Design and Fabrication of Smart All-in-one Chip for Electrochemical Measurement

Tomoyuki Yamazaki^{1,2}, Takaaki Ikeda¹, Makoto Ishida^{1,3}, and Kazuaki Sawada^{1,3}

¹Department of Electrical and Electronic Engineering Toyohashi University of Technology

1-1 Hibarigaoka, Tempaku-cho, Toyohashi 441-8580, Japan,

Phone: +81-532-44-1306 E-mail: yamazaki-t@int.ee.tut.ac.jp

²HIOKI E.E. E. CORPORATION, 81 Koizumi, Ueda, Nagano, 386-1192, Japan

³JST, CREST, 1-1, Hibarigaoka, Tempaku-cho, Toyohashi 441-8580, Japan

1. Introduction

Electrochemical sensors have potential applications in the field of fuel cell industry, environment assessment, bio-industry, etc. A significantly small sensing system is desirable especially for measuring a living tissue due to less invasiveness and capability of local measurement. The system makes it possible to analyze a detailed mechanism of organic activities. In addition to sensor electrodes, signal processing circuits are expected to be miniaturized to realize this due to two factors, 1) the fully miniaturized system reduces burdens while measuring, and 2) amplification near the sensor can reduce ambient noise coupling on the transmission line.

There are only few reports on miniaturizing the full sensing system [1] because of the following limitations. First, a reference electrode (RE) which is an indispensable factor for conducting electrochemical measurement is usually external. Common RE is made of Ag/AgCl surrounded by solution whose chloride ions (Cl⁻) maintained at constant level and connected to the sample solution through a glass container, which is usually much larger in size than the chip. Second, standard CMOS production site does not contain instruments for fabricating sensor electrodes including a platinum electrode. Third, voltage applying circuits are generally off chip to generate signals of various wave forms. Due to these limitations it is difficult to fabricate sensors and circuit on the same chip. Recently reported CMOS based electrochemical sensor does not include RE or signal generating circuits on the chip [2-4].

In this study, initially, an operational amplifier (OPAMP) composing a potentiostat was improved from our previous report [4] to acquire stabilized signals. Furthermore, in order to integrate every function for electrochemical sensing to realize a chip-sized electrochemical measurement system, we have designed and fabricated the functional chip. Only supply voltages are needed to conduct cyclic voltammetry (CV). This is the first time ever reported all the components of electrochemical sensing incorporated on a single chip.

2. Experimental

The equivalent circuit diagram of sensor electrodes and the signal processing circuit is shown in Fig. 1. The output terminal of OPAMP1 is connected to the counter electrode (CE), which is a large capacitive load of about 500 pF. A single staged OPAMP, telescopic OPAMP was designed as OPAMP1 because of its stability for a larger capacitive load. The SpectreS, Cadence simulation result of the OPAMP1 characteristics with 500 pF load capacitance is shown in Fig. 2. A phase margin at unity gain frequency is calculated to be 90° .

Fabrication process was based on 5.0 μ m silicon technology starting from 4-inch n-type substrate and p-well process. The threshold voltage of NMOS and PMOS were achieved experimentally 0.68 V and -1.18 V, respectively, which fits well to the designed value of 0.76 V and -1.19 V, respectively.

After dicing, a 5 mm square chip was attached to a 17 mm square package, and then chip was wire-bonded and molded. Ag/AgCl ink was put on the chip and dried. (See Fig. 3) Then chip was cleaned by using piranha solution $(H_2SO_4 : H_2O_2 = 3:1)$.

The triangular wave was generated as an input signal by using OPAMP oscillation. Signal generating circuit diagram is in Fig. 4. OPAMPs are fabricated on the chip, while capacitance and resistance are external but installed beside the chip.

3. Results and Discussion

Triangular wave was generated using OPAMP inside the chip. Cyclic voltammetry (CV) measurement was conducted to evaluate the chip, where sample solution of well-studied potassium ferricyanide (K₃[Fe(CN)₆]) was used at various concentrations. The potassium ferricyanide was dissolved in 0.1 M phosphate buffer solution (PBS) and saline in order to keep the Cl⁻ concentration constant and to stabilize RE potential. The sample volume of 20 µl was put on the chip and potential between RE and WE was swept upward and then downward through the potentiostat. The reaction current at WE was monitored and clear CV curves were achieved. The CV curves of 0.0 mM to 2.0 mM of potassium ferricyanide are shown in Fig. 5. The cathodic peak current dependence of sample for different concentration is shown in Fig. 6. The obtained linear trend is similar to the predicted theoretical behavior [5].

4. Conclusion

We have demonstrated for the first time the electrochemical sensor chip where the signal generator, a potentiostat, and the sensor electrodes are integrated. The chip circuit and layouts were designed, simulated and fabricated. By measuring $K_3[Fe(CN)_6]$ in 0.1 M PBS and saline solution, clear CV curves were observed. The cathodic CV peak current dependence of varying sample concentration showed a linear relationship, fitted well to the theoretical trend. In addition, one of the OPAMPs which compose a potentiostat was improved to drive large capacitive load as

500 pF.

The chip-sized electrochemical measurement will intensify the trend of miniaturizing sensing system and open up a new opportunity for less-invasive and local measurements for living things.

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Fig. 1 Equivalent circuit diagram of electrochemical measurement system composed of three electrodes (working electrode (WE), counter electrode (CE), and reference electrode (RE)), potentiostat which contains two operational amplifiers (OPAMPs), and signal generating unit V1. R1 is read out resistance.



Fig. 2 Simulation results using SpectreS, Cadence. Gain (solid line) and phase (dashed line) characteristics of a telescopic operational amplifier with capacitive load of 500 pF. At unity gain frequency (90 kHz), phase margin is calculated to be 90° indicating robustness for large capacitive load.



Fig. 3 Packaged chip. Three types of electrode; working electrode (WE), counter electrode (CE), and reference electrode (R), and circuits (under adhesive) are incorporated on the chip.



Fig. 4 Triangular wave generation circuit. External R1 to R3, and C1 are connected to the on chip operational amplifier (OPAMP). Under the condition of R1 = 660 Ω , R2 = 2 k Ω , R3 = 1.5 M Ω , and C1 = 3.3 μ F, oscillation frequency was about 0.91 Hz.



Fig. 5 (a): Triangular wave generated by oscillation circuit (right axis). (b): Cyclic voltammetry (CV) curves acquired at 0.0, 1.0, and 2.0 mM of K_3 [Fe(CN)₆] / 0.1 M phosphate buffer solution (PBS) and saline (left axis). Peak current increases with increasing concentration of the solution.



Fig. 6 Cathodic peak current versus K₃[Fe(CN)₆] concentration.