Photonic Crystal Nanolaser Biosensors

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1. Photonic Crystal Nanoalser Sensors

Photonic crystal nanolaser [1] is a tiny laser suitable for sensing applications [2]. It is simply fabricated by patterning and etching an epiwafer and operated by photo-pumping. Owing to a small device area of ~(10 μm)^2, large-scale integration of many nanolasers is also straightforward. The nanolaser acts as a sensor because it changes its wavelength and emission intensity with the surrounding index and electric charges, respectively. Our main target is sensing bio-molecules toward medical diagnoses, sanitary supervision, etc. For detecting biomarker proteins, ELSA is widely used. However, it needs complicated procedures, resulting in a high cost. Moreover, the detectable concentration by standard ELISA is in the sub-pM regime, which is sometimes insufficient for reliable diagnoses from human blood. The nanolaser sensor has achieved a sensitivity and selectivity higher than ELISA's.

2. Sensing Characteristics

The index sensitivity for bulk liquids is higher than 400 nm/RIU. The chemical adsorption of BSA protein and specific binding of biotin-streptavidin were observed through the spectral shift in the nanolaser. The lowest concentrations detectable were in the 100 fM and sub-aM regimes, respectively. The difference between the two values comes from their different affinity constants. The specific binding was observable even when 10^{13} times higher amount of BSA was included as a contaminant.

3. Biomarker Sensing

In sensing actual biomarker proteins, their antibodies are functionalized in advance, and the antibody-antigen reaction is observed through the spectral shift. In recent studies, we succeeded in detecting PSA for prostate cancer and CRMP2 for Alzheimer disease, both from the concentrations two orders lower than detection limits of ELISA. Figure 1 shows an example result for PSA, showing the detection limit lower than 1 fM. This performance was maintained when 10^{10} times higher amount of BSA was included. For CRMP2, the performance was confirmed a sample from human blood.

4. Endotoxin Sensing

Endotoxin is a bio-toxin widely distributing in the environment. The inspection of Endotoxin is crucial in medical treatments because the mixing of Endotoxin into blood in the human body causes serious fever and septic shock. Usually the limulus amebocyte lysate (LAL) assay is used, but it takes more than 1 h to confirm if the critical concentration of 0.001 EU/ml is included. The nanolaser was applied to detecting the reaction of LAL and succeeded in shortening the detection time to 33 min.

5. Multi-Sensing

So far, such cavity-based photonic sensors have been used for monitoring the change of the environmental index through the spectral shift. As for nanolasers, we discovered that the emission intensity is also changed by surface charges [4, 5]. The simultaneous sensing of spectral shift and emission intensity allows the investigation of adsorption and discrimination of biomolecules. We succeeded in detecting negatively-charged DNA hybridization from both sensing signals, which suggests a potential that DNA can be detected using neither labels nor spectroscopy, which will reduce the cost of DNA screening.

6. Cell-Imaging

The large-scale integration of nanolasers was applicable to imaging cells cultured on the nanolaser array. Tracking the spectrum of all nanolasers, the evolution of HeLa cells was imaged. Although the spatial resolution is limited by the size of each nanolaser of several microns, this image sensor will be advantageous when one needs to observe cells without labels with a high index resolution.

Aknowledgments

This work was supported by Grant-in-Aid for Scientific Research No. 16H06334 from JSPS.

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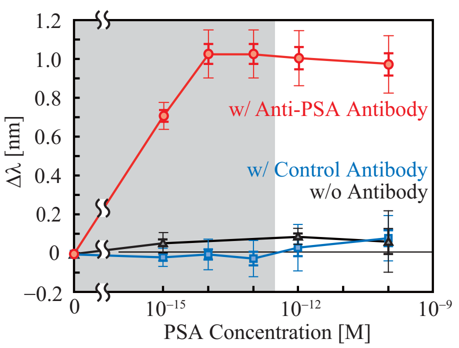

Fig. 1 PSA sensing using nanolaser where ethanolamine was injected as a surfactant. Thin and thick error bars show the standard deviation and standard error for 10–25 nanolasers. Gray area shows the undetectable range of the concentration by ELISA.