別紙４－１（課程博士（英文））

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Abstract (Doctor)

Title of Thesis	Implantable microelectrode devices for chronic neuronal recordings in mice

Approx. 800 words

To elucidate brain function, it is necessary to measure the neural activity in the brain with the high spatial and temporal resolution for long period in chronic. In particular, several critical human diseases including Parkinson disease, Alzheimer disease and major depressive disorder need knowledge of the basic nervous system from mammal model.
For studying these human diseases, mice frequently have been used as a model organism. However, the conventional study using mice provides data hard to quantitative evaluation from the behavioral test. Recent advances in microelectromechanical system technology enable us to fabricate multi-channel neuronal electrode devices and to record the electrical signals including spike signals and LFP signals. however, these devices have some challenges with the failure mode of the neural electrode including the mechanical origin and biological origin.
In this study, I provide several of the neuronal electrode and implant systems for chronic recording with high spatial and temporal resolution using mice. For the low invasive device placement, I proposed surgical methods by PEG dissolvable material using states of "solid phase" and "liquid phase".

As the first, I proposed the parylene-thread microelectrode was fabricated, and the tissue was penetrated by guiding the tungsten microneedle based on the sewing mechanism. The fabricated thread-bioprobe enabled us to acquire EMG signals from a mouse's MG muscle and neuronal signals of LFP and spike from the mouse's visual cortex in vivo. The proposed thread-bioprobe device that exhibits the features of device flexibility, electrode position controllability, and implantation capability will contribute to both acute and chronic in vivo electrophysiological recordings. The sewing method of the flexible thread device using a dissolvable material of PEG has been proposed to prevent physical stress on the tissue. These features of both flexible thread-device and the surgical method proved unachievable earlier using conventional methods and devices.

As the next, I proposed a chronic neuronal recording in mice, in which a 5-μm-diameter microneedle electrode penetrates the brain tissue with dissolvable material–based detachment, and the device is placed on it without fixing the device to the cranium, achieving the floating electrode architecture. For the device placement, I proposed the penetration method of a microelectrode into the brain tissue and the device detachment with dissolvable material of PEG. The method showed the advantage of the reduction of the physical stress to the tissue during the device placement as well as the detachment from the manipulator. The electrode shows the stable recording with no significant degradation of the signal-to-noise ratios for 6 months, and minimized tissue damage is confirmed compared to that when using the other cranium-fixed electrodes with the same needle geometry. Although the electrode device needs further improvements, such as miniaturization and wireless recording system, the proposed recording technology showed clear advantages of the high SNR during the implantation and the minimized tissue damage.

Finally, we proposed a microneedle-electrode-assembled flexible-film device for chronic in vivo recording with high spatiotemporal resolution multi-signal and low invasive implantation. The fabricated microneedle-electrode-assembled flexible-film device enabled us to record the LFP signals and spike signals in an acute in vivo experiment. Furthermore, the fabricated device was placed on the brain tissue using PEG, and the device implantation for chronic in vivo recording. The implanted device showed the LFP signal and spike signal for 4 months. In addition, the SNR during the implantation was analyzed. As the result, the SNRs for 4 months showed no significant difference. From these results, the proposed microneedle-electrode-assembled flexible-film device provide the signals with high spatial and temporal resolution and low invasive chronic implantation.

These studies demonstrated chronic in vivo recordings for the microelectrodes that enable recording the signal with high spatial and temporal resolution using mice. Furthermore, the implant method using PEG provides the recording without inflammation due to the factors including tissue damage during device penetration, the elastic mismatch between the neural electrodes and the neural tissue in the context of relative micromotion, chronic breach of the blood–brain barrier in mice brain. I hope that this research result will be used as a powerful tool to accelerate the elucidation of brain function in the future.