

**【Grant-in-Aid for Scientific Research(S)】**  
**Science and Engineering (Engineering D)**



**Title of Project : Ultra-high sensitivity biomarker sensor with extreme light localization of nano-slot lasers**

Toshihiko Baba  
(Yokohama National University, Department of Electrical and Computer Engineering, Professor)

Research Area : Bio photonics

Keyword : biosensing, biomarker, photonic crystal, nanolaser, nanoslot

**【Purpose and Background】**

Blood biomarkers (specific proteins characterizing diseases) have been extensively studied because early diagnoses are crucial for medical treatments of severe diseases. However, it is still difficult to detect a very small amount of marker proteins with a high accuracy and high selectivity against contaminants without complicated procedures of functionalizing fluorescent labels, filtering of contaminants, and condensation of targets.

In this study, we aim at investigating ultimate physics of light localization in photonic crystal nanolasers with a *nanoslot*, and super-sensitive detection of proteins without labels. Furthermore, we develop the efficient surface treatment to give a much higher selectivity than conventional sensors. This is a fused study of nano-photonics, surface and fluid chemistry, and medical applications.

**【Research Methods】**

Three main contents are summarized as follows:

(1) Theoretically, narrower nanoslots enhance the light localization and sensitivity for proteins exponentially. We develop a technology of forming nanoslots of <30 nm width and investigate nano-scale physics of light localization. We also fabricate the nanoslot in a passive slab and nanocavity to enhance the Raman spectrum, which is effective for the detailed analysis of molecular bindings and verifying the results of the nanolaser sensing.

(2) We elucidate the behaviors of proteins from a remote distance to the nanolaser and the fluidic mechanism that carries proteins to the nanolaser. We also cover the device surface with a polymer to suppress the electro-static noise in blood or enhance the signals using the electro-static effects. We adopt a biomarker suitable for effective diagnosis and study the immobilization of antibodies, enabling the specific binding with a selectivity over  $10^9$ .

(3) We develop low-cost and high-throughput production of sensor chips, array integration for the statistical and quantitative evaluation, parallel detection of multi-targets, and condensation method of antibodies using the optical gradient

force. In addition, we build a portable setup and perform the sensing experiments in hospital to get the feedback from medical venues.

**【Expected Achievements & Significance】**

In protein analyses, HPLC and ELISA have been used, while pM-level low-concentration biomarkers suitable for high-accuracy diagnoses of diseases are still difficult to detect. Conventionally some biomarkers are detected through pre-processes and functionalizing labels, resulting in high cost and low throughput. Therefore, high sensitivity and selectivity, label-free, and low-cost are strongly demanded. Our nanoslot nanolaser is a promising candidate that satisfies all the requirements and becomes the first practical sensor chip for medical applications based on photonics.

**【Publications Relevant to the Project】**

- S. Kita, K. Nozaki, S. Hachuda, H. Watanabe, Y. Saito, S. Otsuka, T. Nakada, Y. Arita and T. Baba, "Photonic crystal point-shift nanolaser with and without nanoslots --- design, fabrication, lasing and sensing characteristics", IEEE J. Sel. Top. in Quantum Electron., vol. 17, no. 6, pp. 1632-1647, 2011 (Invited Paper)
- S. Kita, S. Otsuka, S. Hachuda, T. Endo, Y. Imai, Y. Nishijima, H. Misawa and T. Baba, "Super-sensitivity in label-free protein sensing using nanoslot nanolaser", Opt. Express, vol. 19, no. 18, pp. 17683 - 17690, 2011.
- S. Kita, S. Otsuka, S. Hachuda, T. Endo, Y. Imai, Y. Nishijima, H. Misawa and T. Baba, "Photonic crystal nanolaser bio-sensors", IEICE Trans. Electron., vol. E95-C, no. 2, pp. 188-198, 2012 (Invited Paper).

**【Term of Project】** FY2012-2016

**【Budget Allocation】** 152,800 Thousand Yen

**【Homepage Address and Other Contact Information】**

<http://www.baba-lab.ynu.ac.jp/babalabe.htm>