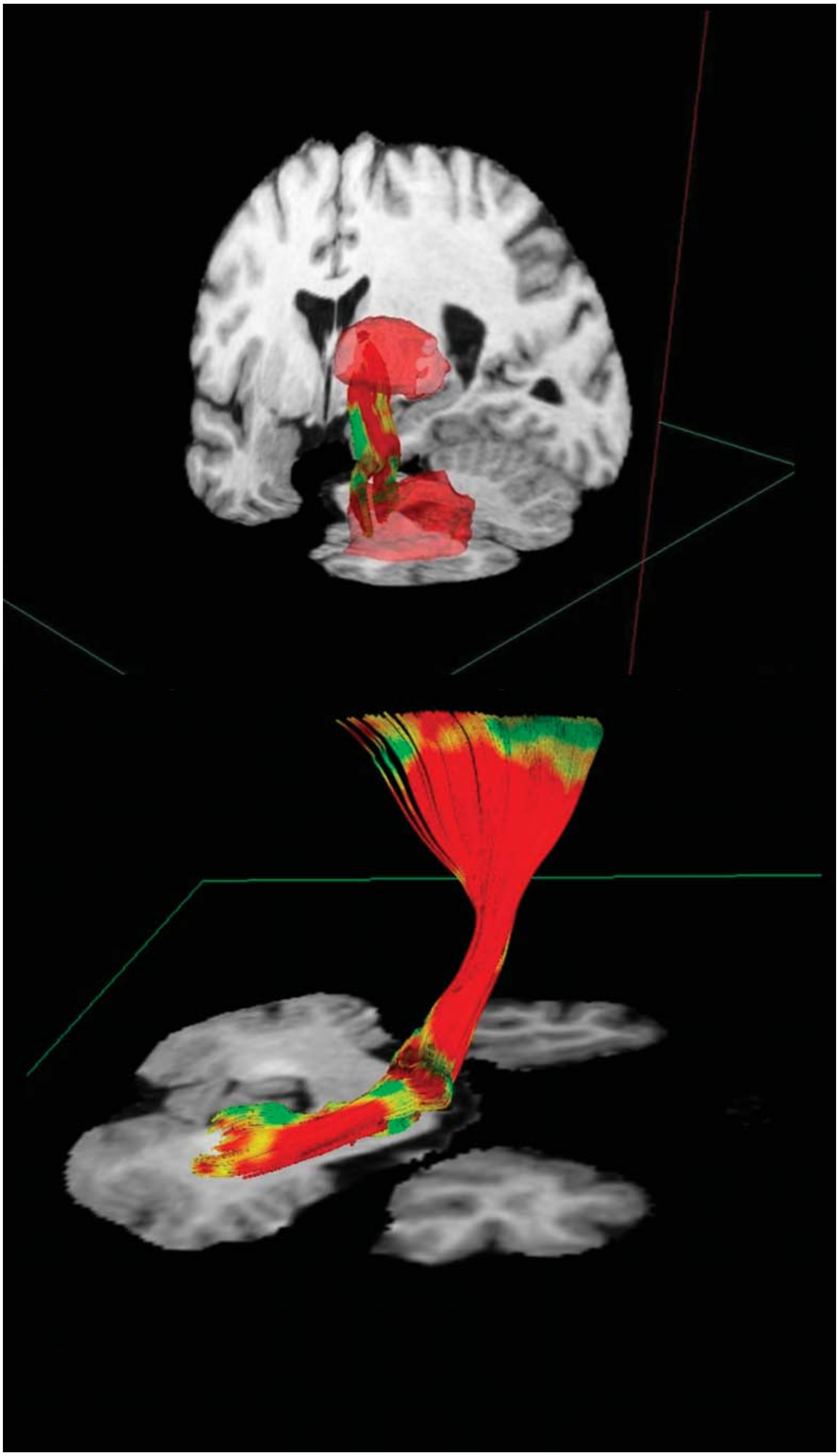
BRAIN IMAGING

Diffusion Tensor Imaging

Kelvin Lim is using a new brain-imaging method to understand schizophrenia.

FLIPPING THROUGH A PILE OF BRAIN scans, a neurologist or psychiatrist would be hard pressed to pick out the one that belonged to a schizophrenic. Although schizophrenics suffer from profound mental problems—hallucinated conversations and imagined conspiracies are the best known—their brains look more or less normal. This contradiction fascinated Kelvin Lim, a neuroscientist and psychiatrist at the University of Minnesota Medical School, when he began using imaging techniques such as magnetic resonance imaging (MRI) to study the schizophrenic brain in the early 1990s. Lim found subtle hints of brain structures gone awry, but to understand how these problems led to the strange symptoms of schizophrenia, he needed a closer look at the patients' neuroanatomy than standard scans could provide. Then, in 1996, a colleague told him about diffusion tensor imaging (DTI), a newly developed variation of MRI that allowed scientists to study the connections between different brain areas for the first time.

Lim has pioneered the use of DTI to understand psychiatric disease. He was one of the first to use the technology to uncover minute structural aberrations in the brains of schizophrenics. His group



DTI YIELDS images of nerve fiber tracts; different colors indicate the organization of the nerve fibers. Here, a tract originating at the cerebellum is superimposed on a structural-MRI image of a cross section of the brain.

has recently found that memory and cognitive problems associated with schizophrenia, major but undertreated aspects of the disease, are linked to flaws in nerve fibers near the hippocampus, a brain area crucial for learning and memory. "DTI allows us to examine the brain in ways we hadn't been able to before," says Lim.

Conventional imaging techniques, such as structural MRI, reveal major anatomical features of the brain—gray matter, which is made up of nerve cell bodies. But neuroscientists believe that some diseases may be rooted in subtle "wiring" problems involving axons, the long, thin tails of neurons that carry electrical signals and constitute the brain's white matter. With DTI, researchers can, for the first time, look at the complex network of nerve fibers connecting the different brain areas. Lim and his colleagues hope this sharper view of the brain will help better define neurological and psychiatric diseases and yield more-targeted treatments.

In DTI, radiologists use specific radio-frequency and magnetic field–gradient pulses to track the movement of water molecules in the brain. In most brain tissue, water molecules diffuse in all different directions. But they tend to diffuse along the length of axons, whose coating of white, fatty myelin holds them in. Scientists can create pictures of axons by analyzing the direction of water diffusion.

Following Lim's lead, other neuroscientists have begun using DTI to study a host of disorders, including addiction, epilepsy, traumatic brain injury, and various neurodegenerative diseases. For instance, DTI studies have shown that chronic alcoholism degrades the white-matter connections in the brain, which may explain the cognitive problems seen in heavy drinkers. Other DTI projects are examining how the neurological scars left by stroke, multiple sclerosis, and amyotrophic lateral sclerosis (better known as Lou Gehrig's disease) are linked to patients' disabilities.

Lim is pushing the technology even further by combining it with findings from other fields, such as genetics, to unravel the mysteries of neurological and psychiatric disorders. Lim's group has found, for instance, that healthy people with a genetic risk for developing Alzheimer's disease have tiny structural defects in specific parts of the brain that are not shared by noncarriers. How these defects might be linked to the neurological problems of Alzheimer's isn't clear, but the researchers are trying to find the connection.

Lim and others also continue to refine DTI itself, striving for an even closer look at the brain's microarchitecture. For example, current DTI techniques can easily image brain areas with large bundles of fibers all moving in the same direction, such as the corpus callosum, which connects the two hemispheres of the brain. But it has difficulty with areas such as the one where fibers leave the corpus callosum for other parts of the brain, which is a tangle of wires.

Researchers hope tools for studying white matter, like DTI, will help illuminate the mysteries of both healthy and diseased brains. Lim believes his own research into diseases like schizophrenia and Alzheimer's could yield better diagnostics within 10 to 20 years—providing new hope for the next generation of patients. **EMILY SINGER**

COURTESY OF VINCENT MAGNOTTA

OTHER PLAYERS
DTI

Researcher	Project
Peter Basser *National Institute of Child Health and Human Development*	Development of higher-resolution diffusion imaging techniques
Aaron Field *University of Wisconsin-Madison*	Neurosurgery planning
Michael Moseley *Stanford University*	Assessment and early treatment of stroke

INTERNET SECURITY

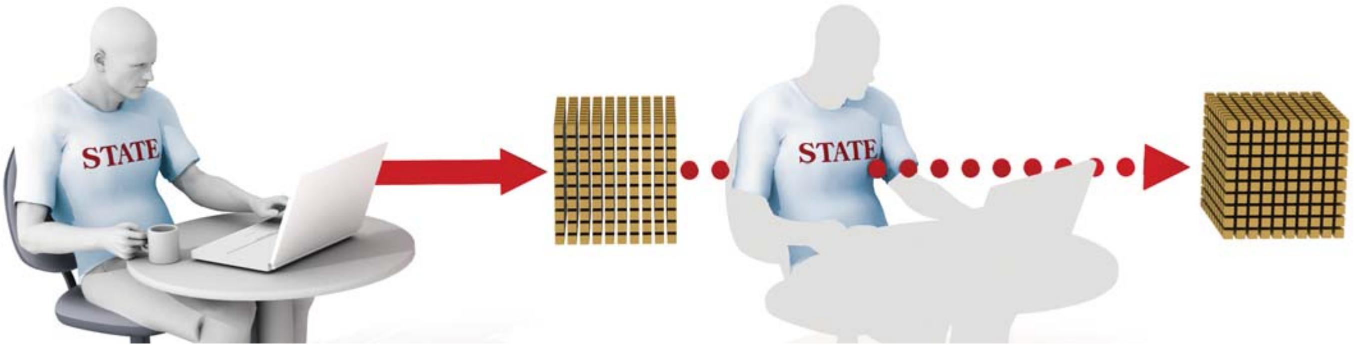
Universal Authentication

Leading the development of a privacy-protecting online ID system, Scott Cantor is hoping for a safer Internet.

IF YOU'RE LIKE MOST PEOPLE, YOU'VE established multiple user IDs and passwords on the Internet—for your employer or school, your e-mail accounts, online retailers, banks, and so forth. It's cumbersome and confusing, slowing down online interactions if only because it's so easy to forget the plethora of passwords. Worse, the diversity of authentication systems increases the chances that somewhere, your privacy will be compromised, or your identity will be stolen.

The balkanization of today's online identity-verifying systems is a big part of the Internet's fraud and security crisis. As Kim Cameron, Microsoft's architect of identity and access, puts it in his blog, "If we do nothing, we will face rapidly proliferating episodes of theft and deception that will cumulatively erode public trust in the Internet." Finding ways to bolster that trust is critically important to preserving the Internet as a useful, thriving medium, argues David D. Clark, an MIT computer scientist and the Internet's onetime chief protocol architect.

Scott Cantor, a senior systems developer at Ohio State University, thinks the answer may lie in Web "authentication systems" that allow users to



SECURITY WITH PRIVACY: Shibboleth software could create a far more trustworthy Internet by allowing a one-step login that carries through to many online organizations, confirming identity but preserving privacy. In this example, a student logs in to his university's site, then clicks through to a second university. Shibboleth confirms that the person is a student but doesn't give his name.

hop securely from one site to another after signing on just once. Such systems could protect both users' privacy and the online businesses and other institutions that offer Web-based services. Cantor led the technical development of Shibboleth, an open-standard authentication system used by universities and the research community, and his current project is to expand its reach. He has worked, not only to make the system function smoothly, but also to build bridges between it and parallel corporate efforts. "Scott is the rock star of the group," says Steven Carmody, an IT architect at Brown University who manages a Shibboleth project for Internet2, an Ann Arbor, MI–based research consortium that develops advanced Internet technologies for research laboratories and universities. "Scott's work has greatly simplified the management of these Internet-based relationships, while ensuring the required security and level of assurance for each transaction."

OTHER PLAYERS

Universal Authentication

Researcher	Project
Stefan Brands *McGill University*	Cryptology, identity management, and authentication technologies
Kim Cameron *Microsoft, Redmond, WA*	"InfoCard" system to manage and employ a range of digital identity information
Robert Morgan *University of Washington*	"Person registry" that gathers identity data from source systems; scalable authentication infrastructure
Tony Nadalin *IBM, Armonk, NY*	Personal-identity software platform

Shibboleth acts not only as an authentication system but also—counterintuitively—as a guardian of privacy. Say a student at Ohio State wishes to access Brown's online library. Ohio State securely holds her identifying information—name, age, campus affiliations, and so forth. She enters her user ID and password into a page on Ohio State's website. But when she clicks through to Brown, Shibboleth takes over. It delivers only the identifying information Brown really needs to know: the user is a registered Ohio State student.

While some U.S. universities have been using Shibboleth since 2003, adoption of the system grew rapidly in 2005. It's now used at 500-plus sites worldwide, including educational systems in Australia, Belgium, England, Finland, Denmark, Germany, Switzerland, and the Netherlands; even institutions in China are signing on. Also in late 2005, Internet2 announced Shibboleth's interoperability with a Microsoft security infrastructure called the Active Directory Federation Service.

Critically, the system is moving into the private sector, too. The science and medical division of research publishing conglomerate Reed Elsevier has begun granting university-based subscribers access to its online resources through Shibboleth, rather than requiring separate, Elsevier-specific logins. And Cantor has forged ties with the Liberty Alliance, a consortium of more than 150 companies and other institutions dedicated to creating shared identity and authentication systems. With Cantor's help, the alliance, which includes companies such as AOL, Bank of America, IBM, and Fidelity Investments, is basing the design of its authentication systems on a common standard known as SAML. The alliance, Cantor says, was "wrestling with lots of the same hard questions that we were, and we were starting to play in the same kind of territories. Now there is a common foundation.... we're trying to make it ubiquitous." With technical barriers overcome, the companies can now roll out systems as their business needs dictate.

Of course, Cantor is not the only researcher, nor Shibboleth the only technology, in the field of Internet authentication. In 1999, for instance, Microsoft launched its Passport system, which let Windows users access any participating website using their e-mail addresses and passwords. Passport, however, encountered a range of security and privacy problems.

But thanks to the efforts of the Shibboleth team and the Liberty Alliance, Web surfers could start accessing multiple sites with a single login in the next year or so, as companies begin rolling out interoperable authentication systems. **DAVID TALBOT**

BRYAN CHRISTIE DESIGN

MOLECULAR BIOLOGY

Nanobiomechanics

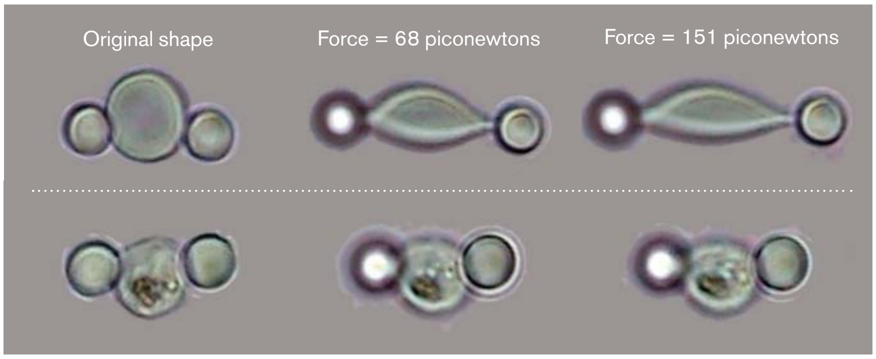
Measuring the tiny forces acting on cells, Subra Suresh believes, could produce fresh understanding of diseases.

MOST PEOPLE DON'T THINK OF THE human body as a machine, but Subra Suresh does. A materials scientist at MIT, Suresh measures the minute mechanical forces acting on our cells.

Medical researchers have long known that diseases can cause—or be caused by—physical changes in individual cells. For instance, invading parasites can distort or degrade blood cells, and heart failure can occur as muscle cells lose their ability to contract in the wake of a heart attack. Knowing the effect of forces as small as a piconewton—a trillionth of a newton—on a cell gives researchers a much finer view of the ways in which diseased cells differ from healthy ones.

Suresh spent much of his career making nanoscale measurements of materials such as the thin films used in microelectronic components. But since 2003, Suresh's laboratory has spent more and more time applying nanomeasurement techniques to living cells. He's now among a pioneering group of materials scientists who work closely with microbiologists and medical researchers to learn more about how our cells react to tiny forces and how their physical form is affected by disease. "We bring to the table expertise in measuring the strength of materials at the smallest of scales," says Suresh.

One of Suresh's recent studies measured mechanical differences between healthy red blood cells and cells infected with malaria parasites. Suresh and his collaborators knew that infected blood cells become more rigid, losing the ability to reduce their width from eight micrometers down to two or three micrometers, which they need to do to slip through capillaries. Rigid cells, on the other hand, can clog capillaries and cause cerebral hemorrhages. Though others had tried to determine exactly how rigid malarial cells become, Suresh's instruments were able to bring greater accuracy to the measurements. Using optical tweezers, which employ intensely focused laser light to exert a tiny force on objects attached to cells, Suresh and his collaborators showed that red blood cells infected with malaria become 10 times stiffer than healthy cells—three to four times stiffer than was previously estimated.



COURTESY OF SUBRA SURESH

OPTICAL TWEEZERS stretch a healthy red blood cell (top row), increasing the applied force slowly, by a matter of piconewtons. A cell in a late stage of malarial infection is stretched in a similar fashion (bottom row). The experiment illustrates how the infected cell becomes rigid, which prevents it from traveling easily through blood capillaries and helps cause the symptoms of malaria.

OTHER PLAYERS
Nanobiomechanics

Researcher	Project
Eduard Arzt *Max Planck Institute, Stuttgart, Germany*	Structure and mobility of pancreatic cancer cells
Peter David and **Geneviève Milon** *Pasteur Institute, Paris, France*	Parasite-host interaction; mechanics of the spleen
Ju Li *Ohio State University*	Models of internal cellular structures
C. T. Lim and **Kevin Tan** *National University of Singapore*	Red-blood-cell mechanics

Eduard Arzt, director of materials research at the Max Planck Institute in Stuttgart, Germany, says that Suresh's work is important because cell flexibility is a vital characteristic not only of malarial cells but also of metastasizing cancer cells. "Many of the mechanical concepts we've been using for a long time, like strength and elasticity, are also very important in biology," says Arzt.

Arzt and Suresh both caution that it's too early to say that understanding the mechanics of human cells will lead to more effective treatments. But what excites them and others in the field is the ability to measure the properties of cells with unprecedented precision. That excitement seems to be spreading: in October, Suresh helped inaugurate the Global Enterprise for Micro-Mechanics and Molecular Medicine, an international consortium that will use nanomeasurement tools to tackle major health problems, including malaria, sickle-cell anemia, cancer of the liver and pancreas, and cardiovascular disease. Suresh serves as the organization's founding director.

"We know mechanics plays a role in disease," says Suresh. "We hope it can be used to figure out treatments." If it can, the tiny field of nanomeasurement could have a huge impact on the future of medicine. MICHAEL FITZGERALD

NETWORKS

Pervasive Wireless

Can't all our wireless gadgets just get along? It's a question that Dipankar Raychaudhuri is trying to answer.

IN NEW BRUNSWICK, NJ, IS A LARGE, white room with an army of yellow boxes hanging from the ceiling. Eight hundred in all, the boxes are actually a unique grid of radios that lets researchers design and test ways to link mobile, radio-equipped computers in configurations that can change on the fly.

The ability to form such ad hoc networks, says Dipankar Raychaudhuri, director of the Rutgers University lab that houses the radios, will be critical to the advent of pervasive computing—in which everything from your car to your coffee cup "talks" to other devices in an attempt to make your life run more smoothly.

Wireless transactions already take place; anybody who speeds through tolls with an E-ZPass transmitter participates in them daily. But Raychaudhuri foresees a not-too-distant day when radio frequency identification (RFID) tags embedded in merchandise call your cell phone to alert you to sales, cars talk to each other to avoid collisions, and elderly people carry heart and blood-pressure monitors that can call a doctor during a medical emergency. Even mesh networks, collections of wireless devices that pass data one to another until it reaches a central computer, may need to be connected to pagers, cell phones, or other gadgets that employ diverse wireless protocols.

Hundreds of researchers at universities, large companies such as Microsoft, Intel, and Nortel, and small startups are developing embedded radio devices and sensors. But making computing truly pervasive entails tying these disparate pieces together, says Raychaudhuri, a professor of electrical and computer engineering at Rutgers. Finding ways to do that is what the radio test grid, which Raychaudhuri built with computer scientists Ivan Seskar and Max Ott, is for.

One problem the researchers are addressing is that different devices communicate using different radio standards: RFID tags use one set of standards, cell phones still others, and various Wi-Fi devices several versions of a third. Linking such devices into a pervasive network means providing them with a common protocol.

Take, for example, the issue of automotive safety. Enabling cars to communicate with each other could prevent crashes; in Raychaudhuri's vision, each car would have a Global Positioning System unit and send its exact location to nearby vehicles. But realizing that vision requires a protocol that allows the cars not only to communicate but also to decide how many other cars they should include in their networks and how close another car should be to be included. As programmers develop candidates for such a protocol, they try them out on the radio test bed. Each yellow box contains a computer and three different radios, two for handling the various Wi-Fi standards and one that uses either Bluetooth or ZigBee, short-range wireless protocols for personal electronics and for monitoring or control devices, respectively. The researchers configure the radios to mimic the situation they want to test and load their protocols to see, for instance, how long it takes each radio to detect neighbors and send data. "If I want cars not to collide, it cannot take 10 seconds to determine that a car is nearby," says Raychaudhuri. "It has to take a few microseconds."

The Rutgers radio grid is the first large-scale shared research facility that researchers can use to study multiple wireless devices and network technologies. "The sort of real-world complexity, dealing with real-world numbers that [the test bed] allows you to do, is something that really makes it quite unique," says Tod Sizer, director of the Wireless Technology Research Department at Lucent Technologies' Bell Labs.

Sizer's group is working with Raychaudhuri to build cognitive-radio boxes that can be programmed to employ a wide variety of wireless standards, such as RFID, Wi-Fi, or cellular-phone protocols.

While hordes of researchers are developing new networked devices, Raychaudhuri says it is the standardization of communications protocols that will make pervasive computing take off. In just five years, he believes, networks of embedded devices will be all around us. His aim is to reduce "friction" in daily life, eliminating lines, saving time in searching for objects, automating security checkpoints in airports, and the like. "You save 10 seconds here, two minutes there, but it's significant," he says. He claims that just a 2 percent reduction of friction in the world's economy could be worth hundreds of billions of dollars in productivity. "Each transaction is small, but the benefit to society is very large."

NEIL SAVAGE

OTHER PLAYERS

Pervasive Wireless

Researcher	Project
David Culler *University of California, Berkeley*	Operating systems and middleware for wireless sensors
Kazuo Imai *NTT DoCoMo, Tokyo, Japan*	Integrating cellular with other network technology
Lakshman Krishnamurthy and **Steven Conner** *Intel, Santa Clara, CA*	Wireless network architecture

STEVE MOORS

Dipankar Raychaudhuri

MICROELECTRONICS

Stretchable Silicon

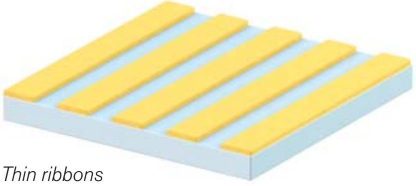
By teaching silicon new tricks, John Rogers is reinventing the way we use electronics.

THESE DAYS, MOST ELECTRONIC CIRCUITRY comes in the form of rigid chips, but devices thin and flexible enough to be rolled up like a newspaper are fast approaching. Already, "smart" credit cards carry bendable microchips, and companies such as Fujitsu, Lucent Technologies, and E Ink are developing "electronic paper"—thin, paperlike displays.

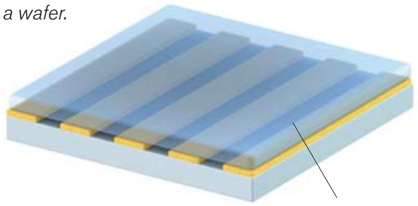
But most truly flexible circuits are made of organic semiconductors sprayed or stamped onto plastic sheets. Although useful for roll-up displays, organic semiconductors are just too slow for more intense computing tasks. For those jobs, you still need silicon or another high-speed inorganic semiconductor. So John Rogers, a materials scientist at the University of Illinois at Urbana-Champaign, found a way to stretch silicon.

If bendable is good, stretchable is even better, says Rogers, especially for high-performance conformable circuits of the sort needed for so-called smart clothes or body armor. "You don't comfortably wear a sheet of plastic," he says. The potential applications of circuitry made from Roger's stretchable silicon are vast. It could be used in surgeons' gloves to create sensors that would read chemical levels in the blood and alert a surgeon to a problem, without impairing the sense of touch. It could allow a prosthetic limb to use pressure or temperature cues to change its shape.

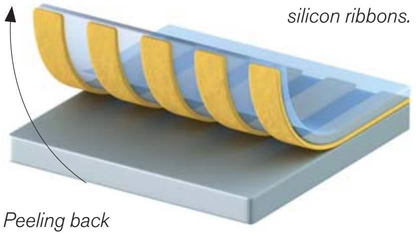
What makes Rogers's work particularly impressive is that he works with single-crystal silicon, the same type of silicon found in microprocessors. Like any other single crystal, single-crystal silicon doesn't naturally stretch. Indeed, in order for it even to bend, it must be prepared as an ultrathin layer only a few hundred nanometers thick on a bendable surface. Rogers exploits the flexibility of thin silicon, but instead of attaching it to plastic, he affixes it in narrow strips to a stretched-out, rubberlike polymer. When the stretched polymer snaps back, the silicon strips buckle but do not break, forming "waves" that are ready to stretch out again.



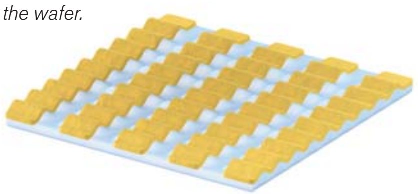
Thin ribbons of silicon are deposited on a wafer.



A stretched elastic is bonded to the silicon ribbons.



Peeling back the elastic lifts the ribbons off the wafer.



Releasing the tension on the elastic produces "waves" of silicon that can later be stretched out again as needed. Such flexible silicon could be used to make wearable electronics.

Rogers's team has fabricated diodes and transistors—the basic building blocks of electronic devices—on the thin ribbons of silicon before bonding them to the polymer; the wavy devices work just as well as conventional rigid versions, Rogers says. In theory, that means complete circuits of the sort found in computers and other electronics would also work properly when rippled.

Rogers isn't the first researcher to build stretchable electronics. A couple of years ago, Princeton University's Sigurd Wagner and colleagues began making stretchable circuits after inventing elastic-metal interconnects. Using the stretchable metal, Wagner's group connected together rigid "islands" of silicon transistors. Although the silicon itself couldn't stretch, the entire circuit could. But, Wagner notes, his technique isn't suited to making electrically demanding circuits such as those in a Pentium chip. "The big thing that John has done is use standard, high-performance silicon," says Wagner.

Going from simple diodes to the integrated circuits needed to make sensors and other useful microchips could take at least five years, says Rogers. In the meantime, his group is working to make silicon even more flexible. When the silicon is affixed to the rubbery surface in rows, it can stretch only in one direction. By changing the strips' geometry, Rogers hopes to make devices pliable enough to be folded up like a T-shirt. That kind of resilience could make silicon's future in electronics stretch out a whole lot further. **KATE GREENE**

OTHER PLAYERS

Stretchable Silicon

Researcher	Project
Stephanie Lacour *University of Cambridge, England*	Neuro-electronic prosthesis to repair damage to the nervous system
Takao Someya *University of Tokyo*	Large-area electronics based on organic transistors
Sigurd Wagner *Princeton University*	Electronic skin based on thin-film silicon

BRYAN CHRISTIE DESIGN