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High-frequency QCM Biosensor Fabricated with PDMS Polymer Process

PDMS 樹脂プロセスを用いた高周波水晶振動子バイオセンサ

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1. Introduction

Recently, the immunotherapy is watched with interest as the treatment of serious diseases such as cancer. This treatment suppresses the action of the antigen cells, which is secreted from disease sites, utilizing and controlling the immune cell positively. The evaluation of binding affinity between the antigen and antibody is important in the field of new pharmaceutical development for the immunotherapy. The quartz crystal microbalance (QCM) biosensor is a candidate which can evaluate the affinity quantitatively, and so is attracting more attention as the effective equipment.

However, the QCM biosensor is low sensitive for the low-molecular-weight materials because of the mass detection device [1)]. Therefore, the high-frequency QCM biosensor, which becomes more sensitive, has been desired in the field which investigates the low-molecular-weight materials, for instance, the cutting-edge drug discovery. The QCM biosensor becomes higher frequency as the quartz oscillator becomes thinner. However, thin quartz plate is very fragile, and so it is easy to break when it is fixed mechanically. Furthermore, the leakage of vibration energy occurs from the fixed part. The resonance frequency of the general QCM biosensor used in the fields such as pharmaceutical science, medical science and the like is around 5-30 MHz, and moreover the resonance frequency enhancement has long been extremely difficult. In order to solve these problems, the RAMNE-Q (resonance acoustic microbalance with naked embedded quartz) biosensor, which has the thin quartz plate which is supported by the micropillars without fixing and packaged in the microchannel, was developed [2), 3)]. This sensor is allows high-frequency operation (approximately >500 MHz), and small in size [4)]. The whole analysis system, however, becomes large in scale because the ready-made pump and silicone tube are used in the investigation.

In this study, the RAMNE-Q biosensor chip was made with PDMS (Polydimethylsiloxane) silicone, which is widely used as the material for the micropump [5)], to miniaturize the analysis system through the integration between the sensor chip and liquid transfer unit (e.g., pump, fixture), and then the dynamic characteristics were evaluated.

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2. Fabrication

We developed the RAMNE-Q biosensor chip using PDMS silicone which allows fabrication of submicron scale structure (**Fig. 1**).

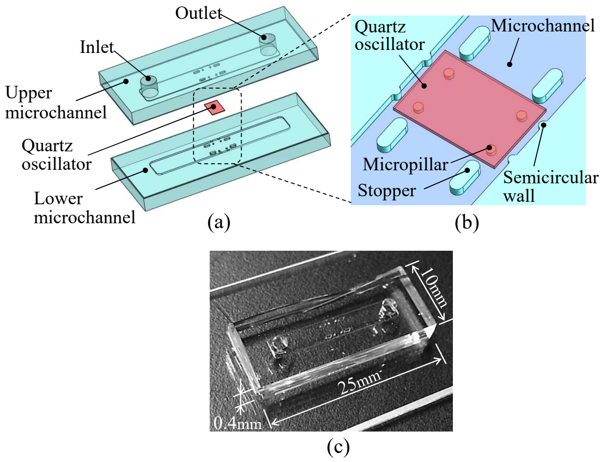

Fig. 1 (a) Exploded view of the PDMS RAMNE-Q biosensor chip, (b) Enlarged view, (c) Assembled chip.

The photoresist mold process was applied in this fabrication (**Fig. 2**). At first, the photoresist was casted on a silicon wafer, and then the master mold was formed by the photolithography (i). The photolithography was repeated twice because the depths from the surface to the bottom of channel and the top of pillar were different. Next, the PDMS prepolymer was poured into the space consisted of two molds (ii). The air bubbles in the prepolymer were removed by degas, and then the prepolymer was thermally cured after making it reach in every corner (iii). After cooling, the replica PDMS substrate was peeled off from the molds (iv), and the quartz oscillator (fundamental resonance frequency 56 MHz) was installed in the state supported by the pillars (v). The bonding surface was activated by oxygen plasma, and the side-chain methyl group was replaced by hydroxyl group (iv). This process makes the binding surface hydrophilic. Another replica substrate, which becomes the upper channel, was activated similarly. At the end, the upper and lower substrates were bonded via the covalent bond by overlapping each hydrophilic surface in room temperature (vii).

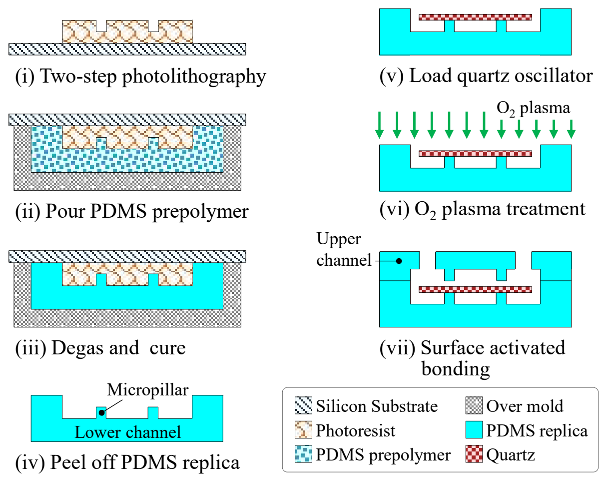

Fig. 2 Fabrication steps using the photoresist mold.

3. Experimental

Fig. 3 shows the experimental setup of the sensor chip. With the previous system, the silicone tubes and sensor chip were connected via the dedicated fixture. They were, however, connected with the adhesive directly in this study because both ingredients were silicone resin, and consequently the analysis system was miniaturized. The solution was transferred by the precision pipette. The sensor chip was operated wirelessly by the express card or LAN based network-analyzer which allows system miniaturization. The electromagnetic wave provided successively from the copper foil antenna, which was attached to the outside of the sensor chip, generates the vibration of the quartz oscillator through the inverse piezoelectric effect. Concurrently, this vibration induces the electric charge on the quartz surfaces through piezoelectric effect, and it was detected as the electromagnetic wave by another copper antenna.

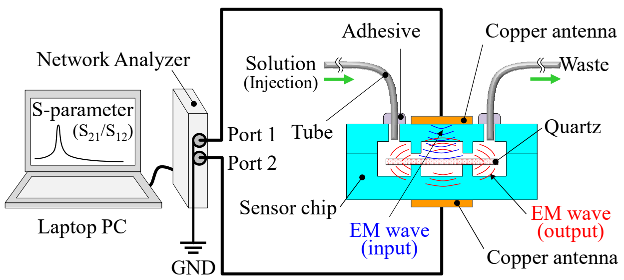

Fig. 3 Schematic of the experimental setup.

4. Results and Discussion

Fig. 4 shows the resonance spectrums of the PDMS RAMNE-Q biosensor chip in the atmosphere and the ultra-pure water filled in the microchannel. The quality factor (Q-factor) was defined by the half bandwidth method, and the Q-factors were approximately 17000 in the atmosphere and 1000 in the solution, respectively. This results indicates that the structural damping (i.e., leakage of vibration energy through the structure) of the quartz oscillator is very low, therefor the PDMS RAMNE-Q biosensor chip, which has the quartz oscillator supported the entire side by the pillars and stoppers without mechanical fixing, has potential for high-resolution analysis of the biomolecular reaction, as with the conventional RAMNE-Q biosensor made of glass and silicon.

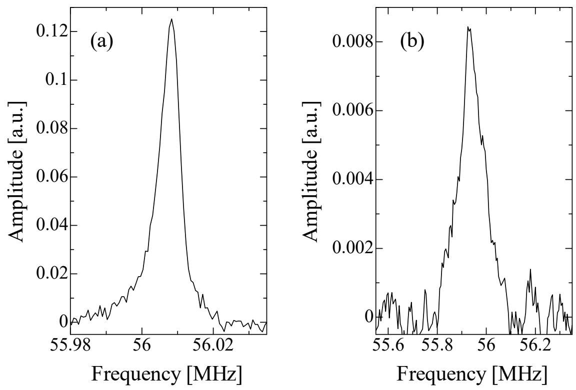

Fig. 4 Output spectrums of the sensor: (a) in atmosphere, (b) in ultra-pure water.

5. Conclusion

We developed the PDMS RAMNE-Q biosensor chip applying the photoresist mold process, and then found that the chip achieves high Q-factor through the evaluation of dynamic characteristic. This suggests that the developed chip is useful equipment for the high-resolution analysis. In the future, the small and high sensitive QCM biosensor that hasn't been around until now can be realized through the integration of the sensor chip and pump made of PDMS silicone.

References

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