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Biosensor using an acoustic wave manipulator for micro droplet

弾性波による微小液滴搬送を利用したバイオセンサ

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1. Introduction

A droplet manipulation is one application of a surface acoustiv wave (SAW) device [1]. The Piezoelectric substrate is used for generating the SAW. The SAW radiates a longitudinal wave into the droplet. For this wave, we can manipulate a droplet. But when we consider the bio-reaction measurement, there is a problem that SAW device get dirty. Therefore, it is necessary to permit disposable system. To solve the problem, we have proposed to use three-layer structure device of sensor plate/matching layer/piezoelectric substrate which is named micro-laboratory [2]. In this paper, enzyme reaction is measured by using the micro-laboratory.

2. Measurement system and micro-laboratory

Experimental system in this study is shown in **Fig. 1**. A sinusoidal signal of 50 MHz from a synthesized signal generator (Leader 3220) and a pulse signal from a multifunction synthesizer (nf WF1943B) were mixed and amplified by using an RF power amplifier (R&K A1000-510). Then the signal was fed to an interdigital transducer (IDT) via an antenna tuner. The antenna tuner was used for impedance matching. The IDT was fabricated on the 128YX-$LiNbO_3$ for generating the SAW. Center frequency of the IDT was designed as 50 MHz, width of a finger electrode and space between electrodes were 20 μm, and an aperture of the IDT was 2 mm. An interdigital electrode (IDE) was fabricated on the cover glass. Three different widths and spaces of 5, 10, and 20 μm were prepared for the IDE. The IDE was connected to an LCR meter (HP 4285A or Hioki 3522-50) for detecting droplet impedance. When frequency is larger than 75kHz, HP 4285A was used.

The micro-laboratory consists of transparent cover glass (thickness of 200 μm)/water layer/128 YX-$LiNbO_3$. Fabrication process of the micro-laboratory is shown in **Fig. 2**. A liquid droplet which is distilled water (DW) in this study is placed on the 128 YX-$LiNbO_3$. Then the cover glass with the IDE is put on it.

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Droplet manipulation on the micro-laboratory is shown in **Fig. 3**. When a radio frequency (RF) signal is applied to the IDT, the SAW is generated. At the matching layer and 128 YX-$LiNbO_3$ interface, the SAW becomes a leaky-SAW and the longitudinal wave is generated into the matching layer. When the longitudinal wave is reflected at the glass interface, a bulk acoustic wave (BAW) is generated [3]. A droplet on the cover glass is moved due to a longitudinal wave radiation from the BAW.

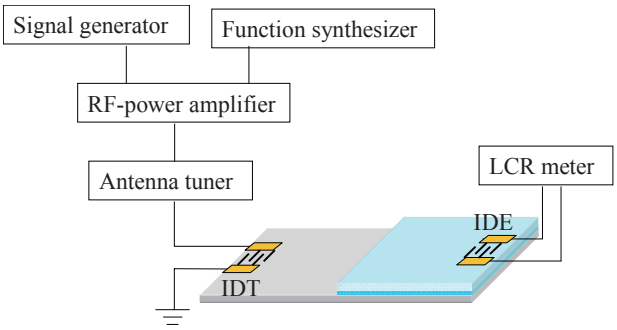

Fig. 1 Experimental setup in this study.

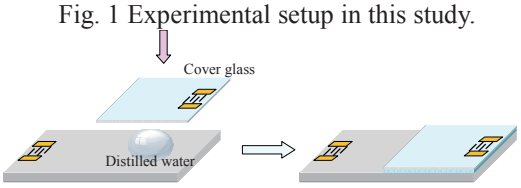

Fig. 2 Fabrication method of the micro-laboratory.

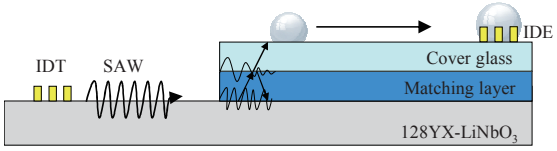

Fig. 3 Schematic illustration of the micro-laboratory.

3. Urease catalytic reaction measurement

The urea is hydrolyzed due to a catalytic reaction of the urease as following equation.

$$(NH_2)_2CO + 2H_2O + H^+ \xrightarrow{urease} 2NH_4^+ + HCO_3^- \quad (1)$$

As conductivity of droplet increases due to the catalytic reaction, droplet impedance decrease. Using the LCR meter, impedance change was measured.

4. Result and discussion

Sample solutions of urease and urea were prepared using distilled water. Volumes of urease and urea droplets are 4 μL and 7 μL, respectively. Concentration of droplets was varied. At the measurements, a droplet of urea solution was placed on the IDE and a droplet of urease solution was manipulated. Two droplets were mixed on the IDE and impedance was measured by using the LCR meter. All measurements were performed at room temperature. LCR meter was fixed at 100 kHz. Applied voltage to the IDT was 28 $V_{p\text{-}p}$.

Typical time response of the urease reaction is shown in **Fig. 4**. Width and space of the used IDE were 20 μm. Concentrations of urease and urea droplets were 0.1 wt% and 1mM, respectively. After SAW was generated, the urease droplet was manipulated and mixed with the urea droplet. Then impedance of the binary-mixed droplet decreases due to the reaction. Similar measurements were performed at different concentrations of urease and urea. The results of impedance shift are shown in **Fig. 5**. In the figure, parameters are the urease concentration. The figure shows the calibration curve for urea. The impedance shift does not depend on the urease concentration because of the catalytic reaction.

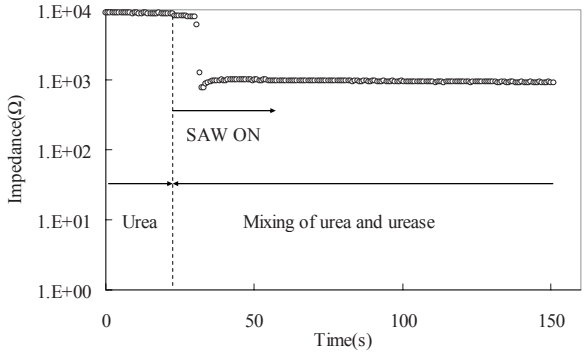

Fig. 4 Time responses of the urease catalytic reaction. Concentrations of urease and urea droplets are 0.1wt% and 1mM, respectively.

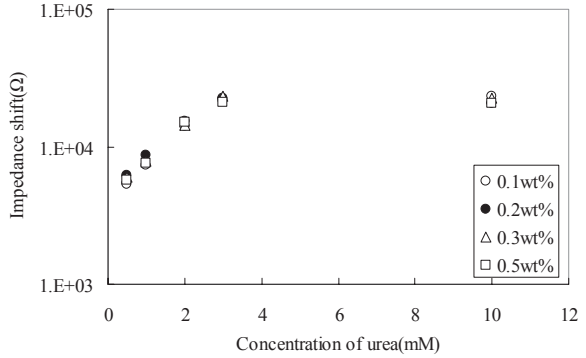

Fig. 5 Impedance shift for concentration of urea solution.

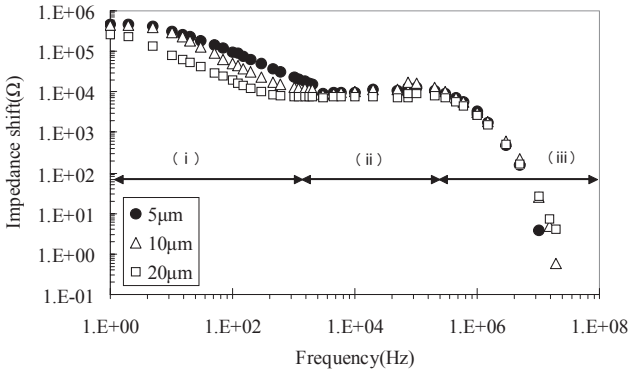

Fig. 6 Impedance shift as a function of frequency. Parameter is electrode width of the IDE.

We varied the finger electrode width and space between electrodes as 5, 10, and 20 μm. The 1mM urea solution of 7 μL was placed on the IDE and then the 0.1wt% urease solution of 4 μL was added. Then the impedance shift was measured. The frequency of the LCR meter was varied. Results are shown in **Fig. 6**. From the figure, the impedance shift has three sections. The impedance shift in the frequency range of (ii) and (iii) does not depend on frequency. Meanwhile, frequency range of (i) depend on the width of the IDE. Also, magnitude of the impedance shift increases with decreasing the frequency. Therefore, high sensitive detection of the urease catalytic reaction is possible with lower frequency of the LCR meter and with narrower width of the IDE.

5. Conclusions

In this paper, urease catalytic reaction was measured by using a micro-laboratory which is consisted of cover glass/matching layer/128 YX-$LiNbO_3$. Because cover glass is cheap, the micro-laboratory is disposable application. Therefore, the proposed micro-laboratory can detect a reaction with attending impedance change, such as other enzyme reactions and immunoreactions.

References

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