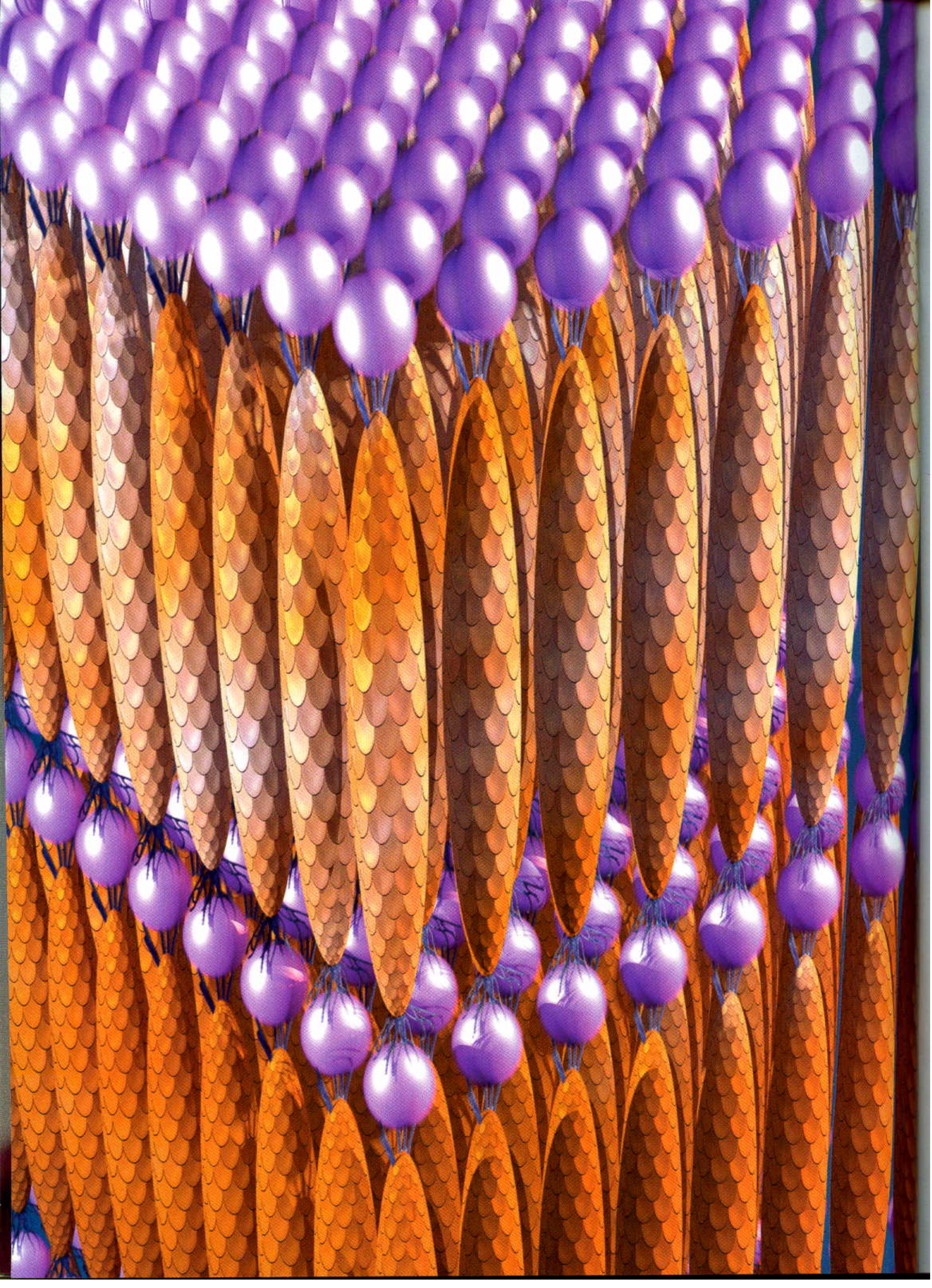


VIRAL NANO ELECTRONICS

M.I.T. breeds viruses that coat themselves in selected substances, then self-assemble into such devices as liquid crystals, nanowires and electrodes

By Philip E. Ross

For many years, materials scientists wanted to know how the abalone, a marine snail, constructed its magnificently strong shell from unpromising minerals, so that they could make similar materials themselves. Angela M. Belcher asked a different question: Why not get the abalone to make things for us?

She put a thin glass slip between the abalone and its shell, then removed it. "We got a flat pearl," she says, "which we could use to study shell formation on an hour-by-hour basis, without having to sacrifice the animal." It turns out the abalone manufactures proteins that induce calcium carbonate molecules to adopt two distinct yet seamlessly melded crystalline forms—one strong, the other fast-growing. The work earned her a Ph.D. from the University of California, Santa Barbara, in 1997 and paved her way to consultancies with the pearl industry, a professorship at the Massachusetts Institute of Technology, and a founding role in a start-up company called Cambrios in Mountain View, Calif.

Belcher had a grand plan to develop biological agents that could move molecules around like so many bricks, building structures from the ground up, a strategy known in the nanotechnology world as self-assembly. But to begin the task, she needed a critter more tractable than the abalone, a high-maintenance animal that grows slowly and is something of a one-note Charlie. She wanted something small, spry and flexible—a cross between Maxwell's famous molecule-sorting demons and Santa's elves.

3-D LIQUID CRYSTAL depicted in this artist's representation consists of multiple copies of a phage (a bacteria-infecting virus) called M13 (*gold*) that bound to inorganic nanocrystals (*pink*) and assembled themselves into an ordered array. Such films could be used in flexible displays.

PHIL SAUNDERS *Space Channel Ltd.*

Belcher looked at monoclonal antibodies because they can be engineered to stick to many different things, but they proved hard to work with. Then, in the mid-1990s, she learned about the M13 phage, a long, skinny virus that parasitizes bacteria but is harmless to humans. The phage, which is roughly six nanometers wide and a micron long, encloses its single strand of DNA in a protein coat, with some 2,700 copies of one kind of protein lining the filamentous body and a few copies each of several other kinds of protein capping the ends. The different kinds of proteins can be engineered to vary from phage to phage, making for a billion possible permutations, each conferring particular chemical affinities. A phage might stick to one material along its sides, another at one end, and still another at the opposite end.

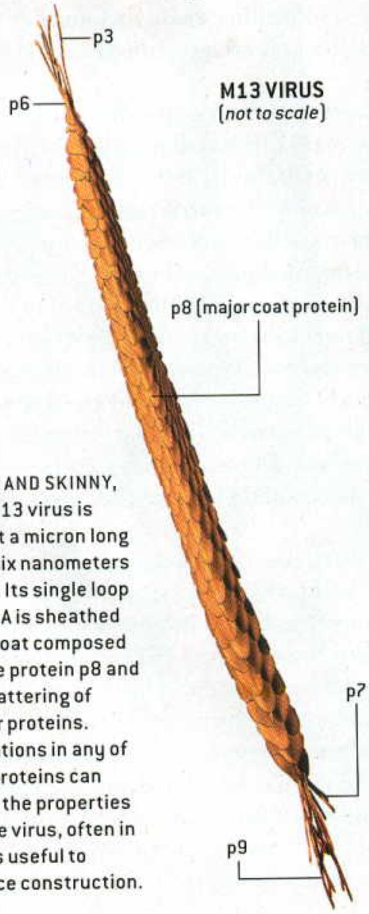
Such chemical specificity has long been exploited by biologists, who use M13 phages that bind to particular organic substances to identify unknown samples. Belcher was the first to demonstrate that the virus could also tag and manipulate inorganic molecules, such as the metals and semiconductors that lie at the heart of so many useful products. It was a rare example of the physical sciences borrowing from the biological sciences: because the biologists had done the spadework, Belcher could go out and buy a vast collection of phage variants, called a phage display library, for approximately $300.

To get a phage that binds to the right molecule, Belcher uses a process called directed evolution. "We throw our billion possibilities into a beaker with some material, wash it off and see what sticks to the material," she says. "We remove the ones that stick by changing their interaction with the surface, say, by lowering the pH, then collect whatever stuck and infect it into host bacteria, to amplify the phage."

Phage Feats

AMPLIFICATION provides trillions of copies of a promising subset of phages for another stage of evolution. This time the conditions in the solution are altered to make it a little harder for the phages to bond to the target material; again, the less sticky variants are washed off, the survivors are amplified, and the process is repeated under still more demanding conditions. At the end of the process, which can take three weeks, only one phage variant remains—the most selectively sticky of them all.

Put a phage with a highly specific taste for gold into a solution containing gold ions, and it will gild itself into a wirelet a micron long, suitable for connecting adjacent elements in a microcircuit. A variant of this phage will even link up with its fellows to form a gold wire many centimeters long, which can be spun like thread and woven into cloth fabric. Such a wire, bonded to chemically sensitive receptors, might detect toxic or biologically threatening agents.



LONG AND SKINNY, the M13 virus is about a micron long and six nanometers wide. Its single loop of DNA is sheathed in a coat composed of the protein p8 and a smattering of other proteins. Variations in any of the proteins can alter the properties of the virus, often in ways useful to device construction.

A year or two ago Belcher got yeast cells to fix gold, in an experiment that as yet has no practical applications (although the cells' six-micron width might make them easily visible as fluorescent markers in certain experiments). In the meantime, her M.I.T. students who are learning how to use organisms as a basis for materials perform the gold fixing as an exercise.

Although Belcher continues to examine the experimental merit of various other organisms, she focuses on M13, in part because its immense length-to-width ratio makes it naturally assemble into more complex shapes. "Think of crayons in a box," Belcher says. "If you shake just a few of them up, they'll settle randomly, but if you increase their concentration, they'll tend to pack." She has gotten selected M13 phages to form a film 10 centimeters square and less than a micron thick, a structure she then fixes into a stable sheet by throwing in the odd chemical cross-linkage.

Right now Belcher—along with M.I.T. collaborators Yet-Ming Chiang, Paula Hammond and Ki Tae Nam—is developing such sheets as electrodes for an ultralight lithium-ion battery, a project funded by the U.S. Army. "Battery weight is a big issue for them. The first few planes into Baghdad were full of batteries," Belcher says. "Our electrodes weigh 40 to 50 milligrams, versus grams for the conventional kind."

The negative electrode can be formed from a sheet of phages bred to encrust themselves in gold and cobalt oxide—the gold to increase conductivity, the cobalt oxide to exchange ions with the battery electrolyte. Such ion exchange is what moves charge from one electrode to the other. The electrode assembles directly on a prepatterned polymer electrolyte, forming a bilayer. Now the group is getting phages to grow a positive counter-electrode that will stick to the other side of the electrolyte.

A NEW KIND OF BATTERY

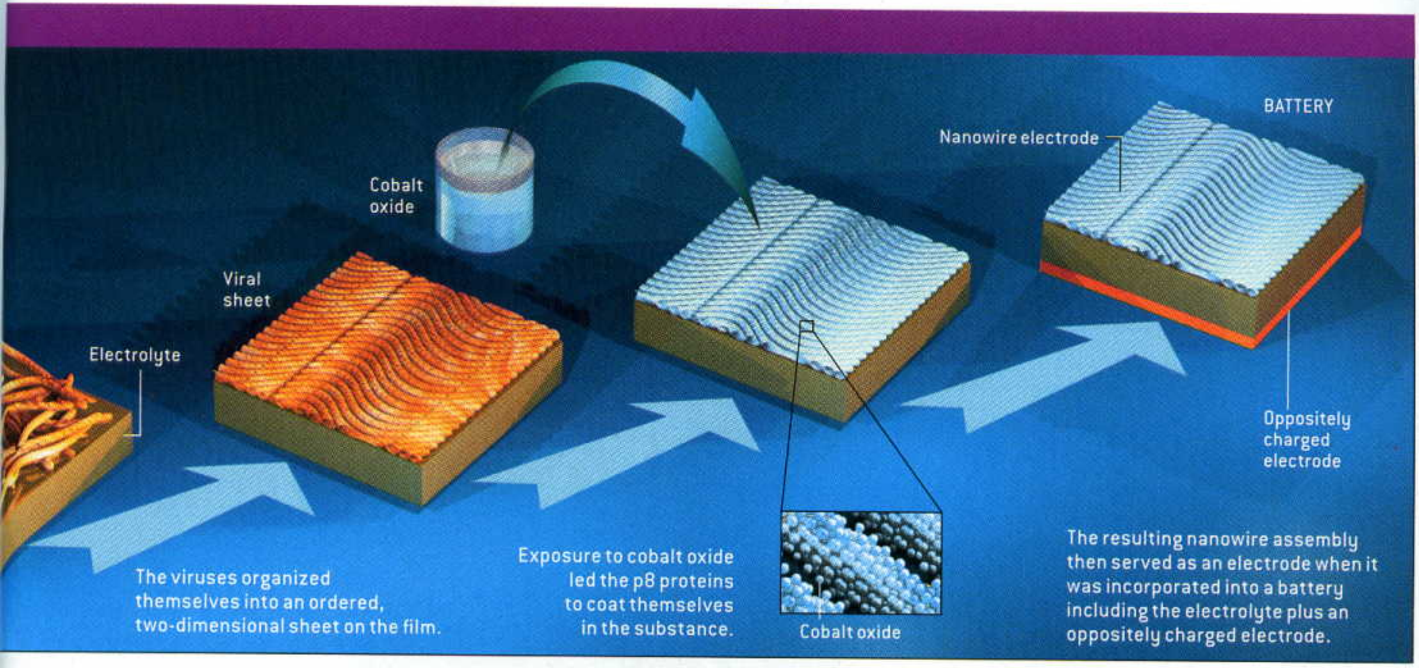
Angela Belcher and her colleagues at M.I.T. are testing selected M13 variants as building blocks for electrodes in flexible, lightweight lithium-ion batteries. One recent experiment is depicted.

The group selected an M13 variant that can bind to cobalt oxide, a substance able to store lithium ions. They put copies of the virus on an electrolyte film containing lithium.

The goal is to shape the sheets into a solid with positive and negative electrodes alternating on the surface so they may be connected in series for higher voltage. The short distances between electrodes permit fast charging and discharging and allow for the optimal use of components. The battery will also mold to whatever space a designer may have. It will thus save both weight and space, features critical to everything from military electronics to ultrathin MP3 players.

There seem to be no elements and compounds that phages cannot tell apart. One phage is specific for the semiconductor gallium arsenide and is insensitive to its close cousin gallium nitride, giving it a power of discrimination that might allow it to detect flaws in chips. Chipmakers sometimes grow crystals of one of these substances on top of some other semiconductor so that the slightly different spacing of the crystalline lattices will induce mechanical strain, which in turn will affect electronic behavior. When the crystals do not mesh properly, the occasional atom will jut out where it should not, creating a defect to which a phage can stick. If such a phage also bears a fluorescent tag, it will then glow under the right conditions, and a microscope can pinpoint the defect.

PHIL SAUNDERS *Space Channel Ltd.* (*left and above*)



The viruses organized themselves into an ordered, two-dimensional sheet on the film.

Exposure to cobalt oxide led the p8 proteins to coat themselves in the substance.

The resulting nanowire assembly then served as an electrode when it was incorporated into a battery including the electrolyte plus an oppositely charged electrode.

Big Plans

BELCHER WANTS TO TAKE the technology even further, though. "We want to see if we can transition over to finding manufacturing defects in things like an airplane wing," she says. Her group also wants to coax M13 phages into building complete transistors from molecules of semiconductors, and then churn them out by the billion. She admits that viral transistors might not be smaller and better, but because they would be made without harsh chemicals, their manufacture should yield less toxic waste.

Belcher also hopes to return a favor to biochemistry by getting M13 to bind both to cancer cells and to nanodevices known as quantum dots that show up in medical body scans. Quantum dots have yet to be tried in humans, in part because of concerns over the toxicity of their constituent heavy metals, notably cadmium. Belcher is trying to get her phage to attach to safer particles made of gallium nitride, indium nitride or some other semiconductor. The National Cancer Institute is funding this research.

Most of Belcher's M.I.T. projects are years away from finding commercial applications, but Cambrios needs to work on applications that can go to market within about two years, before it burns through its capital. Michael Knapp, president and CEO, notes that in the three years since it began, the company has raised $14 million in two rounds of financing, opened a lab and hired 20 people, which makes for a "burn rate" of $5 million a year. He says Cambrios is pursuing a niche product that will yield high profits on low volumes: a touch-sensitive screen on a flexible plastic sheet.

The army wants a flexible screen to slap onto a windshield so that a computer interface can be quickly put within the driver's field of vision; designers also want to build the screen into a computer display that can be rolled up when not in use, saving space. Today's production techniques cannot build flexible screens, because they work at temperatures that would melt the plastic backing.

"We're planning on launching a product in the middle of next year," Knapp says. "We'll be involved in the production one way or another, but because the electronics industry prefers to buy from someone they know, it's almost certain that we will have partners."

Belcher continues to consult regularly with Cambrios on its various projects, and she also conducts research on her own. She notes that although the company has rights to her viral manufacturing technique, she, along with M.I.T., retains the intellectual property from her current pursuits. Her M.I.T. group worked on the battery, for instance, whereas Cambrios devised the touch screen in-house.

"I really liked developing the basic science and transitioning to a company," she says, adding that she wants to do it again. She won't think out loud about what her next company will do, except to say that, like Cambrios, with its viral assemblers and inorganic building blocks, it will involve connecting things that do not usually go together.

Philip E. Ross is a science writer based in New York City.

MORE TO EXPLORE

Ordering of Quantum Dots Using Genetically Engineered Viruses. Seung-Wuk Lee, Chuanbin Mao, Christine E. Flynn and Angela M. Belcher in *Science*, Vol. 296, pages 892–895; May 3, 2002.

Viruses as Vehicles for Growth, Organization and Assembly of Materials. Christine E. Flynn, Seung-Wuk Lee, Beau R. Peelle and Angela M. Belcher in *Acta Materialia*, Vol. 51, Issue 19, pages 5867–5880; November 25, 2003.

Spontaneous Assembly of Viruses on Multilayered Polymer Surfaces. Pil J. Yoo et al. in *Nature Materials*, Vol. 5, pages 234–240; March 2006.

Virus-Enabled Synthesis and Assembly of Nanowires for Lithium Ion Battery Electrodes. Ki Tae Nam et al. in *Science*, Vol. 312, pages 885–888; May 12, 2006.

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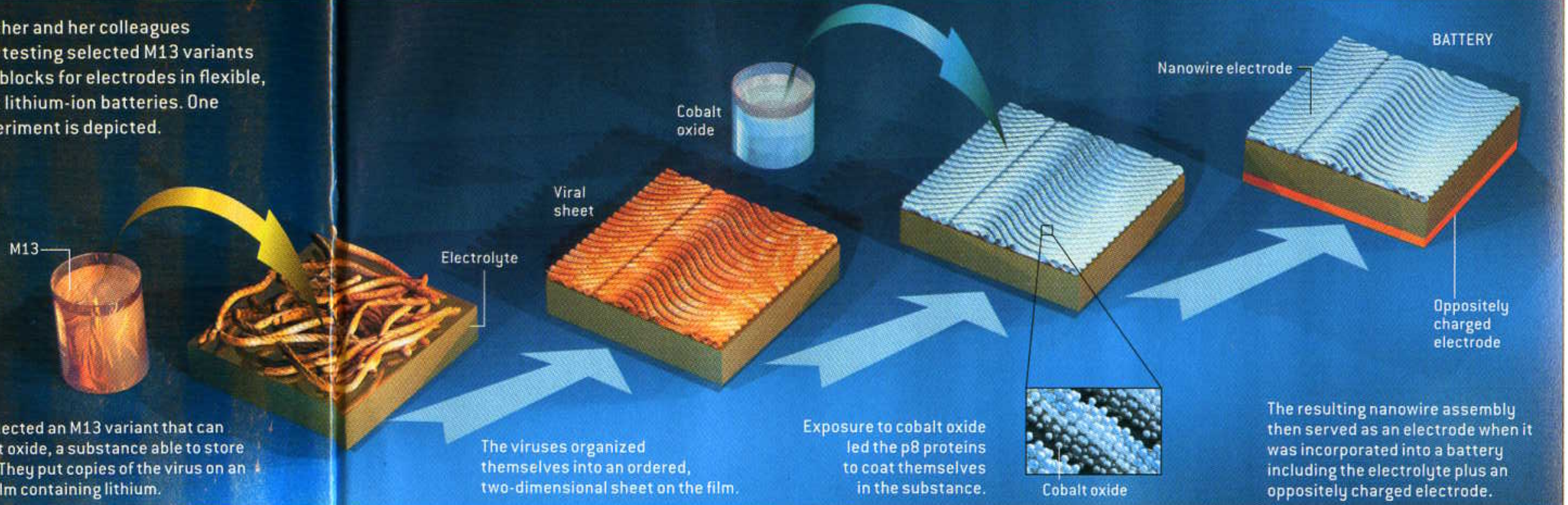

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