Development of Multi-Functional Microfluidic Device using *Caenorhabditis elegans* as a Bioindicator

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ABSTRACT

The nematode *Caenorhabditis elegans* (*C. elegans*) receives attention as a bioindicator in a micro environment for many reasons: microscopic size, short life span, transparent body, well known genome map, and relevance to human diseases. The advances in microfluidics and micro electromechanical system (MEMS) have enabled a microfluidic device to be applied to the study of *C. elegans*, but it has the same limitation as the conventional work used a NGM agar plate that it needs an imaging system to observe *C. elegans*. In this thesis, to overcome this limitation, two sensors such as the capacitance sensor and the resistance sensor were developed to monitor the condition of *C. elegans* without a microscope.

First, the capacitance sensor could assess the body volume of *C. elegans*. The body volume was one of the features to show the condition of a worm, because it was easily affected by an external stimulus such as heavy metal. Hence, from the body volume measurement, we analyzed the status of *C. elegans*. The capacitance sensor was comprised of a micro channel and a pair of electrodes. The electrodes were used to measure the capacitance change by *C. elegans*. When a *C. elegans* passed through the electrodes, the capacitance was measured. The capacitance change was proportional to the body volume of the worm, thus the body volume was assessed from the capacitance change. Based on the capacitance sensor, the multifunctional microfluidic device was developed. It had chambers, pneumatic valves, and the capacitance sensor. The device could culture *C. elegans*, apply an external stimulus to worms, and analyze the condition of each worm. For demonstrating the capability of our device, it was applied to examine the effect of cadmium on *C. elegans*, and the condition of each worm was analyzed by the capacitance change without an imaging system.

For adding the other function to conduct multi exposure test at the same time, a no-moving-parts (NMP) valve was developed. The NMP valve enabled unidirectional movement of *C. elegans* in a chamber: once *C. elegans* was loaded into the chamber, it could not exit, regardless of the flow direction. To show the ability of the NMP valve to handle worms, the microfluidic device with three chambers was developed. Each chamber incorporated the NMP valve and was used to expose worms to Cd and Cu solutions, and K-medium. A pair of electrode was installed in a chamber to analyze the condition of *C. elegans*: it was the same method as that already used in our previous works. From this experiment, we confirmed that the different solutions induced

differences in the capacitance changes for each group.

Secondly, the resistance sensor was developed to detect the locomotion of *C. elegans*. The locomotion of *C. elegans* gave us the information on the functionality of the neuronal and muscular system and was more sensitive than the body volume of *C. elegans* depending on the external stimulus. Among the behavior patterns of *C. elegans*, the resistance sensor was designed to measure the speed of the worm. The resistance sensor was composed of three PDMS layers. The second PDMS layer was a thin PDMS layer in which the flexible electrode was incorporated. The resistance of electrode was changed depending on the locomotion of *C. elegans*. Using our proposed sensor, we succeeded to measure the speed *of C. elegans* in a sinusoidal channel.

Overall, the microfluidic devices developed in this thesis demonstrates the new method to observe the condition of *C. elegans* without an imaging system. They have great capability to apply a microfluidic device to the portable *C. elegans* observation system as well as to contribute in *C. elegans* researches to serve as a platform for analyzing *C. elegans* without an imaging system.