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Scientists find nanowires capable of detecting individual viruses

Findings could point the way to ultra-powerful new diagnostic tools and bioterror detectors

CAMBRIDGE, Mass., Sept. 22, 2004 — Harvard University scientists have found that ultra-thin silicon wires can be used to electrically detect the presence of single viruses, in real time, with near-perfect selectivity. These nanowire detectors can also differentiate among viruses with great precision, suggesting that the technique could be scaled up to create miniature arrays easily capable of sensing thousands of different viruses.

The work was reported in the most recent issue of the *Proceedings of the National Academy of Sciences*.

"Viruses are among the most important causes of human disease and are of increasing concern as possible agents of biowarfare and bioterrorism," says author Charles M. Lieber, Mark Hyman Jr. Professor of Chemistry in Harvard's Faculty of Arts and Sciences. "Our work shows that nanoscale silicon wires can be configured as ultra-sensitive detectors that turn on or off in the presence of a single virus. The capabilities of nanowire detectors, which could be fashioned into arrays capable of detecting literally thousands of different viruses, could usher in a new era for diagnostics, biosafety, and response to viral outbreaks."

Lieber and his colleagues merged nanowires conducting a small current with antibody receptors for certain key domains of viruses — such as agglutinin in the influenza A virus. When an individual virus came into contact with a receptor, it sparked a momentary, telltale change in conductance that gave a clear indication of the virus's presence. Simultaneous electrical and optical measurements using fluorescently labeled influenza A confirmed that these conductance changes corresponded to binding and unbinding of single viruses from nanowire devices.

In addition to influenza A, the Lieber group tested nanowire arrays outfitted with receptors specific to paramyxovirus and adenovirus. The researchers found the detectors could differentiate among the three viruses both because of the specific receptors used to snag them and because each virus binds to its receptor for a characteristic length of time before dislodging -- leaving only a minuscule risk of a false positive reading.

"The fact that a nanowire array can detect a single virus means that this technology is the ultimate in sensitivity," Lieber says. "Our results also show that these devices are able to distinguish among viruses with nearly perfect selectivity."

While there are many ways for researchers to assay viruses, most are laborious and appropriate only in laboratory settings. The use of nanowires provides immediate verification of a given virus's presence without any specialized biochemical manipulation.

Lieber says nanowire arrays could be scaled up not only to detect many different viruses, but also to detect common strains as well as variants genetically engineered by would-be bioterrorists. By making an array sensitive to numerous domains of a given virus, the chances of even a modified virus escaping detection would be very low.

In a clinical setting, the extreme sensitivity of nanowire arrays means they could detect viral infection at very early stages, when the immune system is still able to suppress virus populations. It's at this stage of viral activity that symptoms often begin to appear, but with viruses still present in limited numbers, they can be difficult to detect and treat.

The nanowire arrays detect viruses suspended in fluids, whether bodily or otherwise. Lieber says that any anti-bioterror device built around nanowires' virus-detecting capabilities would most likely marry the technology with a microfluidic apparatus that would draw in air, suspend any airborne particles in a liquid, and then run this solution past the nanowire array.

Lieber's co-authors are Fernando Patolsky, Gengfeng Zheng, Oliver Hayden, Melike Lakadamyali, and Xiaowei Zhuang, all of Harvard's departments of chemistry and chemical biology, physics, and Division of Engineering and Applied Sciences. The work was supported by the Defense Advanced Research Projects Agency, National Cancer Institute, Ellison Medical Foundation, Office of Naval Research, and Searle Scholar Program.

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