Nano Focus

Photonic-crystal nanolasers shown to be highly sensitive biosensors

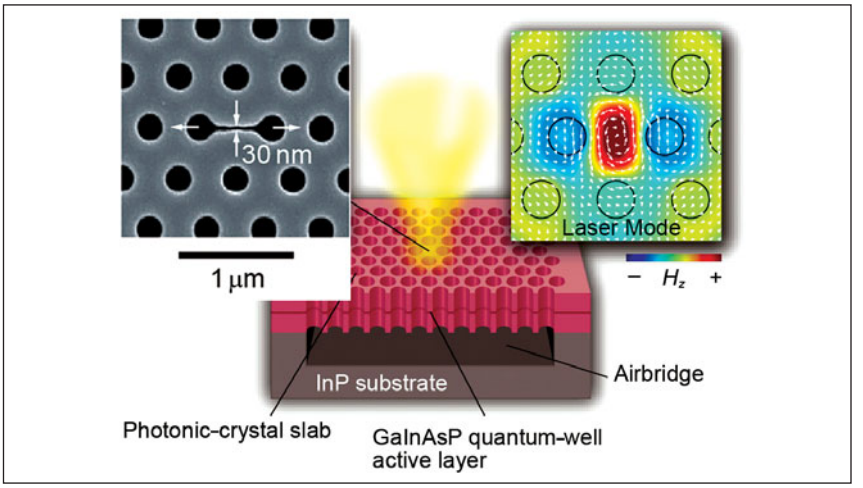
Move over, ELISA. While the Enzyme-Linked ImmunoSorbent Assay has long been one of the most popular ways of detecting and quantifying the presence of antibodies or antigens in solution, nanolasers may be poised to share the spotlight on the biosensor stage.

Using a photonic-crystal nanolaser developed by their team, engineering professor Toshihiko Baba and colleagues at Yokohama National University's Department of Electrical and Computer Engineering in Japan have demonstrated the utility of their device as a disposable sensor for several biomedical applications. Their experiments, presented in *MRS Communications* (DOI: 10.1557/mrc.2015.73) show promise for detecting targets including proteins, endotoxins, and DNA sequences.

Enzyme immunoassays determine whether body fluids contain proteins related to certain diseases. Contemporary immunoassays often require expensive fluorescent labels and complicated procedures. Furthermore, their detection limit can be insufficient for many important proteins. Now, Baba aims to provide "an immunosensor beyond the current standard technology," exploiting the nanolaser's sensitivity to changes in refractive index and surface charge.

"Our interest is using the nanolaser for immunosensing. But it has the potential to detect toxins, cells, and chemicals. However, photonic sensors are not [yet] available for medical applications. ELISA has been superior to those reported so far," says Baba.

The Yokohama group fabricated a nanolaser from an indium gallium arsenide phosphide wafer with a lattice of holes comprising the photonic crystal separated by an air layer from an indium phosphide substrate. Shifting several holes resulted in a nanolaser cavity that lases at ~1550 nm when pumped with light at 980 nm. As the refractive index of the fluid in the cavity changes upon immersion in solution containing various concentrations of proteins, so does the nanolaser wavelength.



Schematic of nanolaser biosensor and laser mode profile. (Top right): Modal profile without nanoslot; mode is most intense at the nanoslot position. (Bottom): GaInAsP slab of quantum wells on InP substrate. Periodic holes, which form a photonic crystal, are modified to form the central slot (top left), which is the main part of the sensor. Credit: Toshihiko Baba/Yokohama National University.

Functionalizing the nanolaser with a molecule known to bind with the target molecule provides biological specificity. To detect a protein, this means fixing an antibody to the nanolaser surface.

"We can detect a smaller amount of protein than the limit of ELISA. This means we can use a lower concentration of protein as a biomarker for severe diseases, which offers a higher diagnostic probability," adds Baba.

Proteins in body fluids help to identify particular diseases. However, existing tests are limited by detection sensitivity. If lower concentrations could be detected, diagnoses could be improved.

For prostate cancer screening, current tests for detecting the prostate-specific antigen are useful at the threshold, but not at lower levels. Experiments using the nanolaser in blood proxy bovine serum albumin suggest that detection could be achieved below sub-picomolar (pM = 10^{-12}M) concentrations, well below the range needed for post-surgical monitoring. Additionally, Baba's team detected the antibody-antigen reaction of a protein biomarker for Alzheimer's disease at 10 pM concentration in cultured cells and in lymphocites, two orders of magnitude better than ELISA.

The nanolaser's sensitivity to a variety of surface modifications also allows sensing of other molecules. Endotoxins are detected rapidly; gel formation during reaction with a reagent is the current, but slow, method. Baba's team detected the wavelength shift due to gelation faster than is possible with standard assays. For DNA, they showed that hybridization to a probe attached to the nanolaser is detectable through changes in both wavelength and laser emission intensity. This eliminates the need for traditional labels in detecting specific sequences.

Other photonics-based methods of label-free protein sensing show promise too, but they face the challenge of distinguishing signal from noise caused by nonspecific binding and other contamination. The nanolaser sensor's suitability results from a combination of selectivity for target proteins, minimal sample damage, repeatability, low cost, and experimental simplicity.

"The study implies that we can have large sensitivity, and also scalability. But specificity is still dependent on the functionalization, not solely on the laser," says Arka Majumdar, an electrical engineer and physicist at the University of Washington, who was not involved in the study.

Baba plans to continue the investigation, to deliver superior stability and quantification for each target biomolecule.

Rachel Berkowitz