Measurement of signal from Cardiac Cell of Rat by High-Tc SQUID

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Abstract— **Stem cells in developing tissues give rise to the multiple specialized cell types that make up the heart, lung, skin, and other tissues. For the scientists, it is important to know the stages of the stem cell development. We propose a new method to know the cell development stages by using a high Tc SQUID magnetometer. In the first step of the experiment, we used Wister rat myocardial cells incubated for 12-14 days in a culture dish as a sample and tried to measure the signal by SQUID magnetometer. We successfully measured the signals. A beat signal with period of 0.6 sec was observed. The peak - peak value was about 400pT. The beat oscillation was continued for 10 sec and stopping for 10 sec. This wave set could be periodically repeated. This phenomenon showed a good agreement with a result of microscopic observation.**

I. Introduction

Research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease, which is often referred to as regenerative or reparative medicine. Stem cells are important for living organisms for many reasons. Stem cells in developing tissues give rise to the multiple specialized cell types that make up the heart, lung, skin, and other tissues. When unspecialized stem cells give rise to specialized cells, the process is called differentiation. Scientists are just beginning to understand the signals inside and outside cells that trigger stem cell differentiation [1].

For the scientists, it is important to know the stages of the stem cell development. Growing cells in a laboratory is known as cell culture. Stem cells are isolated by transferring the inner cell mass into a plastic laboratory culture dish that contains a nutrient broth known as culture medium. The scientist are using a patch clump method, which includes a microscope, a microprobe and micro voltmeter to investigate the development stages of the cell. Figure 1 shows the patch clump method. One can know the growth stage by reading the voltmeter corresponding to the action potential of the cell. In this method, you need much skill to insert the micropipette. And also this method is not applicable to the tissue for cell-based regenerative therapies because of its invasive method. The stem cell is fragile and easily broken by touching or sting into the surface [2]-[5].

We propose a new method to know the cell development stages by using a high Tc SQUID magnetometer. This method is perfectly invasive and does not break the cell. In this paper we describes the system for the measurement and the results using rat myocardial cells.

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II. Experimental

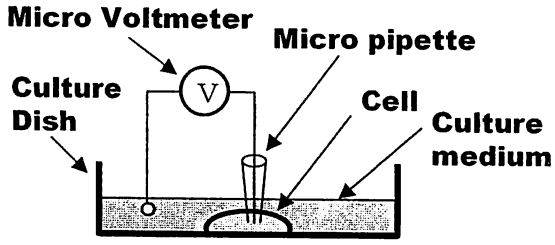

Fig. 1. Patch Clump Method. One can know the growth stage by reading the voltmeter corresponding to the action potential of the cell. In this method, you need much skill to insert the micropipette.

A. Cell samples

We used neonatal Wister rats. All animals were kept in a temperature-controlled room with a 12-hour light-dark cycle, and had free access to water and standard laboratory diet. All experiments were carried out in compliance with guidelines on the care and use of laboratory animals from Toyohashi University of Technology. Cardiac muscle tissues were taken from 1- to 3-day-old Wister rats under CO_2 anesthesia and were sliced into small pieces. They were cultured in a plastic laboratory culture dish at 32 degree for 12-14 days. The inner surface of the culture dish was coated with collagen and contained 2mL of HMEM based culture medium. The size of

the cultured cell array was about 500 um in diameter and 50 um in height.

The cells were attached in the bottom of the culture dish after three days. After four days, unstable heartbeat motion in part of the cellular structure, which showed systole and diastole could be confirmed by microscopic observation. The cells cultured for 12-14 days were used for our experiments. In this stage, it could be seen that the whole cellular structures beat periodically in the culture dishes.

B. Measurement System

The SQUID magnetometer is made of $Y_1Ba_2Cu_3O_{7-y}$ thin film. The junctions utilized in the SQUID are of the step-edge type. The magnetic flux noise in the white noise region was about 10 - 20 $\mu\phi_0/Hz^{1/2}$. The cryostat was specially designed for a SQUID microscope. The SQUID sensor was located inside a vacuum and separated by a 200μm thick sapphire window. A more detailed description can be found elsewhere [6]-[10].

All of the experiments were performed inside a magnetically shielded room (MSR), with a shielding factor of –50dB at DC. The schematic layout of the system and the data acquisition system is shown in Fig. 2. The SQUID was operated in a flux-locked loop with a flux modulation frequency of 256 kHz. The output voltage of the SQUID electronics is passed through a low pass filter at a frequency of 5kHz and also through a 60Hz band elimination filter. The signal voltage is coupled to an A/D interface board and stored in a PC.

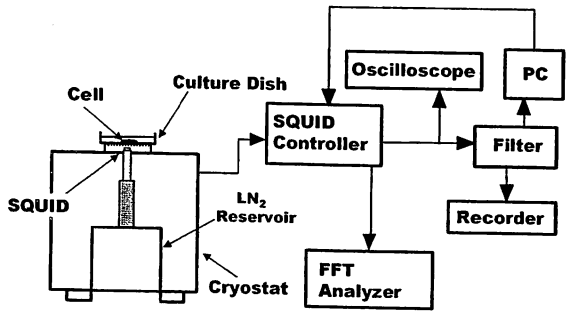

Fig. 2. The schematic layout of the system. The SQUID was operated in a flux-locked loop with a flux modulation frequency of 256 kHz. The sample in the plastic culture dish was placed on the top of the vacuum window. The signal voltage was coupled to an A/D interface board and stored in a PC.

C. Measurement

The sample in the plastic culture dish was placed on the top of the vacuum window. Then the magnetic signals were recorded. The total spacing between the cell sample and the SQUID magnetometer is approximately 1.8mm.

III. Result and Discussions

The typical result of the measurement of the cultured rat cell is shown in Fig. 3. A beat signal with period of 0.6 sec can be observed. The peak - peak value is about 400pT. The beat oscillation was continued for 8 to 10 sec and stopping for 10 sec. This wave set could be periodically observed. This phenomenon showed a good agreement with a result of microscopic observation. This suggests that this method can be applicable to measurement of action potential of cultured cells.

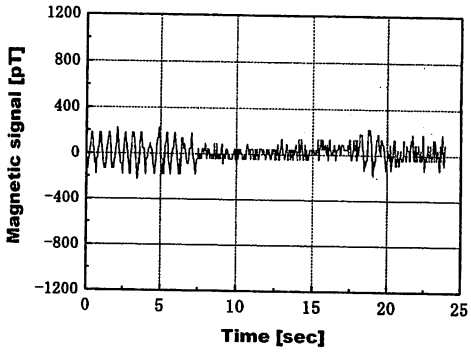

Fig. 3. Measured magnetic signal from the rat cell. A beat signal with period of 0.6 sec was measured. The peak - peak value is about 400pT. The beat oscillation is continued for about 8 to 10 sec and stopping for 10 sec. This wave set could be periodically observed.

We believe this result has not been reported to date.

IV. Conclusion

We have proposed a new method to know the cell development stages by using a high Tc SQUID magnetometer. As the first step of the experiment, we used rat myocardial cells incubated for 12-14 days in a culture dish and tried to measure the signal by SQUID magnetometer. As a result, the signal from the cellular structure could be successfully detected.

This method must be effective for measurement of action potential of cultured cells because of a non- invasive advantage.

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