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Novel biosensor technology could allow rapid detection of Ebola virus

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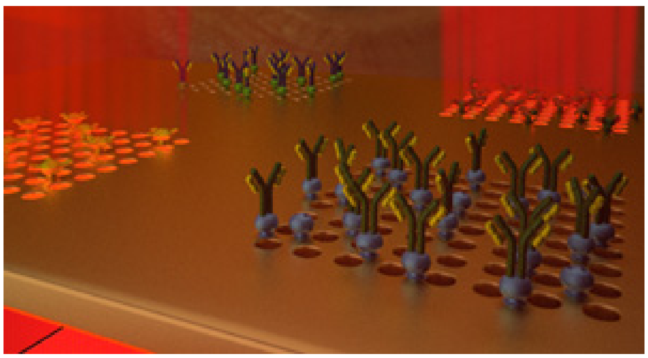


The transmission of light through plasmonic nanohole arrays changes with the binding of specific proteins or virus particles, as shown in this illustration.

In 2010, Ahmet Ali Yanik published his first paper on the rapid detection of Ebola virus using new biosensor technology he and colleagues at Boston University had invented. But he found there was little interest at the time in developing the technology further.

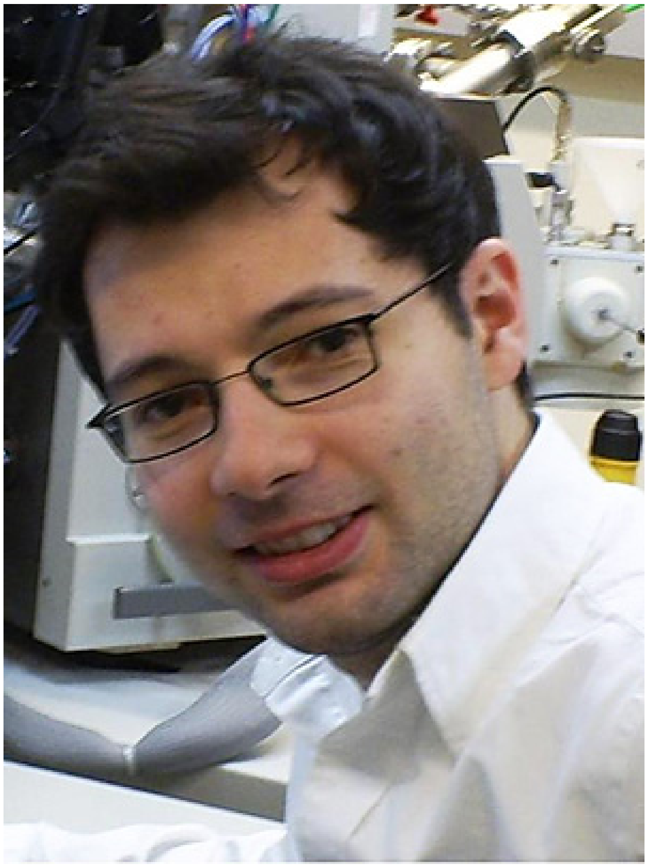
"People told me that there wasn't any profit in it because this disease only affects people in the developing world," Yanik said.

Now, however, Ebola hemorrhagic fever has captured the attention of first world countries in a big way. The current outbreak in West Africa began spreading out of control just as Yanik was setting up his lab as a new faculty member at UC Santa Cruz, where he is an assistant professor of electrical engineering. Yanik plans to resume his work on virus detection in addition to ongoing projects involving biosensors for other biomedical applications. The current Ebola crisis may subside before his technology can be perfected, since there are still many challenges to overcome, but the need will remain for simple and inexpensive virus detection techniques, he said.

"The truth is that Lassa virus, which is related to Ebola and also causes hemorrhagic fever, infects nearly half a million people every year in Africa and kills more people than Ebola, but it doesn't make the news. So there has been an ongoing crisis with hemorrhagic fever viruses, and now it's finally getting some serious attention," Yanik said.

His goal is to create a low-cost biosensor that can be used to detect specific viruses without the need for skilled operators or expensive equipment. "We need a platform for virus detection that is like the pregnancy tests you can use at home," Yanik said. "The initial symptoms of hemorrhagic fever are similar to the flu, and you just cannot treat every person with flu symptoms as a potential Ebola-infected patient. It needs to be simple and cheap."

Nanotechnology



Ali Yanik

Nanotechnology may provide a solution. Advances in nanotechnology have enabled researchers to fabricate novel materials with precise structures on the scale of nanometers (a nanometer is one billionth of a meter). A "plasmonic nanohole," for example, is a tiny hole a few hundred nanometers across. Yanik's 2010 paper described a biosensor based on arrays of nanoholes in a metallic surface that interact with light in predictable ways. Using antibodies on the sensor surface to bind specific viruses, the researchers showed that binding of the virus caused a detectable change in the color of light transmitted by the nanohole arrays.

Detecting the color change, however, required the use of a spectrometer.

Yanik later figured out how to make a sensor that could be read with the naked eye, without any need for electronic instruments. "You can use sunlight as the light source and the human eye as the detector," he said.

He published that technique in a 2011 paper in the *Proceedings of the National Academy of Sciences*. The sensor technology involves realms of physics far more complex than the relatively straightforward enzymatic reactions involved in a pregnancy test. Light transmission through nanohole arrays occurs through a phenomenon known as "surface plasmon resonances," which involves the oscillations of free electrons in a metallic surface. Yanik's 2011 paper showed that light transmission could be greatly enhanced by exploiting a phenomenon called Fano resonances (named for Italian physicist Ugo Fano).

Label-free detection

"This effect causes a huge difference in light transmission that you can see with the naked eye," Yanik said. Unlike conventional laboratory tests such as PCR and ELISA (currently the standard tests for Ebola infection), Yanik's approach does not rely on labeling with fluorescent tags or other markers to see the results. "The results can be read immediately after the pathogen binds to the sensor," he said.

Further work is needed, however, to improve the sensitivity of the sensor to the point where it could be effective for virus detection in routine "point-of-care" clinical evaluations. Yanik plans to work with Jin Zhang, professor of chemistry and biochemistry at UC Santa Cruz, to develop a new version of the sensor. Zhang's research group works on advanced nanomaterials for a wide range of applications.

"He has the exact technology I need to make the biosensor more sensitive for virus detection, so we are working on a proposal to combine his approach with ours," Yanik said.

Another major focus of Yanik's research is the detection and isolation of circulating tumor cells (CTCs) in the blood of cancer patients. CTCs can spread cancer to other parts of the body (metastasis), and detecting them in blood samples can have important prognostic and therapeutic implications. Yanik is working on methods for capturing CTCs with high efficiency and isolating them for molecular analysis. He began this work as a research associate at Harvard University Medical School and Massachusetts General Hospital before coming to UC Santa Cruz. At UCSC, he is working with Zhu Wang, an assistant professor of molecular, cell, and developmental biology, who studies genetic alterations in prostate cancer.

"It was a natural match," Yanik said. "We met during an orientation meeting for new faculty, and our collaboration spun off from there."

Both plasmonic biosensors and CTC technology are crowded fields with lots of competition, but Yanik has confidence in the methods he has developed. "There are a lot of different approaches to these problems, but we have achieved some unprecedented results with our technology," he said. "I am pretty optimistic that we can make a difference in people's lives."

Provided by University of California - Santa Cruz

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