um would then contain genes to make both components of the antigen-binding portion of an antibody, and a very large number of light-heavy chain combinations could be produced. "Now you can make a library with 10^{12} members," Lerner says. "You have as much diversity as the animal has, or even more."

Lerner and his colleagues also devised a rapid method for screening this multitude of clones to pick out just those that produce antibody fragments with the desired specificity. In this case, they were looking for antibody fragments that bind the chemical *p*-nitrophenyl phosphonamidate. They found them in only about 2 days—approximately 100 in 1 million clones screened. Although this may seem like a low success rate, the number of positive clones obtained was a big improvement over what might be expected from standard monoclonal antibody technology, Lerner says.

"Richard was very brave in taking the total combinatorial approach," Winter remarks. "I'm very glad that it worked out. It shows that the system may be even easier to manage than we thought."

So far the researchers have not produced complete antibody molecules, but for some applications that may not be necessary. As long as the fragments produced bind antigens specifically, as they do, they can be used in purifying proteins or for catalyzing chemical reactions. But Lerner says that the viral vector he is using to transplant the antibody genes into the bacteria can accommodate longer gene segments, so it should be possible to make full-size antibodies if they are needed. He notes, incidentally, that a patent application on the vector is being filed, but he intends to make it available to any researcher who wants it.

Also, the light and heavy chain combinations produced by the cloning method are probably not going to be the same as those produced by antibody-producing cells, but that may not matter as long as the desired specificities are produced.

Moreover, once an antibody with the desired specificity is identified, a researcher will be able to tinker with it to improve its antigen-binding or catalytic activity. This can be done by introducing mutations into the cloned antibody genes or by varying light and heavy chain combinations. "Someday," Lerner says, "we'll be sitting around reminiscing about monoclonal antibody technology and saying 'remember when we used to do *that*.' " ■ **Jean Marx**

ADDITIONAL READING

R. Orlandi, D. H. Güssow, P. T. Jones, G. Winter, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 3833 (1989).
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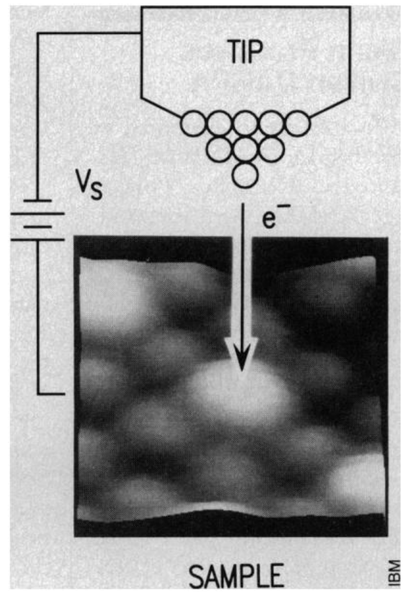
A Small, Small, Very Small Diode



Microswitch. *As the tip of a scanning tunneling microscope is placed near a defect site on the silicon surface (bright area), it creates a tunnel diode effect.*

Two recent experiments have shown that it may someday be possible to build electronic devices as small as a few atoms across. "This is really the ultimate limit on size," says physicist Peter Bedrossian. "Devices will never get smaller than atomic sizes."

Bedrossian's team at Harvard University's Lyman Laboratory in Cambridge, Massachusetts, and a group at IBM's T.J. Watson Research Center in Yorktown Heights, New York, have independently reproduced the essential features of a tunnel diode in structures that consist of only a few atoms. However, although the existence of these structures shows that atomic-scale electronics may be feasible, the researchers caution that it will be many years before practical development catches up with laboratory demonstrations.

Normal-sized tunnel diodes are important in a number of applications that require high-speed circuitry, such as fast switches used in digital signal processing and high-frequency oscillators used in microwave instruments. Their value depends on an unusual property called negative differential resistance: As the voltage across the diode increases, the induced current goes down, at least for a certain range of voltages. A diode switch can be turned on by a low voltage and off by a high one. And tunnel diodes are very fast because electrons need to travel only a short distance in them.

As with all electronic devices, trying to diminish the size of a tunnel diode by simply decreasing its dimensions soon runs into a fundamental limit. Once a device gets small enough, quantum effects start to dominate its electronic behavior, and it begins to act very differently. So the two groups did not actually shrink a tunnel diode; they mimicked it with a new, atom-sized structure in which negative differential resistance is produced by quantum effects instead of electronic effects.

In-Whan Lyo and Phaedon Avouris of IBM reported their work in the 22 September *Science*. Lyman Lab's Bedrossian, Dongmin Chen, Klaus Mortensen, and Jene Golovchenko, who performed their experiment at the Rowland Institute for Science in Cambridge, announced the result in the 16 November *Nature*.

Both groups created the atomic-scale tunnel diode effect by bringing the tip of a scanning tunneling microscope down near the surface of a boron-doped silicon crystal. A voltage applied between the tip of the scanning tunneling microscope and the crystal created a tunneling current between them. When the microscope was positioned over certain sites on the surface, the tunnel diode effect appeared—the current dropped as the voltage increased.

The spots on the surface that exhibit this negative differential resistance seem to be isolated defect sites. "Our interpretation is that the detailed nature of the sites does not appear to be important," IBM's Avouris says. Instead, the essential requirement for the tunnel diode effect, he says, is the presence of localized quantum states on the surface of the sample and on the probe of the scanning tunneling microscope. Such localized states, he says, are usually found over defect sites on the surface and at the tip of the probe, which consists of only one or a few atoms. "It's a general effect—you can probably cook up many combinations that work," Avouris adds.

Golovchenko warns that although they have shown how to produce an atomic-scale tunnel diode effect, this doesn't mean practical applications are around the corner. "The interesting parts of the system are very small—a couple of atoms on one side and a couple of atoms on the other—but the surrounding hardware is enormous," he says. What it does mean is that researchers now have something to shoot for in the quest to make electronic devices as small as possible. ■ **Robert Pool**