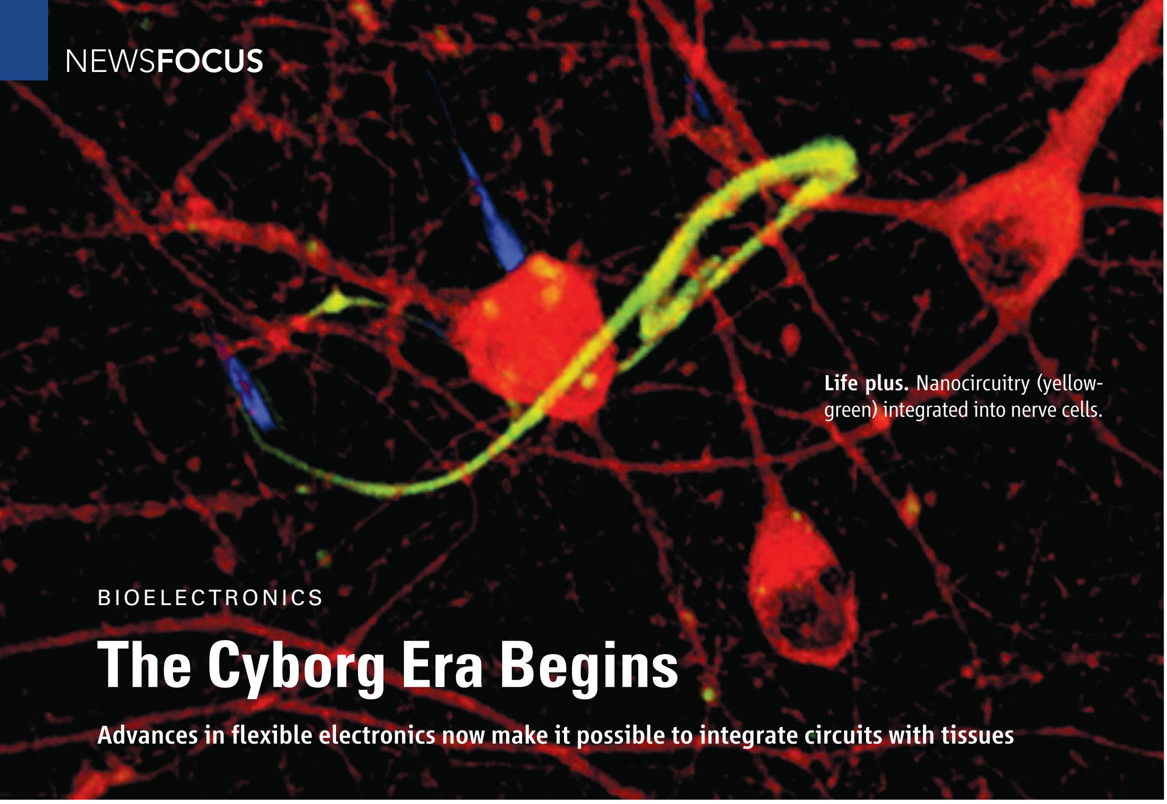


Life plus. Nanocircuitry (yellow-green) integrated into nerve cells.

BIOELECTRONICS

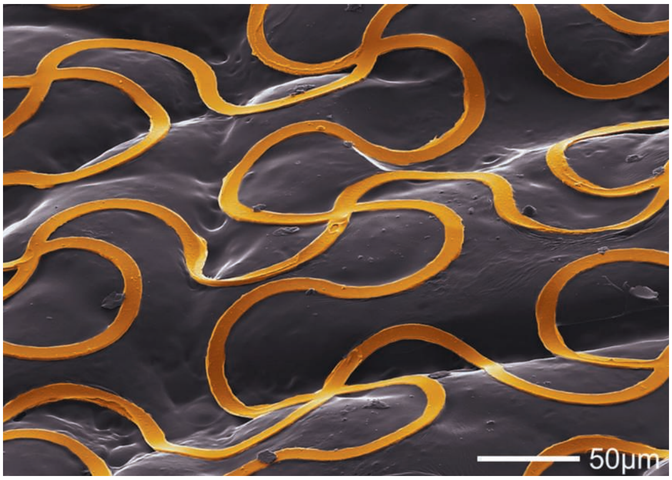
The Cyborg Era Begins

Advances in flexible electronics now make it possible to integrate circuits with tissues

John Rogers doesn't look like a cyborg yet, but his transformation has begun. As he delivered a talk at a recent conference in San Francisco, Rogers, a materials scientist at the University of Illinois, Urbana-Champaign, picked up a penlike microscope connected to the projector that beamed the PowerPoint slides on his computer for all in the audience to see. As Rogers pressed the pen-scope against his forearm, viewers got a close-up view of the craggy hills and valleys of his skin, as well as an array of squiggly gold lines and square pads. The lines and pads, it turns out, were components of arrays of circuits—not the Intel or ARM variety found in your laptop or cell phone, but a postage stamp–sized collection of flexible, stretchable, and nearly transparent devices that molded perfectly to the contours of Rogers' skin.

That intimate contact, Rogers explained, will allow his team to use flexible circuitry to monitor body temperature, heart rate, and blood pressure and wirelessly transmit the data to a nearby computer. Using similar arrays, Rogers's team has also been able to track arm motion, allowing researchers to control a toy helicopter's flight path with a wave of the arm. Through a startup company that he founded called MC10, Rogers has teamed up with NBA and NFL stars such as Grant Hill and Matt Hasselbeck to use the technology to monitor head impacts during sports. Working with the stars "is pretty cool," Rogers says. "It gives you a lot of credibility with your 10-year-old son."

Fanciful as such technology sounds, it's just the beginning. Additional devices shown by Rogers and others at the Materials Research Society (MRS) meeting went even further. Cling wrap–like circuitry draped over the hearts of test animals can not only independently track the activity of each of the heart's four chambers, but it can also emit pulses of heat that kill tiny patches of tissue that initiate potentially deadly arrhythmias. Other arrays penetrate brain tissue to monitor the abnormal nerve firing patterns in epilepsy or induce gene expression in the brain tissue of mice and monitor the results to study developmental biology. One team has even made a 3D printed bionic ear complete with cartilage cells and wiring able to tune in to both Beethoven's "Für Elise" and ultrasonic bleats that humans cannot hear.



Rise and fall. Electrode arrays flexible enough to hug the contours of human skin make it possible to measure temperature and muscle contraction.

Meet your future self. The beginnings of a cyborg world have arrived. These early prototypes are pale shadows of the Hollywood versions, such as the humanoid Cylons in *Battlestar Galactica* or the Borg in *Star Trek* who claim that resistance to incorporation into their collective is futile. Nevertheless, research progress is real, as a mix of biologists, materials scientists, and nanotechnology experts are chipping away at a host of challenges. "I see it as building a seamless interface between cells, tissues, and electronics," says Aleksandr Noy, a bionanoelectronics expert at Lawrence Livermore National Laboratory and the University of California, Merced. For now, most of these efforts focus on providing better health care and quality of life for patients. But over time, expect devices that will make us better athletes and soldiers, or even improve our complexion.

"A few years ago these things were science fiction. Now we are seeing the emergence of real devices and applications," Noy says. And fast, says Zhenan Bao, an organic electronics expert at Stanford University in California: "The competition is furious."

Stretching the limits

The idea of fusing man and machine has long tantalized humanity. Over the past century, Rogers points out, researchers have pioneered myriad efforts to use electronics to measure biological activity and sometimes even alter it. They tailored metal electrodes that could be taped to the skin for use in electrocardiograms. They devised brain stimulators that can be inserted deep within brain tissue to disrupt the neural firing patterns that cause debilitating tremors in patients with Parkinson's disease. And they created cochlear implants capable of converting sound to electrical impulses that can be registered by the inner ear.

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Published by AAAS

The early technologies were crude: rigid devices that were strapped and glued to the skin or stabbed through soft tissue. The latest iterations are more about tailoring electronics to mimic the body's pliability. Efforts range from the macroscale of things we can see to the microscopic scale at which electronics are being entwined with individual cells.

At the upper end of the scale, Michael McAlpine, a mechanical engineer at Princeton University, and colleagues reported in the 1 May issue of *Nano Letters* that they've made the first 3D printed functional organ: a bionic ear that hears acoustic sound and ultrasound. "We're trying to see if one could introduce augmented functionality that a human wouldn't ordinarily have," McAlpine says.

Three-dimensional printers work by using a computer-driven laser printer to build up layers of material-based inks, usually made from plastics. McAlpine's team started with three different inks: one made from silicone; another with silicone infused with silver nanoparticles; and a third with chondrocytes, cells that produce cartilage, along with a gel to promote their growth. Numerous groups have used 3D printing to make tissues, but they have typically printed only scaffolding material and cells. McAlpine's team added a level of sophistication to the technology. The researchers printed out a metal coil in the center of the engineered ear that serves as an antenna capable of picking up acoustic signals and converting them to electrical pulses for the inner ear, à la a conventional cochlear implant. The antenna can also detect ultrasonic waves that dogs and other animals can hear but humans cannot.

Another macroscopic project is electronic skin, complete with tactile, temperature, and even chemical sensors. Such skin could potentially be integrated into prosthetic limbs, enabling users to feel and touch their world again, and perhaps give robots a new sense of their surroundings. For electronic skin to work, it must be soft, flexible, and stretchable, much like our own. That rules out conventional computer electronics made from rigid glass and ceramic chips.

But such skin is around the corner thanks to progress in organic electronics. Nearly all organic solids are insulators: They don't readily conduct electricity. But in the 1970s and 1980s, researchers discovered how to tweak the structures of some organic compounds to make them metal-like conductors or semiconductors, with the ability to switch a current on and off—a property critical to transistors and other devices. That advance opened the door to creating electronics on soft, flexible substrates. By the 2000s, researchers had honed their skills to make arrays of devices and pattern them cheaply. Compared with top-shelf electronics in computers and cell phones, flexible electronics remained big and slow. But they could now go places that rigid silicon could not.

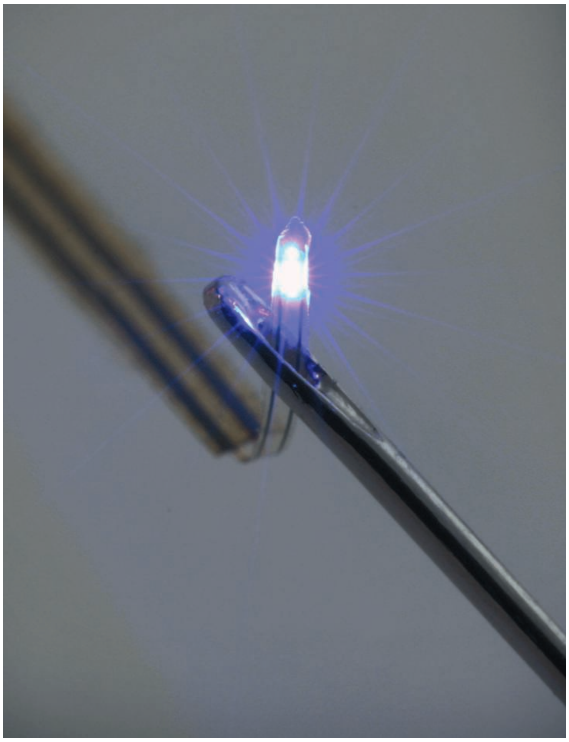
In the past few years, numerous groups have unveiled flexible and stretchable arrays of touch and temperature sensors. For example, 2 years ago Bao and her colleagues at Stanford made an array of flexible organic pressure sensors so sensitive that it could detect the weight of a butterfly sitting on top. More recently, at the MRS meeting, Bao reported how she and her colleagues had used a miniature array, roughly 144 square millimeters in area, to detect heartbeat and blood pressure from a simple watch-style wristband. Bulky wristwatch heart rate monitors exist, but the Stanford team's devices are paper-thin. "Human skin is a great inspiration," says Bao, whose group has also produced flexible chemical sensors and devices in which metal nanoparticles can move to fill in cracks so that damaged devices can heal themselves.

Feel that? Flexible electronic sensors could give robots and prosthetic limbs more realistic ways of detecting touch, temperature, and strain.

CREDIT: SOMEYA-SEKITANI GROUP/UNIVERSITY OF TOKYO

According to the online rumor mill that follows everything that the electronics giant Apple has in the works, the company is testing the use of flexible electronics in a sleek iWatch that will have a screen for surfing the web, as well as monitoring time, temperature, and fitness information such as how many calories a jogger wearing the device is burning up. Apple isn't alone. MC10 and fitness giant Reebok have developed prototypes of wearable sensors to monitor concussion risk in athletes playing contact sports like football or hockey. If the device senses strong enough head impacts—as determined by measurements of rotational acceleration, multidirectional acceleration, and the location and duration of the blow—it lights up a panel of light-emitting diodes (LEDs) that alerts the coach to take the player out of the game.

Other researchers are shrinking devices to pack more into a patch. One technology at this frontier is touch sensors. Most touch sensors work by spotting how pressure changes the electrical resistance of current flowing through a device array. Chemist Zhong Lin Wang of the Georgia Institute of Technology in Atlanta and his colleagues have come up with an alternative based on piezotronics, in which increasing the strain on a material changes its polarization, or the distribution of positive and negative charges, which can be read out as a signal. Unlike the conventional transistor approach, Wang notes, piezotronics enable researchers to fashion tiny devices, making it possible to create arrays with ultrahigh resolution. In the 24 May issue of *Science* (p. 952), the group reported packing piezotronic transistors at the density of 8464 devices per 1 centimeter square—thousands of times denser than tactile sensors in human skin. Such arrays, Wang says, could eventu-



Big and small. Bioelectronic advances include using tiny light emitters to study brain development (*left*) and engineering a functional ear (*above*).

ally be useful in providing high-resolution touch sensing to prosthetic limbs, or giving robots a tactile sense sharp enough to identify what they're touching, or making signature readers capable of sensing not only the swoops of a handwritten signature but characteristic changes in pressure as well.

Flexible sensors are going way past skin deep. Rogers's team reported last year in the *Proceedings of the National Academy of Sciences* that ultraflexible circuitry could cling to the surface of beating hearts of pigs and rabbits and, at each of more than a dozen points in the array, continuously register the electric signals that fire muscle cells in the beating heart. This allowed them to image waves of muscle fiber contraction as blood is pumped throughout different chambers. The fine detail also makes it possible to map patches of heart tissue that misfire during arrhythmia, a condition that affects up to 5% of people in the United States.

Rogers and his colleagues also integrated temperature sensors and tiny heating pads into their array. By turning on the pads—emitting heat instead of measuring it—they ablated tiny tissue patches in their test animals, opening the door to using similar arrays to cure arrhythmia.

Going deep

Perhaps the boldest direction in bioelectronics is the emerging effort of marrying tissue and electronics at the cellular level. At Harvard University, chemist Charles Lieber and his colleagues have spent much of the past 2 decades pioneering efforts to grow ultrathin nanowires from the atomic scale up and to design them to work as transistors and other electronic devices. Nanoscale devices are the right size to monitor and influence biology inside cells. "It's really the natural length scale for electrical interface," Lieber says. Ion channels in neurons are less than 10 nanometers in width, synaptic connections between nerves are less than 100 nanometers across, and neurons themselves are on the order of a micrometer. Devices at those scales could be revolutionary.

Using nanowires, Lieber's team has made nanoscale computer memories, LEDs, and photovoltaics. In a series of recent papers, Lieber and his colleagues used their devices to track nerve firing. And they've placed multiple transistor-based recorders on nanowire probes that can be inserted inside neurons, making it possible for the first time to track neural signals as they traverse the interior of a cell. Patch clamp probes have made it possible to monitor the firing of individual cells since the late 1970s, but that approach can't track action potentials inside a cell. The new nanowire approach "is really the first fundamentally new recording method since the patch clamp," Lieber says.

Another new device in the nano tool chest is one that uses pulses of light to control gene expression in mice. Optogenetic tools of late have become a valuable way for biologists to initiate the expression of target genes in lab animals and track the effect. To use them, however, researchers typically must tether animals to complex electronic gear that distorts their natural behavior. In the 12 April issue of *Science*, Rogers and his colleagues described patterning nanoscale LEDs on the end of a flexible nanoscale filament (p. 211). These nano LEDs were then injected deep within the brain tissue of mice engineered to turn on particular genes in response to light. The nanoribbons were designed to pick up nearby radio waves and convert them to electricity. By placing a radio source next to the heads of the mice, the researchers turned on the LEDs, which, in turn, triggered gene expression. The new technique, Rogers says, foreshadows applications in which self-powered bioelectronics embedded in a variety of organs will regulate their function.

Some of the latest work by Lieber's group makes that day seem close at hand. As described in the November 2012 issue of *Nature Materials*, his team created a 3D mesh of silicon nanowires with built-in transistors. They used the mesh as scaffold for growing tissue, either heart muscle cells or neurons. The transistor array could monitor the electrical activity of the growing tissues and track their response to drugs such as noradrenaline, which stimulates cardiac cell contraction.

Such devices are only the beginning of a brave new world of bioelectronics. Better hope that it is more benign than *Star Trek*'s soulless collective, because make no mistake: With so much to gain, we *will* be assimilated.

–ROBERT F. SERVICE