Getting an Eyeful of Biomolecules

In the 1970s, television's "Six Million Dollar Man" embodied the dream of high-tech replacement limbs and organs—the most spectacular of them being his mechanical eye. Technology is getting closer to the television dream. But there's a twist: Instead of wires and hardware, it looks as if the first bionic eye might rely on wet, squishy biological materials.

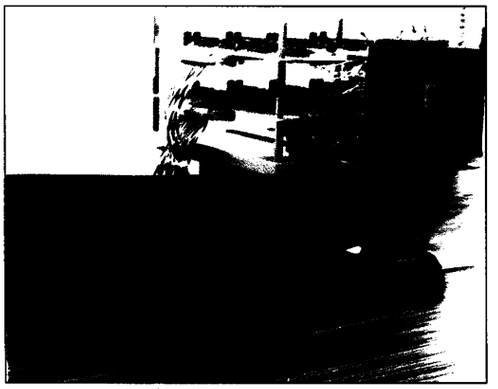
That's the implication of work reported by Tsutomu Miyasaka and his colleagues in this issue of *Science* (see page 342). Working at Japan's Fuji Photo Film Company, the engineers have constructed a retinalike light sensor based on a protein extracted from a saltwater bacterium. Miyasaka's biomolecular sensor rivals the most sophisticated silicon-based sensors in its ability to imitate some functions of the eye, but it does so in a far simpler and more compact package than its rivals.

The most eyelike feature of Miyasaka's sensor, other researchers say, is its ability to react within microseconds to changes in intensity while ignoring constant light—an attribute known as differential response. That means it can react to features of contrasting brightness when they move or the sensor is scanned across them. Such sensitivity enables animals such as frogs to detect moving prey, and it's also important in human vision, says University of Syracuse chemist Robert Birge, who is building other devices based on the same bacterial protein.

To imitate any biological retina, a sensor has to convert light information into electrical impulses almost instantaneously. That's where biological molecules have the advantage over electronics. While the retina uses a pigment called rhodopsin for this light-to-electricity conversion, the sensor makes use of a cheaper imitation—bacteriorhodopsin. Though the bacteria that make this purplish substance use it not to see but to harvest solar energy, the protein closely resembles its sight-giving cousin, says Miyasaka.

To turn the protein into a light sensor, Miyasaka spread it in a thin film sandwiched between an oxide electrode and an electrically conductive gel. When light strikes the film, the bacteriorhodopsin molecules respond by changing shape. The shape change creates a displacement of charge, which generates an electrical signal that travels through the electrode. Because the protein relaxes back to its original shape when the light hitting it remains constant, it delivers just a quick pulse of current to the electrode and then sends nothing more until the light intensity changes again.

Perhaps the most notable competitor in the quest for an artificial eye, electrical engineer Carver Mead of Caltech, is impressed.



MIYASAKA, ET AL.

The eye has it. *A biomolecule-based sensor deciphers a letter that was scanned across it.*

Mead achieved the same differential sensitivity in an all-electronic "silicon retina," but he concedes that doing so took a lot of electronic circuitry. "The potential advantage of the biological materials is that you can make things smaller," he says.

Then again, Mead defends his approach by noting that the choice of using protein in place of hardware is a trade-off. Because proteins are often unstable, delicate, and sensitive to conditions of moisture and chemistry, "it is an unknown territory," he says, adding that "silicon is a tried-and-true material."

Miyasaka isn't worried. He says he has overcome some of the problems that beset biological systems. The protein layer is exceptionally stable, able to last as long as several years, in part because the bacteriorhodopsin is kept saturated with water. With some further development, he thinks, his sensor might be ready to endow industrial robots with vision.

But don't assume that a few months and, say, $6 million (or its equivalent in yen) will get you a full-fledged artificial eye. The human eye has many capabilities neither Miyasaka nor Mead are ready to mimic—its ability to work within a vast range of brightness conditions, from starlight to the midday sun, for example. Says Mead: "It's easy to make something that can rival the eye in just one aspect, but it is impossible to get one that compares with the eye in others. As soon as you try to mimic [those other features of the eye], you gain an enormous respect for the biological system." ■ FAYE FLAM

Gene Therapy for CF Advances

A team of researchers at the National Heart, Lung, and Blood Institute (NHLBI) has taken a big step toward achieving gene therapy for cystic fibrosis, the most common hereditary disease in Caucasians. In the 10 January *Cell*, a research team led by molecular biologist Ronald Crystal of the NHLBI reports that they have introduced a functional cystic fibrosis gene into the lung cells of living cotton rats. If the same thing can be done in human patients, it may correct the biochemical defect produced in their lungs by their own malfunctioning cystic fibrosis gene. "It's an important piece of work. It's going to push the field," says Richard Boucher of the University of North Carolina at Chapel Hill, who also works on potential new cystic fibrosis therapies.

To get the cystic fibrosis gene into the rats' lungs, Crystal and his colleagues first put it into the DNA of an adenovirus, which infects lung cells but was modified to prevent it from reproducing itself (see *Science*, 19 April 1991, pp. 374 and 431). They then administered the virus directly into the rats' lungs. The result: the human cystic fibrosis gene was active in the rat lung cells for at least 6 weeks.

But while that's an encouraging result, some significant safety hurdles will have to be cleared before a similar gene-transfer technique can be used on human patients. The biggest concern, Crystal says, is that even though the genes needed for the virus to reproduce have been deleted, it might regain the ability if a natural adenovirus also infects the patient's lungs and provides the missing genes.

If that happens, the viral proteins might trigger an immune response in the lungs against the virus used for gene transfer. And that could cause problems since it's likely that the gene therapy would have to be periodically repeated because the adenoviral DNA—and the cystic fibrosis gene it carries—do not become permanently incorporated in the cellular genome. Such an immune response might simply render further treatments useless, but it might also lead to inflammation of the lungs. "I'm sure we could do it safely once," Crystal says, "but I'm not sure what would happen the second time." He nonetheless thinks that if additional animal testing can allay the safety concerns, human trials might begin in as little as a year. ■ JEAN MARX