Construction of detection system for intracellular changes using a micro single-sided transient hot rectangle method

Yoshiyuki Takashima, Yuta Yagami, Takashi Katayama, Kaoru Uesugi and Keisuke Morishima
Department of Mechanical engineering, Osaka University, 2-1, Yamadaoka, Suita, Osaka, 565-0871, Japan

Abstract:
Development of a technique for minimally invasively measuring the state of a living organism is desired. We proposed the µ-STHR (The micro single-sided transient hot rectangle) method [1] that can detect dissipated heat as a minute signal and add heat pulse to a sample on a sensor. Our purpose is to construct an ultra-sensitive and biocompatible measurement system for biomaterials. By applying this µ-STHR method, the state of cells can be evaluated quantitatively with low invasiveness. Furthermore, by incorporating this system into a microscope, it will be possible to visually observe changes in cells by measuring them (Fig. 1).
As the first step in this research, we report on the influences of microscope light source to the sensor output.

1. INTRODUCTION

In recent years, the diagnosis of living tissues and cells is mostly based on visual information using a microscope. In the development of regenerative medicine, we expected that the state of cells will need to quantitatively evaluate without staining before transplanted into the body. As such a minimally invasive measurement system, we proposed a measurement system using heat [2]. Molecules present in normal and abnormal cells are different. Since heat represents the behavior of the molecules, the dissipation of heat within each cell is different. We considered that the state of the cell can be measured by electrically measuring this dissipation of heat. As a problem, cells change the composition of substances inside them by life activity for every day. Without visual information, we cannot judge what state cells are being measured. Therefore, by linking the visual information with the measured value of the µ-STHR method, it becomes more accurate as data.

This measurement system can detect temperature change with a standard deviation of 0.0007K. The light source of the microscope influences the measured value as a disturbance. In order to construct a system to detect intercellular changes, the influence of the light source of the microscope was investigated.

2. EXPERIMENT

2.1 Apparatus Overview
A photo image of experimental setup apparatus was shown in Fig. 2. The sensor of the µ-STHR has a small rectangular region which has 5 µm (height) by 10 µm (width) on a glass substrate made of Ni thin film. Joule heat is induced by the electrical current pulse introduced to this rectangular region. The heat diffuses into the measurement sample. By utilizing the temperature dependence of the electric resistance, it is possible to detect the change in the average temperature of the electrode surface. We developed a unique circuit. As a performance characteristic, the current is 5 mA and the time width of the pulse is 10 µs. The device set on a copper heatsink. The copper heatsink was connected to a circulating

Fig. 1 Schematic image of the experimental set up of the ultra-sensitive measurement system

Fig. 2 Photo image of the experimental system
thermostat controlled by a temperature regulator. The temperature fluctuation of the copper heat sink was ± 0.02 K or less. A halogen lamp of 100 W and 12 V manufactured by Nikon was set on the top of the device. It was equipped with standard infrared ray cutoff filter. Illuminance of the halogen lamp was maximized, and the device was irradiated.

2.2 Measurement procedure
The temperature of the device controlled to 27.5 °C by a heat sink. As a measurement sample, we selected water and ethanol. The measurement procedure is as follows. Water (400 μL) was poured into the chamber and waited steady for 1 hour. Water was measured for 30 minutes while the halogen lamp was non-lighting. The halogen lamp was turned on and water was measured for 30 minutes. The halogen lamp was turned off and water was measured again for 30 minutes. After the halogen lamp was turned off, water in the chamber was removed and methanol (400 μL) as a reference was poured and waited steady for 10 minutes. Methanol was measured for 30 minutes.

3. Result and Discussion
The measurement results were shown in Fig. 3. The horizontal axis represents the measurement time and the vertical axis represents the sensor output. It could be confirmed that the sensor output was slightly lowered when the halogen lamp is turned on. The value was about -0.0005 V which is compared with Lighting and Non-Lighting. It was found that irradiation of the halogen lamp affects the absolute value of sensor output.

Next, the standard deviation of the measured values in each measurement was shown in Fig. 4 Comparing the time when the halogen lamp was Lighting and the Non-lighting, it was confirmed that the variation slightly affected the data dispersion. Since it was close to five to the power of minus four, it was confirmed that highly accurate detection was maintained.

4. Conclusion
As a system to detect intracellular changes, the influence of the light source of the microscope on the sensor could be evaluated quantitatively. As a result, it was confirmed that there was a difference in sensor output when irradiating the halogen lamp. However, the illuminance which is used to observe cells compared with this experiment is strong. Therefore, the actual influence is thought to be smaller than this. As a future task, we will construct a system that can control the temperature on the stage of the microscope and perform measurements while actually visually confirming the change of the cell.

References