論文の内容の要旨

論文題目
A high resolution biosensor using microcantilever resonating at air/ liquid interface
（気液界面で共振するカンチレバーを用いた高感度バイオセンサー）

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The purpose of the study is to develop a high-resolution biosensor to detect biomolecules in a microfluidic system. The microfluidic system is also called 'Lab-on-a-chip' because functions of chemistry laboratory such as reaction, separation and detection can be integrated on a small chip. It can handle an extremely tiny amount of biomolecules in a micro-scale chamber or a channel in much faster reaction time. Therefore it has successfully been applied to biotechnology. However, its detection method depends mainly on optical means; this results in the need for a rather bulky optical system and expensive fluorescent-regents or the difficulty in continuous monitoring for long-time. Electrical detection using biosensors integrated in the microfluidics system can provide a good solution to the problem. I have compared electrochemical sensors and mechanical sensors and chose a mechanical biosensor based on a resonating microcantilever because of its high sensitivity, easy functionalization and simple structure. The microcantilever has high mass sensitive in vacuum and air but not in water due to excess damping. The thesis proposes the biosensor using the microcantilever (80μm x 20μm x 5μm) resonating at air/ liquid interface to realize high sensitivity and easy integration to the microfluidics. The cantilever is fabricated on a SOI wafer and placed on the bottom of a microchannel, which is actuated efficiently by a photothermal laser. Its surface facing to liquid layer is functionalized for label-free detection, while opposite side is exposed to air to improve the resonance characteristics. However, the resonance frequency of the new cantilever is susceptible to a surface tension on the meniscus surface at a micro-slit and liquid pressure changes in the microchannel, besides loaded mass on the surface. The thesis explores methods to eliminate such undesired effects and confirms the performance of the biosensor.

The thesis consists of 8 chapters. Chapter 1 introduces background, purpose and significance of the thesis, and chapter 2 explains a principle and characteristics of the biosensor. Chapter 3, 4 and 5 shows resonance frequency shift by loaded mass (ch. 3), surface tension (ch. 4) and liquid pressure in a microchannel (ch. 5). Chapter 6 is related on a construction of the novel biosensor system summarizing results in ch. 3, 4, and 5. Chapter 7 shows its possibility as a biosensor and the thesis is concluded in chapter 8.

Chapter 2 shows the concept of design and its characteristics. The novel cantilever improves 62% of resonating amplitude, 50% of quality factor (15) and eight times higher signal-to-noise ratio, because liquid damping acts on only one-side and there is no obstacle between laser detector and the cantilever.

According to improved results, the novel cantilever is characterized by about 25 times higher frequency resolution with mass sensitivity down to 1.54fg (femto-gram).

Chapter 3 verifies the resonance frequency shift by mass loading on the cantilever. To apply the silicon resonator to a biosensor, the surface should be functionalized using antibodies that are cross-linked to amino-group of APTES (self-assembled monolayer) on SiO_2 layer sputtered on the cantilever. The functionalizing process is optimized using three different concentrated fluorescent antibodies, 20, 40, and 80μg/ml, under a fluorescent microscopic observation and verified their each reaction kinetics by the resonance frequency measurement.

Chapter 4 describes that a surface tension changes is susceptible to the resonance frequency theoretically and experimentally. Though the micro-slit keeps liquid with its meniscus surface, it affects on additional elastic property causing changes of the resonance frequency. Different width of micro-slit down to 10μm and several concentration of surfactant (Tween20) are tested to understand the effect on surface tension to the resonance frequency. The narrower width of a micro-slit and lower concentration of surfactant has the higher resonance frequency, which is correlated to theoretical calculation.

In chapter 5, the resonance frequency is stabilized during injecting flow into the microchannel. A peristaltic pump and push/ pull type of syringe pump are tested to balance liquid pressure between an inlet and outlet of the microchannel using microscopic method and resonance frequency measurement. Finally, we optimize fluidic resistance adjusting length and diameter of PTFE tube linked to both side of a microchannel, to achieve an imaginary ground level of liquid pressure at the cantilever.

Chapter 6 suggests method to measure the loaded mass using the novel biosensor and to reduce side effect introduced in chapter 4 and 5. In this regard, chapter 7 shows the cantilever as a biosensor to detect low concentration of insulin (6.3ng/ml, highest concentration level *in vivo*) and other applications.

In chapter 8, significance and prospect of the novel sensor is explained to conclude the thesis. Moreover, I want to introduce new type of sensor to measure the surface tension in a microfluidic system, which was a drawback for a mass sensitive biosensor. In addition, I prospect that the cantilever resonating at air/ liquid can apply to various purposes such as AFM to work in liquid.