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Fabrication of Microfluidic Channel Type Smart Electrochemical DNA Sensors with Operational Amplifiers

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1. Introduction

Smart micro chips, which are integrated several circuits in a sensor, are attractive candidate for human sensing tools, because they will sense some physical and/or chemical phenomena with high sensitivity and high functionality. DNA chips are one of the tools for gene diagnosis. Previously we reported novel microchips integrated microfluidic reactors and sensors in a same chip [1]. In the proposed integrated DNA chip, hybridization of DNAs is successively carried out using laminar flow in microchannel reactor and the hybridizations are detected by electrochemical method. In this paper, we present new smart micro DNA chips, which integrated with electrochemical sensor, microreactor and operational amplifiers. Conventionally relatively big and expensive measurement system is necessary for electrochemical measurement. By the proposed smart chip, a simple electric power source will only be required.

2. Fabrication and Structure

The integrated smart DNA-chip has two-layer structure of glass/silicon. Microfluidic channel reactor (width 1mm, depth 10μm, capacity 100nl) was formed at surface of glass wafer, and Au electrodes (100μm × 900μm), for electrochemical measurement, were fabricated on silicon wafer. Glass and silicon were bonded by anodic bonding technique. The integrated signal processing circuit consists of two operational amplifiers. The designed operational amplifiers are nMOSFET composition. The signal processing circuits are fabricated on a silicon substrate by 5μm n-MOS process.

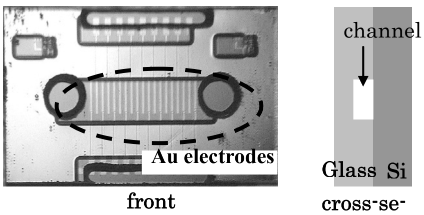

Fig.1. DNA chip for electrochemical measurement

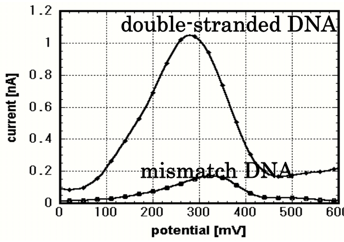

Fig.2. Differential Pulse Voltammograms of double-stranded DNA and mismatch DNA

3. Experiments and Results

Microfluidic Electrochemical DNA Sensor

To confirm the possibility of hybridization detection in the microfluidic channel without fixed probe DNA on electrodes, a flow channel type device as shown in Fig.1 was fabricated and evaluated. Hybridized DNA solution (1μM, 22 bases) with electrochemically active intercalator (25μM) was measured electrochemically in the microchannel. In this experiment the solution was prepared in another conventional chamber previously. For comparison, mismatch DNA solution was measured in the chip similarly. This experiment result is shown in Fig.2. An electrochemical signal from match DNA was observed much higher than that from mismatch DNA. It was confirmed that hybridization detection using microfluidic channel without fixed probe DNA is successively carried out.

Electrochemical DNA Sensor with Two Branch Microfluidic Channel Reactor

Schematic diagram of integrated electrochemical DNA sensors with two branch microfluidics channel reactor is shown in Fig 3. Two kinds of solutions are flowed from each inlet and the solutions make laminar flow in a microchannel. It was expected that hybridization of DNAs occur at a boundary in laminar flow. To detect hybridization by electrochemical method, Au electrodes are placed at the center of the microchannel. Other electrodes are also placed at the side of the channel. Hybridization is only occurred at the boundary and is not reacted on the side electrochemical signal from side electrode is used as reference signal. The proposed microchip integrated with electrochemical sensor and microreactor for hybridization using laminar flow microchannel was fabricated as shown in

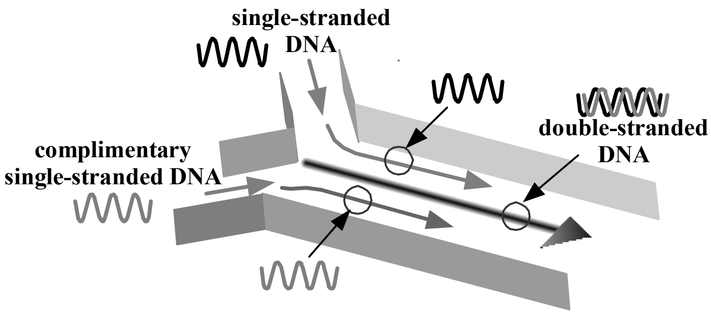

Fig. 3. Schematic diagram of integrated electrochemical DNA sensors with microfluidics channel reactor

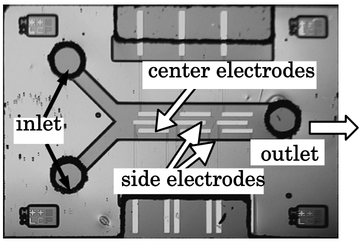

Fig.4. DNA chip (10mm × 7mm) integrated electrochemical sensor with microreactor

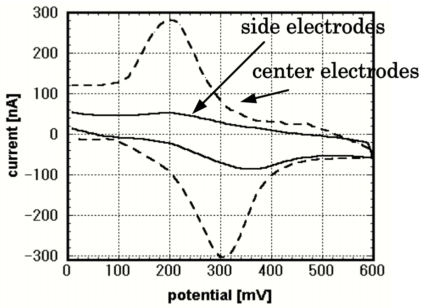

Fig.5. Cyclic Voltammograms of center electrodes and side electrodes

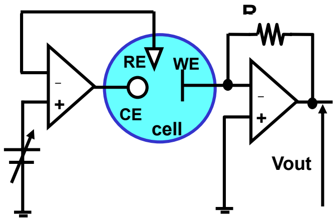

Fig.6. The measurement system configuration for Cyclic Voltammograms by Operational Amp.

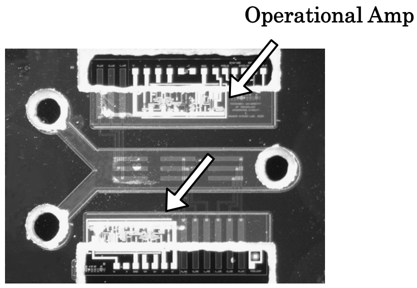

Fig.7. Smart DNA chip (10mm × 7mm) integrated electrochemical sensor, two branch microfluidics channel reactor and two operational amplifiers.

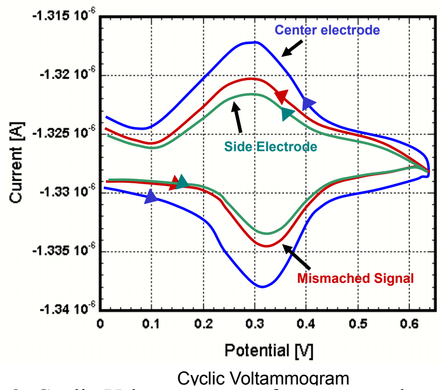

Fig.8. Cyclic Voltammograms from center electrodes, side electrodes, and mismatched DNA

Fig.4. Probe DNA solution (1μM, 22 bases) and complementary target DNA solution (1μM, 22 bases) was flowed into microchannel from each inlet. Probe DNA and complementary target DNA solution, which was added electrochemically active intercalator, have flowed into a micro channel. The microchip has detected hybridization of DNAs only at the center portion as shown in Fig.5. Therefore, signal from side electrode is able to use reference signal. DNA solutions, mismatched each other, were flowed from the inlet of each micro channel, and electrochemical measurement was performed, and Cyclic - Voltammograms signal is small compared with matched DNA solutions. From these results, detection of DNA hybridization can be performed using the integrated DNA chip.

Smart DNA Sensor with Operational Amplifiers

Smart microfluidic-DNA sensor with the signal processing circuit for the electrochemical analysis is fabricated. Generally electrochemical measurement system is relatively large and expensive. Using the proposed smart chip, the Cyclic-Voltammograms signal will be measured by only a simple electric power source. The analogue signal processing circuit consists of two operational amplifiers. The measurement system configuration is shown in Fig.6. The operational amplifiers are designed by nMOSFET. A photograph of the smart microfluidic DNA sensor is shown in Fig.7 Using this sensor, electrochemical measurement was carried out without special measurement system. The results are shown in Fig.8, and hybridization signal was observed using this smart chip. The Cyclic- Voltammograms signals are same as that by special measurement equipments. The signal from the center electrodes and the side electrodes were detected, and the differences were observed. From these results, we can fabricate smart micro-fluidic DNA sensor.

4. Conclusions

Smart micro DNA chips, which are integrated with electrochemical sensor, microreactor and operational amplifiers, were fabricated, and .electrochemical measurement was carried out without special measurement system. The hybridization signal was successively observed using this smart chip.

Acknowledgements

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References

[1] C.Oda, K.Sawada, T.Tsuchiya, H.Takao. M.Ishida, Proceeding of μ-TAS2003 (Seventh International Conference on Minitureized Chemical and Biochemical Analisys Sysytems) (2004) 371.