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Ion Sensor Array For Electronics – Biological Matter Interface

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Abstract

It is demanded to realize ideal interface device between Electronics and Cell, because electronic devices will be implanted in our body near future. However, in the present, we don't have enough interface yet. A lot of researcher interest electric spike signal for interface. But the electric spike signal is a results in movements of ions in cell. Generally, cells are communicated by Chemical. For example, as a chemical stimulation was done, the ion or neurotransmitter is emitted from the synapses. We thought that the most ideal interface between electronics and cells is ion. If we realize these Ion I/O devices, which can realize ion emission and detection, LSI and cell are fused as one devices.

1. Introduction

One of the merits of fusion for LSI technology with sensor technology is arraying. The LSI sensor technology is able to array more than several thousand devices, and it becomes tools for visualization. Among the five senses of human being, information from our eyes is about 80%. To visualize a phenomenon, it is easy to understand the phenomenon intrusively. Fusion of the sensor technology with the LSI technology change a worth of the sensor from "tools for measurement" to "tools for understanding".

In a biomedical field, imaging technology has become important to understand information of organic activity. Solid state type bio image sensors fused bio-sensor technology with Complementary Metal Oxide Semiconductor (CMOS) technology is an attractive device for bio/chemical imaging tools, because an optical image sensor combined photodiodes and CMOS read out circuits is fabricated with state of art technology. The CMOS based bio image sensor have a potential to acquire local distribution of neurotransmitters, ions and chemical species in a solution and organic matters without optical label.

2. CMOS Ion Image Sensor based on Charge Transfer Technique

An ion image sensors based on a Charge-Transfer-Technique have been studied [1, 2], and have applied them to the field of bio-chemical analyses [3, 4]. We have been developed CMOS based ion image sensor with 32 × 32 (1K) pixel arrangement [5], a 128 × 128 (16K) pixel configuration [6], and1024×1024 (1M) [7] A Charge Coupled Device (CCD) based hydrogen ion image sensor with 1320 ×976 (1.5 M) pixels and 3.75um pixel was developed [8]. These sensors have achieved outputs with lower variability between each pixel than those achieved by other groups because these ion image sensors are handle electrons corresponded on an ion concentration. We believe that optical CMOS/CCD image sensors, which handle electrons, have been developed to realize low noise characteristics with high pixel density and small sensor size [9]. An ion image sensor with a high special resolution, more pixels and a higher frame rate, are required for the underatanding of cell membranes and for the responses of neural networks.

3. Applications for Bio-imaging

Mechanisms of neurotransmitters have been discussed, and these findings are expected to contribute to a deep understanding of a lot of brain functions [10–12]. Acetylcholine (ACh) is an important neurotransmitter in both the central and periperal nervous system [13]. At synapses in neurons, ACh is released and chemically transmitted between neurons and networks. By using the conventional optical approaches involving fluorescence probes and dyes, the neurotransmitter-operated signal propagation was observed [14]. The direct measurement of 2-dimensional distribution of ACh is also possible by the mass spectroscopy [15], however, the cell sample should be fixed before the recording. In terms of real time observation of distribution and/or diffusion of ACh in the living neurons, there is no established methods. In this session, we are introduced a chemical imaging method of the neurotransmitters based on the CMOS type hydrogen ion image sensor [16]. The distribution and diffusion of ACh was able to visible by combining the hydrogen ion image sensor with the ACh-sensitive layer, which consists of acetylcholine esterase (AChE) immobilized with a polyion complex [4] or biotinylated AChE magnetic nano-bead [17]. The developed ACh image sensor could detect the generated hydrogen ion by the ACh-AChE reaction. The enzyme-type image sensor detected a concentration change of hydrogen ion generated by the Ach - AChE enzyme reaction.

A cortical slice was placed on the hydrogen ion image sensor in a slice-side-down configuration. The ion concentration of the images of extracellular hydrogen ion concentration in the cortical slice putting on the sensor surface was slightly lower in the corresponding area where images of slices were observed by a bright field microscopy. No significant changes

were observed in the extracellular hydrogen ion concentration before stimulation. At the resting states, the extracellular hydrogen ion concentration of the slice was 7.35pH. After stimulation with 1 mM glutamate, the extracellular hydrogen ion concentration gradually decreased, and the degree of decrease was more than 0.5pH. The extracellular hydrogen ion concentration stimulated by glutamate decreases were dependent on the presence of AChE, which generate hydrogen ion enzymatically with the reaction of ACh. These results strongly indicate the extracellular hydrogen ion concentration decrease highly reflects the increase of the ACh concentration inside the slice. The ACh should be released from the neurons induced by glutamate. The continuous decrease of extracellular hydrogen ion concentration may be caused by a signal propagation in the neurons or amplification of the ACh release by the unknown mechanism. The spatio-temporal analysis of glutamate-induced ACh dynamics in the non labelled brain slice was carried out by using the bio-image sensors utilized enzymes.

4. Summary

Imaging is an effective way to understand organic activity by visualizing information of organic matters or cells intrusively. It indicates that the fusion changes a worth of the sensor from "tools for measurement" to "tools for understanding". We are certain that the bio- image sensors become a potential tool for the microbiological and medical field and might help to make a new finding of unknown chemical phenomena in micro-scaled structures such as single cells, cell groups and neuronal networks.

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