BIOSENSORS

Incredible shrinking optics

A radical departure from the current generation of large and expensive optical research instruments will change the way some scientists conduct experiments.

The relentless decrease in the size and cost of computer components has resulted in wider usage than their inventors ever dreamed of. A similar process is now underway with optical devices. Microscopes and other instruments that use light to allow detailed observations of the microscopic world are usually large and expensive. Developments now underway herald an age when optical instruments will be available at a fraction of their present size and cost.

Two recent reports demonstrate how researchers have exploited the unique optical properties of microscopic objects to turn them into sensitive measurement devices. The first of these objects is an unusual entity called an optical microcavity that can confine light within its small volume by resonant recirculation.

Kerry Vahala at the California Institute of Technology has worked on optical microcavities for years. Now he and his colleagues describe the creation of a sensitive biosensor based on one of these microcavities (Armani *et al.*, 2007). This sensor is essentially an optical tuning fork made out of silica in the shape of a microtoroid (**Fig. 1**). When light is pumped into the microtoroid, it recirculates with a specific resonance wavelength, but the light can interact with molecules binding to the surface, causing a tiny red-shift of the resonance wavelength.

A large red-shift owing to thermal heating from the pumped light typically masks these small resonance shifts. Vahala and colleagues neutralized this shift by immersing the microcavity in water, greatly enhancing sensitivity of the technique. It was then quite simple to turn this into a sensor for specific proteins.

The researchers coated the microtoroid with antibodies to interleukin-2 (IL-2) and flowed mixtures containing IL-2 past the microtoroid. Binding of IL-2 to the antibody-coated surface resulted in dose-dependent changes in the resonance shift. At the lowest concentrations, they could see step shifts in resonance wavelength caused by the binding of individual molecules.

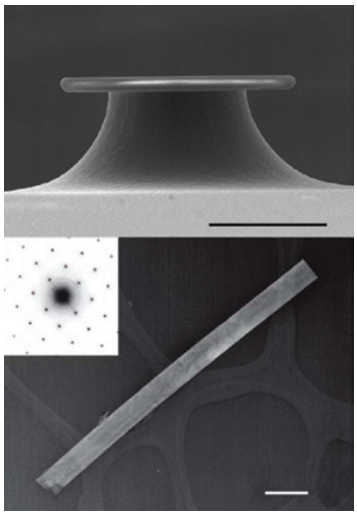

Figure 1 | Microscopic optical devices. Scanning electron microscope image of a microtoroid optical resonator (top) and transmission electron microscope image of a potassium niobate nanowire (bottom) with an electron diffraction pattern of the nanowire (inset). Scale bars, 45 μm (top) and 200 nm (bottom). Reprinted from *Science* (with permission from AAAS; top) and *Nature* (bottom).

Microcavities are not the only microscopic optical devices being exploited for potential biological application. Nanowires (**Fig. 1**) also show promise because of their ability to guide light. Members of Peidong Yang's and Jan Liphardt's laboratories at the University of California, Berkeley, have been collaborating for several years in an effort to use optical tweezers to assemble nanowires into optical microcircuits. They started wondering whether the light of the optical tweezers could be used as more than just an assembly tool.

Basic optics theory says that if you place a nonlinear optical material into a laser beam it should double the frequency of light. Many people unknowingly exploit this phenomenon when using a green laser pointer. The green light emanates from a piece of potassium niobate illuminated by an infrared laser diode.

Liphardt says, "So quite naturally we asked, 'what would happen if we took a nanowire of potassium niobate and trapped it using the existing setup?'" It turns out that green light emanates from both ends of a potassium niobate nanowire held in their infrared optical tweezers, and this works even in a liquid environment (Nakayama *et al.*, 2007).

"At this point we knew green light was radiating out the ends, and we knew that we could move this nanowire in [three dimensions]. The next thing was to try to utilize this to build a microscope," says Liphardt. They added a light detector and tested the system by imaging a test sample composed of parallel gold bars spaced at decreasing intervals. The researchers scanned the radiating nanowire over the sample while collecting the transmitted light from below, and this allowed them to measure the distance between the bars.

"What I think you are beginning to see is the glimmerings of circuits and detectors where a lot of the detection and signal preprocessing is going to be done very locally," explains Liphardt. Yang adds, "The development of a tunable nanoscale light source and probe will enable our future research in the direction of single-cell endoscopy on the cell surface and the inside."

Liphardt believes that in 10–20 years, imaging devices may be roughly the same scale as the cells being studied. "One thing that is clear is these methods are all a lot cheaper," says Liphardt. This will be welcome news to many.

Daniel Evanko

RESEARCH PAPERS

Armani, A.M. *et al.* Label-free, single-molecule detection with optical microcavities. *Science* **317**, 783–787 (2007).

Nakayama, Y. *et al.* Tunable nanowire nonlinear optical probe. *Nature* **447**, 1098–1101 (2007).