Conformal multi-electrode arrays using organic electrochemical transistors

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Since the organic electronic device has mechanical flexibility and biocompatibility, it was expected to be utilized as a tool for measuring the signal of electrophysiology of a neuron circuit. Low mobility and high driving voltage of organic semiconductors were the factors that interfered with practical applications to bioelectric signal sensors. In recent years, organic electrochemical transistors (Organic Electrochemical Transistors; OECTs) have been attracting attention as bio signal sensors because they exhibit high transconductance of 1 mS or more with low voltage driving of 1V or less. Due to high amplification, single OECT have been demonstrated to measure nerve activity on the cortical surface, with superior a signal-to-noise ratio (SNR) to that of conventional electrodes. However, it have been not realized the active array which can significantly reduce the number of wires. In practical applications, it is necessary to develop an active multielectrode-array (MEA) with high temporal and spatial resolution in order to access large area signal environment over the whole brain surface area of a large mammal. Therefore, in this paper, we aim to fabricate ultra-thin conformal active MEA array that can harmonize with living organisms using organic electrochemical transistors and to measure signals by *In-vivo* experiments to show practical applicability.

Chapter 1 Background of Bio signal Sensor

The origin of the bioelectric signal is the action potential created by the movement of ions during neurotransmission. Previously, the rigid device based on Si or Ag/AgCl was used for measure bio potentials. However, to make higher conformable, stabile devices, the flexible device was required. Recently, passive arrays of bio-electrical sensors have been developed on a flexible substrate. Furthermore, in order to obtain high spatiotemporal information on a large area, it is necessary to develop a multielectrode arryay (MEA) using a transistor active array. In this chapter, we described past researches in order of conventional, flexible and stretchable devices, and also showed the points to overcome the studies reported so far.

Chapter 2 Development of Flexible MEA using Integration of OFETs and OECTs

In this section, a study to realize a 5 × 5 Active MEA showing high temporal and spatial resolution by the integration of OECT and Organic Field Effect Transistors (OFETs) on a thin film substrate was described. In order to drive OECT with low resistance, we developed a method of miniaturizing the OFET channel by photolithography. Also, in order to prevent thermal degradation of the organic semiconductor layer DNTT, we succeeded in stabilizing the operation in water by cold crosslinking PEDOT: PSS which is a channel of OECT for a long time at 55 ° C. A biosignal sensor including one OECT and one OFET could read a signal with a cutoff frequency of ~ 3 kHz with a transconductance of 1 mS or more. An integrated device with a total thickness of 2.0 μm including a substrate and a sealing film measures biopotential signals by in vivo experiments of measuring evoked potentials on the surface of the muscle tissues of transgenic rats in which nerves are stimulated by light. In order to make evoked potentials artificially, the motor nerve on the muscle was locally stimulated by a laser beam having a wavelength of 473 nm. The 2.0-μm device was able to smoothly adhere to the living body surface, so artificial movement due to the dynamic motion of the muscle could be neglected. Integrated devices of OFET and OECT were able to detect electromyography (EMG) of evoked potentials with temporal resolution of 1 ms or less. The reference signal current through the integrated device was about 245 μA and the spike representing myocyte activation showed an amplitude of about 1 μA (0.4% modulation) with a noise level of 50 nA. The results in this chapter were published in the journal *Advanced Materials* under the title "Integration of Organic Electrochemical and Field-Effect Transistors for Ultraflexible, High Temporal Resolution Electrophysiology Arrays".

Chapter 3 Development of Transparent Flexible MEA using OECTs

In this section, it was stated that a transparent active MEA is fabricated on a parylene substrate with a thickness of 1.2-μm. Devices composed of transparent OECT and transparent metal grid wiring realized high transparency throughout the region. The Au grid wiring with a line width of 3 μm fabricated on a parylene substrate with a thickness of 1.2 μm was much smaller than the typical size of the neuron and showed high transparency of 60% and low sheet resistance of 3 Ω / sq . Mechanical durability of the Au grid was achieved by applying it to a 100% pre-stretched PDMS substrate and applying compressive strain. As a result, the ITO transparent electrode which was widely used in the past deteriorated from 79 Ω / sq to 378 Ω / sq when 50% of compression strain was applied, whereas the Au grid electrode ranged from 3 Ω / sq to 7 Ω / sq and showed better mechanical properties than conventional transparent electrodes. Even when a strong laser beam (150 mW) was irradiated on the transparent OECT channel, current fluctuation of OECT was suppressed to less than 0.1%. In order to exclude the OFET used in Chapter 2, we have devised a new circuit design array that can suppress cross-talk with only transparent OECT elements in each cell. Simulation and experiments demonstrated that a new circuit does not exhibit cross-talk when wiring resistance and output resistance are close to 0 Ω. Based on the invented circuit, a 3 × 5 transparent OECT array was fabricated with a total thickness of 3 μm, each OECT showed a large transconductance of 1.1 mS and a fast response time of 363 μs. Finally, by mapping the evoked response (Electrocorticography; ECoG) with an amplitude of about 800 μV to the exact location where the cortical surface of the transgenic rat, practicability of the transparent active MEA have been demonstrated. The results in this chapter were published in the *PNAS* magazine titled "Transparent, conformable, active multielectrode array using organic electrochemical transistors".

Chapter 4 Development of Biocompatible Flexible MEA capable of Elongation and Shrinkage Using OECTs

In this chapter, the realization of biocompatible, stretchable active (4 × 4) MEA using OECT was described. This device was able to show high compatibility and biocompatibility by using PMC 3 A coating material for OECT on a 1.2-μm-thick stretchable parylene honeycomb grid. The stretchability of OECT on a honeycomb grid showing a linewidth of 40 μm was demonstrated by applying 15% elongation strain at 1000 cycles. Biocompatibility of PMC3A was demonstrated by platelet adhesion tests on devices or films. On the substrate with low biocompatibility, platelet membrane is formed due to the activation of platelets, which interferes with signal measurement, resulting a decrease in the time response of OECT. PMC3A uncoated OECT deteriorated from 0.5 hour platelet adhesion until the response rate of 60 μs exceeded 50 ms on the other hands, the response rate of PMC3A coated OECT increased 60 μs to 87 μs even after 2 hours. Finally, the practicality of biocompatible, stretchy active (4× 4) MEA is to record electrocardiography (ECG) in dynamically moving hearts of rats with multiplexing. We succeeded in stably mapping ECG signals on a dynamically moving heart using a 4 × 4 OECT array coated with PMC3A. The results of this chapter are currently prepared for another publication.

Chapter 5 Summary

In this study, we developed an active MEA that can be driven by multiple driving using OECT or OFETs fabricated on a flexible substrate with a thickness of 1 μm or less. Ultra-thinness gives the device high conformality and can be easily contacted with complicated surfaces such as complex brain surfaces and dynamically moving hearts. Conformal MEA has been demonstrated to be mechanically stable even under severe deformation such as compression. Furthermore, from the mechanical stability and high amplification degree of the conformal MEA using OECTs, bio-medical feasibility was demonstrated by recording various bioelectric signals such as electromyogram (EMG), electroencephalogram (ECoG), electrocardiogram (ECG). Conformal MEA also has transparency, stretchability, and blood compatibility, for measurement compatibility with different biological environments.