NEED TO KNOW

Microscope-on-a-Chip Is Small in Size, Big in Scope

The future of microscopy is coming into focus for a team of researchers at the **California Institute of Technology** (Caltech; Pasadena, CA; www.caltech.edu). In a dramatic departure from conventional microscopy design, the team has developed a microscope-on-a-chip that operates without the use of lenses. Claiming the instrument as the smallest microscope in the world, the researchers have set their sights on also making it the world's cheapest to mass-produce.

While seemingly every product has been reduced to fit on a chip these days, advancements in conventional microscope system development have mainly involved adding more functionality, such as achieving higher resolutions and better imaging, according to Changhuei Yang, assistant professor of electrical engineering and bioengineering at Caltech. "What that means is that the microscope becomes more and more sophisticated, which is good for high-end applications," he says. "But there's nothing that really provides a clinician or bioscientist with a very cheap, compact microscope that is a direct replacement of the conventional microscope system."

However, characteristics of conventional microscopes have created barriers to miniaturization. It is neither cheap nor easy to fabricate tiny and precise lenses on chips, and the space requirements for microscopes are significantly more than what is available on a chip. Because of these obstacles, the team elected to design a miniature microscope from scratch and take a completely different approach.

Researchers at Caltech have developed a miniature microscope system that enables imaging without the use of lenses or optics and may be relatively inexpensive to mass-produce.

The design model for the microscope drew inspiration from *floaters*—the specks people sometimes see floating in their field of view, most noticeably when looking up at a clear blue sky. Floaters are actually debris that cast a shadow on the retina when exposed to uniform illumination, such as the clear sky. Such phenomena are an example of direct projection imaging, which allows an observer to view an object without lenses or optics. The Caltech team concluded that a microscope could operate in a similar way.

To achieve this goal, the team coated a layer of metal onto a linear sensor array in order to block light and then punched tiny holes in the metal layer. The addition of a microfluidic channel on top of the entire chip resulted in a system that is capable of direct projection imaging via optofluidic microscopy. By moving the object to be viewed across the line of holes, a light scan is obtained; the resolution is equal to the size of the holes in the metal layer.

"The way that we pattern the holes is the nonintuitive part of it," Yang says. "The fact that we are using the microfluidic channel to actually translate the object as a way to do scans is also a novel aspect of the project."

Yang predicts that within the next five years, diagnostic applications for the optofluidic microscope-on-a-chip could come to fruition. He speculates that the system could be used for such purposes as diagnosing urinary tract infections and evaluating blood samples for parasites. It also could come in handy in areas such as treating patients on the battlefield. Farther down the road—in perhaps 15 to 20 years—the team envisions the instrument as a component in implantable devices designed to analyze the blood stream that can alert patients to seek treatment before symptoms arise. The researchers estimate that the chip could be mass-produced for around $10 per unit.

"The whole field of biomedicine right now is pretty much dominated by the conventional microscope system," Yang remarks. "We think that once we start providing clinicians with hundreds of thousands of microscopes that can operate in parallel, then new applications would also evolve. We can then begin to do things that are too impractical to do right now with the conventional microscope system."

—*Shana Leonard*