

Amperometric Electrochemical Sensor Array for On-Chip Simultaneous Imaging

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Abstract

We presented an amperometric electrochemical sensor array using CMOS technology. The proposed sensor successfully demonstrated the individual and simultaneous measurements of multi-point redox currents.

1. Introduction

Recently, there has been a growing interest in array-based biosensors for rapid and high-throughput analyses [1,2]. Fluorescence measurement with high sensitivity and a variety of commercially available tools has been developed. However, it has two drawbacks: one is performance degradation due to shielding by a turbid solution or vessels, and another is necessity for labeling nonfluorescent species. An electrochemical detection method outperforms fluorescence measurement because it can eliminate optical interference and thus achieves low cost and simplicity. Amperometric electrochemical sensor array with microelectrode arrays (MEAs) has great potential for multi-point rapid detection. The principle of amperometry is based on the measurement of the current induced by a redox reaction at the working electrode (WE). The microelectrode has a steady-state current response in unstirred solutions and addressable microelectrodes can be arrayed in an integrated circuit [3,4]. However, since it takes a few or tens of seconds before reaching a steady state, rapid multipoint measurement cannot be achieved with a simple switching scheme. Until now, we have proposed a MEA structure with auxiliary electrode (AE) to suppress diffusion layer expansion over MEA [5]. In this work, we designed and fabricated CMOS amperometric electrochemical sensor array circuit exploiting MEA with AEs. The proposed circuit successfully demonstrated the individual and simultaneous measurements of multi-point redox currents.

2. Switching Circuit with Dual Switch

The multi-point measurement requires switching of the readout electrodes. Fig. 1 shows the proposed amperometric electrochemical sensor array circuit. Each electrode is connected to two switches. The electrode being measured is connected to the readout circuit via switch SWA, and on stand-by, the potential is fixed via switch SWB to maintain the steady-state current. When the reading electrode is switched, either switch of the two is kept closed. Therefore, the switching is carried out while the steady-state current is maintained. In order to suppress electrode potential fluctuation due to the switching, we employ a current buffer circuit.

In this case, the role of dual switch is to keep the output voltage of current buffer circuit constant and eliminate the charging and discharging of data-line, providing a rapid measurement. Besides the role that electrode potential is fixed at a certain voltage, low input impedance and low-current detection are required for current buffer circuit. The designed current buffer circuit consists of a source follower, a differential amplifier and a current mirror to copy current ($I_{out}=I_{in}$) (Fig 2(a)). The measured electrochemical reaction using the current buffer circuit is shown in Figs. 3(a) and (b). From the results, the detection lower limit found to be approximately 1 pA.

3. MEA structure

The implemented MEA structure in this study is shown in Fig. 4(c). The WE is surrounded by a grid AE, and the redox reaction opposite to the WE occurs in the AE [5]. Therefore, the diffusion layer is confined around the WE, and the overlap of diffusion layers is decreased. As shown in Fig. 4(d), current in conventional MEA continuously decreased and steady-state current was not obtained. By way of contrast, in the case of MEA with AEs, the steady-state current is obtained and amplified by redox cycling and the time required for reaching the steady-state is dramatically reduced.

4. Implementation of Amperometric Sensor Array

Using the current buffer circuit, a 16×16 amperometric sensor array was designed and fabricated, as shown in Fig 5(b). We integrated an on-chip I - V converter and a digital control circuit to address the electrodes individually (Fig. 5(a)). The read-out control circuit was employed to address the microelectrodes individually one at a time. The I - V converter amplifies the current and converts it to voltage. The measured readout time for all electrodes is approximately 0.7 ms and the measured power consumption is 0.425 W/chip. Fig. 6(b) shows the four cyclic voltammograms of 256 simultaneous measurements for 10 mM $K_4[Fe(CN)_6]$. On-chip gold microelectrodes (10 μ m×10 μ m), external Ag/AgCl, and a Pt wire were utilized as working, reference, and counter electrodes, respectively. Steady-state limiting currents of 20 nA was confirmed.

5. Conclusions

We have proposed an amperometric electrochemical sensor array circuit for rapid and simultaneous measurement. Local amperometry using MEA surrounded by a grid AE and the multi-point simultaneous measurement were demonstrated by using the proposed circuit. These results

indicate that this amperometric sensor circuit can apply to the local concentration measurements and analysis of diffusion processes of target molecules.

References

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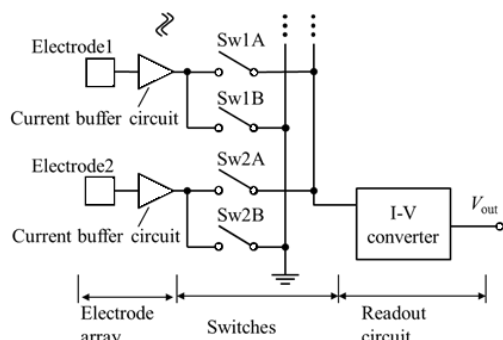


Fig. 1 Proposed amperometric electrochemical sensor circuit. Each electrode is connected to two switches. An electrode under measurement is connected to the readout circuit via "switch A", and otherwise the potential is fixed to maintain steady-state current via "switch B" during stand-by. Current buffer circuit suppress electrode voltage variation due to the switching

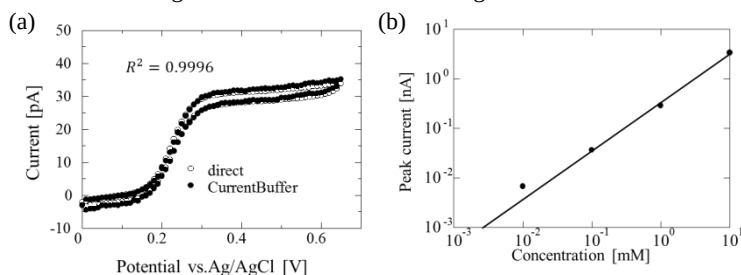


Fig. 3(a) Cyclic voltammograms for 0.1 mM $K_4[Fe(CN)_6]$ in 100 mM Na_2SO_4 using current buffer (black dots) and without circuit (white dots). Off-chip gold microelectrodes (10mm diameter), Ag/AgCl, and a Pt wire were used as working, reference, and counter electrodes, respectively. (b) Peak current of CV measurement at each concentration. From the results, the detection lower limit is approximately 1 pA.

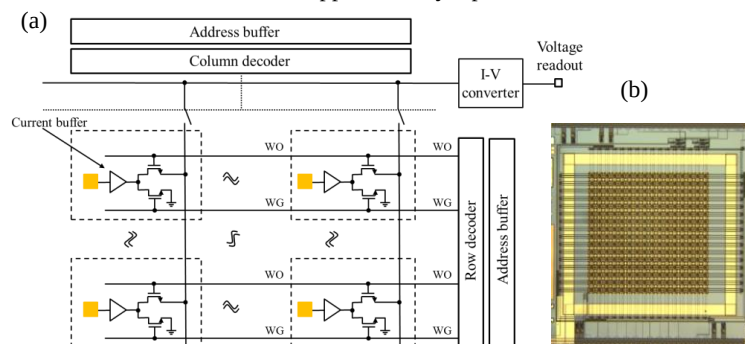


Fig. 5 (a) Block diagram of the amperometric sensor array CMOS chip. We integrated an on-chip I-V converter and a digital control circuit to individually address the electrodes. (b) Microphotograph of the 16x16 amperometric sensor CMOS chip. The chip size is 7.5mmx7.5mm.

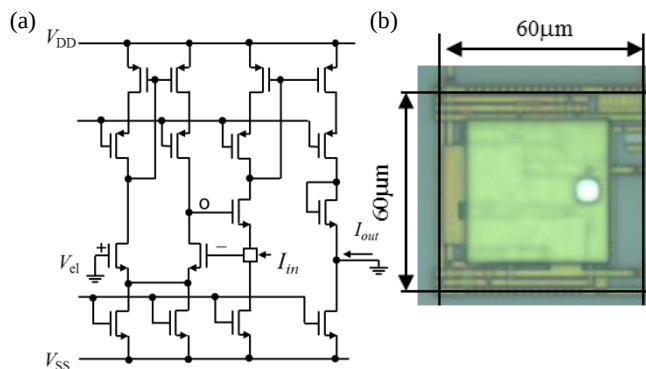


Fig. 2 Current buffer circuit.

(a) Schematic diagram. (b) Microphotograph. Chips were fabricated with a 0.6 μm , 2-poly, 3-metal standard CMOS process. This circuit employs source follower and differential pair to fix electrode potential at V_{el} as well as current mirror to copy current ($I_{out} = I_{in}$).

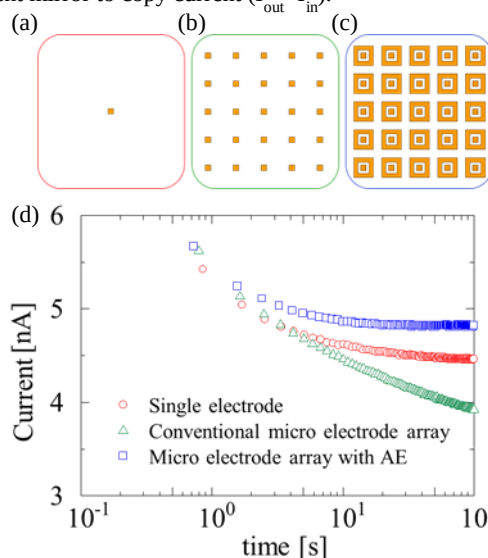


Fig. 4(a) Single electrode. (b) Conventional micro electrode array. (c) Micro electrode array with AE. (d) The time course of the electrochemical current of 100 mM Na_2SO_4 and 1 mM $K_4[Fe(CN)_6]$ measured. On-chip gold microelectrodes (25 μm x25 μm), Ag/AgCl, and a Pt wire were used as working, reference, and counter electrodes, respectively. The WE and the AE potential were fixed at 0.65 V and 0 V (vs Ag/AgCl), respectively. The steady-state current is amplified by redox cycling, and the time to reach the steady-state is reduced.

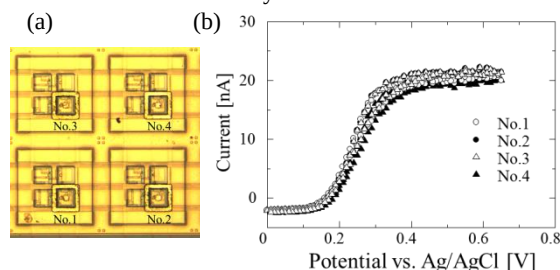


Fig. 6 (a) Microphotograph of on-chip sensor units. (b) Four cyclic voltammograms of 256 simultaneous measurements for 10 mM $K_4[Fe(CN)_6]$ in 100 mM Na_2SO_4 . On-chip gold microelectrodes (10 μm x10 μm), external Ag/AgCl, and a Pt wire were used as working, reference, and counter electrodes, respectively.