lies close to the skin. Competitors are skeptical that stimulating this small branch will cause sufficient changes in the brain, but Cerbomed cites studies showing that its stimulator produces a pattern of neural activation similar to that produced by more typical forms of VNS. The company is now conducting a clinical trial for the treatment of epilepsy and has experimented with treatments for migraine, schizophrenia, and tinnitus as well.

YOU MIGHT THINK ELECTROCORE'S noninvasive vagus nerve stimulator would have makers of more conventional systems worried. It doesn't. For those companies, it's all a matter of compliance and control.

Compliance is the ability or willingness of a patient to follow through with a therapy. As former Cyberonics staffer Morris points out, some of the company's patients may be too sick to reliably use a self-administered system. Some epileptic patients, for example, can feel their seizures coming on and activate their implants, but others don't experience such foreshadowing. Implanted stimulators can deliver their therapies automatically. What's more, it can take months or even a few years for epileptic patients to get the full benefits of vagus nerve stimulation, he says. "If he's not getting relief, a patient might quit before it gets there."

Companies making invasive vagus nerve stimulators also like the guarantee that they can control the delivery of a precisely tuned signal to the vagus nerve alone. Cyberonics is also working on a heart-failure therapy, in which the doctor carefully ramps up the electrical signal over many weeks. Morris thinks this progression would be too difficult to control without an implant.

The Dallas-based company MicroTransponder is developing an implanted device to treat tinnitus and stroke. The company's chief scientific officer, Navzer Engineer, says external stimulators couldn't match the timing precision and signal integrity of his system. "We know it works and we know the parameters," he says. "I'm not sure we'd know these parameters if we used a noninvasive system."

> "Epilepsy might be just one end of the spectrum"
>
> —**J.P. Errico**, ElectroCore Medical

ElectroCore's Errico acknowledges that compliance may be a problem for some patients, but he's convinced that his company's device has exact enough control to treat a broad range of ailments.

Perhaps the biggest advantage of the noninvasive approach is the economics. Implants must operate inside the body for years without being damaged or causing problems themselves, and that doesn't come cheap: The U.S. government insurance program Medicaid pays about $20,000 for the Cyberonics epilepsy device and its implantation. At that price, it's not surprising that implants are often a last resort. By contrast, ElectroCore's noninvasive system costs the equivalent of $200 to $400 in Europe, depending on how many doses are programmed into the device.

At that price, Medical University of South Carolina brain-stimulation scientist Mark S. George imagines a scenario that would be a win for both invasive and noninvasive technology. Like any therapy, VNS doesn't work for everybody. Even in its most established use, epilepsy, VNS helps only about 40 percent of those who get the implant. George suggests that patients might start with noninvasive stimulation, and if they respond to it, they could go ahead with the implantation procedure knowing ahead of time that they'll benefit. This would cut costs overall, because fewer patients would needlessly get implants.

In any case, ElectroCore still has a lot to prove: While its device has met Europe's regulatory standards as a treatment for migraines and other headaches, U.S. market approval requires more rigorous clinical trials, which are now being reviewed by the Food and Drug Administration. And the company's scientists are still investigating potential applications in gastroenterology, psychiatry, and pulmonology.

If clinical trials eventually prove this system's worth for other chronic ailments, its low price tag would make it competitive with standard drug treatments. And unlike pharmaceutical treatments, the nerve stimulator seems to have no major side effects. Hence the buzz about electroceuticals. Anyone who will ever suffer from one of those ailments or cares about someone who does–in other words, just about everyone–may soon benefit from this new electronic age of medicine. ■

POST YOUR COMMENTS at http://spectrum.ieee.org/vagusnerve0615

GIVING YOUR BODY A "CHECK ENGINE" LIGHT

CONTINUED FROM PAGE 31

apps that use Biostamp data will have to comply with the security requirements of the Health Insurance Portability and Accountability Act in the United States and analogous privacy regulations around the world. But unlike other data-gathering devices, Biostamps also have the potential of making health information more secure. Because it can't be removed without being destroyed, a Biostamp can be a physical key used to control access to data, whether in a patient's smartphone or at a nurse's workstation.

The early tests of different Biostamps have shown encouraging results, but they were labor intensive, requiring Rogers's group to design each sensor from scratch. So while medical researchers have plenty of ideas about how a proposed sensor could help patients, creating it can take months or even years. And the stamps' limited memory and external power restrict the kinds of applications that are feasible.

To address this issue, Rogers and MC10 have developed a version of the Biostamp that's larger (about the size and shape of a Band-Aid, though slightly thicker), reusable, and equipped with a variety of sensors, batteries, and memory. The patch can be placed on a variety of spots on the body, and the signals it collects can be analyzed by smartphone or tablet apps. This reusable version includes off-the-shelf dies (chips stripped of their packages) for NFC or Bluetooth Low Energy communications and multiple sensors, small squares of lithium-ion batteries, and, for linking these components together, the kind of serpentine coils that Rogers invented for the stretchable circuits used in the tattoo-like Biostamp.

Researchers have started using these patches in clinical trials and as a platform for the development of new applications, some of which may migrate to the smaller skinlike Biostamp. MC10 is planning to market these larger, reusable Biostamps as a competitor to today's health-tracking devices in 2016. This gadget will be functional as long as its batteries are able to hold a charge. Depending on how often you end up recharging it, that's likely to be two years or more.

WITH SKINLIKE WEARABLE ELECTRONICS ON THE VERGE OF commercialization, Rogers is turning his attention from what can be sensed from outside the body to electronics that can be worn on the inside. He's collaborating with researchers at the University of Pennsylvania on an array of some 400 electrodes that can be draped across brain tissue to map activity that signals an epileptic seizure. The researchers have conducted trials with cats and will begin primate trials soon.

Other researchers are using excised hearts from organ donors to test Biostamps that could be laminated directly onto the heart's surface. This type of sensor–and, eventually, a mesh one that wraps completely around the heart and harvests energy from its beating–would give detailed information about arrhythmias and could provide finer control for pacemakers, which currently monitor a single point in the organ.

Lately, Rogers has begun to mull over a new challenge. Some parts of the body, like the brain and the heart, have twists and turns and crevices that cry out for a 3-D solution rather than his 2-D one. "We'd like to be able to not only transform circuits from planar wafers into thin, soft sheets that can be wrapped onto complex surfaces," he says, "but to induce them to self-assemble into open, 3-D formats, with filaments and arrays of interconnected structures that completely permeate a biological system. That capability would bring us into an entirely new realm of biointegration."

Such an application remains more than a decade away. But Rogers's nearer-term vision is pretty compelling, too. This enthusiastic inventor fully expects that within a decade, nearly everyone in the developed world will be wearing one or more Biostamps, at least some of the time.

FAST-FORWARD TO 2025. AT THIS POINT, IF ROGERS'S AND MC10's dreams come true, a baby in a developed country will be tagged with several Biostamps at birth. One, on a wrist or ankle, will serve as a high-tech hospital bracelet–and will be far harder to lose than today's plastic cuffs. Others on the torso or arm will allow nurses to perform quick scans of temperature, oxygen saturation, and pulse without disturbing a sleeping infant. The mother of that baby will also wear a few Biostamps, allowing nurses to monitor her vital signs as she recovers; no longer will an automatically inflating blood pressure cuff wake up an exhausted new mom.

In that same hospital, cardiac patients will wear vital-sign Biostamps plus two more on their ankles to check for swelling, an early sign of heart failure. After the cardiac patients are discharged, the stamps will continue that monitoring at home. Even the nurses will wear Biostamps, to enable them to unlock doors and log on to their computers; these devices will provide far more security than scan cards or pass codes.

Outside, the joggers running past the hospital will wear Biostamps to monitor their progress toward fitness goals. Though a typical jogger probably isn't suffering from serious medical conditions, the fitness Biostamps will spot early signs of cardiac problems or movement disorders like Parkinson's disease and suggest that the wearer check in with a doctor.

Meanwhile, passengers lining up to board a cruise ship in the nearby harbor will be busily adding one more Biostamp to the ones they usually wear. Designed with the cruise ship logo on it, it will act as a secure ID to permit them to board the ship. It will also unlock their cabin doors, allow them to charge their drinks at the bar, and even monitor their sun exposure over the course of the week and warn them when it's time to reapply sunscreen.

This coming ubiquity of the Biostamp may be hard to imagine, given that most people haven't even seen one yet. But technology sometimes surprises us. iPhones and Androids were still on the drawing board 10 years ago, and now we rely on them for constant access to information about the outside world. A decade from now, if Rogers succeeds in ushering in the world of the Biostamp, we'll know just as much about our internal worlds. ■

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DIABETES HAS A NEW ENEMY: ROBO-PANCREAS

CONTINUED FROM PAGE 35

problems with responses in the form "if this happens, do that; if that happens, do this," says Aaron Kowalski, a medical geneticist who heads artificial-pancreas research for the JDRF.

A third kind of algorithm tries to model human physiology, for instance by considering how quickly food passes through your system and how long the insulin takes to work. "The beauty of this approach is that it's like chess programming: You reset the variable when your opponent makes his move–that is, when new data arrive," says Kowalski.

Tuning these algorithms requires big data, gathered from both the individual patient and the larger community of patients. Hovorka's group at the University of Cambridge is conducting trials of advanced systems in the home, not just in controlled settings. Hovorka is also working with a corporate partner, but he won't say which one. (He notes, however, that only two companies are pushing the closed-loop solution now: Medtronic and Animas Corp., in West Chester, Pa.) He says his algorithms learn by doing and so adapt to the patient.

"The algorithm analyzes during the day and between days for short-term learning and also longer term," Hovorka says. "If somebody goes skiing, you can see a drop-off in blood sugar, and the system has to be able to cope. Every 10 to 12 minutes we run the algorithm for predictive control. We have a number of models running in parallel, with each given a probabilistic value based on how well it fitted the data in the past.

"We can achieve what no other technology can do now," he says. "Hypoglycemia [low blood sugar] is down 30 to 50 percent," Hovorka says. Patients spent 20 percent longer in the targeted zone for blood sugar–not too high and not too low.

"It's good enough to use now–I believe so," he insists.

ONE OF THE MOST FRAUGHT QUEStions in the robo-pancreas community has been whether to stick with insulin alone or to add a pump for the hormone glucagon. Insulin lowers blood sugar by helping the body–particularly the liver–store it. In the liver, glucose is converted to glycogen, a kind of animal starch. Glucagon works in the opposite direction by stimulating the liver to turn that starch back into sugar and dump it into the bloodstream. People with diabetes often carry a special pen charged with glucagon for others to use on them in case they faint from low blood sugar.

In a dual-hormone pump, insulin serves as the accelerator and glucagon as the brake, in principle allowing for finer control. But at a diabetes technology conference held in Paris this past February, funding organizations appeared to have doubled down on the simpler one-hormone system in the hope that it will get approved more easily.

One cause of the change was a recent report by researchers from IRCM. They compared the one- and two-hormone systems and found no significant advantage for the dual-hormone method. Their report seems to have had an effect.

"Prior to Paris, I'd have said the jury was still out," says IRCM's Remi Rabasa-Lhoret, one of the authors of the report. "Now I believe the jury is not out. Other teams working on the single-hormone approach have progressed immensely. The JDRF told us in a private meeting: You are doing a good job, and we want to put all our money on bringing the closed loop to market."

What's next? As the millions of people with type 1 diabetes work out the kinks in the new technology, it will spread to the hundreds of millions with type 2 diabetes, many of whom would also benefit from insulin but shy away from it because of the needles and the bother.

Now that the artificial pancreas is finally within reach, we can look back at this as the perfect case study of excessive technological optimism. A machine that senses which way your blood sugar is going and keeps it on the right track–how hard could it be? How long could it take?

Hard as hell. And 50 years. ■

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THEIR PRESCRIPTION: BIG DATA

CONTINUED FROM PAGE 52

Kathy's case dramatically illustrates this transitional moment in medicine. Her diagnosis and preliminary imaging were done at a hospital that wasn't part of the SHRINE system; when she switched to Beth Israel Deaconess for her cancer care, she hand-carried a CD containing her mammograms and other records. Her two hospitals couldn't exchange information via e-mail, much less search each other's databases. About a year later, in October 2012, John and Kathy stood with the governor of Massachusetts to celebrate the launch of Mass HIway, a health information exchange that lets hospitals, doctors, labs, pharmacies, and other health care organizations securely transmit data. As a demonstration, the Halamkas sent Kathy's medical records over the wire.

Creating such networks could enable smarter and more responsive medicine. In today's atomized medical system, it can take 10 to 20 years for a major treatment advance to become ubiquitous, says John—but linking and cross-correlating institutional records can speed up the dissemination of knowledge. In such a network, hospitals that conduct clinical trials could continually publish results and update their guidelines, and everyone on the network could access that information. A doctor running a query could then get the response: "This is the protocol you should use as of last Friday," John says.

There's plenty more to be done in order to turn today's data into tomorrow's wisdom. If tools like SHRINE can be augmented with natural-language-processing capacities, they'd be able to mine the unstructured text in doctors' notes. And the query tools have to be ready for big data to get a whole lot bigger: The cost of a full genome scan has plummeted to about US $1,000, which means that health records may soon be stuffed with patients' digitized gene sequences. How useful that data will be for research or customized treatment plans remains to be seen—but as soon as it's in the databases, innovators will certainly start trying to use it. John, who sits on advisory boards of several health care startups, is helping the big electronic-records vendors create a secure interface for nimble software companies, letting them build apps to work with the vendors' medical records. "All these big companies are fine, but do we really think the next cool innovation is going to come out of an 8,000-person company?" John asks. "No. It's probably a two-person garage operation."

As John and Kathy finish their frittata lunch and their story, the February sun is fading. John pulls on his winter gear and heads out to his chores in the barn and poultry coop. Kathy is looking forward to the spring thaw, when she'll restock the beehives and plant vegetables. As the seasons go by and Kathy's checkups continue to return a clean bill of health, all the details of her happy outcome will be recorded in her electronic health records. That means her case will now be part of the data that will guide the treatment of the next 49-year-old Asian woman with stage III breast cancer. Kathy's just another statistic—and that suits her fine. ■

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THE RACE TO BUILD A REAL-LIFE TRICORDER

CONTINUED FROM PAGE 41

on the smartphone and Aezon's app to count white blood cells with computer vision. "It's got everything," says Samson. "It's small, it's cost effective, it's doable."

BETWEEN JUNE AND DECEMBER OF THIS YEAR, XPRIZE WILL assess the teams' prototypes at the UC San Diego Medical Center. The effort will involve recruiting nearly 500 people—three consumer testers per device, per condition—to obtain a representative result for each condition with each tricorder.

The winning team will be the one that has the highest health assessment score (based on the tricorder's ability to correctly identify the condition that the user has) while also being among the five teams with the highest "consumer experience" score (based on the tricorder's aesthetic appeal, ease of use, and functionality).

"These devices must be able to function in such a way that a typical person with some understanding of smartphones should be able to understand how to operate them," says Campany, the Tricorder XPrize director. "We've put 45 percent of the score on the consumer experience, because that's how important we think it is."

This assessment won't be a clinical trial, which would be far more difficult. Even if some of the tricorders work well, there will still be a long list of questions that will need to be answered before the devices can be commercialized. Are they safe? Do they keep a user's medical data private? Who's liable if there's a misdiagnosis?

A month after my visit to Johns Hopkins, I check in with Rypinski to see how things are going. Aezon has finalized the design of its tricorder and is now tweaking its components to make sure they work well together and offer a cohesive user experience. Rypinski doesn't know how she will feel when the prototype finally ships to XPrize—and there's nothing more that her team (or any of the other teams) can do, besides wait for the results of the consumer testing. Right now she can barely find time to eat lunch.

"We have a really tight deadline to meet," she says. "After that, we'll have all the time in the world." ■

POST YOUR COMMENTS at http://spectrum.ieee.org/tricorder0615

Excerpts from the monograph entitled

Why laws such as Young's law and Ohm's law should be abandoned, and the laws that should replace them.

Eugene F. Adiutori
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Abstract
The history of engineering methodology is reviewed, and modern engineering methodology is critically examined. The examination reveals that the manner in which the dimensional homogeneity of parametric equations is currently achieved should be abandoned because it:

- Is based on an *irrational* premise.
- Makes it *impossible* to have laws that are *always* obeyed.
- Results in laws (such as Young's law and Ohm's law) that are obeyed if the behavior of concern is proportional, but are *not* obeyed if the behavior of concern is nonlinear.
- Requires *two* methodologies in each branch of engineering:
  - One methodology for problems that concern proportional behavior, and are solved using proportional laws such as Young's law and Ohm's law.
  - A second methodology for problems that concern nonlinear behavior, and are solved *without* using proportional laws such as Young's law and Ohm's law.

In this monograph, dimensional homogeneity is achieved in a manner that results in laws that are *always* obeyed, and *one* methodology that applies to *both* proportional and nonlinear behavior.

The laws are presented, and their application is demonstrated in example problems that concern proportional and nonlinear behavior in stress/strain engineering, electrical engineering, and heat transfer engineering.

The example problems reveal the marked improvement in methodological scope and simplicity that results when laws such as Young's law and Ohm's law are replaced by laws that are always obeyed.

1. Introduction
For 2000 years, scientists such as Euclid, Galileo, and Newton agreed that different dimensions *cannot* rationally be multiplied or divided.

Dimensional homogeneity was achieved by requiring that equations consist of ratios in which the numerator and denominator were the *same* parameter.

Because different dimensions could not be multiplied or divided, parametric equations such as "force equals mass times acceleration" were considered irrational.

Two centuries ago, Fourier performed experiments to determine the laws of convective and conductive heat transfer. Fourier recognized that the thermal behavior he induced could be described by quantitative, homogeneous laws *only* if dimensions could be multiplied and divided.

Fourier convinced his contemporaries that, for 2000 years, the scientific community had been *wrong* in maintaining that different dimensions cannot be multiplied or divided. He convinced his contemporaries that it is *rational and necessary* to multiply and divide dimensions. Fourier is generally credited with the modern view of homogeneity.

3.4 Why Clerk Maxwell (1831-1879) would abandon Ohm's law and electrical resistance.
In the following from *Electricity and Magnetism* (1873), Clerk Maxwell explains why Ohm's law is a law, and why electrical resistance has scientific value.

. . . the resistance of a conductor . . . is defined to be the ratio of the electromotive force to the strength of the current which it produces. The introduction of ***this term would have been of no scientific value*** *unless Ohm had shown, as he did experimentally, that . . . it has a definite value which is altered only when the nature of the conductor is altered.*

In the first place then, the resistance of the conductor is ***independent*** *of the strength of current flowing through it.*

The resistance of a conductor may be measured to within one ten thousandth, . . . and so many conductors have been tested that our assurance of the truth of Ohm's Law is now very high

In other words, if some conductors did *not* obey Ohm's law, then Ohm's law would ***not*** be a true law, and electrical resistance would have ***no scientific value***.

If Maxwell were alive today, he would surely abandon Ohm's law and electrical resistance because of the many electrical devices that do *not* obey Ohm's law.

6. Why the modern view of homogeneity is irrational.
The modern view of dimensional homogeneity is irrational because it is based on the irrational premise that dimensions can be multiplied and divided.

"Multiply six times eight" *means* "add six eights". Therefore "multiply meters times kilograms" *means* "add meter kilograms". Because "add meter kilograms" has no meaning, it is irrational to multiply dimensions.

"Divide twelve by four" *means* "how many fours are in twelve?" Therefore "divide meters by minutes" means "how many minutes are in meters?" Because "how many minutes are in meters?" has no meaning, it is irrational to divide dimensions.

In modern engineering, the multiplication and division of dimensions are indicated symbolically. But that does not prove that dimensions can actually be multiplied and divided.

7. Why laws such as Young's law and Ohm's law are irrational.
It is self-evident that dissimilar things *cannot* be proportional.

- Because alligator and house are dissimilar, they *cannot* be proportional. Therefore it is irrational to state that alligator is proportional to house.
- Because stress and strain are dissimilar, they *cannot* be proportional. Therefore it is irrational to state that stress is proportional to strain.
- Young's law is *irrational* because it states that stress is proportional to strain, and similarly for Ohm's law, and Fourier's laws of heat transfer, and other proportional laws.

"Stress is proportional to strain" is generally understood to mean "The *numerical value* of stress is proportional to the *numerical value* of strain". The *understood* meaning of the statement is rational, but the statement itself is irrational. And similarly for laws such as Young's law, and Ohm's law, and Fourier's laws of heat transfer.

4.1 Fourier's experiments and conclusions, and why laws such as Young's law and Ohm's law are *in*homogeneous.
Fourier performed comprehensive experiments in both convective and conductive heat transfer. From data he had obtained, Fourier induced that:

- Convective heat flux q_{conv} is proportional to boundary layer temperature difference ΔT_{BL}. Expressed in equation form,

$$q_{conv} = b \, \Delta T_{BL} \qquad (7)$$

- Conductive heat flux q_{cond} is proportional to temperature gradient $\mathrm{d}T/\mathrm{d}x$. Expressed in equation form,

$$q_{cond} = c \, \mathrm{d}T/\mathrm{d}x \qquad (8)$$

Equations (7) and (8) are inhomogeneous. In order to make them homogeneous, Fourier assigned the required dimensions to constants b and c, and replaced b and c with h and k.

Fourier's laws of heat transfer are *in*homogeneous because, in the modern view of homogeneity, dimensions may *not* be assigned to constants. (In Fourier's view, dimensions *may* be assigned to constants.)

Similarly, the homogeneity of laws such as Young's law and Ohm's law is achieved by assigning dimensions to constants, and they also are *in*homogeneous.

8. Fourier's error of induction.
Fourier's induction resulted in the conclusion

> Convective heat flux is proportional to boundary layer temperature difference.

But the proportional relationship Fourier observed in his data was *not* between heat flux and temperature difference. The proportional relationship was between the *numerical value* of heat flux and the *numerical value* of temperature difference. Therefore the result of Fourier's induction *should* have been

> The *numerical value* of convective heat flux is proportional to the *numerical value* of boundary layer temperature difference.

9. How Fourier's error of induction affected his methodology and conclusions.
If Fourier had correctly induced that the *numerical value* of convective heat flux is proportional to the *numerical value* of boundary layer temperature difference, his methodology and conclusions would have been affected in the following ways:

- His parameter symbols would have represented numerical value but *not* dimension.
- He would have stated that the dimension units that underlie parameter symbols in quantitative equations must be specified in accompanying nomenclatures.
- He would *not* have assigned dimensions to constants b and c in Eqs. (7) and (8) because all symbols in both equations would have represented numerical value but *not* dimension. Therefore Eqs. (7) and (8) would have been dimensionally homogeneous *as written*.
- He would *not* have conceived the modern view of dimensional homogeneity because it would not have been required in order to transform Eqs. (7) and (8) from inhomogeneous to homogeneous.
- He would *not* have conceived "heat transfer coefficient" or "thermal conductivity" because they would not have been required in order to transform Eqs. (7) and (8) from inhomogeneous to homogeneous.
- He would have accepted Eq. (7) as the law of convective heat transfer, and Eq. (8) as the law of conductive heat transfer.
- His view of homogeneity would have been that parametric equations are *inherently* homogeneous because parameter symbols represent numerical value but *not* dimension.

If you would like to receive a hard copy of the monograph, please send five USA dollars or five pounds or seven euros to

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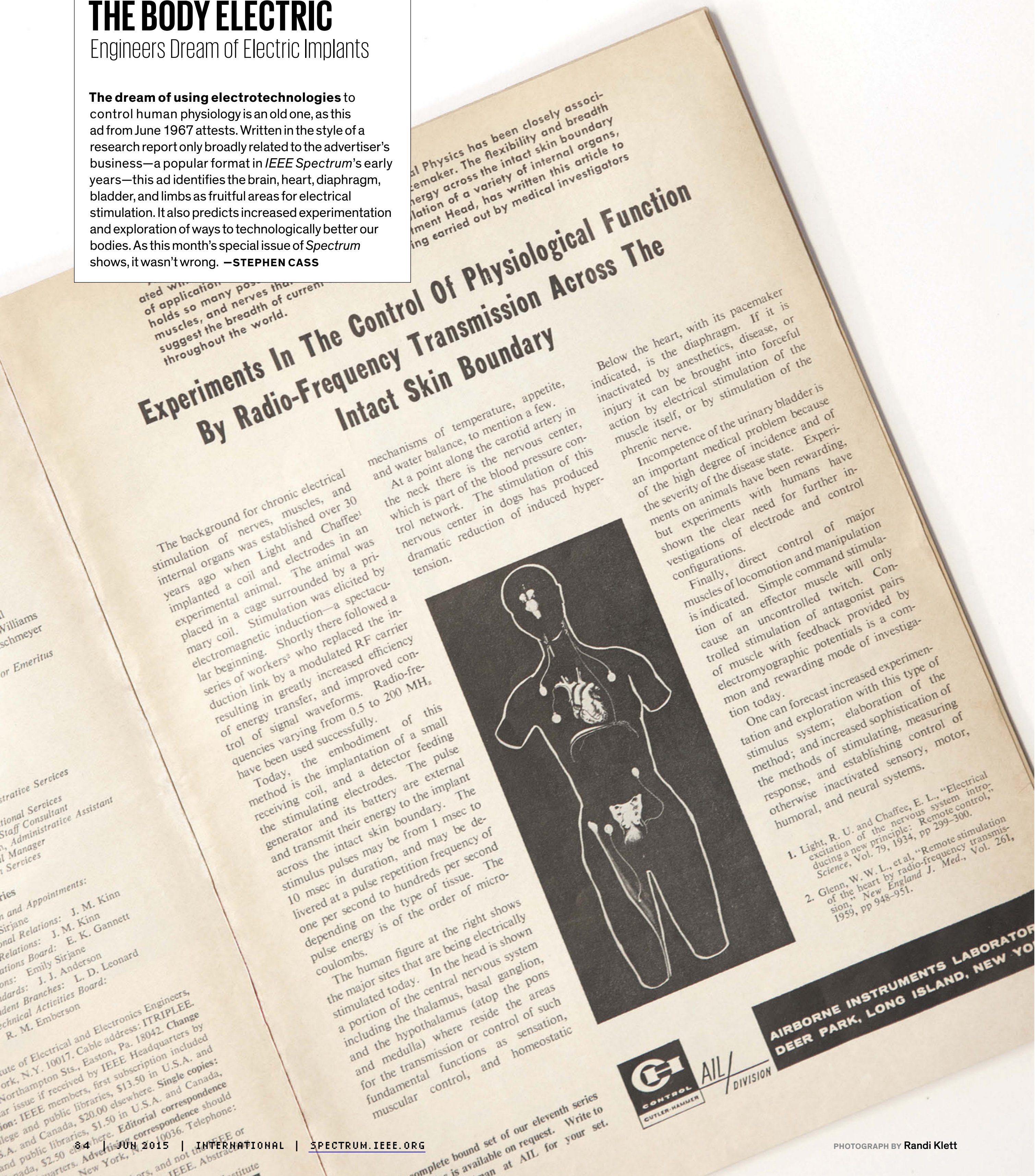
THE BODY ELECTRIC

Engineers Dream of Electric Implants

The dream of using electrotechnologies to control human physiology is an old one, as this ad from June 1967 attests. Written in the style of a research report only broadly related to the advertiser's business—a popular format in *IEEE Spectrum*'s early years—this ad identifies the brain, heart, diaphragm, bladder, and limbs as fruitful areas for electrical stimulation. It also predicts increased experimentation and exploration of ways to technologically better our bodies. As this month's special issue of *Spectrum* shows, it wasn't wrong. —STEPHEN CASS



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Experiments In The Control Of Physiological Function By Radio-Frequency Transmission Across The Intact Skin Boundary

The background for chronic electrical stimulation of nerves, muscles, and internal organs was established over 30 years ago when Light and Chaffee[1] implanted a coil and electrodes in an experimental animal. The animal was placed in a cage surrounded by a primary coil. Stimulation was elicited by electromagnetic induction—a spectacular beginning. Shortly there followed a series of workers[2] who replaced the induction link by a modulated RF carrier resulting in greatly increased efficiency of energy transfer, and improved control of signal waveforms. Radio-frequencies varying from 0.5 to 200 MHz have been used successfully.

Today, the embodiment of this method is the implantation of a small receiving coil, and a detector feeding the stimulating electrodes. The pulse generator and its battery are external and transmit their energy to the implant across the intact skin boundary. The stimulus pulses may be from 1 msec to 10 msec in duration, and may be delivered at a pulse repetition frequency of one per second to hundreds per second depending on the type of tissue. The pulse energy is of the order of microcoulombs.

The human figure at the right shows the major sites that are being electrically stimulated today. In the head is shown a portion of the central nervous system including the thalamus, basal ganglion, and the hypothalamus (atop the pons and medulla) where reside the areas for the transmission or control of such fundamental functions as sensation, muscular control, and homeostatic mechanisms of temperature, appetite, and water balance, to mention a few.

At a point along the carotid artery in the neck there is the nervous center, which is part of the blood pressure control network. The stimulation of this nervous center in dogs has produced dramatic reduction of induced hypertension.

Below the heart, with its pacemaker indicated, is the diaphragm. If it is inactivated by anesthetics, disease, or injury it can be brought into forceful action by electrical stimulation of the muscle itself, or by stimulation of the phrenic nerve.

Incompetence of the urinary bladder is an important medical problem because of the high degree of incidence and of the severity of the disease state. Experiments on animals have been rewarding, but experiments with humans have shown the clear need for further investigations of electrode and control configurations.

Finally, direct control of major muscles of locomotion and manipulation is indicated. Simple command stimulation of an effector muscle will only cause an uncontrolled twitch. Controlled stimulation of antagonist pairs of muscle with feedback provided by electromyographic potentials is a common and rewarding mode of investigation today.

One can forecast increased experimentation and exploration with this type of stimulus system; elaboration of the method; and increased sophistication of the methods of stimulating, measuring response, and establishing control of otherwise inactivated sensory, motor, humoral, and neural systems.

1. Light, R. U. and Chaffee, E. L., "Electrical excitation of the nervous system introducing a new principle: Remote control," Science, Vol. 79, 1934, pp 299–300.
2. Glenn, W. W. L., et al, "Remote stimulation of the heart by radio-frequency transmission," New England J. Med., Vol. 261, 1959, pp 948–951.

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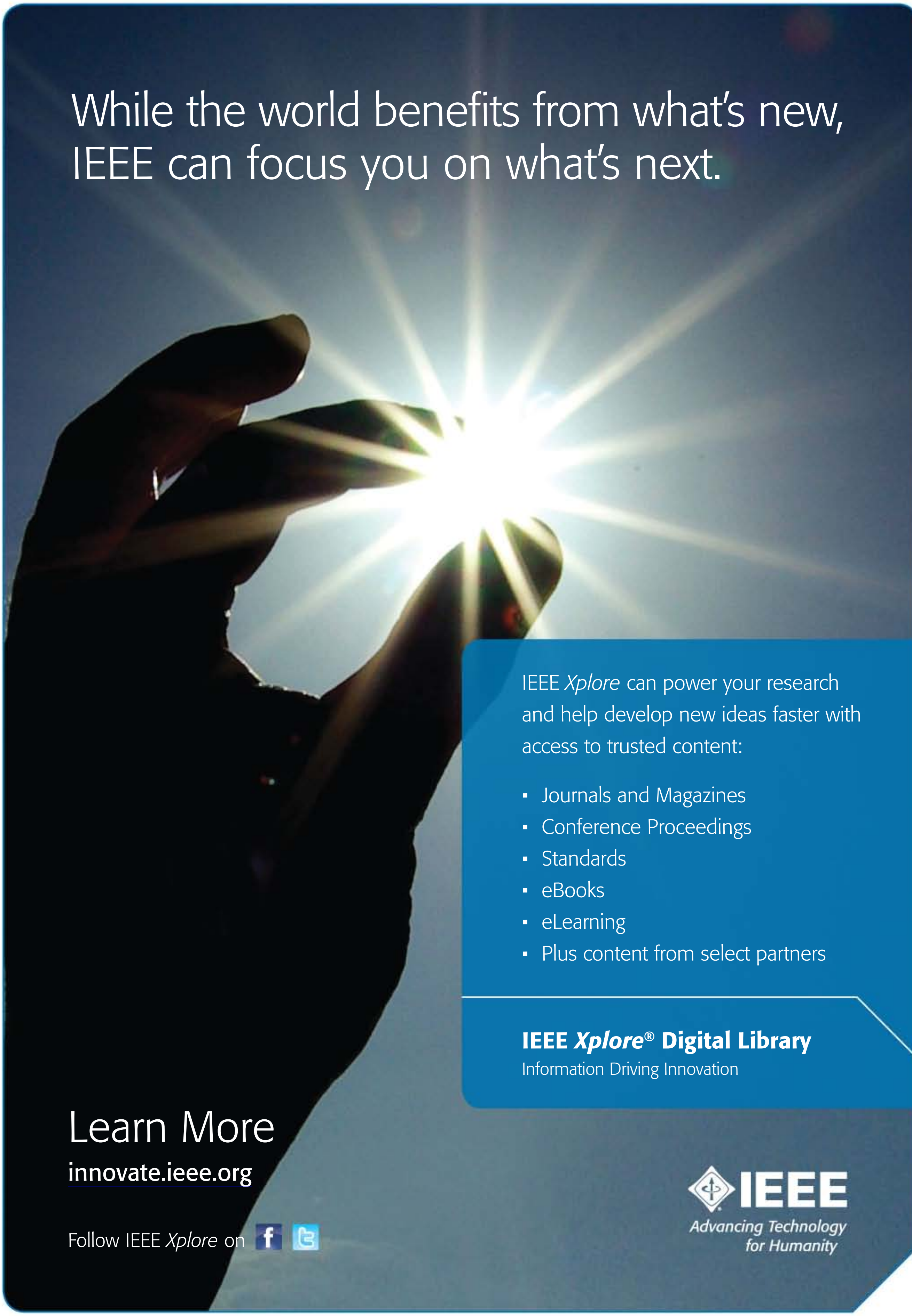
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