An Integrated Potentiostat

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Abstract **- This paper proposes an integrated potentiostat circuit to realize a compact, power-efficient, and cost-efficient biosensor driving circuit. The proposed potentiostat consists of two integrated operational amplifiers, each of which can be configured with negative feedback to perform potentiostat functionality. When configured as a potentiostat, the control operational amplifier controls the voltage of the counter electrode of the sensor to make the voltage difference between the reference and the working electrodes of the sensor to be identical to the input voltage fed by an external digital-to-analog converter. The other operational amplifier is configured as a transimpedance amplifier which converts the sensing current to the voltage, which is digitally converted by an external analog-to-digital converter. In the experiment, the proposed potentiostat is assembled with digital-to-analog converters, analog-to-digital converters, control-logics, and a laptop computer to form a portable and low-cost bio-sensor platform. With this platform enabled by our chip, users can easily and cost-efficiently generate the necessary control signals such as cyclic waves for bio-sensors.**

I. INTRODUCTION

Various electrochemical biosensors are widely used for health-care or medical applications including monitoring blood glucose levels for diabetic, malaria falciparum, pneumonia, urinary infection, celiac disease [1]. These biosensors are attractive because they do not need experienced staff and large laboratory instruments, and also reduce diagnosis time and cost compared with typical modern medical diagnosis [1].

In order to operate these biosensors at low cost and in a convenient way, a potentiostat, which is a driving circuit for the biosensors, must be miniaturized. For example, potentiostats implemented on a printed-circuit board using an FPGA controller reduced the cost of these biosensors as well as improved the user convenience [1]-[3].

In this paper, we report an integrated potentiostat fabricated in 0.35 μm CMOS technology operating at 3.3 V to further improve the cost and power efficiency of the potentiostat. The potentiostat consists of two operational amplifiers, each of which can be configured with negative feedback to form a potentiostat functionality. A two-stage operational amplifier sets the proper voltage level between the reference and the working electrodes of a sensor while the other three-stage operational amplifier is configured as a transimpedance amplifier to detect small sensing current.

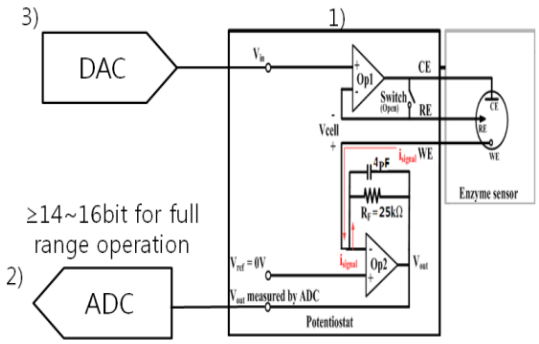

Fig. 1. A typical potentiostat driving an enzyme-based bio-sensor; 1) a potentiostat circuit; 2) an analog-to-digital converter; 3) a digital-to-analog converter.

II. BACKGROUND

Fig. 1 shows a typical potentiostat driving a typical enzyme-based biosensor. A typical enzyme-based biosensor has three electrodes: the working electrode (WE), the reference electrode (RE), and the counter electrode (CE) [1]. At the WE surface, electrochemical reaction takes place. The CE is a conductor that supplies the biosensor output current i_{signal} required for the electrochemical reaction at the WE [1]. The RE is a potential reference to measure the working electrode potential [1]. No actual electrochemical reaction occurs on the RE because current does not flow through the RE due to the large input impedance of the control amplifier (Op1) [1]. By feedback from RE, the control amplifier adjusts the CE voltage and i_{signal} to maintain voltage difference V_{cell} between WE and RE at a constant level V_{in}: the input voltage of the control amplifier driven by a digital-to-analog converter (DAC) [1]. Biomarkers concentration can be measured by monitoring i_{signal} which is proportional to biomarker concentration [1]. This monitoring is usually done by the transimpedance amplifier (Op2), which ideally provides zero-input impedance not to disturb the operation of the bio-sensor

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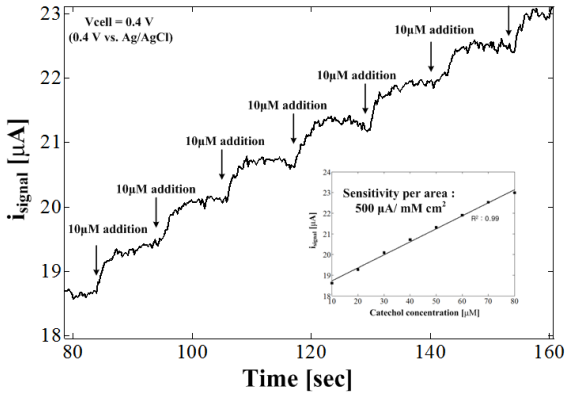

Fig. 2. Steady state current response (amperometry) of the laccase to successive 10μM increments of catechol in PBS [1]. The applied Vcell voltage is 0.4V vs. Ag/AgCl. Inset: isignal vs. catechol concentration.

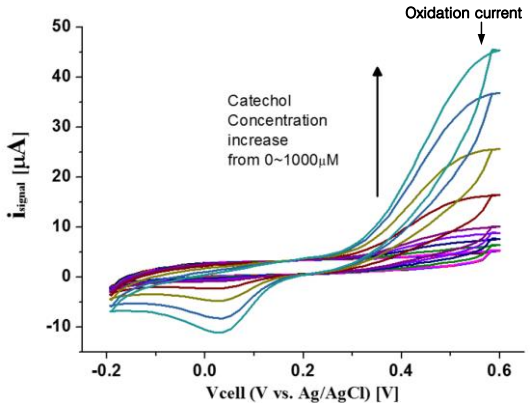

Fig. 3. Cyclic voltammetry curves with various catechol concentrations [1].

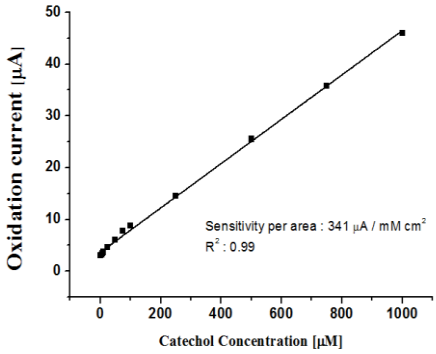

Fig. 4. Oxidation current measured at V_{cell}=0.58V in the cyclic voltammetry of Fig. 3 [1].

while the sensing current i_{signal} is converted to the proportional voltage, so that the following analog-to-digital converter (ADC) can easily read the sensing result in digital code. This current-to-voltage conversion is typically preferable because most commercially available analog-to-digital converters are designed for the voltage inputs. In our design, the two operational amplifiers are integrated in a chip while their input and output nodes are connected through I/O.

III. DRIVING SCHEMES OF BIO-SENSORS

Potentiostats are usually used to measure concentration of bio-materials typically in two ways: amperometry and cyclic voltammetry [1].

In amperometric measurement, the input voltage of the control amplifier (Op1 in Fig. 1) is set to a constant DC voltage while the sensing current is continuously read by the transimpedance amplifier (Op2 in Fig. 1). With a constant input voltage V_{in} in Fig. 1, the V_{cell} voltage must be set to the same DC voltage by the feedback of the control amplifier. With this condition, the sensing current flowing through the bio-sensor is only determined by the concentration of the target bio-material. Hence, by reading the output voltage of Op2, which is linearly proportional to the sensing current, the concentration of the target material can be measured.

Fig. 2 shows an example measurement of amperometric response of a laccase immobilized sensor to successive increments of catechol [1]. In the experiment, a catechol biosensor fabricated by immobilizing laccase on a 250BT electrode is used [1]. In the amperometric measurement, the V_{cell} is fixed to at 0.4V vs. Ag/AgCl, and the sensing current is continuously measured upon the simultaneous catechol addition [1]. In response to successive 10 μo catechol addition, the amperiometric response of the biosensor shows the stair-like sensing current i_{signal} increment. The i_{signal} vs. catechol concentration graph is plotted in Fig. 2 too; i_{signal} in Fig. 2 were obtained from the saturation currents after repetitive addition of 10 μe catechol [1]. As can be seen in Fig. 2, if the sensing current i_{signal} is properly measured, then the concentration of the catechol is proportional to i_{signal}. Therefore, just by applying the appropriate DC input voltage to the potentiostat and continuously monitoring the output voltage, the concentration of the target bio-material can be measured by amperometry.

Cyclic voltammetric measurement method can be also used for the same measurement. Fig. 3 shows an example measurement of catechol concentration by cyclic voltammetry using a potentiostat [1]. Catechol concentration ranging from 0 to 1000 μM is measured at room temperature in the experiment [1]. During cyclic voltammetric measurement, a triangular voltage wave is applied to the input voltage (or equivalently V_{cell}) of the control amplifier (Op1 in Fig. 1). The maximum and the minimum voltages of the applied triangular wave were 0.6 V and -0.2 V, respectively [1]. The scan rate, which is the slope of the triangular wave, was 200 mV/s [1]. While continuously applying the triangular wave, the sensing current i_{signal}, or equivalently the output voltage of the transimpedance amplifier (Op2 in Fig. 1), is continuously monitored. From this measurement, the pair of the measured i_{signal} and V_{cell} are plotted 2-dimensionally in Fig. 3 [1]. The oxidation current of this plot (Fig. 3) is the current level at V_{cell} of 0.58 V, and the measured oxidation current versus the concentration of the catechol is plotted in Fig. 4 [1]. As can be seen Fig. 4, the measured current level is proportional to the catechol concentration. Therefore, the concentration of the target

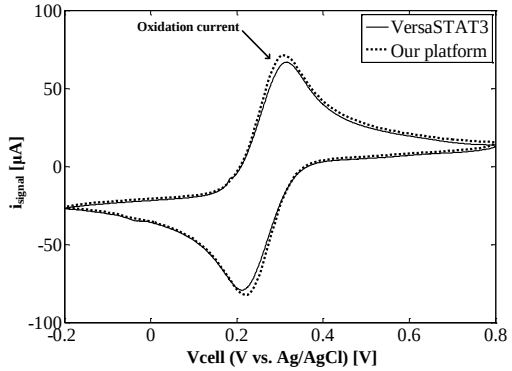

Fig. 5. A cyclic voltammetry curve of 5.0 mM $K_3Fe(CN)_6$ in PBS buffer [1].

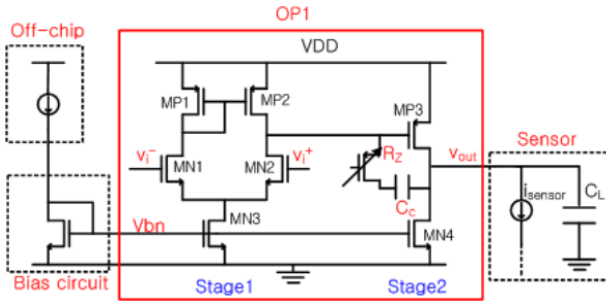

Fig. 6. A schematic diagram of the control amplifier (Op1 in Fig. 1).

bio-material can be measured by cyclic voltammetry by feeding the proper triangular voltage wave the potentiostat and by continuously monitoring the sensing current at the appropriate V_{cell} level.

Although operation of the potentiostat in amperommetric measurement is easier to implement than the counter part in the cyclic voltammetric measurement, cyclic voltammetric measurement has many other advantages. Firstly, the cyclic voltammetry has less random additive noise (Fig. 3) than the amperommetry (Fig. 2). As can be seen in Fig. 2, the sensing current measured in the amperommetry has more random noise than the cyclic voltammetry. Because of the Brownian motion, the measured current has large portion of random noise which cannot be easily distinguished from the sensing current caused by the target bio-material. Secondly, the cyclic voltammetry has much better selectivity to distinguish different bio-materials because different bio-materials have different V_{cell} voltage levels by their nature. For example, $K_3Fe(CN)_6$ has the oxidation current at about V_{cell} of 0.35 V (Fig. 5) [1] whereas Catechol has the oxidation current at V_{cell} of 0.58 V (Fig. 3). Therefore, by reading the sensing current at different V_{cell} levels, we can distinguish the measured concentrations of different materials mixed in the same sample.

Because various kinds of bio-materials are mixed in the sample in a realistic bio-sensing scenario, cyclic voltammetry is more preferable than amperommetry. Therefore, the target operation scheme of the proposed potentiostat is cyclic voltammetry.

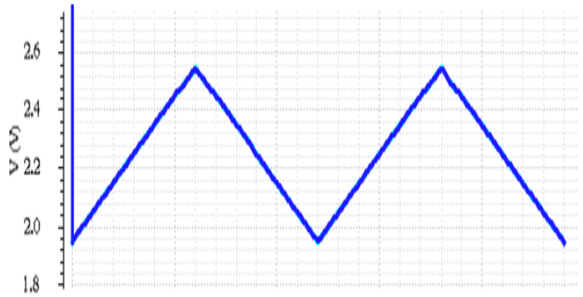

Fig. 7. A simulated output waveform of the designed Op1 in cyclic voltammetry.

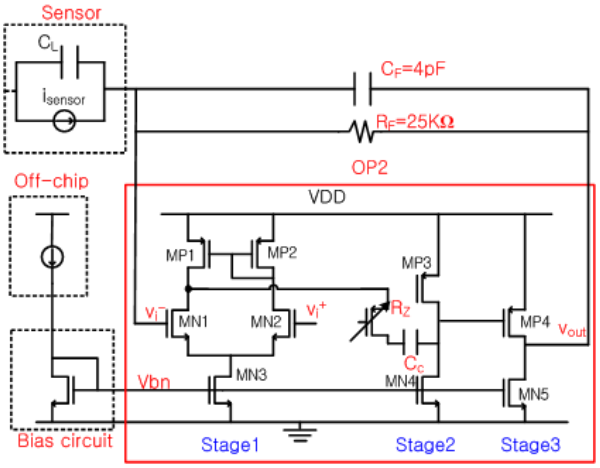

Fig. 8. A schematic diagram of the transimpedance amplifier (Op2, in Fig. 1).

III. CHIP DESIGN

Fig. 6 shows a schematic diagram of the designed control amplifier Op1. The Op1 is designed as a simple two-stage operational amplifier having a pole-zero compensation feedback. In sensor applications, the capacitance of the sensor is not determined because various sensors can be used for the integrated potentiostat, Since the stability of the Op1 strongly depends on the capacitance of the sensor, the pole-zero compensation feedback path is designed so that the feedback resistance can be adjusted. The feedback resistor is a simple MOSFET transistor whose resistance value can be adjusted by tuning its gate voltage. The bias current of Op1 can be adjusted by external reference current. The input nodes v_i^+ and v_i^- as well as the output nodes V_{out} are connected to PADs so that they can be externally observed. For stability, a resistor, which is implemented by a MOSFET transistor, and a series capacitor are used for compensation. Because the supply voltage levels are 3.3 V and 0 V, the reference level in Fig. 1 is increased from 0 V to 1.65 V to realize negative V_{cell} voltage in the actual design. The simulated output waveform of the control amplifier Op1 during cyclic voltammeric measurement is shown in Fig.7.

The transimpedance amplifier Op2 is also designed in a similar fashion. Fig. 8 shows the schematic diagram of the

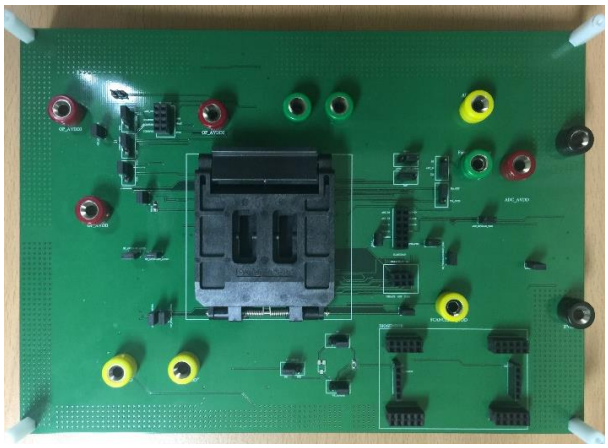

Fig. 9. A photograph of the printed circuit board (PCB) used to assemble the platform.

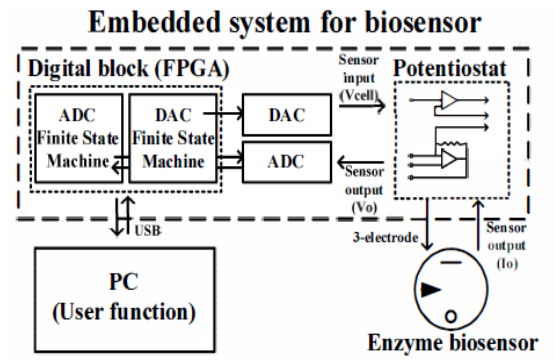

Fig. 10. An overall block diagram of the portable biosensor platform using the fabricated potentiostat [2].

transimpedance amplifier (Op2). The Op2 is driving the current flowing through the load sensor and converts the current to the voltage, which will be read by an ADC. For this transimpedance amplification, the Op2 is supposed to be configured in negative feedback through a 25 kΩ feedback resistor in parallel with the 4 pF feedback capacitor (Fig. 8). Because the 25 kΩ is connected to the output node of the Op2, it can significantly reduce the gain of the Op2 by reducing the total impedance at the output node of the Op2 if Op2's output impedance is not significantly smaller than the 25-kΩ feedback impedance. Because the reduction of the feedback gain of the Op2 will worsen the linearity of the transimpedance amplifier, it will also significantly reduce the accuracy of the overall potentiostat. Therefore, in this design, the Op2 is designed as a three-stage amplifier to guarantee large gain even with a gain reduction by a 25-kΩ feedback impedance. Like the Op1, the Op2 also has the pole-zero compensation feedback circuit between the first and the second stages.

When they are configured as Fig. 1 and connected to a biosensor, the Op1 and Op2 work as a potentiostat and can drive a biosensor with good accuracy.

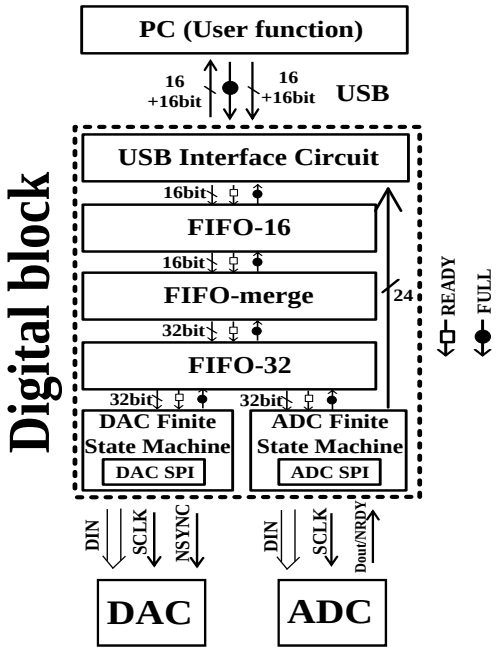

Fig. 11. A block diagram of the digital block implemented in an FPGA. READY: this signal is high, when the transmitting module is ready to transfer data; FULL: it becomes high whenever a receiving module cannot receive data because the buffer is full [2].

IV. IMPLEMENTATION

The chip was fabricated using magna-chip 0.35 μm technology, and 3.3 V supply was used. The effective chip area is only about 1mm x 1mm.

Using the fabricated chip, a compact, completely portable, low-cost biosensor platform is implemented. The platform is assembled on a custom-designed printed-circuit board (PCB) (Fig. 9). Fig. 10 depicts the block diagram of the implemented platform. Our biosensor platform consists of four main block: 1) the analog potetntiostat circuit to process a biosensor signal, 2) interface blocks (ADC and DAC) between analog and digital, 3) digital blocks which generate various control signals for ADC and DAC and also provide a USB interface with a computer, 5) a computer and a software that provides a user-friendly interface easily to run the platform. The fabricated chip is connected with commercial DAC and ADC as shown in Fig. 1 so that it can be digitally operated. The DAC and ADC require fine digital control signals, and these control signals are generated by the control logic which can be commanded by a personal computer (PC) through a USB interface block. The PC can run the designated software to give the command through USB. When a user runs a function of the software, the PC transfers the corresponding message through USB to the digital block implemented in the FPGA (OpalKelly XEM 6002) [1]. The digital blocks are designed based on atomic message passing via first-in-first-out (FIFO) (Fig. 11). All commands and data are carried by messages, whose transfer between buffers are atomically controlled by READY and FULL signals just like handshaking but much more efficiently [4]. In the digital block, the message containing command received from the PC is transmitted to a 12-bit DAC (Digilent PmodDA4) via a FIFO and then is converted to a DAC input by a DAC state machine [1]. Upon receiving the DAC input, the DAC generates the

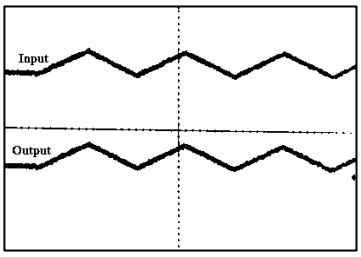

Fig. 12. Measured input and output voltages of the fabricated potentiostat chip.

voltage input V_{in} and the reference V_{ref} [1]. These voltages are fed to the designed chip setting the control voltages V_{cell} (Fig. 1) [1]. When appropriately driven, a biosensor conducts sensing current to the transimpedance amplifier Op2 which converts this current into the proportional voltage [1]. A 24-bit ADC (Digilent PmodAD5) reads this voltage corresponding to the sensing current and converts it into digital number [1]. This number can be acquired and analyzed by the user-friendly software running on PC through the digital blocks and a USB port [1]. By analyzing this digital number, we can obtain the biosensor output current that reveals the target concentration [1].

V. EXPERIMENT

Because the bio-sensors were not fully prepared at the moment of the experiment, R-test is carried to test the fabricated potentiostat [1], [2]. In R-test, the control amplifier Op1 is configured as a voltage follower and a resistor is connected between the output node of the control amplifier Op1 and the transimpedance amplifier Op2. The resistance values are the typical nano-mesh electrode impedance values of an enzyme based biosensor. The input to Op1 is a triangular wave generated by an off-chip DAC and the corresponding output of Op2 is fed to an off chip ADC.

Fig. 12 shows the input and the output of our potentiostat as captured on a digital oscilloscope. The shape of the measured input and output waveforms are almost identical, but the measured noise level is high. The peak-to-peak input-referred noise level is about 1 μA for a nominal input current level of 15 μA.

VI. CONCLUSIONS

We have proposed an integrated on chip potentiostat as a biosensor driving circuit. With our chip, users can easily and cost-efficiently generate the necessary control signals such as cyclic waves for bio-sensors. The potentiostat consists of two operational amplifiers, each of which can be configured with negative feedback to perform potentiostat functionality. The measurement shows that the potentiostat achieved 1-μA peak-to-peak input-referred noise level in R-test.

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