In vitro Bio-circuit Sensing with Integrated Bio/Semiconductor Platform

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Abstract — This research concept is based on bio-sensing for various biological phenomena such as DNA hybridization, antigen-antibody reaction, metabolism of living cells and so on. Basically, we develop and explore bio-sensing technology by use of semiconductor principle because this unique principle allows to detect ionic charges such as cation, DNA molecules, protein, ionic behaviors resulting in cell-cell communication and so on. These ionic behaviors are fundamental elements of bio-functions, that is, we can understand the ionic behaviors with charges as fundamental media of "bio-circuit". In this paper, we would like to introduce the possibility of semiconductor-based biosensing device for bio-functional analysis in vitro on the basis of "bio-circuit" concept.

In our laboratory, we focus on a direct detection of ions or ionic molecules through ion-channels at cell membrane, because various bio-molecules have charges and most of cell functions are closely related to transferring of charged conductors from cell to cell. In this study, we have clarified that a principle of semiconductor devices based on field effect realizes to detect ion charges in a direct, label-free, real-time and noninvasive manner for bio-functional analysis [1-5]. The principle of semiconductor-based biosensing devices is based on the potentiometric detection of charge density changes induced at a gate insulator/solution interface accompanied by specific bio-molecular recognition events. Ionic charges of ions or bio-molecules at the gate insulator electrostatically interact with electrons in silicon crystal across the thin gate insulator resulting in the threshold voltage change. Particularly, we are interested in DNA molecular recognition events, antigen-antibody reaction, ion transportations through membrane proteins such as ion-channels and ion-pumps at cell membrane and trying to detect ionic behaviors based on biological phenomena using a bio-coupled gate semiconductor. The semiconductor-based biosensing devices have good advantages of label-free, real-time and noninvasive method and we can make an arrayed device for a multi target analysis by use of the conventional semiconductor processes.

In this research, we propose the device structure with three components such as target, signal transduction interface and detection device. Since we utilize the bio-coupled gate semiconductor, we are trying to design the signal transduction interface in order to detect ion charges specifically and selectively based on bio-molecular recognition or each cell function.

In order to detect drug effect on cancer cells, we need to detect ion charges based on programmed cell death “apoptosis” using the bio-coupled gate semiconductor and develop the signal transduction interface to trap them. The previous work showed the possibility of potassium ions, chloride ions and water release from cells in the early stage of apoptosis. Therefore, we have focused on potassium ion release based on apoptosis and succeeded in the real-time, direct and noninvasive monitoring of their flow. In particular, this result was accomplished by use of crown ether monolayer to trap selectively potassium ion as signal transduction interface of the bio-coupled gate semiconductor. Moreover, we have found the possibility of multi-target detection for high throughput screening of drug effect using the bio-coupled gate semiconductor with some transfected cancer cells in this study. Using the bio-coupled gate semiconductor, furthermore, we have succeeded in the real-time and noninvasive monitoring of various cell functions, as follows.

- Interaction between substrate and transporter at cell membrane for drug effect detection
- Embryo activity based on in vitro fertilization (IVF) for assisted reproductive technology (ART)
- Glucose response of pancreatic be-ta cells for insulin secretion
- Differentiation of stem cells such as murine or human iPS cells
- Autophagy for accommodation to starvation
- Other cell functions

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References