Development of Voltage Amplifier Electronic Reader for Multiplex Detection of Two Electrode Electrical Biosensors

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Abstract. Amperometric electrical biosensors have small current variations at nano to micro range. There are limited number of electrical based two electrode electronic readers for biosensors are commercial available because of the amplification and noise issues at nano to micro ampere current range. The electronic reader focused on design a voltage amplifier circuit to capture and amplify three different range of current as nano, micro and mili ampere and convert it to detectable voltage range as an output voltage signal. Current input as nano, micro and mili current were flown through 10 KΩ, 10 Ω and 10 mΩ resistors, respectively to convert different current inputs to the similar range in micro voltage. Then, MAX 4238 op-amp IC was used to amplify micro voltage to mili voltage. Arduino Uno circuit was act as the process and control circuit to read the output voltage from the amplifier circuit. Arduino Uno circuit will convert analog signal to digital signal and then the output voltage value is display in the LCD screen. The Proteus 8 Pro software was used to design, simulate and calibrate the amplifier circuit and Arduino Uno circuit. While, Arduino software was used to create a programming code and to upload in Arduino Uno circuit. Start your abstract here.

1. Introduction

The experiments of amperometric electrical based biosensor are expensive and time consuming [1], [2]. Because of the detectable range of biomarkers usually in pico molar (pM) to micro molar (µM) concentration and limit of detection (LOD) even goes down to femto molar concentrations for some early detection cases [3]–[5]. Thus, current variation for these concentrations, usually in nano ampere to micro ampere range and some time it goes down to pico ampere range. Therefore high precise equipment is necessary for biosensor research. Commercialization of the biosensors are critical because of the complexity and the large size of the detector systems [6]–[9]. Moreover, most of the electronic reader design only for 3 electrode type instead 2 electrode type for electrical biosensors. Usually most of the electronic readers used 3 electrode type were blood glucose meter which integrated with micro range amplifiers [3], [10]–[14]. Nowadays, very few electronic readers used 2 electrode type for electrical biosensors and capability to detect low current until nano range in commercial. In addition, the use of biosensors included hand held electronic reader provide more potential for commercialization [15]–[19].

Conventional methods of biomarker detection have many draw backs as time consuming, low detectable range, high expensive, depend on lab base experiment and required knowledgeable people...
for testing. Usually this type of methods can identify single disease per time. By using electrical biosensor, the device able go to multiplex analyse [20], [21]. Apart from that, with an electronic reader, lab result can be retrieved much more rapidly, thus saving time and money and in case of emergency, these readers can provide critical information to emergency care provider with the accurate result [22]. Simple devices and techniques such as using proper grounding method, shielded and twisted wire, signal averaging methods, filter, and differential input voltage amplifiers can control the noise in most measurements. Some techniques prevent noise from entering the system, while other removes extraneous noise from the signal [23]–[25].

Almost every industry is now computerized and digitized for rapid data retrieval and trend analysis. In recent years, Arduino microcontroller based open-source hardware projects now popular for control the electrical systems. Moreover, this Arduino microcontroller is not a separate piece but a single board, used to code and upload computer code to the physical board. Other than that, in order to load new code onto Arduino microcontroller can simply use a USB cable. The most important, the Arduino microcontroller hardware is reasonable priced and development software is open-source [26]–[29]. Thus, it can be easily used.

In this paper, we have designed and developed hand held electronic reader which included voltage amplifier and Arduino Uno microcontroller unit (MCU). The reader is specific to two electrode amperometric electrical biosensors and capability to detect until nano, micro and mili ranges. Apart from that, the electronic reader can be used for multiplex analyse. The voltage amplifier is amplified extra small current through sensors from nano-micro-mili ampere range to mili voltage. The MAX 4238 op-amp is used as the amplifier. The mili output voltage through to analog input port of Arduino Uno board. Arduino Uno convert analog signal to digital signal and display the result to LCD display.

2. Material and methods

2.1. Apparatus, equipment and software

The MAX 4238 op-amp was used as operational amplifier to amplify micro voltage to mili voltage. The voltage converter using shunt resistor was used to convert input current into input voltage to the amplifier. Then, LM 358 operational amplifier was used as to supply virtual ground for MAX 4238 op-amp and TPS 3809 was used as battery testing. The external voltage source 9 V DC battery was used to supply power for Arduino Uno circuit. The Arduino Uno Board was act as control circuit and isolate internal voltage source to others circuit. Arduino Uno internal voltage source was used to supply 3 V to amplifier circuit, 1 V to sensor circuit and 5 V to LCD display. Arduino Uno control circuit was used to read the amplify output voltage from MAX 4238 op-amp. LCD display was used to display the amplify output voltage and analog sensor value. Aluminium clip was used as the two electrode electrical biosensor connector. The voltage source was used to supply voltage through variable resistors that acts as a replacement of biosensors to input current to the sensor ports. The Arduino Uno software was used to write program code and uploaded it into microcontroller Arduino Uno board. The Proteus 8 Pro software was used to design and simulate the circuit.

2.2. The Circuit design

Figure 1 shows the detail block diagram for a voltage amplifier for three different range as nano, micro and mili for electrical biosensors. There are six major parts of electronic reader device consists of aluminium clip sensor connection, switches sensors, low noise amplifier, Arduino Uno circuit, DC power supply, and LCD display. The amplifier circuit as voltage converter and voltage amplifier. Sensor circuit input system has included sensor input connectors and three dual select switches to select appropriate sensor to resistors. Arduino Uno has included in isolate power supply and main control circuit. As shown in the figure, amplified voltage output can be detected using microcontroller Arduino Uno and LCD display, acts as a replacement detected using multimeter.
Voltage amplifier circuit was designed using Proteus 8 Pro software as shown in Figure 2. There are four major voltage amplifier circuit parts, voltage converter, MAX 4238 op-amp, power supply circuit, and virtual ground supplying circuit. Figure 2 (a) shows the sensor selection circuit with current to voltage converter by using shunt resistor. There are three switches to select the respective resistor for selected sensors in three different current as nano, micro and milli ampere. Figure 2 (b) shows the MAX 4238 op-amp circuit and Figure 2 (c) shows the power supply circuit which was included with TPS 3809 as battery testing circuit. Figure 2 (d) shows the virtual ground supplying circuit to MAX 4238 op-amp IC. The voltage amplifier circuit was simulated using Proteus 8 Pro software.

Arduino circuit design was act as replacement for multimeter to read the milli output voltage amplifier. As shown in Figure 3, there are four major Arduino Uno circuit parts, included Arduino Uno main control circuit, Arduino Uno internal voltage, LCD display and three selection switches. Figure 3 (a) shows the “ELS ELECTRONIC READER” on LCD display after the Arduino Uno circuit switch ON. Figure 3 (b) shows the “ECOLI” pathogen type with analog value and milli output voltage amplifier on LCD display after the first selection switches been selected. While, Figure 3 (c) and Figure 3 (d) shows the “LISTERIA” and “SALMONELLA” pathogen type with analog value and milli output voltage amplifier on LCD display after the second and third selection switches been selected.
Figure 3. Arduino circuit design simulation using Proteus 8 Pro software.

Figure 4. Complete operation of electronic reader.

Figure 4 shows the complete operation of electronic reader circuit using Proteus 8 Pro software. Electronic reader consists of combination voltage amplifier circuit and Arduino circuit. The electronic reader design was simulated using simulator on Proteus 8 Pro software. The theoretical and experimental result were recorded and compared to identify the accuracy of the electronic reader circuit [29], [30]. These formula was used to calculate the theoretical output voltage through the voltage amplifier circuit and Arduino Uno microcontroller. Based on the equation, sensor input current $I_i$ (A), shunt resistance for appropriate range $R$ (Ω), and input voltage $V_i$ (V) as defined. As shown in Equation (1), the calculation to find the input current to sensor switches port using voltage source and variable resistor. Equation (2) shows the calculation to find the input voltage.

$$I_i = \frac{V_R}{R}$$  \hspace{1cm} (1)

$$V_i = I_i \times R$$  \hspace{1cm} (2)

After converting input current to input voltage, the input voltage will apply directly to the non-inverting (+) input terminal as shown in Figure 5. It means the output signal is in-phase with the input signal. The signal at the output is not inverted when compared to the input. Moreover, the feedback control of the non-inverting operational amplifier is done by applying a small part of the output voltage
signal back to the inverting input terminal via an \( R_f - R_2 \) voltage divider network [31]. This closed-loop configuration produces a non-inverting amplifier circuit with very good stability, a very high input impedance, as no current flows into the positive input terminal and a low output impedance [16]. Equation (3) and Equation (4) shows the equation of the gain and the output voltage (\( V_o \)). Based on the calculation, the gain of MAX 4238 op-amp IC is 100. The voltage drop across shunt resistor in micro voltage, the analog to digital in microcontroller Arduino read only in mili voltage range. Then, the amplifier need to amplify the signal with gain 100 [3].

![Non-inverting Operational Amplifier](image_url)

**Figure 5.** Non-inverting Operational Amplifier.

\[
\text{Gain, } A_v = \frac{V_{out}}{V_{in}} = \frac{R_2 + R_f}{R_2} = 1 + \frac{R_f}{R_2} \tag{3}
\]

\[
V_o = V_i \times G \tag{4}
\]

After amplify the micro input voltage to mili output voltage, the voltage value will through to Arduino Uno microcontroller on analog input “AO” port. Arduino Uno converted the analog voltage to discrete value. The reference voltage (\( V_{ref} \)) used in the Arduino equal to 1 V. Equation (5) shows the calculation for microcontroller Arduino Uno read the output voltage amplifier and display to LCD display.

\[
\text{Sensor Value} = \text{Analog Read}
\]

\[
\text{Output Voltage} = (\text{Sensor Value} / 1024) \times V_{ref} \tag{5}
\]

Figure 6 shows the electronic reader hardware setup consists of low noise amplifier, microcontroller Arduino Uno, LCD display and aluminium clips included sensor connectors. Figure 6 (a) shows the separate circuits of the electronic reader. After testing of each separate circuit, the separate circuit were assembled to make one complete device as shown in Figure 6 (b). After designing the software and hardware circuit, Proteus 8 Pro software was used to convert the electronic reader schematic design to PCB design layout.
Figure 6. Electronic reader hardware setup, (a) separate circuit, (b) integration of separate circuit.

2.3 Fabrication and assembly of PCB

Proteus 8 Pro software was used to convert the electronic reader schematic design to PCB layout as shown in Figure 7 (a). Then, the PCB layout convert to 3D visualizer layout as shown in Figure 7 (b). The circuit design layout was transferred onto copper clad board to make PCB, after removed first and second layer as shown in Figure 7 (c) and Figure 7 (d). After that, assembled all the components to make the portable amplifier device as shown in Figure 7 (e) and Figure 7 (f).

Figure 7. Fabrication process of the electronic reader PCB board. (a) PCB layout of the electronic reader circuit, (b) PCB layout convert to 3D visualizer layout view, (c) copper clad board without first layer, (d) copper clad board without second layer, (e) top view of the electronic reader and (f) bottom view of the electronic reader.

3. Result and Discussion

Figure 8 shows the measurement setup for testing the performance of the electronic reader circuit. This project was focus in three different current ranges consists of nano, micro and mili current. Voltage source and variable resistor acts as a replacement of biosensor input current. The electronic reader was validated by comparing the output voltage on LCD display with theoretical output.

As shown in Figure 8, a different current input was supplied using the voltage source that supply through the different range of variable resistor 20 MΩ for nano ampere range and 10 KΩ for micro ampere range. While, 100 Ω and 10 Ω used for mili ampere range. Therefore, the input current shows in range 0 to 1000 µA for nano and micro. While, the input current for mili range shows in range 0 to 300 µA. The current flow through voltage converter by using shunt resistor to produce input voltage in micro voltage value. Apart from that, there are three different switches on the voltage converter to select as the input current range as nano, micro and mili ampere with different value of resistors as 10 KΩ, 10 Ω and 10 mΩ respectively to convert three different range values to same range in micro input voltage.
Figure 8. Measurement setup for testing the performance of the electronic reader circuit.

Table 1. Theoretical and experimental result for nano ampere range.

| Voltage Regulator (V) | Resistor (Ω) | Input Current (nA) | Input Voltage (µV) | Output Voltage (mV) | Analog Value | Output Voltage (mV) | Output Voltage (mV) | Percent Error (%) |
|-----------------------|-------------|--------------------|--------------------|---------------------|--------------|---------------------|---------------------|------------------|
| 0                     | 20M         | 0                  | 0                  | 0                   | 0            | 0                   | 0                   | 0                |
| 2                     | 20M         | 100                | 1000               | 100                 | 77           | 97.43               | 2.57                | 2.57             |
| 4                     | 20M         | 200                | 2000               | 200                 | 179          | 196.20              | 3.80                | 1.90             |
| 6                     | 20M         | 300                | 3000               | 300                 | 281          | 294.60              | 5.40                | 1.80             |
| 8                     | 20M         | 400                | 4000               | 400                 | 383          | 393.50              | 6.50                | 1.63             |
| 10                    | 20M         | 500                | 5000               | 500                 | 484          | 492.30              | 7.70                | 1.54             |
| 12                    | 20M         | 600                | 6000               | 600                 | 592          | 591.80              | 8.20                | 1.36             |
| 14                    | 20M         | 700                | 7000               | 700                 | 692          | 690.70              | 9.30                | 1.33             |
| 16                    | 20M         | 800                | 8000               | 800                 | 794          | 789.40              | 10.60               | 1.32             |
| 18                    | 20M         | 900                | 9000               | 900                 | 895          | 887.80              | 12.20               | 1.35             |
| 20                    | 20M         | 1000               | 10000              | 1000                | 995          | 971.80              | 28.20               | 2.82             |

Table 1 shows the theoretical and experimental result of output voltage for input current in nano ampere range. The different voltages through 20 MΩ resistor were supplied the input current. The range of input current was between 0 to 1000 nA. The result shows a small different in mili voltage with 1.76 % average percent error. While, for micro and mili ampere input current were followed same calculation procedure. The output voltage for theoretical and experimental result for micro and mili current input were shown average percent error was 1.8 % and 3.15%. The factors for overall voltage amplifier electronic reader accuracy depend on PCB design, components grounding, thermoelectric EMFs, and electrostatic interference [20], [21]. Hence, the results were obviously shown that the voltage amplifier electronic reader capable to detect biomolecules in biosensor application. Figure 9 shows the graph comparison between theoretical and experimental result for nano, micro and mili ampere range.
4. Conclusion
An electronic reader for detection of different detectable range as nano, micro and mili ampere current was designed and fabricated successfully. The design and programming was done using Proteus 8 Pro software and Arduino software, respectively. Electronic reader was tested for different current inputs with different ranges via voltage source coupled with variable resistors. Apart from that, the theoretical and experimental results of electronic reader were recorded and compared. The average percent error for nano, micro and mili range were 1.76 %, 1.8 % and 3.15 %, respectively. Appropriate precautions should be taken to reduce the noises and error. The experimental results were approximately similar with theoretical result. The processing and control part was successfully done using Arduino software and results were displayed in LCD screen successfully. According to the results, the electronic reader can successfully function to detect and produce output voltage in mV for two electrode based biosensor applications.

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