Thinking Small

From quantum materials design to "voodoo physics" in the nanoscientists' weird world

by JONATHAN SHAW

NANOSCIENTISTS MANIPULATE OBJECTS and forces at a scale one-millionth the size of the period at the end of this sentence. At that size, matter behaves differently. Light and electricity resolve into individual photons and electrons, particles pop in and out of existence, and other once-theoretical oddities of quantum mechanics are seen to be real. Nanoscale research encompasses communications, new materials, and the study of life, as well as weird quantum phenomena and incidental things that exist in the real world, like diesel exhaust and dust and viruses. Physics, mechanical and electrical engineering, materials science, chemistry, biology, and medicine converge here. This is the realm of the lowest common denominator.

"Nano-," from a Greek word meaning "dwarf," refers to a billionth part of something. An atom is a nanometer-scale object, of course, so everything around us, in its smallest constituent parts, has nanoscale components, threatening to swamp the term and turn a promising realm of inquiry into a grab bag of science and pseudoscience. To merit the label, most scientists agree, nanoscience must involve investigative control and controlled integration of matter in which the small size leads to a significant change in physical properties. At Harvard, scientists are delving into the secrets of this tiny world, a strange place of apparent parallel realities, of proton-powered molecular biomotors, and of zero-dimensional objects, artificial atoms with adjustable numbers of individual electrons: a place where distances are measured in nanometers—billionths of a meter—and it is possible to *engineer* an empty space.

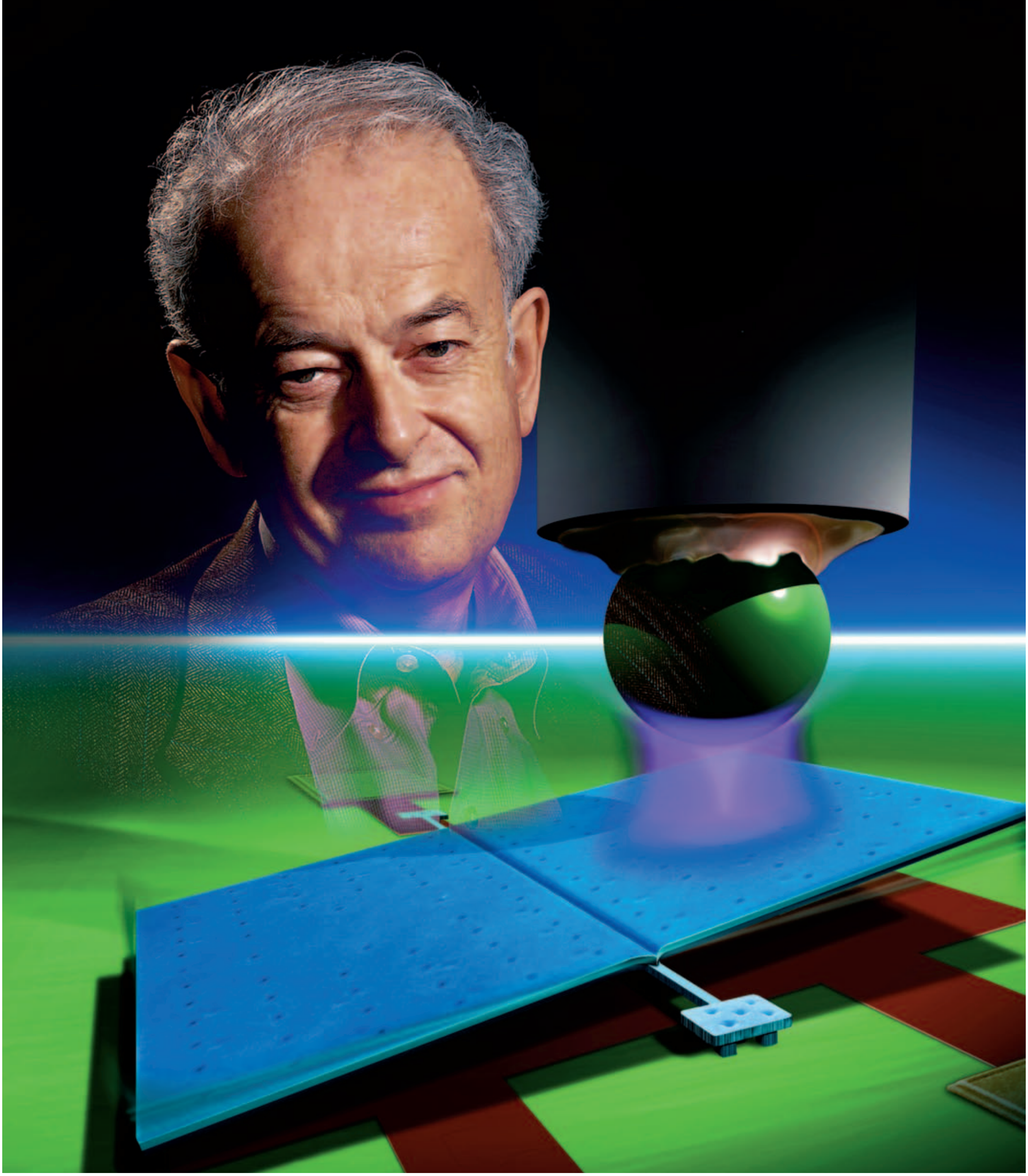
The Quantum Designer

FEDERICO CAPASSO, A SPRIGHTLY and enthusiastic man about five and a half feet tall, is the Wallace professor of applied physics and Hayes senior research fellow in electrical engineering. Ebullient and friendly, he has nevertheless just made a mischievous claim: "I can engineer the vacuum." A perfect vacuum, something akin to deep space, is a place from which all matter has been removed: not even one molecule remains.

Great classical physicists like Aristotle and Sir Isaac Newton defined a vacuum that way. In the macroscopic world we inhabit, vacuums are, for the intents and purposes of daily living (and even for much work in scientific laboratories), empty. But actually a vacuum is a busy place and, at the nanoscale, that has physical effects.

The current view of vacuum, Capasso explains, "is that you have continuous activity as particles or quasiparticles bubble in and out of existence. They could be photons or electrons that pop up for an infinitesimal time and then disappear. The beauty is that this activity, which is called vacuum energy, has effects that you can measure over fairly large distances, like a tenth of a micron." (A human red-blood cell is about 7 or 8 microns in diameter, but even a tenth of micron is large compared to a nanometer, which is one hundredth the size.)

"The laws of physics allow lots of stuff," continues the animated Capasso. "Lately, I have been pushing the frontier." He is attempting an experiment, which, he says in Italian-accented English, "if it works, will be fantastic." If two plates are put very close together, vacuum energy will cause an attractive force between them. "This is very weird," he notes, because the plates themselves carry no charge of any kind. This attraction, named the Casimir force for the late Dutch physicist who predicted it, has a classical analogy that makes it easy to understand.



OVERLAY ILLUSTRATION COURTESY OF KEITH DRAKE/FEDERICO CAPASSO LABORATORY

Federico Capasso with a microelectromechanical seesaw that makes high-precision measurements of the attraction between the metal sphere and the metal plane beneath it. This attraction, named the Casimir force after a Dutch theoretical physicist, arises from quantum fluctuations of the vacuum rather than from electric charges.

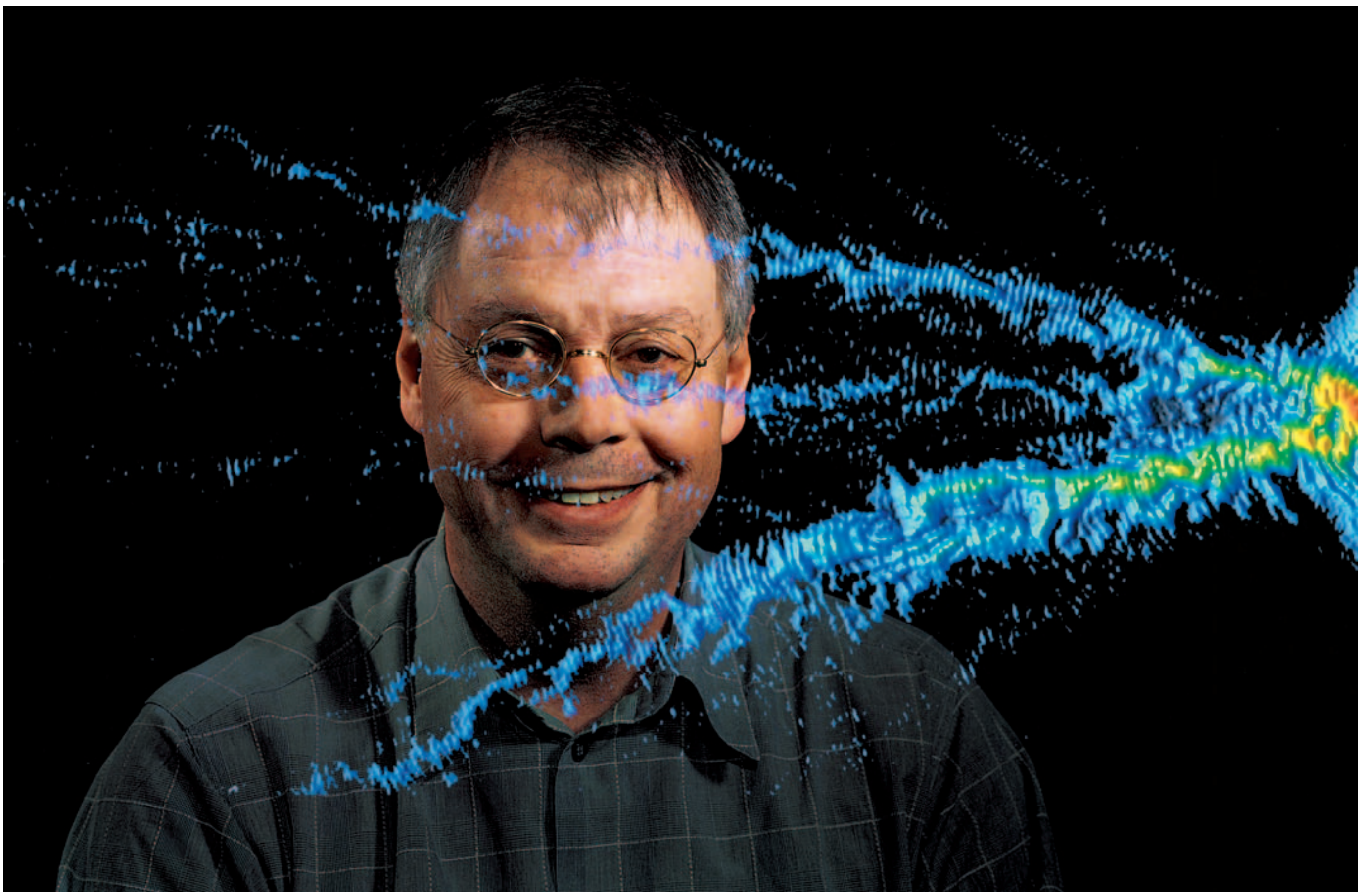
In the era of tall ships, navigators noticed that if two schooners traveling side by side in relatively rough seas "were sufficiently close, [they] crashed into each other mysteriously. A smart physicist," says Capasso, "writing a few years ago in the *American Journal of Physics,* made a connection with the Casimir effect: between the two ships, you have all the ocean waves of certain wavelengths—the ones that can fit. But outside, in the open ocean, you have all possible waves. The waves inside tend to push out, but there are fewer of them than there are waves outside, which tend to push in. The result is a net pressure inward, so the two ships attract each other, and collide."

At the nanoscale, the Casimir effect, whose existence was conclusively verified just a few years ago, works the same way, Capasso explains. "In the vacuum—now there is no real light there, but you can think of vacuum fluctuations as photons popping in and out—these photons are of certain wavelengths. Only certain wavelengths can fit between the plates, but outside them you have all wavelengths. So the net effect of quantum fluctuation, or vacuum energy, is to give an effective pressure inwards"—just like the ocean waves.

Perhaps most startling for those not familiar with the truly tiny distances that can be controlled in nanoscience is the fact that the two plates can be positioned closer to each other than the wavelengths of visible and ultraviolet light. As a matter of reference, visible light has a wavelength of between 4,000 and 8,000 angstroms, or 400 to 800 nanometers, and ultraviolet wavelengths are shorter than that. Capasso, by changing the shape of the plates (making them half-spheres, for example) or by changing the nature of the materials, can manipulate the force arising from the vacuum fluctuations, thus "engineering the vacuum."

Jeremy Munday, one of Capasso's students, and Davide Iannuzzi, one of his postdoctoral fellows, are currently at work on "a beautiful experiment" that uses an effect related to that of Casimir to enable a precise measurement of the torque generated by quantum fluctuations. This torque was predicted decades ago, but never verified experimentally. Under certain circumstances, Capasso explains, things can be engineered so that two plates of suitable materials, with a suitable intervening liquid, develop a net *repulsive* (rather than attractive) force between them due to quantum fluctuations. If one plate is positioned above another, the two then settle close together at the point where the weight of the upper plate is counterbalanced by the repulsive force; the upper plate essentially floats above the lower one, in what Capasso describes as a "quantum mechanical bearing"—like a ball bearing, but frictionless—an extraordinary feat of engineering in and of itself. But Capasso is after more than this. By making the upper and lower plates from special birefringent crystals that naturally attempt to align themselves with a polarized light source, he can actually use a light to rotate the upper plate relative to the lower one. What he wants to know, and to measure, is whether, when the light source is cut off, quantum fluctuations will rotate the plate back to its original equilibrium position.

The experiment is classic Capasso, a mixture of pure physics and engineering that could as easily lead to a fresh theoretical insight as to a new technology. But don't expect to find frictionless bearings in your local hardware store anytime soon; whether they will ever find an applied use outside the laboratory is difficult to say.



OVERLAY IMAGE COURTESY OF ROBERT WESTERVELT LABORATORY

Robert Westervelt with an image of electron waves and their interference patterns flowing from a point source across the plane of a two-dimensional semiconductor. The image was made with a liquid helium-cooled scanning probe microscope.

The Casimir effect, however, could play a role in future technologies. Capasso notes that microelectromechanical devices (MEMs), with moving parts, are becoming commonplace. An MEM activates the airbags in automobiles, and as these devices become smaller, perhaps one day shrinking to the scale of nanomechanical devices, the minute distances would cause them to interact via Casimir forces. Hendrik Casimir himself, who was director of research for electronics-industry giant Philips, is famous for describing the "spiral of science and technology," in which a basic advance feeds new technology, and a new technology feeds new science. Capasso is an exemplar of the scientist who understands both. Well he should: his most famous invention, the quantum cascade laser, was enabled by a new technology that made possible, for the first time, materials engineering at the atomic scale.

The Mastery of Materials

Semiconductors are widely used in electronics for making chips as well as light-emitting devices, and their name comes from having properties intermediate between those of conductors, like metals, and those of insulators, like rubber, which carry no electricity. Small as a grain of salt, semiconductor lasers send billions of bits of information per second over land and under sea along thousands of miles of optical fibers; closer to home, they read music engraved in compact discs. They are based on a simple principle: by applying a small voltage across a sandwich of two semiconductor materials, negative electric charges (the electrons) and positive ones (known as "holes" or electron vacancies) are injected into the center of the sandwich, called the active region, where they "annihilate," giving off photons. The energy and therefore the wavelength (or color) of these light quanta is determined by a key material parameter called band gap. This is the gap between the valence band of electrons surrounding an atom (those electrons that are part of the material's elemental structure) and the conduction band of electrons that flow in the presence of voltage. For a laser to emit light, an electron has to "jump the band gap," i.e., drop down into one of the "holes" in the valence band precisely by this band-gap amount, emitting a photon of equivalent energy, which thereby determines the light's wavelength. If one wishes to have semiconductor lasers emitting vastly different wavelengths, one has no other choice but to make them out of very different materials with widely different band gaps.

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In the early 1990s, while working at Bell Laboratories, Capasso realized that, using an entirely different principle, he could design a new kind of semiconductor laser that didn't rely on band gaps: the quantum cascade laser. Using an advanced materials-fabrication technique called molecular beam epitaxy (MBE), capable of precisely growing artificial man-made substances, it is possible to spray-paint materials, one atomic layer at a time, onto a flat surface in a vacuum. The materials can be changed for each layer, making it possible to create an intricate, multilayered sandwich of substances, each with its own special properties.

MBE made it possible to create crystals with alternating layers of different semiconductors. Those with higher band gaps form energy barriers or "walls" that constrain electrons present in the lower band-gap material, so that they cannot easily move across the structure. Electrons are not circus fleas, but they are capable of other tricks besides jumping across band gaps. If the semiconductor forming the wall is sprayed in a very thin layer, just a few atoms deep, then electrons in the neighboring layers can traverse it. In classical physics, when you throw a ball against a wall, it bounces back. The ball can only only blast through if it has a higher energy than the barrier. But at the nanoscale, when the particle is sufficiently small and the wall extremely thin, it can pass through. Scientists refer to this quantum mechanical phenomenon as "tunneling," an effect that is at the heart of the quantum cascade laser (QCL).

Before Capasso's invention of the QCL in 1994, no one had "ever actually been able to say with a straight face that he or she had *designed* a new material," writes Ivan Amato in *Stuff: The Materials the World Is Made Of,* which provides an accessible and entertaining account of Capasso's achievement. In a QCL, electrons tunnel through multiple layers of materials laid down using molecular beam epitaxy. Capasso realized that if electrically conductive layers were arranged in a series of steps, with intervening insulating layers of precisely engineered resistance, then the electrons could be induced to "tunnel" down the "staircase"—the energy slope that he would design—emitting a photon of light as they tunneled between each layer. The result is that a single electron entering a QCL will emit not one photon but 25 or more, depending on the number of layers. (In conventional semiconductor lasers, on the other hand, only one laser photon is created as the electron is injected into the active region.) Most importantly, the wavelength of the QCL light is controlled not by the band gap of a particular semiconductor material but instead by the thickness of the layers, and is therefore not limited only to the wavelengths of materials that occur in nature. Materials design of this kind, Amato writes, is "tantamount to breaking the four-minute mile, or breaking the sound barrier...."

Unlike any other light source, the emitted wavelength in a QCL can be tailored across a tremendous range covering most of the invisible spectrum known as infrared. QCLs have already found several applications and are now becoming commercially available. Hundreds of times more powerful than conventional semiconductor lasers operating at equivalent wavelengths, they can monitor atmospheric pollution or measure emissions, detecting the presence of trace gases down to a few hundred parts per billion. Capasso's success would not have been possible, of course, without benefit of the science and technology spiral—the nanoscale engineering capability provided by molecular beam epitaxy that allows researchers to build things one atomic layer at a time.

The sandwiched layers of materials created by MBE actually trap electrons in a two-dimensional plane, which physicists describe as a kind of skating rink. An insulator acts as the floor of the rink, a conductive layer acts as the ice, and then another insulator provides a low ceiling. If you were an electron out for a Sunday afternoon skate, you would wish to stand up, to operate in three dimensions as you glided around. But in this rink the ceiling is so low that you practically have to crawl on your belly just to enter. This is what electrons are forced to do in the two-dimensional rinks made by MBE, and it drives them a little crazy—which is why they sometimes tunnel out.

Being able to confine electrons in this way—the technical term for the skating rink is a "two-dimensional electron gas"—has led to new discoveries in physics, one of them recognized with the 1998 Nobel prize.

Making the Caged Bird Sing

Creating such exotic-sounding materials is relatively straightforward, according to Robert Westervelt, Mallinckrodt professor of applied physics and of physics. Physicists have fancy tools that let them image and imprint and cut and drill tiny nanoscale structures. They can take a two-dimensional skating rink and then cut out a tiny sliver, just a wavelength wide (about 40 nanometers in this case). The result is a wire-like, one-dimensional structure. Chop a tiny bit off the end of the wire and you get a dot, a zero-dimensional structure. Scientists refer to these as quantum dots, and they are already the subject of lots of basic research. After all, physicists have reasoned, if confining electrons to two dimensions leads to exciting new physics, might a smaller cage—one or even zero dimensions—be even better?

Westervelt is the kind of scientist who wants to understand how everything works. How do confined electrons behave? What does their movement look like? Nanoscale research is providing the answers. Scientists can see things that used to be purely theoretical. Westervelt's lab, for example, was among the first to image electrons moving in real space through a two-dimensional electron gas. His research also focuses on those quantum dots—tiny semiconductor structures that contain a finite number of free electrons.

Quantum dots are so small, in fact, that their size is what determines the number of electrons they can contain. Make them too small and they will contain none at all. They are exciting research tools because they exhibit quantum mechanical behaviors such as the quantization of electron charge and spin, much as real atoms do. ("To understand quantization of electrons in a dot," says Westervelt, "imagine people entering a subway car. They enter one at a time, and a crowded car can only hold so many before it is full.") Unlike atoms, quantum dots can be connected to electrodes, making them easier to study.

A single quantum dot with electrical leads attached can be made to behave like a transistor, switching on and off at voltage levels corresponding to the energy needed to add an additional electron to the dot. In the mid 1990s, Westervelt's group and others made an artificial molecule by bringing two quantum dots together, essentially creating a chemical bond between two artificial atoms. Being able to connect two or more quantum dots makes it theoretically possible to build circuits, and that could in turn open up a whole new area of research in electronic and magnetic devices, such as computers. Furthermore, Westervelt's group has created quantum dots that contain just a single electron. Having one electron, because it is easy to control, has expedited research into the new field of spintronics (electronics based not on an electron's charge, as in a traditional transistor, but on its spin) and into the development of systems for quantum information processing.

Electrons have spin that is either up or down—but spin can also be *both* up and down simultaneously in what is called a superposition. And superpositions, it is thought, are what will someday allow the construction of quantum computers that are exponentially more powerful for solving certain kinds of problems than conventional computers. (More on this later.)

But even with respect to conventional computers, the electronics industry is "beginning to ask academic people to think about new ways of representing information," says Westervelt, who is director of a National Science Foundation-funded Nanoscale Science and Engineering Center (NSEC) based at Harvard. The NSEC is an interdisciplinary research collaboration among scientists at Harvard, MIT, and the University of California, Santa Barbara, who also work with researchers at the Sandia, Oak Ridge, and Brookhaven National Laboratories and internationally at Delft University of Technology, the University of Basel, and the University of Tokyo. As the semiconductor industry reaches the limits of how small it can make a silicon chip, industry researchers are looking for new ways to make computers faster. A new approach might be to use the quantum states of nanostructures instead of the electron charge to represent information. "Understanding ideas like these," says Westervelt, "we can create new types of nanoscale electronics."

Voodoo Physics

Charles Marcus works on an entirely different timescale. "The things we explore," he says, "might be useful or might only be interesting in the abstract, or might only be useful for my great-grandchildren." Though his research lies in a realm that appears barely poised on the edge of reality, it couldn't be more grounded: nanoscale science enables Marcus to study the physical manifestations of the strangest quantum mechanical effect of all, one that defies normal intuition and logic: a phenomenon called "entanglement."

Marcus, fortunately, is a master of simple explanations. "Before life gets weird," he says with a grin, "let's cover what we're familiar with. An electron doesn't have a lot of machinery. It has a charge: negative. It has a mass, so it weighs something. It has a position in space: it's somewhere. It has a momentum: it's going somewhere. And about those last two, there's a trade-off: if you know one precisely, then you don't know the other.

"But that isn't so otherworldly, in fact. If you want to see where something is, you've got to shine some light on it or something like that, otherwise you're in the dark and you can't see it. A little thing like an electron gets a real knock from having light shined on it," Marcus explains, "and gets speeded up by the light hitting it. The better the look you want to get—by using shorter wavelengths of light—the bigger a knock you give it. So you can't measure where it is without messing up its momentum."

Another property of electrons is that they have angular momentum, or spin. "The earth," says Marcus, "in addition to mov-

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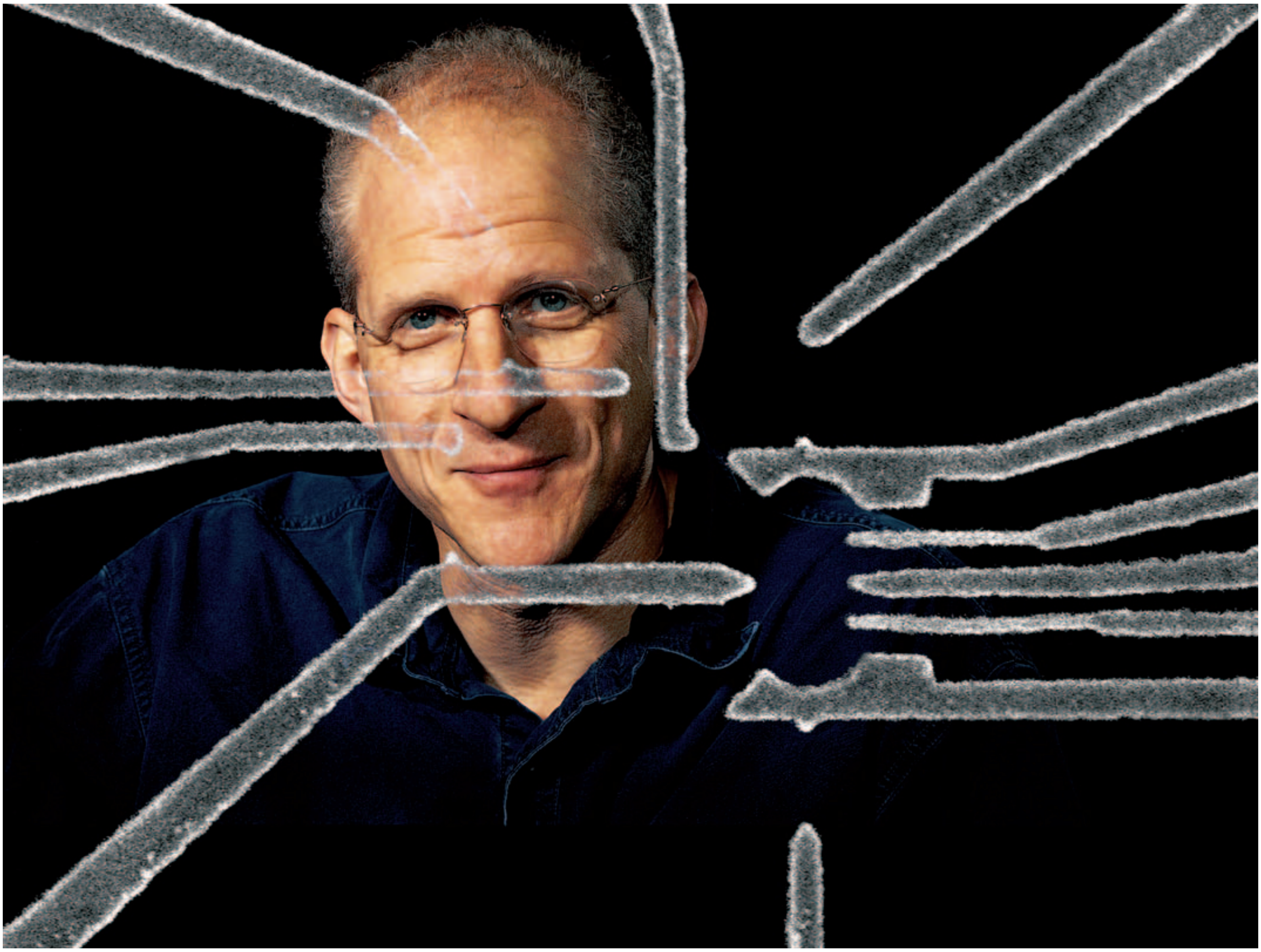


OVERLAY IMAGE COURTESY OF CHARLES MARCUS LABORATORY

Charles Marcus with metal gates that he uses to control the movement of electrons trapped in a two-dimensional semiconductor plane. Marcus uses the gates, which are made using electron beam lithography, to study the quantum mechanical behavior of electrons.

ing around the sun, is spinning on its own axis, and so it not only has momentum—it's moving through space—but it has angular momentum, and a magnetic field that's related to that spinning motion. The same for electrons: they have momentum if they are moving, but they also have angular momentum as if they are spinning, and a magnetic field around them aligned with that angular momentum.

"So far, so good. Nothing too strange yet." Now imagine you are in deep space, where there is no up or down, and the electron could be spinning in any direction at all. "Here's where it gets a little weird. When you ask an electron if it is spinning up or down, it will always give you 'Up' or 'Down' as an answer. It won't answer, 'You asked me the wrong question—I'm pointing sideways to the direction that you asked me.'"

Considered alone, this is not a terrible problem, says Marcus. But when you consider the consequences, things start to become very strange. Say you have a particle whose angular momentum is zero, which then explodes into two parts that go flying off in opposite directions with opposite spins. "Now I wait until they are a billion miles apart—an hour, a week, a century—however long I want to wait," Marcus explains. "I'm out in deep space now, and say I have a measuring apparatus that lets me query one of the particles in the vertical direction (whatever that means in deep space). I ask it, 'Are you aligned with or against such and such a direction?' And it will say either yes or no—'I'm aligned with' or 'I'm aligned against.' The other particle, now at the far side of the galaxy, will have to give the opposite answer: because they started together, their angular momentums must add up to zero."

But how does the particle that answers second know what question the first one will be asked? "The original inquiry could have been made at any angle: 90 degrees to the left or 45 degrees to the right. The first particle says yes; then the other would become purely, 100-percent-probability-aligned in the opposite direction," Marcus continues, "instantaneously learning what the other one had answered and therefore adjusting its value to the right value."

Einstein himself was deeply troubled by this, Marcus notes. It implies that you either have to abandon the notion that effects are local—that one thing influences another—or believe that the world is completely deterministic, that there is no such thing as free will. In that case, the query itself as well as the answer are preordained.

Either way, this is a non-intuitive situation. "And yet that's the world we live in," Marcus says. "If it doesn't make sense, that is our brain's fault. You do these experiments, and that's what happens." There doesn't seem to be any difference between the crazy predictions of quantum mechanics and the experimental reality. "It's a bit like voodoo: someone pokes a doll over there, and somewhere else a guy is saying, 'Ouch!' OK, with quantum mechanics, the poke to the voodoo doll and the ouch are two consequences of a common cause, but still, the effect is nonlocal. The voodoo part," as Marcus puts it, "is that nothing needs to propagate from one to the other."

The Quest for the Quantum Computer

"Entanglement," the quantum conundrum that Marcus describes, is the key to unbreakable quantum cryptography today, and to quantum computing in the future. Quantum computers have been described by mathematical equations, and the equations stand up to experiment. "The machines are doable, we just don't know how to make them," he says. "It might take a decade or it might take a millennium to figure out how to do it." But they could be immensely powerful. Marcus likens it to the power that was unleashed by nuclear physics. "Quantum computing appears to be a whole reality that we haven't figured out how to take advantage of yet."

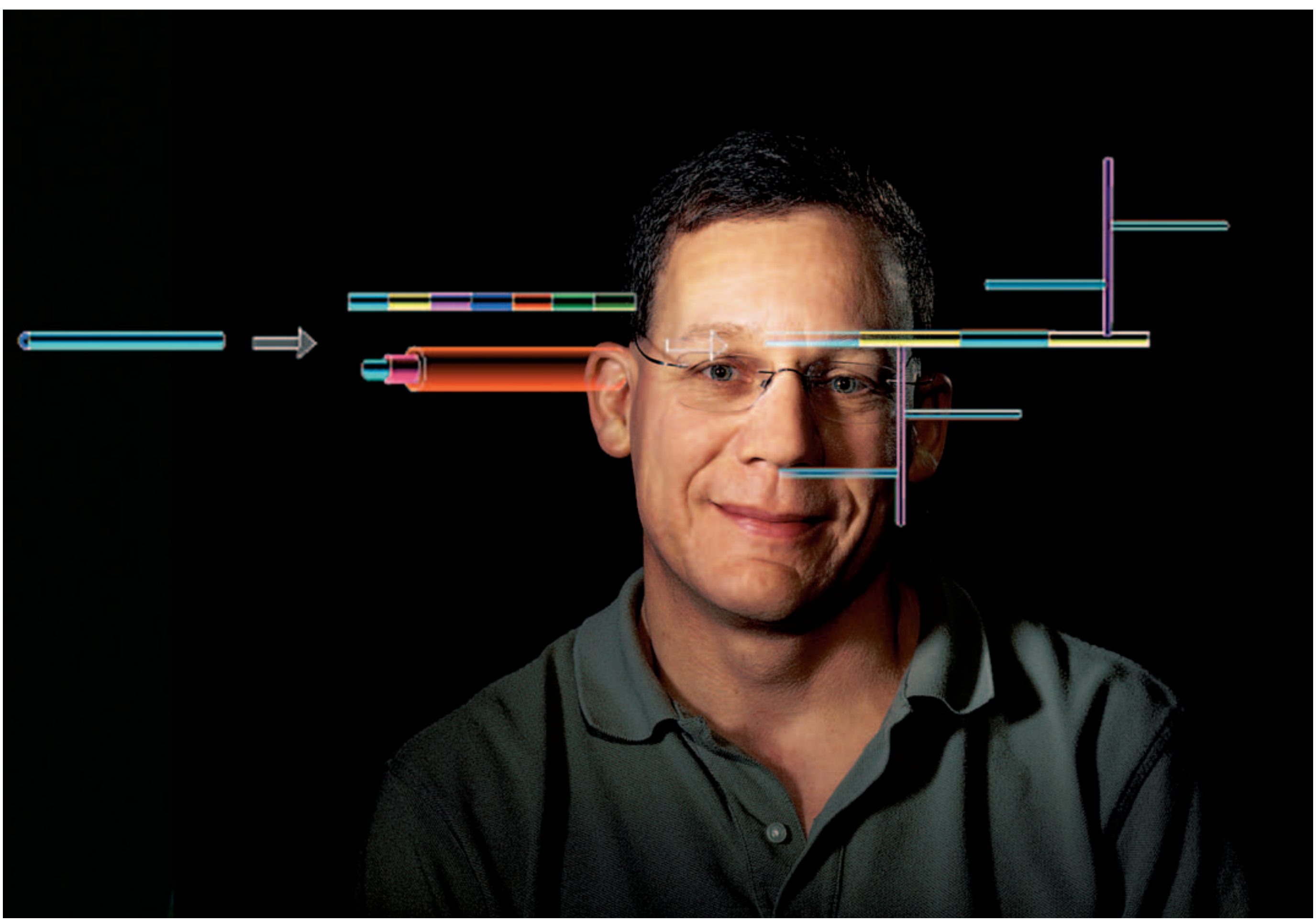
One of the real-world problems that Marcus has been working on in his laboratory involves the first step toward quantum computing: controlling the entanglement of two particles. It is possible for two separate particles to become entangled, much like a single one that has been blown apart.

Marcus achieves this by exploiting a characteristic of electrons: they always seek the lowest energy state, the way a marble in a bowl will roll around until it finds the lowest point. Two identical electrons cannot occupy the same space, just as two marbles cannot share the lowest point in a bowl. But because angular momentum is part of the space where electrons live, if one is spinning up and the other is spinning down, then they can occupy the same lowest-energy position, because they are *not* identical, but instead like a pair of yin/yang marbles fitting together.

Researchers in the Marcus lab can therefore trap one electron spinning up and another down in a low-energy quantum dot on a chip, and then separate them to see how long they remain entangled. The important question that Marcus set out to answer is, Do the electrons maintain their entanglement after they have been sent through transistors and boxes and wires on the chip, or does the entanglement get lost?

One way to establish this is to make the low-energy quantum dot receptive to the returning electrons only if they maintain their entangled state. If, when they return, they no longer have opposite spin, they cannot occupy the same low energy space. Researchers now know that the particles remain entangled for somewhere between a nanosecond and a millisecond, but are seeking a more precise measure. The answer is important because it may limit the

Charles Lieber with chemically engineered nanowires of increasing structural complexity, ranging from uniform wires to structures modulated in the axial and radial directions, and finally to multi-branched materials. Colors indicate variations in material composition, which, like structural complexity, yield increasing diversity in the functional properties possible from a single nanowire.



OVERLAY IMAGE COURTESY OF D. WANG, F. QIAN, AND C. M. LIEBER, HARVARD.

"It's a bit like voodoo: someone pokes a doll over there, and somewhere else a guy is saying, 'Ouch!'"

kinds of calculations that a quantum computer can do, or require discovering a way to prolong entangled states.

A two-particle quantum mechanical system like the entangled electrons seems very simple, like a binary logic state in a standard computer. After all, you have an up and a down particle. But in a quantum system, the sum of the logic states is up-down, down-up; and those probabilities can be added together, so up-down minus down-up is different from down-up minus up-down. It is as if every switch in a computer could be both on and off and off and on at once. "If you have 20 particles all doing this," says Marcus, "heaven help you," because all possible combinations are present simultaneously in what is called a superposition. This is why a quantum computer would be so powerful: all possible solutions to a problem could be represented simultaneously.

"It might seem otherworldly at first," says Marcus, "but it's not. All of this stuff is here, in the lab and in our world. It's true these phenomena don't seem evident when thinking about classical physics, but it's quantum physics that describes our world—microscale and macroscale. Now, can we put it to use in new ways? Let's find out. Let's try."

Bottom-up Computing and the Biological Interface

Charles Lieber is working to build a computer out of the tiniest of components—one that can be assembled cheaply on a lab bench using the principles of chemistry, rather than the expensive lithographic tools employed by physicists and semiconductor manufacturers. His goal is to build a standard, digital computer, ideally with integrated optical circuits. Already, his lab's research has led to new quantum mechanical devices and even biological sensors that can be used to detect disease.

Semiconductor manufacturers can already make electronic components with features smaller than most academic labs can produce because the manufacturers etch the features into silicon; yet the endgame for "Moore's Law," which posits that computing capacity will double every 18 to 24 months based on the shrinking size of transistors, is fast approaching. There is a limit to shrinkage at the nanoscale: atoms, at 0.2 nanometers across, are nature's building blocks, and they don't come any smaller.

Lieber's approach is the opposite of industry's top-down tack: he hopes to build a computer from the bottom up, starting small from the outset. He can make nanowires just three atoms across, and do it cheaply, using materials dissolved in an alcohol solution. The solution is poured into grooved channels in a polymer block to produce an array of parallel wires. Another set of wires can be laid perpendicular to the first simply by rotating the apparatus 90 degrees. Using this method, his lab can produce transistors just 10 nanometers across. Lieber can control various properties of the wire, such as its conductivity, by altering the composition of the alcohol solution to create different "flavors" of nanowire. These can then be mixed and matched depending on the type of transistor one wants to build.

"If all we were doing was making things smaller," says Lieber, "we would already be beaten by a company. But we have made nanoscale computer components with properties that are fundamentally different from [those in] silicon-based components, and then figured out how to organize them in different ways to make computing devices, biological sensors, and optical devices." For example, Lieber can engineer nanowires with properties similar to those created by molecular beam epitaxy. He can make lasing nanowires, tiny wires that emit laser light.

Getting a nanowire to lase is a profoundly important achievement because it means that electrical signals in a computer or other ultra-tiny electrical device can be converted to light (photons) in a highly efficient way. Photons have certain advantages over electrons. Not only are they much faster, but they are less susceptible to the crosstalk, or interference, that is sometimes seen in small electrical circuits. Lieber has forced light to bend at a 90-degree angle within a 100-nanometer device. (This is possible because, in a very small wire, the radius of the curvature is actually small, the way we are very small compared to the curvature of the earth and therefore don't perceive it.) And he has made light-based diodes, or detectors—a key element in an optical logic circuit. His group can modulate light, control its polarization, and use wires for subwavelength guiding. They can even connect two waveguides together (imagine connecting two wires), a process that normally takes a few millimeters or hundreds of microns, in less than a wavelength of light. He can also sort information at the nanoscale ("addressing," in computer parlance) without using lithography by building bits of information into wires before he pours them. And he has made solid-state memory. "All this demonstrates that we are really getting close," says Lieber—"that making a computer [entirely from nanoscale components] is not completely a dream."

"But," he admits, "it is still challenging to connect all the components together and demonstrate that we can process information." His is a fundamentally different approach to computing and will require new kinds of computer architecture to exploit. So Lieber has turned to biology for inspiration about how best to make such connections. Today's desktop computers operate strictly in two dimensions, performing calculations on a flat (planar) chip. Lieber has been laying the groundwork for a much more sophisticated network of connections in three-dimensional devices by engineering branched nanowires, and by studying the architecture of the brain. "If we are always thinking about confining ourselves to a plane," he says, "I just don't see that we are going to do something revolutionary relative to what is going on in electronics today." The goal is not to understand the brain, per se, but to explore ways to connect with the rich variety and scales of organization and interconnections among cells in biology. Biological principles can be used to transmit chemical and electronic information, so it is possible to make hybrid computing devices. "What we have done so far is cool," Lieber says, "but it is not going to change things. Combining biology with nanotechnology to create a new field of science is going to be the future."

Because his lab is a leader in the development of nanoscale biological sensing devices, creating a biological interface is not such a far-fetched idea. Lieber's group has already made sensors for detecting prostate cancer and viruses, and such devices have a bright future. They operate by taking advantage of another special property of nanoscale objects: their surface area is huge relative to their volume, making them highly sensitive to external stimuli. "Things that happen at the surface can therefore affect the whole structure," Lieber explains. While this could cause unwanted interference in an electronic circuit, it can be exploited in biology. "Normally a molecule binding to the surface of a transistor wouldn't have a big effect. But imagine a protein with a charge on it coming up to something very small, where the surface is a big component; the protein biologically or chemically switches the transistor on or off. In essence, you can electrically detect when you have a protein, a nucleic acid, or anything else." The technology could even be modified to detect chemical and biological agents used in warfare.

His nanoscale detectors might be thought of as hard-wired, application-specific devices. They don't run software and, because they are tiny, they really don't have to. Software gives fixed hardware the flexibility to do many things. But with these sensors, Lieber says, you could in principle design a centimeter-square chip to detect a billion things simultaneously, even variations in an individual's DNA.

Once, at a conference, when Lieber raised the possibility of linking the computing power of the brain to the power of digital electronics, he was questioned about the ethics of doing such a thing. (He had shown a slide of a human brain that included a little chip.) He hadn't considered that, he replied. Although that kind of tight integration sounds radical, some people (those who carry their laptops with them all the time?) might welcome it. Such integration is purely hypothetical today, but a partial alternative could be realized with today's nanotechnologies. Flexible electronics, which allow the fabrication of "cheap and powerful displays with the properties of billion-dollar fabrication-line silicon," says Lieber, are easy to make and of high quality. These tiny, flexible plastic screens could even go over the eye, like a contact lens. Such a device might be an ethically palatable intermediate step in the direction of a biological interface.

Robert Westervelt's research group has also been exploring the use of semiconductor technology to create new tools for bioengineering applications. Working with Donhee Ham, an assistant professor in electrical engineering at Harvard, his students have created hybrid chips by building a microfluidic system on top of a custom-designed silicon integrated circuit (IC). The microfluidic system provides a biocompatible environment for the living cells, and the IC brings the power of semiconductor electronics.

The cells have magnetic beads attached, which makes it possible to move them around on a chip and even to pull them apart. Such a system could be used to sort cancer cells from normal cells, or even to assemble artificial tissues. Donald Ingber, Folkman professor of vascular biology at Harvard Medical School, has used magnetic beads like these to explore the effects of mechanical stress on cells. (At the cellular level, breakdowns in function are often due to mechanical failures.)

Westervelt also collaborates with Kit Parker, an assistant professor of biomedical engineering at Harvard who has envisioned a novel application in tissue assembly. "There is a theory," Westervelt explains, "that when someone suffers a heart attack, the heart cells talk to each other. When one cell starts having a heart attack, the other cells feel it and decide to have a heart attack too, causing the whole thing to take off. But this hasn't actually been tested, because we need to get two heart cells, put them together, torch one of them and see whether the other one lights up." By engineering such chips, which are typically just a centimeter square, Westervelt hopes to bring the power of microprocessors to bio-experimentation.

The Expanding Nano Frontier

Biology may be the area that fuels a revolution in nanoscience and technology, says Flowers University Professor George Whitesides, a chemist. Physics gave the field tools for imaging, probing, drilling, cutting, and writing; chemistry has contributed efficient approaches to materials science, an area in which Whitesides is expert; but advances so far have been evolutionary, rather than revolutionary, he says. The study of biological nanostructures might change all that: "The cell is chock full of small structures whose function we can't replicate right now, and that's an area that is intensely interesting."

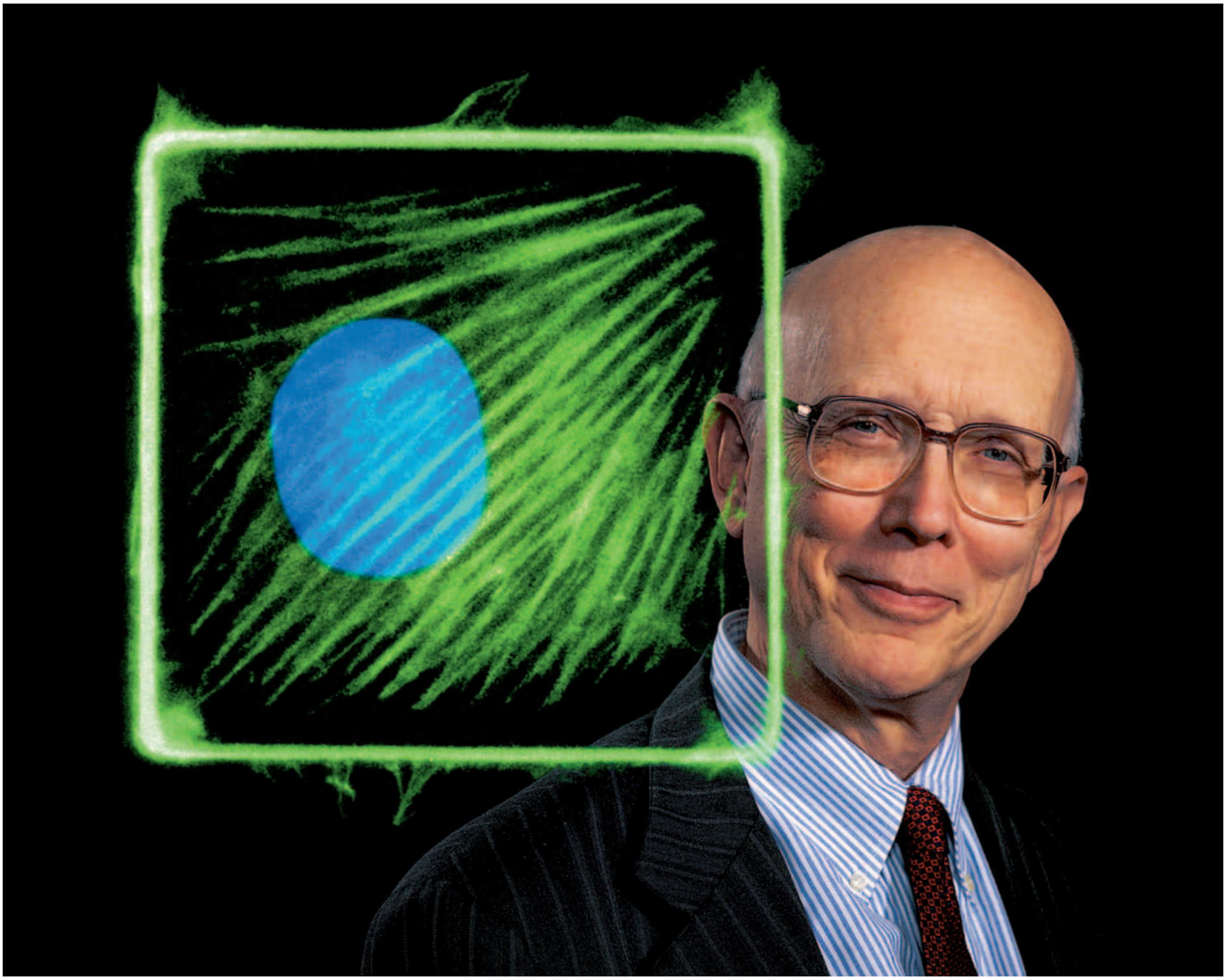
The flagellar nanomotor, which bacteria like *E. coli* use to get around, is a prominent example. It has a central shaft like a motor in a ship, but "is actually completely different in its methods of operation," using the flow of protons to spin a flagellum that propels the cell through fluids. "And it is smaller than any motor human beings can make," Whitesides adds. Understanding the principles of its operation might prove useful in other nanoapplications, he suggests, or the motor might be made to serve a new purpose in a living animal.

Another important area of inquiry lies in understanding how biological structures interact with nano-sized particles such as carbon nanotubes (that can be grown like hair) and buckyballs (named for R. Buckminster Fuller '17). These are unhealthy to inhale, but government safety regulations cover such substances in laboratories, where researchers deal with hazardous materials all the time, says Whitesides. However, in the area of public health, the realization that small particles in the air are a dangerous kind of pollution that can become lodged in the lungs has led to serious concern, particularly about diesel-fuel emissions, which can cause illnesses ranging from asthma to lung cancer.

For Whitesides to be championing research in the biological realm is no surprise. The work done in his laboratory serves as a kind of bridge between the physical and the biological sciences. A polymath with wide-reaching collaborations across disciplines, he works with Capasso, for example, on fluid optics, injecting liquids into a quantum cascade laser without disrupting its ability to lase. The technique could be valuable for spectroscopically analyzing trace chemical or biological elements in fluids and also for controlling the wavelength of the light emitted by the laser.

With these sensors, Lieber says, you could in principle design a centimeter-square chip to detect a billion things simultaneously, even variations in an individual's DNA.

OVERLAY IMAGE COURTESY OF GEORGE WHITESIDES LABORATORY



Chemist George Whitesides, shown with a bovine endothelial cell confined to a square, works at the intersection of materials science and biology. The cell's nucleus is stained blue, while its filamentous actin is stained green.

Capasso "builds things that last forever out of semiconductor materials," says Whitesides. "We make things that are extremely evanescent entirely out of fluids"—such as liquid light channels made from flexible materials. Devices that combine these approaches might lead to fundamentally new ways to manipulate light. "Can it open a window into something else," he asks, "particularly here in biology, which is full of fluids and soft things?"

Fluids are not the only area of research in the Whitesides laboratory with direct application to biology. His group specializes in making nanostructures that "might be fairly simple, but are very cheap and easy to make, so that you don't need fancy 'e-beams' [for cutting and drilling] and elaborate 'clean rooms'" for nanoscale fabrication. "We find ways of making *easily* structures that the electrical engineering and condensed-matter-physics community has made with great difficulty, so that biologists and material-science chemists can get involved in this," Whitesides says. "The economics of these areas are quite different than they are in electronics"—where a semiconductor-fabrication facility might cost billions of dollars.

Whitesides' lab has come up with a method for printing and molding materials called soft lithography; it has been "particularly useful in getting small structures extended into biology, because the methods used for microelectronics are intrinsically too expensive and [made of the wrong materials]," such as hard silicon semiconductors. "These [printing techniques] are very simple methodologies that rely on the contact of one molecule or atom with another," he says, but they allow replication of structures down to about half a nanometer, even smaller than is possible with light-based lithography.

In 1959, the prescient physicist Richard Feynman anticipated the field of nanoscale science and technology. In a lecture titled, "There's plenty of room at the bottom," he explained how it would be possible to one day write the entire contents of the *Encyclopedia Britannica* on the head of a pin. That day has arrived. But Feynman also described far more ambitious ventures, envisioning a day when one might "swallow the surgeon," which would then perform the necessary operation. Though that day has yet to come, hints of its promise are already appearing in Harvard laboratories. Thinking small has a big future.

Jonathan Shaw is managing editor of this magazine