Nano-micro-mili Current to Mili Voltage Amplifier for Amperometric Electrical Biosensors

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Abstract. Amplification of nano and microampere electrical signal to the detectable range is essential in the biosensor field. This research is mainly focused on design an 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 signal to the processing circuit. The Proteus 8 Pro software was used to design, simulate and calibrate the amplifier circuit. Firstly, current input as mili, micro and nano current were flown through 0.1 mΩ, 10 Ω and 10 KΩ resistors, respectively to convert different current inputs to the similar range in micro voltage. The MAX 4238 opamp IC was used to amplify micro voltage to mili voltage. LM 358 dual operational amplifier was used to supply virtual ground to MAX 4238 amplifier. The amplified output voltage of three different current inputs as nano, micro and mili were nearly equal to theoretical outputs.

1. Introduction
The development of simple and portable electronic readers have elevated potential for automation of sensor-based applications. Normally biosensors give extra small electrical output and most of them are amperometric, impedometric and potentiometric [1], [2]. To measure this small electrical outputs, bench type source measurement units and impedance analyzers were widely used [3], [4]. Requirement of portable electronic readers enhance the convenience to retrieve results much more easily and rapidly. Thus, using electronic readers can be saved time, handle out field and save money [5], [6]. Direct current (DC) voltage, DC current and resistance were measured most frequently using present electronic reader and other equipment [7]. Moreover, most industries are still based on the desktop computer and user need to complete the appropriate actions in the laboratory [8][9]. Furthermore, the equipment that used to measure low current was so expensive and inefficient because of the limitation of the detectable range [10]–[13]. In low current amplification there should be considered many factors in order to produce the accurate result such as leakage current or burden voltage. The volume of leakage current or burden voltage will affect the voltage amplifier circuit measured that will be corrupting the measurement contrary with theoretical measurement. Hence, it should be as low as possible the value or leakage current or burden voltage. Moreover, incorrect human handling of PCB also were intentionally contaminated before testing, will affected the measurement. This was similarly a potential source of
contamination resulting from fingerprint, skin oil, and saliva [14]–[16]. In this paper, we designed and developed an amplifier to amplify extra small current through sensors from nano ampere range to mili ampere range. The different range input current has converted to micro voltage and supply to voltage amplifier as input. The MAX 4238 is used to amplify the micro voltage to detectable mili voltage output which can be detect from the multimeter or microcontroller-based processing circuits.

2. Material and methods
2.1 Apparatus, equipment and software
The MAX 4238 was used as operational amplifier to amplify micro voltage to mili voltage. The LM 358 operational amplifier was used as to supply virtual ground for MAX 4238 opamp IC. The TPS 3809 was used as battery testing circuit. The 3 V coin battery was used as the power source to supply power for amplifier circuit and sensors. All ICs and resistors were used in this prototype are from Texas instruments. The Keithley Source Measurement Unit (SMU) was used to compare the resultant current with prototype, in three different current ranges as nano, micro and mili ampere ranges. 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 mili, micro, and nano for electrical biosensors. As shown in the figure there are three major parts included in the amplifier circuit as DC power supply, voltage converter and voltage amplifier. Sensor input system has included sensor input connectors and three dual select switches to select appropriate sensor to resistors. The amplified voltage output can be detected using multimeters or supplied as a input signal for a processing circuit.

Figure 1. Detail block diagram for voltage amplifier.
Figure 2 shows the whole schematic design for voltage amplifier circuit using Proteus 8 Pro software. Figure 2 (1) shows the sensor selection circuit with current to voltage converter. Three switches have designed to select the respective resistor for selected sensors in three different current range as nano, micro and mili ampere. Figure 2 (2) shows the MAX 4238 opamp IC circuit. Figure 2 (3) shows the power supply circuit which was included with TPS 3809 as battery testing circuit and Figure 2 (4) shows the virtual ground supplying circuit to the MAX 4238 amplifier IC. After design the circuit, it was simulated using in-built simulator on Proteus 8 Pro software.

2.3 Fabrication and assembly of PCB

The in-built ARES feature in Proteus 8 Pro software was used to convert the circuit diagram to PCB layout as shown in Figure 3 (1). The connection of the component in printed circuit board (PCB) layout can be adjusted the component position and after finish the process, the circuit was transferred to copper clad board to make PCB as shown in Figure 3 (2). Figure 3 (3 and 4) shows the bottom and top view of the PCB after assembled the components to make the portable amplifier device.

Figure 3. Fabrication process of the circuit board, (1) PCB layout of the amplifier circuit, (2) developed PCB on a copper clad, (3) bottom view of the circuit and (4) top view of the circuit.

3. Result and Discussion
Figure 4 shows the measurement setup for testing the performance of the amplifier circuit. Three different current ranges were supplied separately through the sensor connectors while changing the appropriate selection switches. The circuit was validated by comparing the output voltage through the multimeter value with theoretical output.

As shown in the figure 4, current inputs in different ranges were supplied using the external voltage source through the different range of variable resistors (1 GΩ for nano ampere range, 1 MΩ for micro ampere range and 1 KΩ for mili ampere range). The voltage source and variable resistor acts as a replacement of biosensor to input current to the sensor ports. In the voltage converter, the input current will flow through shunt resistor to produce input voltage in micro voltage value. There are three different switches to select the input current range as mili ampere, micro ampere and nano ampere by coupling three resistors as 0.1 Ω, 10 Ω, and 10 KΩ respectively to convert three different range values to same range in micro voltage. The low noise amplifier get this value as input voltage and amplifies the input voltage from micro voltage value to output voltage in mili voltage value. The gain of MAX 4238 opamp IC is 100, the input voltage times with 100 gives the value of output voltage in mili voltage value.

Figure 4. Measurement setup for testing the performance of the amplifier circuit.

Figure 5 shows the operation steps of the amplifier circuit. The theoretical result and experimental were recorded and compared to identify the accuracy of the amplifier circuit. Following formula was used to calculate the theoretical output voltage through the amplifier circuit. The Ohm’s law was used to calculate the input voltage to the amplifier [17]. According to the equation, sensor input current $I_i$ (A), shunt resistance for appropriate range is $R$ (Ω) and input voltage for sensor $V_i$ (V) as defined.

Equation 1 shows the calculation to find the input current to sensor port using power generator and variable resistor. Equation 2 shows the calculation to find the input voltage (V) to voltage amplifier from voltage converter.

\[ V_i = \frac{I_i R}{10} \]
\[
I_i = \frac{VR}{R} \tag{1}
\]

\[
Vi = I_i \times R \tag{2}
\]

Figure 6 shows the opamp circuit in non-inverting mode. After converted current to voltage, it will apply directly to the non-inverting (+) input terminal which means output signal is in-phase with the input signal. Feedback control of the non-inverting operational amplifier is achieved by applying a small part of the output voltage signal back to the inverting input terminal via an \( R_f - R_1 \) voltage divider network. In addition, this closed-loop configuration produces a non-inverting amplifier circuit with very good stability [18]. Equation 3 shows the equation of the gain (G). Equation 4 shows the equation of output voltage (V).

Before integrate the amplifier circuit, burden voltage or leakage current have to be considered [19]–[21]. It will affect the performance of amplifier circuit and contradict with theoretical measurement. Apart from that, poor human handling as a fingerprint, saliva, dust, chemicals, temperature surrounding, can affect the performance of amplifier circuit [22]–[24]. Those contaminants could be reduced by applying PCB protection coating or making a proper casing for the circuit [25]. Equation 5 shows the calculation for difference value for theoretical result and experimental result and Equation 6 shows the percent error for theoretical result and experimental result.

\[
\text{Gain, } G = \frac{V_{out}}{V_{in}} = \frac{R_1 + R_f}{R_1} \tag{3}
\]

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

\[
\text{Difference} = \text{Theoretical Result} - \text{Experimental Result} \tag{5}
\]

\[
\text{Percent error} = \left| \frac{\text{Theoretical Result} - \text{Experimental Result}}{\text{Theoretical Result}} \right| \times 100 \tag{6}
\]

3.1 Comparison of theoretical and experimental values

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

| Voltage Regulator (V) | Resistor (Ω) | Input Current (nA) | Input Voltage (µV) | Output Voltage (mV) | Output Voltage (mV) | Percent Error (%) |
|-----------------------|--------------|--------------------|--------------------|---------------------|---------------------|-------------------|
| 0                     | 1G           | 0                  | 0                  | 0                   | 0                   | 0                 |
Table 1 shows the theoretical and experimental result of output voltage for input current in nanoampere range. The different voltages through 1 GΩ resistor were supplied the input current. The range of input current for theoretical and experimental result was between 0 to 7.6 nA. While, the output voltage for theoretical and experimental result were shown a small different in mili voltage with 6.67% average percent error. The theoretical and experimental result of output voltage for micro and miliampere input current were followed same calculation procedure. The average percent error for micro and miliampere range was 2.26% and 1.04%. The factors for overall accuracy depend on leakage resistance, input loading, thermoelectric EMFs, and electrostatic interference [25]. Therefore, the results were clearly shown that the system can be used to identify biomolecules in biosensor application. Figure 7 shows the graph comparison between theoretical and experimental result for nano, micro and miliampere range.

| Current (nA) | Resistance (GΩ) | Voltage (mV) | Theoretical | Experimental | Error (% Error) |
|-------------|-----------------|--------------|-------------|--------------|-----------------|
| 0.4         | 1               | 0.4          | 0.42        | -0.02        | 5.00            |
| 0.8         | 1               | 0.8          | 0.85        | -0.05        | 6.25            |
| 1.2         | 1               | 1.2          | 1.28        | -0.08        | 6.67            |
| 1.6         | 1               | 1.6          | 1.68        | -0.08        | 5.00            |
| 2.0         | 1               | 2.0          | 2.11        | -0.11        | 5.50            |
| 2.4         | 1               | 2.4          | 2.48        | -0.08        | 3.33            |
| 2.8         | 1               | 2.8          | 2.89        | -0.09        | 3.21            |
| 3.2         | 1               | 3.2          | 3.29        | -0.09        | 2.81            |
| 3.6         | 1               | 3.6          | 3.75        | -0.15        | 4.16            |
| 4.0         | 1               | 4.0          | 4.15        | -0.15        | 3.75            |
| 4.4         | 1               | 4.4          | 4.51        | -0.11        | 2.50            |
| 4.8         | 1               | 4.8          | 4.87        | -0.07        | 1.45            |
| 5.2         | 1               | 5.2          | 5.28        | -0.08        | 1.53            |
| 5.6         | 1               | 5.6          | 5.73        | -0.13        | 2.32            |
| 6.0         | 1               | 6.0          | 6.15        | -0.15        | 2.50            |
| 6.4         | 1               | 6.4          | 6.48        | -0.08        | 1.25            |
| 6.8         | 1               | 6.8          | 6.93        | -0.13        | 1.91            |
| 7.2         | 1               | 7.2          | 7.36        | -0.16        | 2.22            |
| 7.6         | 1               | 7.6          | 7.81        | -0.21        | 2.76            |
4. Conclusion

Nano, micro and mili ampere current to mili voltage amplifier for electrical biosensors has been designed and simulated using Proteus 8 Pro software. The amplifier is high precision in the detectable range. Actual device was tested with dummy current source via voltage source coupled with resistors. Appropriate precautions should be taken to reduce the noises and error in nA range. The theoretical result and experimental result of amplified voltages have been recorded and compared. The results were indicated a small different in each ranges were in the linear pattern. The changes may happen due to the interferences of the connections, components and humidity. Finally, in this experiment shows that the system can successfully detect and produce output voltage in mV for two electrode based amperometric biosensor applications.

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