国立大学法人 豊橋技術科学大学

TOYOHASHI UNIVERSITY OF TECHNOLOGY

PRESS RELEASE

Source: Toyohashi University of Technology, Japan, Committee for Public Relations

Release Title: Development of semiconductor microchip that can detect prostate cancer markers with ultra-high sensitivity

Release Subtitle: Working toward the realization of IoT biosensors

Overview

Associate Professor Kazuhiro Takahashi and Tomoya Maeda (a second-year Master's student) and other members of the Department of Electrical and Electronic Information Engineering at Toyohashi University of Technology have developed a semiconductor sensor capable of detecting ultra-low concentrations of tumor markers, on chips made using semiconductor micromachine technology. The research team succeeded in detecting only prostate cancer antigens by adsorbing disease-derived marker molecules contained in blood and other bodily fluids into the surface of a flexibly deforming nanosheet, using the principle of converting the force caused by the interaction between the adsorbed molecules into the amount of deformation of the nanosheet. Testing chips, formed in sizes of several millimeters across using semiconductor technologies, are expected to be used as IoT biosensors for home-based testing.

Details

Measuring devices that perform disease tests simply and quickly from small amounts of blood, urine, saliva, and other bodily fluids are extremely important for accurate diagnosis and verifying the effectiveness of therapeutic treatments. Substances that change in concentration according to specific diseases contained in such bodily fluids are called biomarkers. As one example, it has been reported that patients with severe cases of COVID-19 have different concentrations of multiple biomarkers in their blood than those with mild cases of the disease, and it is expected that this can be used to predict severity by examining those markers. One of the most widely used marker tests is the PSA test. PSA is a marker that increases in the blood as a result of prostate cancer. Marker screening of saliva is also carried out as a less invasive form of cancer risk testing. The marker testing equipment that has been put to practical use so far is a detection method that reads color changes using a labeling agent. Because it takes time and effort to perform labeling, many of the devices used are relatively large, and the use of this method was limited to testing at large hospitals. Accordingly, if portable IoT biosensors are actualized, it is expected to expand testing opportunities and contribute to the advancement of telemedicine.

The research team is researching a micro-scale testing chip that uses flexibly deforming nanosheets formed using semiconductor micromachine technology to determine the presence or absence of disease. The principle of the method is that antibodies which catch the marker (antigen) molecules to be detected are fixed onto the nanosheet in advance, and the deformation of the thin film—caused by the force of the adsorbed antigens electrically repelling each other—is read. In this sensor—which was designed to deform sensitively in response to the adsorption of biomolecules—however, there was a problem in that the film deteriorated as a result of fixing antibodies to it. In the past, the biological functional layer on the surface was produced by spin coating and ultraviolet irradiation, but ultraviolet irradiation was considered to be one of the factors that degraded nanosheet films. The research team changed the materials used from the conventional method, and instead adopted a method of depositing the functional layer by chemical vapor deposition. As a result, a thinner, more uniform and less degraded sensor chip was created.

Using the biosensors developed on this occasion, the team conducted an experiment detecting prostate cancer biomarkers, and succeeded in detecting 100 attograms* (equivalent to three attomolars in terms of molar concentration) contained in one milliliter of fluid. This lower limit detection concentration is comparable to that of large testing devices using labeling agents, and can be hoped to be applied in ultra-sensitive testing with portable-scale testing devices. Furthermore, since it is possible to detect how nanosheets deform by adsorption of molecules in real time, it is possible to detect disease-derived molecules faster than in comparison with testing equipment using labeling agents.
*Atto: an SI unit prefix denoting 10^{-18} (quintillionth)

Future Outlook

The research team now plans to demonstrate that biomarkers can be detected on semiconductor sensors that integrate analytical integrated circuitry, with a view to practical applications in portable testing equipment. In addition, replacing probe molecules applied to the surface of nanosheets will enable the creation of numerous types of comprehensive disease diagnosis tests, which are expected to lead to the early-stage detection of more diseases in the future. By implementing IoT biosensors in society, the team aims to help create a society where everyone will be able to take tests easily, and undergo medical examinations by physicians remotely.

Reference

Tomoya Maeda, Ryoto Kanamori, Yong-Joon Choi, Miki Taki, Toshihiko Noda, Kazuaki Sawada, and Kazuhiro Takahashi, “Bio-Interface on Freestanding Nanosheet of Microelectromechanical System Optical Interferometric Immunosensor for Label-Free Attomolar Prostate Cancer Marker Detection”, *Sensors*, **2022**, *22*(4), 1356, DOI: 10.3390/s22041356

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Further information

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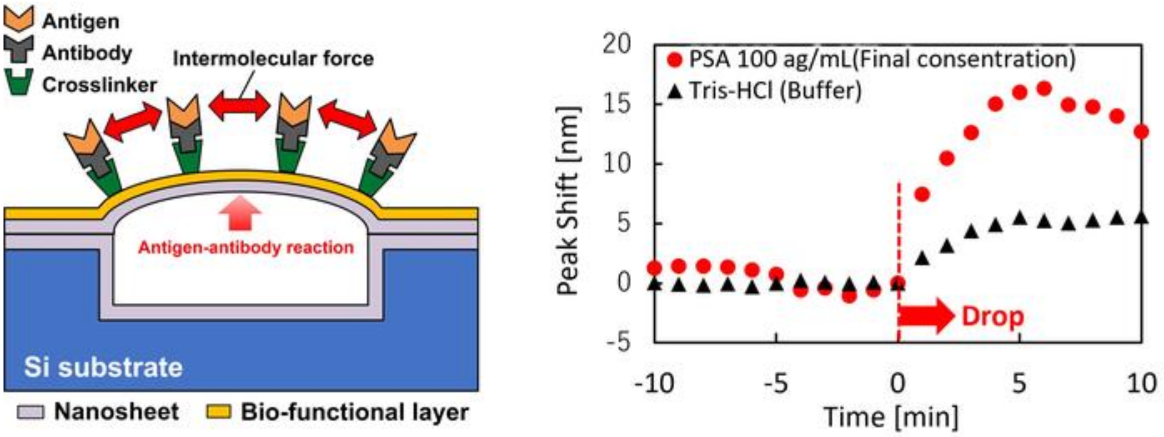
Figure:



Caption: The semiconductor sensor that detects antigen molecules by capturing them on the surface of a nanosheet film. The peak shift amount represents the output value of the sensor proportional to the amount of deformation of the film during marker adsorption.

Movie: https://youtu.be/SOif1-BCA_4

Caption: Peak shift (final concentration 1μg/mL) after PSA drip and microscope image of the sensor

Keywords: Semiconductors, Virus testing, Prostate cancer, Information technology, Cancer research, Biosensors, Biomarkers