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Portable Electrochemical Sensing System Attached to Smartphones and Its Incorporation with Paper-based Electrochemical Glucose Sensor

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ABSTRACT

This paper described the development of a small and low cost biosensor consisting of a smartphone-based electrochemical biosensor device and a paper-based biosensor. The device harvested power from the smartphone and transferred data through audio jack. We designed CMOS circuits including a power supply circuit, a potentiostat, and a ΔΣ modulator. The fabrication of a paper-based biosensor was simple: the three electrodes were directly drawn on chromatography paper using a carbon pencil. The paper-based biosensor was low cost, disposable, portable and friendly to the environment. The sensing system was designed to perform the chronoamperometry measurement, and the glucose concentration in a liquid specimen was detected. Results showed that the sensing system was capable of measuring the glucose concentration as precisely as expensive equipments.

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1. INTRODUCTION

In recent years, preventive health care at a low cost for the medical cost reduction has gathered attention because of the increase of patients with the lifestyle-related disease [1]. Under this circumstance, the point-of-care testing (POCT) market is expected to grow. As a platform for the POCT, the smartphone is a promising device because it has been spread all over the world [2]. Studies utilizing smartphones for biosensing have been actively conducted. These biosensors have been used in various detection methods, such as color-based detection [3], luminescence-based detection [4] and electrochemistry-based detection [5]. Electrochemistry-based detection provides quantitative information by measuring the current, and it is widely used in blood glucose sensors. In order to utilize the smartphone as a platform for the POCT effectively, the miniaturization of a biosensor is crucial. Biosensors based on chromatography paper are attractive because of its small size and low cost. As methods for fabricating the electrode on a paper, pen drawing [6], pencil drawing [7],[8], and inkjet printing [9] have been studied.

The conventional studies report the sensing system connected to the earphone jack of the smartphone [5],[10]. It is capable of drawing electric power from the smartphone without the external power supply devices, and it is also possible to provide an appropriate advice to users by sending the measurement results to the experts. However, these studies have some problems such as the use of the potential measurement which can be used only for limited types of analytes [10], a high cost due to the use of screen printed electrodes (SPE), and inconvenience due to the use of a large device [5]. Therefore, it has not been

able to achieve a small and low cost sensing system. We fabricate a biosensor by merely drawing the electrode with a carbon pencil on chromatography paper [7],[8]. This biosensor is not only fabricated in the simplest way. It also realized a low cost, disposable and portable sensor, so it is considered to be optimal for use in combination with the sensing system attached to the smartphone.

In this paper, using the sensing system attached to the smartphone and a paper-based biosensor by drawing the electrode with a carbon pencil on chromatography paper, we carry out a glucose measurement by the chronoamperometry (CA) method. This study is expected to realize the sensor which can diagnose the health conditions for anyone, anytime and anywhere.

2. EXPERIMENTAL METHOD

We conduct the glucose measurement using the sensing device in connection with the iPod touch (MD723J/A, iOS 9.2, Apple Inc.) (Figure 1(a)). The CMOS chip mounted on the sensor device is designed in our laboratory and fabricated in a standard CMOS process (TSMC 0.35μm 2P4M) (Figure 1(b)). The CMOS chip consists of a power supply circuit, a potentiostat, and a ΔΣ modulator. The selector switch changes the electrochemical potential applied to the solution, and a USB connector is used for the connection with a paper-based biosensor that generates the electrochemical current corresponding to the analyte concentration. The roles of the sensor circuit are measuring the current generated by the reaction of the analytes, and transferring the data to the smartphone via earphone jack.

The block diagrams of the sensing system are shown in Figure 2. The power supply circuit converts the AC voltage from the right channel to the DC voltage to be supplied to the entire circuit (Figure 2(b)). The power supply circuit consists of a transformer, a CMOS bridge rectifier circuit, a storage capacitor, and a regulator (Figure 3). It outputs the constant voltage about 2.7V after amplitude transforming, full-wave rectification and smoothing. The potentiostat conducts the measurement of the electrochemical current generated by the reaction of the analytes, and the output (analog signal) is fed into the ΔΣ modulator (Figure 2(c)). The circuit diagrams of the potentiostat and the operational amplifier are shown in Figure 4 (a) and (b). The potential between the working electrode (WE) and the reference electrode (RE) is controlled by the V_{IN}, and is given by the V_{CM} □ V_{IN}. Since V_{OUT} = □□R_F I_{cell} + V_{CM}, the output voltage reflects the current generated by the electrochemical reaction of the analytes (I_{cell}). The ΔΣ modulator performs analog-digital (A/D) conversion, and its digital output is transferred to the iPod touch via the microphone (Figure 2(d)). The ΔΣ modulator consists of a switched capacitor, an integrator, a clocked comparator, and a 1bit digital-analog converter (DAC) (Figure 5). It performs A/D conversion by the pulse density modulation (PDM) (sampling rate: 2.5 kHz), where the number of the pulse changes according to an analog input value.

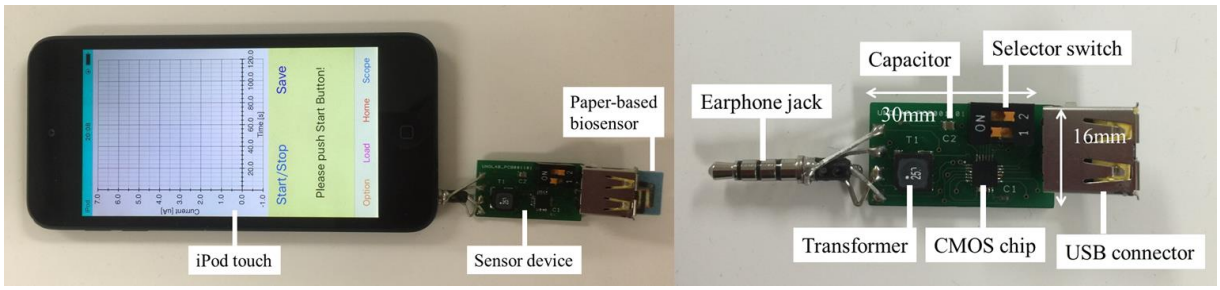
Chromatography paper (Whatman 1CHR) and the carbon pencil (Staedtler Mars 6B grade, Germany) are used for the fabrication of the paper-based biosensor [7],[8]. The pattern of the hydrophobic area is printed by the wax printer (Xerox ColorQube 8580), and then the printed paper is heated in an oven at 120°C for 1 minute. The size of the hydrophilic area is 5mm x 5mm and the total size is 17mm x 12mm (Figure 6(a)). The three electrodes (working electrode (WE), reference electrode (RE), and counter electrode (CE)) are directly drawn on the chromatography paper using the carbon pencil, and the surface areas of all electrodes are 1mm x 5mm (Figure 6(b)). The parasitic resistance value of each electrode is about 10-20kΩ. In order to generate the current in accordance with glucose concentration, it is necessary to provide with an enzyme layer on the electrode. The biochemical reaction shown in Figure 7 is used for detecting glucose in this work:

$$\beta\text{-D-glucose} + \text{GOD-FAD} \rightarrow \text{GOD-FADH}_2 + \delta\text{-D-gluconolactone}, \quad (1)$$

$$\text{GOD-FADH}_2 + 2[Fe(CN)_6]^{3\square} \rightarrow \text{GOD-FAD} + 2[Fe(CN)_6]^{4\square} + 2H^+, \quad (2)$$

$$2[Fe(CN)_6]^{4\square\square} \rightarrow 2[Fe(CN)_6]^{3\square} + 2e^{\square}. \quad (3)$$

Enzyme solution contains a glucose oxidase (GOD, 210units / mg, 074-02401, Wako) (1mg) and a potassium ferricyanide (Ferri, 161-03725, Wako) (2.5mg) in a phosphate-buffered saline (PBS, 0.01mol/l, pH at 25°C 7.0-7.4, 164-18541, Wako) (0.2g). The enzyme solution (5μL) is dropped on the hydrophilic area of the paper-based biosensor, and then it is dried in an oven at 60°C for 5 minutes (Figure 6(c)).



(a) (b)

Figure 1. Overview of the sensing system. (a) Photograph showing the connection of iPod touch, sensor device and paper-based biosensor, (b) The CMOS chip implemented on a PCB board with transformer, capacitor, selector switch and USB connector

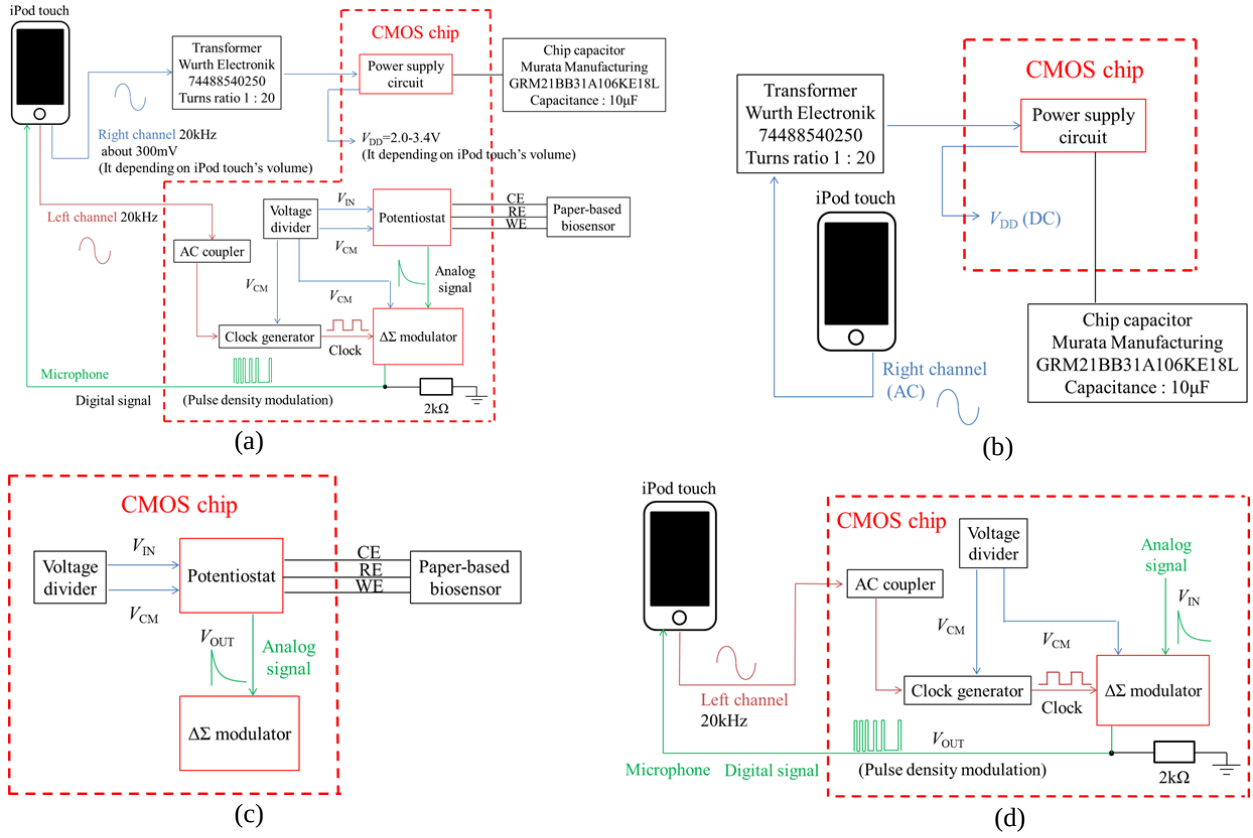


Figure 2. (a) The block diagrams of simplified system: (b) Power supply circuit converts AC voltage from iPod touch to DC about 2.7V supply, (c) Potentiostat transmits resulting output (analog signal) to ΔΣ modulator, and selector switch changes input voltage of potentiostat (V_{IN} = V_{DD}/3 or (17/30) V_{DD}), V_{CM} = V_{DD}/2 is constant, (d) ΔΣ modulator converts potentiostat output to digital signal to be transmitted back to iPod touch via microphone

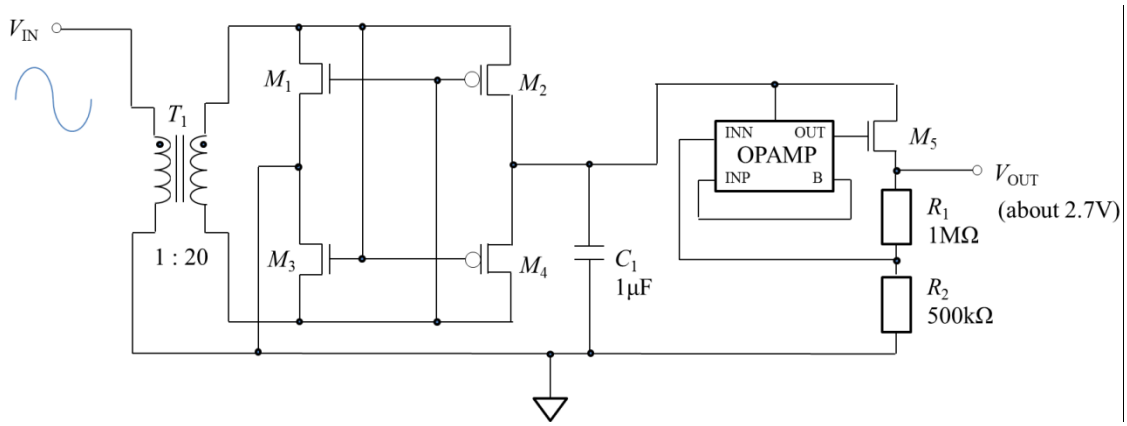


Figure 3. Power supply circuit consists of transformer, CMOS bridge rectifier circuit, storage capacitor, and regulator. The 1:20 transformer boosts input voltage. CMOS bridge rectifiers AC voltage to DC. Regulator outputs about 2.7V

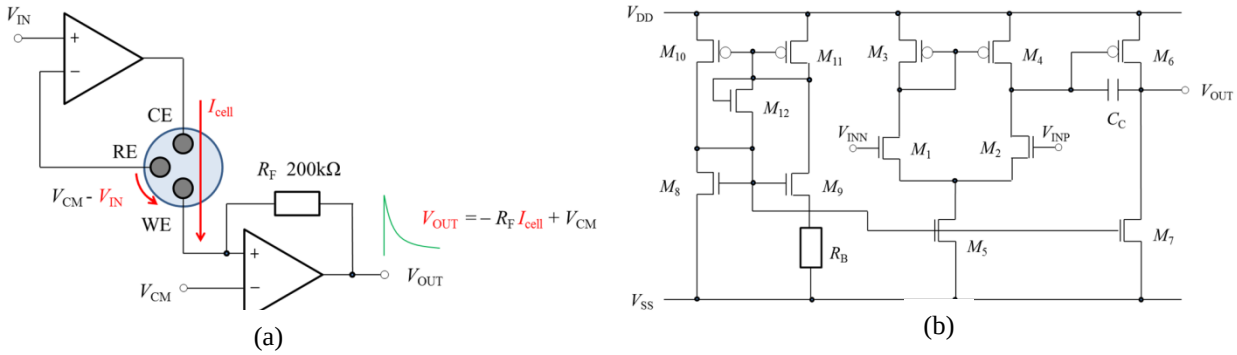


Figure 4. The circuit diagrams of (a) Potentiostat, (b) Operational amplifier. Potentiostat output reflects the current generated by the electrochemical reaction of the analytes (I_{cell})

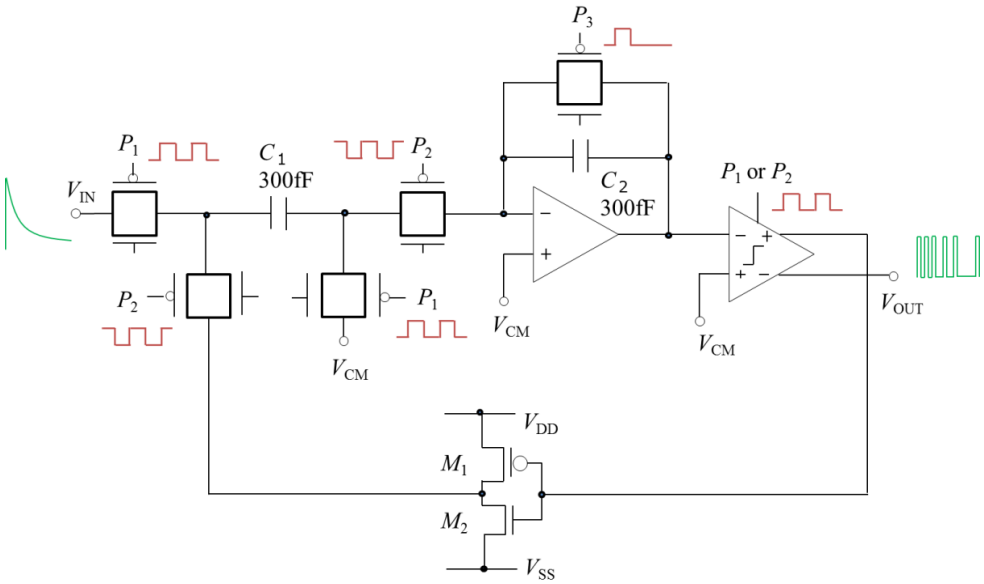


Figure 5. ΔΣ modulator consists of switched capacitor, integrator, clocked comparator, and 1bit DAC. ΔΣ modulator performs pulse density modulation (sampling rate: 2.5 kHz) to transmit digital signal to iPod touch via microphone

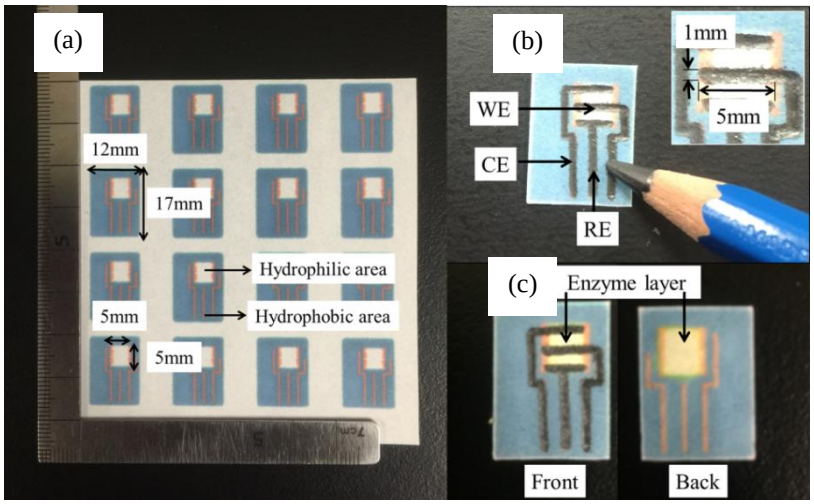


Figure 6. (a) The pattern of the hydrophobic area is printed by a wax printer, (b) Three electrodes (WE, RE, CE) are directly drawn on chromatography paper using a carbon pencil (each electrode is about 10-20kΩ), (c) The enzyme solution is dropped on the hydrophilic area to provide with enzyme layer on the electrodes, and the paper-based biosensor is dried in an oven at 60°C for 5 minutes

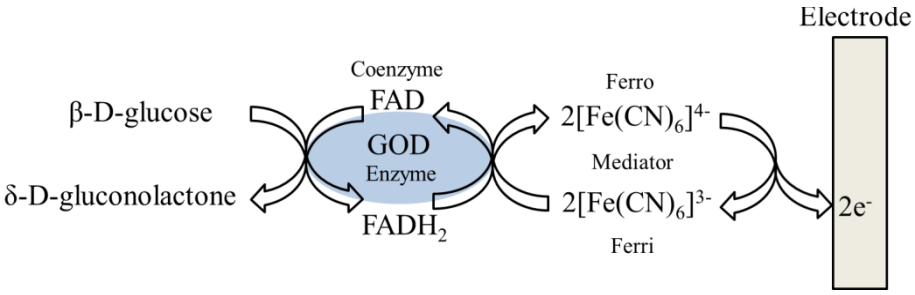


Figure 7. The biochemical reaction for detecting glucose

The measurement method is chronoamperometry (CA), which reads a change in the response current while a constant potential is applied to the electrolytic solution. The time-dependent electrochemical current is represented by the Cottrell's equation as shown below:

$$I = nFAC_{\text{red}}\sqrt{\frac{D_{\text{red}}}{\pi t}}, \quad (4)$$

where n is the number of electrons transferred to the electrode per reaction, F is the Faraday constant, A is the surface area of the working electrode, C_{red} is the concentration of the reduced mediator, D_{red} is the diffusion coefficient of the reduced mediator and t is time. The current increases in proportion to the concentration of the reduced mediator, and decreases inversely proportional to the square root of time. The evaluation of CA measurement is conducted under these conditions (the initial potential between the WE and RE is 0.462V, the sampling period is 0.4096s, and the measurement time is 120s).

3. RESULTS AND ANALYSIS

The CA measurements were conducted using a β-D-glucose (100953, MP Biomedicals,LLC) in a phosphate-buffered saline (PBS, 0.01mol/l, pH at 25°C 7.0-7.4, 164-18541, Wako). We prepared sample solutions of glucose concentrations ranging from 0mM to 10mM. The measurement is started 1 minute after dropping the sample solution (5μL) on the paper-based biosensor by the iOS application developed in our laboratory. The initial potential is applied to the electrodes immediately after the start of the measurement, and then CA measurement is started. The iPod volume was 12 (the maximum volume of iPod touch is 16), and the measurements were conducted 5 times for each glucose concentration.

The screenshots of the application are shown in Fig. 8 ((a) 0mM, (b) 2.5mM, (c) 5mM, (d) 7.5mM, (e) 10mM). The horizontal axis is time [s], and the vertical axis is the current [μA]. A proper operation of the sensing system is confirmed because the current decreases inversely proportional to the square root of time. Fig. 9 shows the average current at each glucose concentration after 120 seconds from the start of the measurement with the application, showing a correlation between the average current and the glucose concentration. The results indicate that the glucose concentration can be successfully determined from the current after 120s.

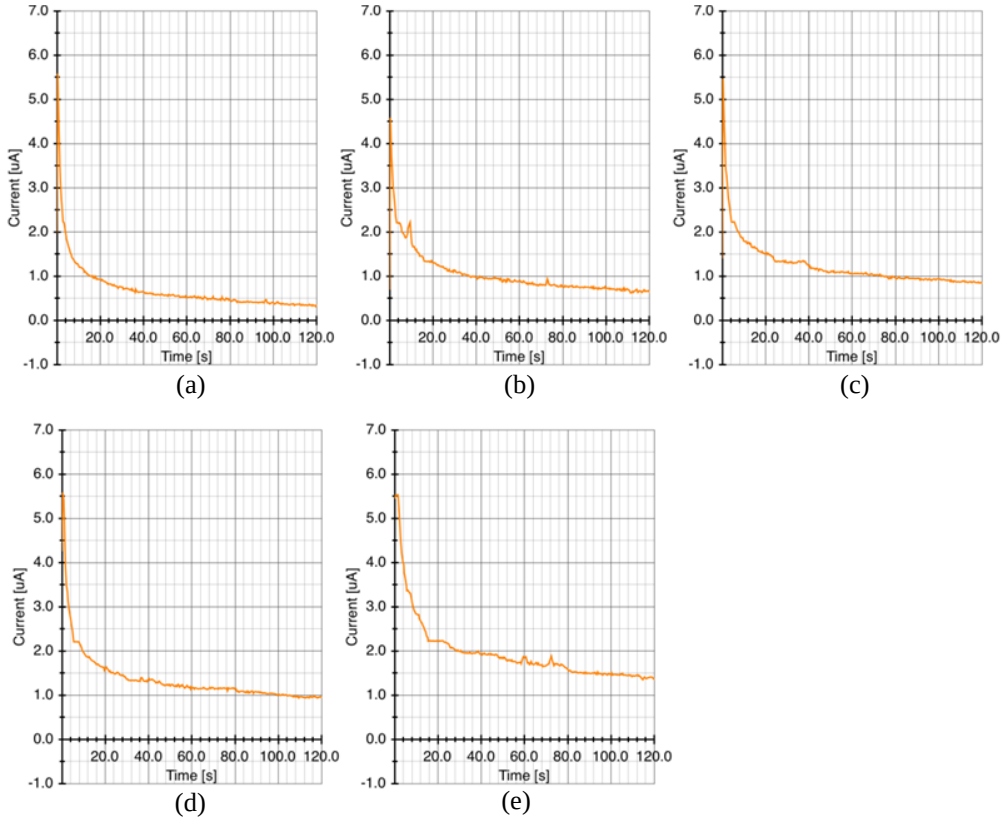


Figure 8. Screenshots of iOS application in the CA measurement. Glucose concentration : (a) 0mM, (b) 2.5mM, (c) 5mM, (d) 7.5mM, (e) 10mM

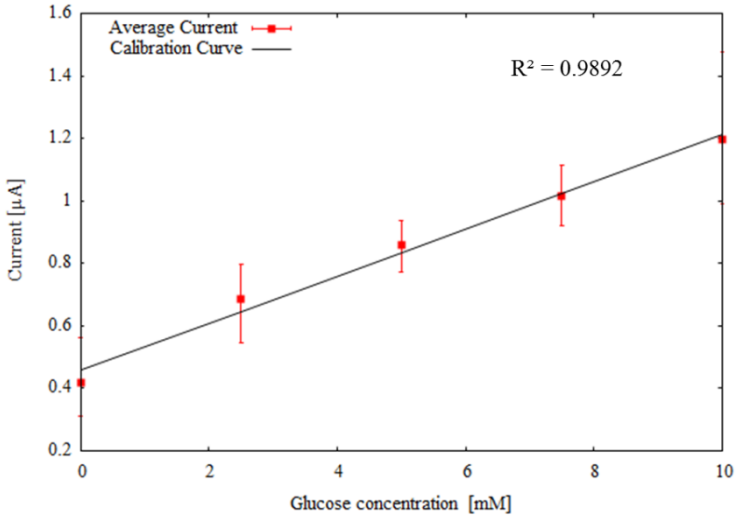


Figure 9. Current vs. glucose concentration at 120s after starting the measurement with an application

4. CONCLUSION

We conducted the glucose measurement ranging from 0mM to 10mM in combination with the sensing system attached to the smartphone and a small and low cost biosensor using chromatography paper and carbon pencil. The capability of the glucose measurement was confirmed because the results show a correlation between glucose concentration and measurement current. The sensing system is expected to be applied to the sensors which are capable of detecting various targets by changing the enzymes and the electron transfer molecules. Further work is in progress for detecting other targets including glycated hemoglobin (hemoglobin A1c) which is one of the indicators of diabetes and identifies the three-month average glucose concentration in blood. Given the possibilities of this small and low cost sensing system, it will contribute to developing mobile health technology.

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