Scientists Create Breakthrough Sensor Capable of Detecting Individual Molecules

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Applied physicists at the California Institute of Technology have figured out a way to detect single biological molecules with a microscopic optical device. The method has already proven effective for detecting the signaling proteins called cytokines that indicate the function of the immune system, and it could be used in numerous medical applications, such as the extremely early detection of cancer and other diseases, as well as in basic biological research.

According to Kerry Vahala, the Jenkins Professor of Information Science and Technology and professor of applied physics, this new detection technology revolves around a previous invention from his lab called an "ultra-high-Q microtoroid resonator."

This is a donut-shaped glass device that is narrower than the width of a human hair and that is able to hold on to light very efficiently. Vahala explains that "the detector relies upon this feature to boost sensitivity to the single molecule level, albeit in a surprising way."

He notes that the original idea was to detect an optical response elicited directly by molecules landing on the donut-shaped device. "As work proceeded, however, we were able to observe single molecule detection events with far greater ease than was originally expected." This pleasant surprise was traced to minute amounts of heat generated when molecules interact with the light stored within the microtoroid resonator. "This thermo-optic response boosts the sensitivity a millionfold," explains Vahala. Andrea Armani, who works in Vahala's laboratory and developed the detector as part of her thesis research, notes that besides being extremely sensitive, the device is also programmable by coating its surface with substances that react to a specific biological molecule.

"The molecule which the device is targeting, whether it is a growth factor or a chemical like TNT, is determined by the surface treatment of the glass microtoroid. Fortunately, the biology and chemistry communities have developed very effective techniques for attaching proteins to glass surfaces, because most microscope slides are glass. All we had to do was adopt those techniques to fit our structure," explains Armani.

Vahala notes that "this combination of single-molecule sensitivity and programmable detection, that is, without labeling of the target molecule, has not been demonstrated before, and enables new kinds of tests and measurement."

Scott Fraser, the Rosen Professor of Biology, professor of bioengineering, and collaborator on the project, explains further that "this technology should lead to many applications for biological experiments, medical tests, and even medical treatments. The advantages are its ability to detect extremely small numbers of molecules, and the fact that there's no need to label target molecules. At this sensitivity level, it is possible even to study growth factors being emitted in real time from a single cell." Fraser adds, "This is the only sensor that currently has the requisite sensitivity and rapidity."

This type of experiment is important in monitoring how environmental changes, such as pH or temperature, can influence a cell's behavior. Currently, these types of experiments must be performed with populations of millions of cells, which often blurs results because it is like trying to pick out a single voice in a choir.

In the July 5 issue of the online journal Science Express, the team reports on its success in detecting a series of different molecules, including one immune response signaling protein, interleukin-2 (IL-2). For the latter, the targeting molecule the devices were coated with was a specific antibody that recognized IL-2. This surface preparation allowed the detector surface to bind the IL-2, while the thermo-optic mechanism provided the sensitivity required to detect the IL-2 at the single molecule level, even in serum (blood with the clotting factors and red blood cells removed).

"What is most exciting about this device is its ability to get single molecule results in real time without labeling. Because it can be programmed to detect almost any biological molecule, it is a universal detector, and as such opens the door to a whole field of new experiments," adds Armani.

Source: Caltech