Reconstruction of neuronal networks in the central nervous system with nano-biotechnology and photoelectronic tools

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Abstract—We developed flexible multichannel microelectrodes by using thin polyimide films and parylene-coating technique (order-made electrode by laser processing) and detected local field potentials in the monkey and rat brains. Control of specific neuronal subsets was achieved with combination of electronic engineering, optogenetics, and nano-drug delivery systems (intelligent nanobeads).

The progress of photolithographic techniques have provided microelectrode arrays to monitor neuronal activities in the brain and silicon-based electrode arrays have advantages over microwire electrodes for multichannel recording. However, hard silicon electrodes cannot catch up with movement of soft brain tissue in the skull and severe brain injury by electrodes limit long-term recording. We developed flexible and durable electrodes by using thin polyimide films and parylene-coating technique (Figure 1). The size and shape of electrodes and the distance between electrodes could be designed freely according to recording purpose of the neuronal experiments with laser processing (order-made electrode). By using the flexible electrodes, we could successfully record exquisite neuronal activities (e.g. event-related desynchronization) in the monkey supplementary motor cortex.

Introduction of the flexible microelectrodes was achieved by (1) insertion sheath or (2) magnetic force. To drive electrode with magnetic force, ion foil patch (50um thick) was attached to the rear surface of the electrode. The magnetic properties of electrode were measured by a high temperature superconducting SQUID gradiometer. The magnetized iron was very effective for making a large guidance force by magnetic force. When an electrode was positioned perpendicularly to the surface of the jelly (simulating hardness of brain, mechanical resistance was 0.8N), the electrode movement was controllable until radial distance of 6 mm and axial distance of 8 mm.

Accurate control of neuronal activity at a neuronal-subregion level is a goal in neurology. Photo-responsive ion channel molecules, such as channelrhodopsins, are now an indispensable tool in brain science, allowing precise regulation of neuronal excitability with blue light. However, simple injection of viral gene vectors into a specific brain region cannot specify neurons expressing the channelrhodopsin gene. Thus, we developed nanobeads expressing viral receptor molecules (intelligent nanobeads). The intelligent nanobeads could induce channelrhodopsin expression only in neurons at the injected site (less than 1mm in diameter, Figure 2). By using the flexible electrodes, we could detect blue LED-induced neuronal activity in the brain areas. Control of specific neuronal subsets could be achieved with combination of electronic engineering, optogenetics, and nano-drug delivery systems (DDS). These techniques would be crucial for future treatment of neurological diseases.

Figure 1
Flexible electrode

Figure 2
Intelligent nanobeads bearing channelrhodopsin2-venus chimera gene constructed in the AAV2 viral vector was injected into the rat striatum (left) (arrow). Four weeks after injection, the gene was expressed only around the injection site (right) (green fluorescence of the venus reporter gene).

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