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HARVARD GAZETTE ARCHIVES

Charles Lieber holds a silicon chip (also inset) containing sensors capable of detecting single viruses that could cause disease epidemics or be used in bioterrorism attacks. (Staff photos Jon Chase/Harvard News Office)

Sensor detects, identifies single viruses

Early warning for disease and bioterrorism

By William J. Cromie
Harvard News Office

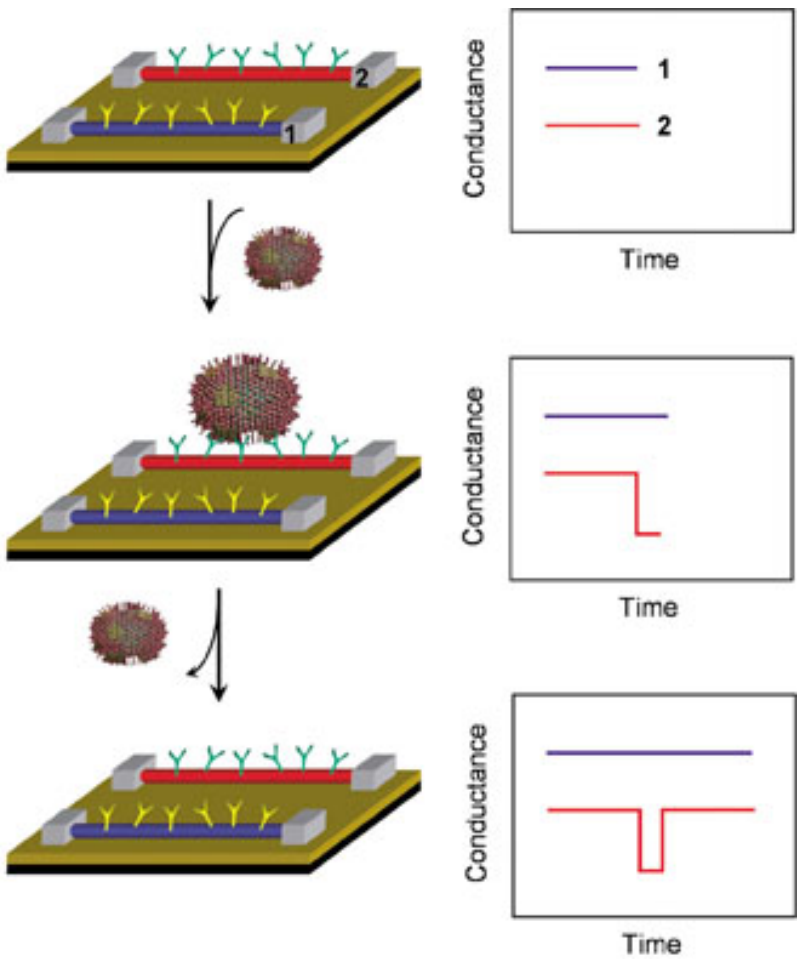
Two of the world's biggest threats may someday be reduced by wires thousands of times thinner than a hair but capable of detecting a single virus. The specter of worldwide viral epidemics is always with us, so detecting them quickly offers the possibility of saving thousands of lives. The pathogens also can be stealthy biological weapons, making their positive detection a vital national defense requirement.

Two-week listing of upcoming events

"We want to find a single virus before it finds you," says Charles Lieber, Hyman Professor of Chemistry at Harvard University. Tests recently completed in his laboratory show that these unimaginably thin nanowires can sense and distinguish between viruses that cause flu, measles, and eye infections. Lieber believes future versions will be able to spot HIV, Ebola, SARS, West Nile, hepatitis, bird flu, and other dangerous viruses.

"Viruses are among the most important causes of human disease and are of increasing concern as agents for bioterrorism," Lieber says. "Our work shows that nanoscale silicon wires can be configured as detectors that turn on or off in the presence of a single virus particle. Such detectors could be fashioned into arrays capable of sensing thousands of different viruses, ushering in a new era for diagnoses, biosafety, and quick response to viral outbreaks."

"Nano" refers to a "nanometer," one billionth of a meter, four hundred billionths of an inch, or about 10 atoms in size. One hundred thousand wires, each 20 nanometers long, would fit on the head of a pin.



A spiky virus binds to Y-shaped receptors built into ultrathin wires carrying a small electric charge. The binding causes a change in electric conductance (middle right) which immediately identifies the germ. When it becomes unbound (bottom), the conductance returns to a set value.

The Department of Defense, Office of Naval Research, and National Cancer Institute all supported Lieber's research, and at least two commercial companies have shown interest in manufacturing nanosensors.

In his office, Lieber shows visitors a two-inch-square silicon and metal chip containg an array of nanowires and two pinhead-size entry ports through which blood, saliva, or other bodily fluids can enter. Air samples put into a fluid solution would also be tested this way.

Surfaces of the nanowires, through which a minute current flows, hold specks of protein (antibodies) to which specific viruses bind. These antibodies, produced naturally by the immune system, can be attached to the surface of the nanowires, and they will, in turn, bind viruses. Such binding causes a change in current, which signals the presence of a virus or viruses, like a burglar alarm detecting intruders.

Immediate alarm

The alarm goes off immediately, a major advantage. Other methods of virus detection involve time-consuming steps such as taking blood samples, which must be sent to a laboratory for analysis. It's easy to imagine adding such sensors to security gates at airports. Dangerous viruses could be spotted before they spread to other passengers and other places in the world.

Besides detection, such laboratories-on-a-chip might someday be employed for monitoring diseases, like following the progress of patients undergoing treatment to stem the activity of HIV, the AIDS virus. Like other viruses, it begins to duplicate itself after it enters a cell. Eventually, the cells burst and spread newborn pathogens to other cells. If such reinforcements can be spotted and treated by drugs before they overwhelm the body's immune system, there is less likelihood that the infection will turn into full-blown AIDS.

Combining selective virus and protein recognition in one nanowire chip could expand its diagnostic potential. Many cancer-related proteins are secreted into the blood. Prostate specific antigen (PSA), for example, is watched as a marker for the seriousness of prostate cancer. Low PSA levels provide one signal that close monitoring of the disease may be a better choice than surgery or radiation, with their distressing side effects of impotence and incontinence. Rather than taking a blood test and waiting for the result, it may be possible to consult a sensor the way diabetics watch their blood sugar daily, or women check for a pregnancy.

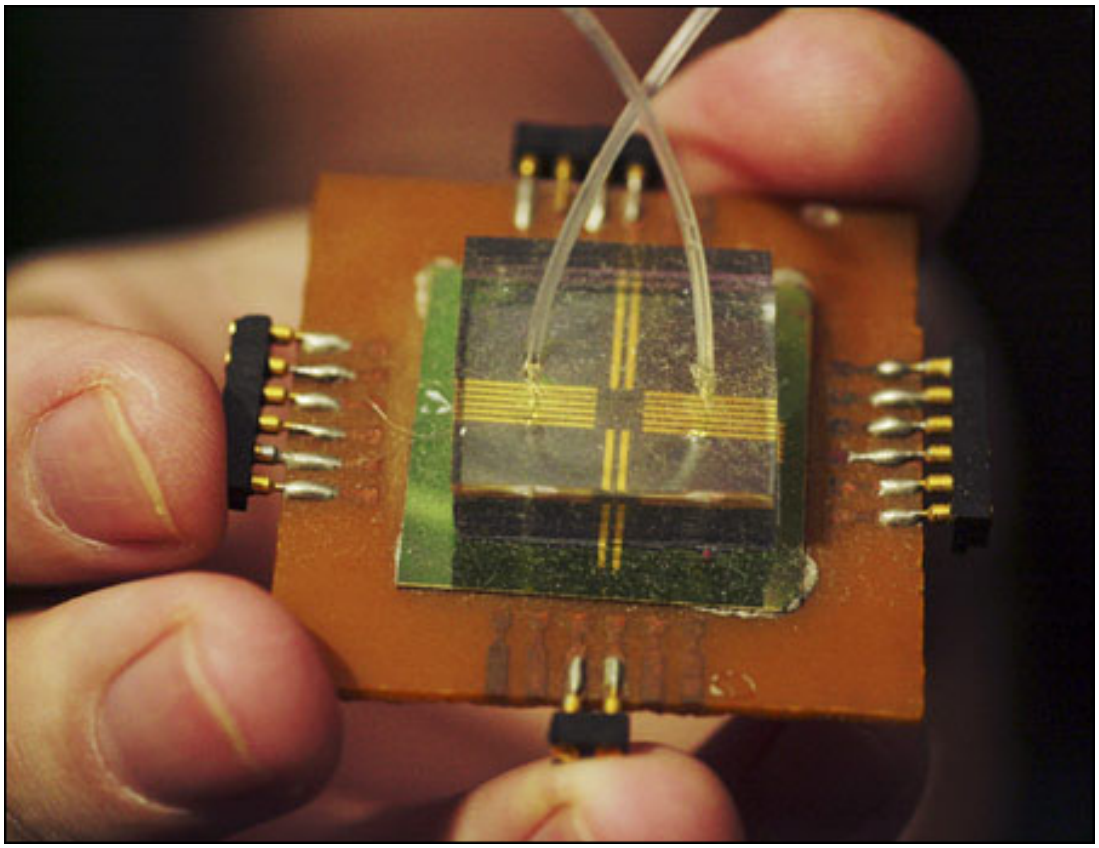
Taking the possibilities one step further, how a virus particle bonds to a cell's surface might be examined closely for ways to prevent such unions. If researchers know exactly what molecules are involved in breaking into and entering cells, they will be better be able to develop drugs and vaccines to prevent losses of cell valuables.

Pushing forward

Such a list of intriguing applications provides what Lieber calls "strong near-term motivation for pushing this work forward."

He and his collaborators have done extensive tests to validate the selectivity of the sensor. First, they fed the device two viruses from different families, one that causes influenza A and one responsible for respiratory and eye infections. The detector sensed the difference.

Then they paired the influenza bug with a closer viral relative that causes mumps and measles. These two boast similar surfaces, but the device was not fooled.



Besides verifying these captures by measuring changes in electrical conductance, researchers marked the viruses with fluorescent dyes so the binding could be seen with very powerful microscopes. The wires involved are only about a hundred atoms across.

The team that did such nanomagic includes students and faculty from Harvard departments of chemistry and chemical biology, physics, and the Division of Engineering and Applied Sciences. They published a detailed description of the research in the Sept. 28 issue of Proceedings of the National Academy of Sciences. The lead author is postdoctoral fellow Fernando Patolsky.

Lieber's team now plans to work on a larger detector, one that could sense up to 100 different viruses simultaneously. Such an array will make it more likely that the federal government and/or private companies will act to move this exciting new technology from a Harvard basement laboratory to a factory floor.