

## BIOMEDICAL // DEVICES

## DEPARTMENTS

## A World-beating TB Detector

To quickly and cheaply diagnose the world's worst infectious disease, engineers have shrunk an NMR machine down to size

BY PRACHI PATEL // MARCH 2010

17 March—To fight tuberculosis, which infects a third of the world's population and kills 2 million people every year, you've got to find and cure the disease before it can spread to new hosts. However, current diagnostic tests require time, money, and full working laboratories, all of which are lacking precisely where the disease is most prevalent.

A faster, cheaper, more sensitive, and more portable TB detector is just what the doctor ordered, and researchers at the Center for Systems Biology at Massachusetts General Hospital

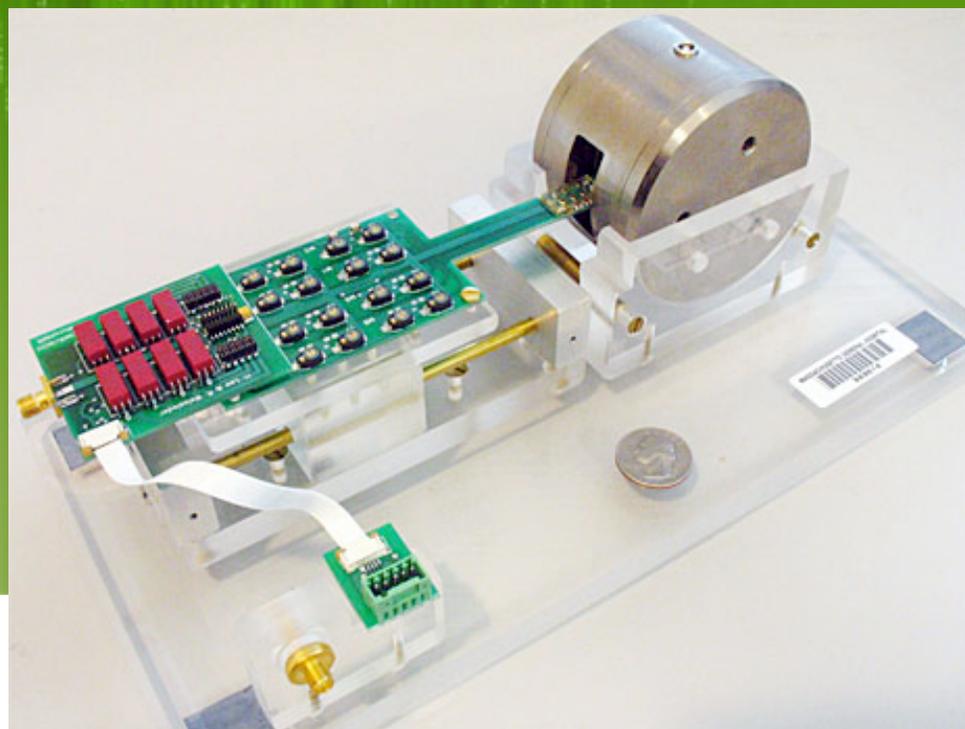


Photo: Hakho Lee

and Harvard Medical School already have a prototype of one. It's the size of a cellphone and should cost just a few hundred dollars to make and another few dollars each time you use it, researchers say. Crucially, it's a thousand times as sensitive and a dozen times as fast as the tests doctors now use.

The conventional diagnostic technique involves staining a coughed fluid sample with a TB-targeting dye and observing it under a microscope. The process requires an entire day and a concentration of about 10 000 bacteria per milliliter of sputum. To confirm the diagnosis, you have to culture the bacteria, which takes several weeks.

Even in the alternative diagnostic test, in which an antigen is injected under the skin to provoke an immunological reaction—a method that won't work in HIV-positive patients—you still need a few days. During that time, "the disease is already advanced, and the patient has spread it to many other people," says Diego Krapf, a professor of electrical and computer engineering at Colorado State University who works on optical methods to detect bacterial proteins.

Even more important than the speed of any new TB test is the simplicity of its use, Krapf says. "The idea is you don't need a great deal of training," he says. "Just put your sample here; the device will tell you if it's positive or negative."

The prototype diagnostic device is hooked up to a computer, which processes the data and gives the bacteria count, says Hakho Lee, a biomedical engineer who's involved in the work. He said the next step is to build a robust, self-

contained laptop-size device to probe the sample and interpret the resulting data. Lee will present the research on 18 March at the American Physical Society meeting.

Lee and his colleagues are working with the Harvard School of Public Health to try the device on clinical samples from patients. They have also planned field tests at a clinic near Durban, South Africa, later this year.

The Harvard detector is a miniature nuclear magnetic resonance (NMR) machine. In such a machine, a magnet aligns atoms so that a radio-frequency (RF) signal can pluck them, as it were, so that they vibrate like a string. In a conventional machine, the magnets must be huge in order to get the atoms to vibrate strongly enough to measure their natural frequency of oscillation. But in the TB detector, the magnets can be a tenth as large because their field only needs to be strong enough to measure the rate at which atoms' vibrations decay over time.

The researchers first liquefy the viscous sputum, then add iron nanoparticles coated with antibodies that stick to TB bacteria. Next they inject the sample through a microfluidics channel in which a membrane filter traps the tagged bacteria in the channel while allowing free nanoparticles out. The metal RF coil and magnet surround this channel. "The presence of magnetic nanoparticles [makes] the NMR signal decay faster compared to cases where there are no nanoparticles," Lee says. The duration of the signal indicates the number of tagged bacteria.

The detection method is technologically sound, says Steve Miller, director of the Clinical Microbiology Laboratory at the University of California, San Francisco. Miller believes the method is akin to an enhanced sample microscopy technique. "[It] would be more sensitive and presumably quicker and easier to do," he says. "It doesn't require a trained person, as microscopy does."

However, testing real sputum samples will be a challenge, because they could contain many bacteria that appear similar to TB, Miller adds. While antibodies that the researchers coat on the nanoparticles are designed to stick only to TB, they might still attach to other species, which would give false positives. "Sputum is really gunky," he says. "Being able to capture TB bacteria and wash away other things is going to be...the biggest technological hurdle."

The new technologies are not yet ready for field-testing, Krapf says. "I think it's going to take a little longer, maybe a few years."

#### About the Author

Prachi Patel, an *IEEE Spectrum* contributing editor, is a Pittsburgh-based science journalist who focuses on energy, environmental and medical technologies. She is also a frequent contributor to *Technology Review*, *Sciam.com*, *Wired* news, *Nature News*, and other publications.

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