LOW COST EXTRACELLULAR VOLTAGE AMPLIFIER

A Design Project Report

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Submitted By

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Abstract

Master of Engineering Program

School of Electrical and Computer Engineering

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Design Project Report

Project Title: Low Cost Extracellular Voltage Amplifier

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Abstract:

Extracellular recording of action potentials is significant in the study of physiology and biology, whether in comparison to intracellular counterparts or the general value of the recorded data. This method of recording action potentials, electrical signals that propagate through various biological media, involves placing electrodes near charged cells and isolating the appropriate potentials. These signals, which can be as small as a few microvolts, require amplification for sufficient analysis. Furthermore, the magnitude of this amplification will differ for different applications of the extracellular recording. In turn, the developed device performs said amplification in a low-cost manner intended for use in student research laboratories, while managing requirements such as noise suppression and tunable gain. This device can boast comparable bandwidth and noise reduction to more costly commercial counterparts, which amount to $1000 per channel, with a price point under $50. Additionally, with a tunable gain of 100, 1000, and 10000, this device presents the necessary versatility for recording action potentials through different varieties of biological media.

Executive Summary: This design seeks to combat the problem of the expense behind extracellular voltage recording, particularly in student lab environments where these expenses are more burdensome. Extracellular voltage recording involves recording electrical potentials propagating through biological media using non invasive means, in the form of electrodes brought into close proximity to the target membrane. These recorded action potentials are extremely small and very susceptible to being lost to pervasive noise in the environment.

The goal of this device is to accomplish similar capabilities as commercial counterparts at a fraction of the cost. These capabilities involve taking the microvolt to millivolt range input signal and amplifying to a recordable range. This requires multiple gain settings, 100 to 1000 to 10000 in this case, to accommodate even the smallest signals to relatively larger potentials. Additionally, the noise issue will have to be diminished to allow for meaningful recording. Altogether, with several other accessibility implements, the device is meant for students in biological research lab environments to have a cheaper alternative to this staple implement of their studies.

The developed device accomplishes these objectives with a great deal of success. With appropriately tunable gain, and well defined output action potentials at a readable scale, as opposed to the 1mV input, this device performs the requirements successfully. Additionally, accessibility and ergonomic features including the small size and rechargeable battery power, the device provides a significant practical boon to research labs, notwithstanding the less than $50 price point.

Further testing with the target user base using the PCB design on laboratory biological specimens, exporting output data over bluetooth, and adding variability to the existing filtering stages is recommended for increased fidelity of the design. Altogether, this design provides a novel and eminently practical solution to cost-effective extracellular voltage recording.

Requirements

Extracellular voltage recording requires a preamplification device to process the directly recorded signals from the electrodes. Due to this type of recording being external to the cell, these signals appear smaller than they are internally and are more susceptible to 60Hz noise from the electrical currents in the environment. Commercial amplifiers of this variety typically go for around $1000 per channel and are proprietary to the manufacturer. In turn, there is significant value in being able to replicate these capabilities with a publicly available design that is easily assembled and utilized in student lab environments at a much lower cost.

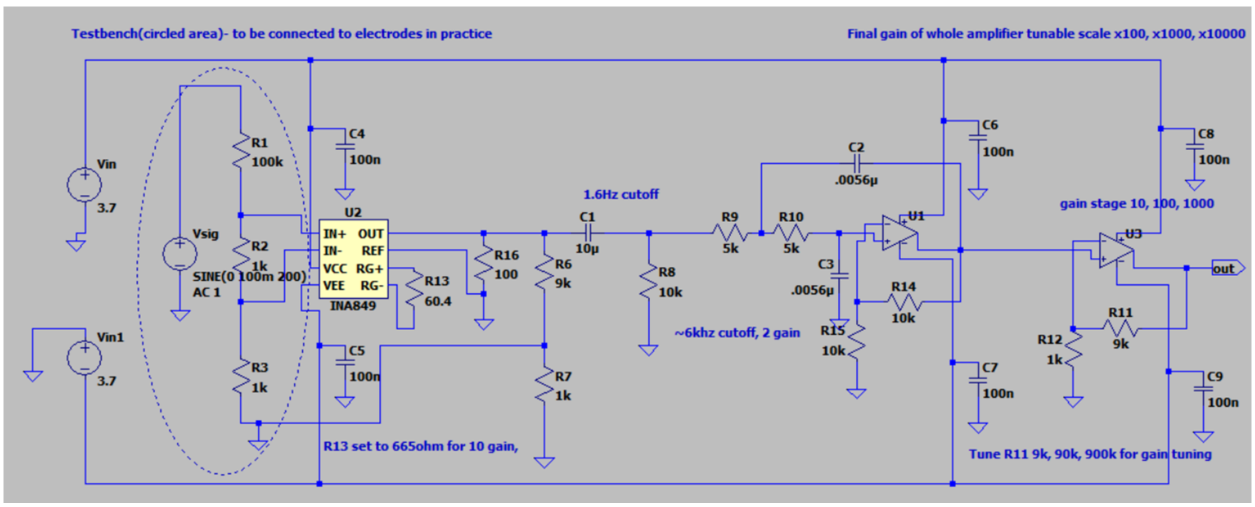

Figure 1: Schematic Design

To determine the angle of approach to the overarching design problem, familiarity with the target of amplification was necessary. These signals are expected to have an amplitude of 10 microvolts to 10 millivolts with a bandwidth of 2-3000Hz. Therefore, for the schematic design, before going ahead with actual lab testing, it is wiser to emulate these signals in a schematic testbench at the input of our prototype device. Figure 1 displays the schematic with the testbench which will take a 200mV sine wave input signal, using a voltage divider to scale down the signal amplitude to millivolt range for testing. It is grounded using another voltage divider within the actual preamplifier to emulate the shielded ground used in extracellular voltage recording probes. This produces an adequate analog for action potentials

In development, it was determined that the frequency bandwidth of the system must be 3kHz to accommodate the magnitude of amplification for signals of this input frequency. Much of the schematic testing revolved around achieving and maintaining this bandwidth and avoiding unexpected attenuation and nonlinearity. Therefore, within the circuit must be sufficient filtering stages to manage the frequency bandwidth to an appropriate level throughout to capture the signal appropriately. With the various gain and filtering stages added to the design iteratively, these unexpected situations arose and had to be dealt with analytically based on the physics and experimentally through tweaking parameters.

While the ratio of resistances and capacitances are set based on the mathematics required for gain and bandwidth, the magnitude of these components must be well controlled. This is due to the impedance between different stages of the circuit that may cause unexpected bandwidth attenuation or nonlinearity. Maintaining similar ranges of resistances and capacitances at the nodes between stages will aid in managing the impedance. However, experimentation beyond the mathematical analysis will be necessary to remedy unanticipated issues at nodes in simulation.

Another point of note early in development was the selection of a power source. With this consideration came the decision to have the preamplifier device be a small battery powered implement for easy use and handling for recording. Therefore, lithium-ion batteries were selected for their charging capabilities. Lithium-ion batteries are 3.7V per cell which was important to take into account as the operational amplifiers used in the design have specific supply voltage necessities. While this met the standard, as op-amps require dual rail positive and negative voltage supplies, two lithium-ion cells, 3.7V each, were used for each supply. All schematic testing utilized 3.7V rails as the power specification for the device. In practice, these cells are required to be connected in series to produce a common voltage ground at the jointed node for use as the main ground source for the circuit. With this requirement balancing charging and powering the device was more nuanced, as the lithium-ion battery charging boards used (TP4056) require a connection to both terminals of the cell. Since during operation, one terminal of each cell is tied up to produce common voltage ground, this would have to be disconnected with a switch and reconnected to the charging chip to charge. As a result, this design will not be able to charge the device and operate the device simultaneously. Ultimately, the tradeoff this requirement presents is necessary as this technique also reduces noise significantly by being disconnected from any charging apparatus during recording.

The noise suppression and tunable gain requirements are some of the fundamental necessary capabilities of this device that had particular priority in the design decisions. The 60Hz noise susceptibility comes predominately from the input to the system. Therefore, determining a noise suppressant solution in the first stage of the circuit limits the negative impact of the noise on further design decisions. After the input gain stage, if the noise is properly eliminated, the signal will be amplified to a level less susceptible to the relatively lower amplitude noise. Furthermore, it was necessary to determine where and how to tune the gain to several different settings. This must occur at one of the gain stages, having it tunable to at least three settings without saturating the output, or any other discrepancies that would cause signal degradation.

During the design process, while there existed base requirements for the device to adhere to, as more design decisions were made and the nuances of the implementation were delved into, these requirements evolved and expanded. Altogether, with consistent monitoring and examination of these developments, a successful design and implementation were achieved.

Approach

The aforementioned design benchmarks, as well as further decisions to be discussed, influenced the overall approach to be taken during the design process. One of the earliest considerations was the problem of noise. Signals this small are very susceptible to various forms of noise, especially with the indirect nature of extracellular voltage recording. Firstly, 60Hz interference from electrical currents in the environment was especially prevalent, due to how the electrodes being positioned outside the cell causes them to capture not only the signal but this interference as well. Additionally, intrinsic amplifier noise constituting thermal, voltage, and current noise was to be noted, considering the amplification stages that would be employed.

The solution that was decided was deliberate component selection to target noise. To elaborate, much of the particular noise vulnerability came from the extracellular recording electrodes being outside the cell and catching 60Hz current noise. By eliminating noise in the input stage the impact of this issue can be stamped out before severely impacting other design decisions. The input stage will ultimately be a gain stage with an op-amp. By selecting an op-amp with a particularly high common mode rejection, this noise issue can be remedied. The INA849 as the instrumentation amplifier used at the input stage, with a 120dB CMRR, accomplishes this quite effectively. This is also an adequately cost-effective measure as this stage would contain an op-amp for gain regardless, and replacing it with a slightly pricier op-amp is an acceptable opportunity cost. Coupling this with balanced and symmetrical component placement, this noise vulnerability can be reduced to the desired level.

With this, component selection for the rest of the stages, as well as determination of what the stages needed to do to the signal was needed. For the rest of the needed op-amps for gain stages, LM358 op-amps were used. Due to not requiring any more noise suppressant capabilities at points besides the input, ordinary well defined op-amps with low cost were usable, which the

LM358 fits well. The decision was to have two gain stages, three if you include a Sallen_key stage at unity gain. The first gain stage would be the aforementioned INA849 set to a fixed 10 gain. The last stage would apply a gain of 10, 100, and 1000 to get the appropriate 100, 1000, 10000 overall gain, through the methods mentioned earlier. Between these two stages would be a high pass filtering stage and a low pass filtering stage. The high pass filtering stage was a simple first order RC filter that set the low cutoff to 1.6Hz. The low pass filter stage was a 2nd order Sallen-Key filter stage set at 3kHz high frequency cutoff. The complexity here was intended to exploit another potential gain stage as well as better selectivity with the sharper cutoff. Ultimately, the final design does not increase the gain beyond unity, since Sallen-Key topology can only stay stable at 3 or less gain, and it was deemed unnecessary to have this magnitude of gain in conjunction with the other stages. The detailed selections and design can be seen in Figure 1.

Notably however, is how the LM358 has a gain-bandwidth product of 0.7 MHz, which means that the gain for an op-amp stage is limited to 100 gain. Therefore, the 10000 gain setting would not work properly as that requires a 1000 gain setting at the output. With the GBWP of the LM358, this 1000 gain would only give an insufficient bandwidth of 700Hz. In turn, an additional gain stage is something necessary to be implemented in further iterations of the design.

Additional additions for future iterations would be having the filtering stages be tunable. While the current high and low cutoff frequencies work for extracellular voltage recording, and much of the unintended noise at 60Hz frequency is handled in the INA849, tuning the filtering can even further improve the versatility of the device, which is one of the most important aspects of the design capability. Ideally, having the low cutoff tunable from 1.5Hz to 150Hz and the high cutoff tunable from 1kHz to 10kHz, in the same way the gain is tunable, the versatility could be improved as these values can improve performance in more specified applications of extracellular voltage recording. This includes ECG and EEG functionality improvement for example. Regardless the current fixed settings, paired with the noise suppression at the input, work well for extracellular recording and present good versatility in high noise environments and for varied input sizes.

With this schematic formulated in simulation, and confirmed to have the correct frequency bandwidth to not degrade the signal, breadboard prototypes were created. With the initial prototype, while testing the functionally of the amplifier was the main objective, testing the lithium-ion battery power supply was possible which was not in simulation. Additionally, it was determined that sending the output of the amplifier over bluetooth would be appealing for accessibility and a more elegant design. This was decided to be done with a Raspberry Pi Pico W using a simple bluetooth script to send a single ADC port output over bluetooth. This data stream could then be loaded onto an oscilloscope program of the user's choosing or plotted using a script. The Pico W will be responsible solely for exporting the data over bluetooth for the user to manipulate. This functionality has yet to be fully implemented and tested due to time limitations.

The approach taken during this project resulted in a device that performed the capabilities required in the conception of this idea well. All the determined requirements were met as well, providing a well defined and efficient device. Ultimately, several improvements could be made as described and it is notable how in the presence of these potential decisions, the design evolved accordingly. In summation, the resultant device produced from this collective approach is well functioning and serves a novel purpose.

Testing and Results

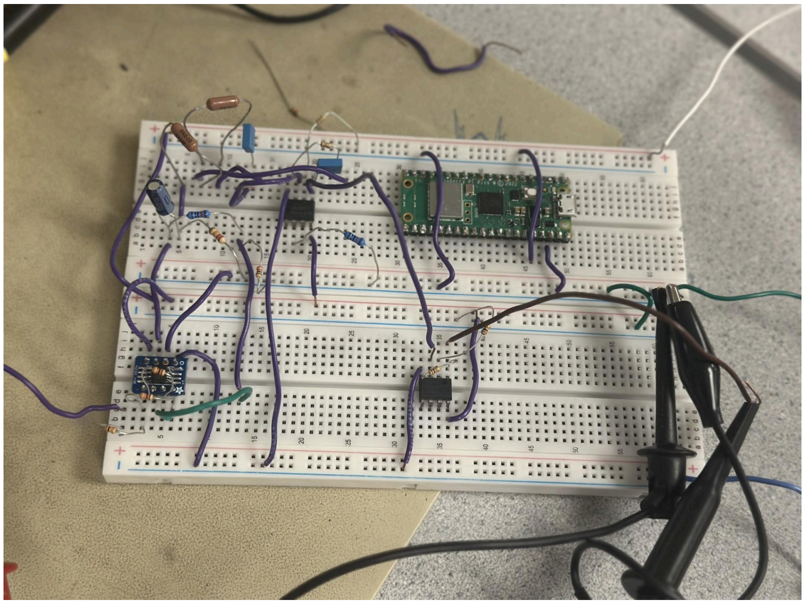

Figure 2: Breadboard Test Prototype

Testing the device began once the breadboard prototype was put together, which can be seen in Figure 2. The testing setup involved connecting the positive and negative power rails with a +3.7V/-3.7V power supply. The battery system was not used yet, to eliminate variables and allow for longer periods of testing. As mentioned earlier, the testbench of the circuit, which can be seen highlighted in Figure 1, involved a voltage divider to minimize the input signal to 1mV. This original signal was produced by a signal generator outputting a sine wave at 200Hz frequency, a mid-band frequency, central between the log scale of 2Hz to 2kHz. Testing involved probing the output at each gain stage, with gain stages disconnected and reconnected. To recall, errors arise with impedance and also human error with misconnects. With extensive testing of separate parts of the circuit, values were tweaked and misconnects were remedied.

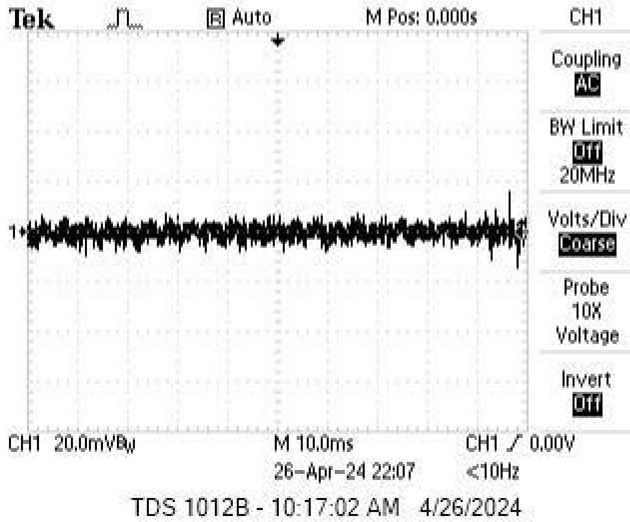

Figure 3: Test Input from Signal Generator

Figure 3 shows the tested input, an extremely small and noisy signal. The noise is the persistent 60Hz noise problem that the device seeks to tackle. This is an approximately 3mV input signal. Figure 4 shows the output with gain set to 1000, as this applies best to an input of that magnitude. The output has a peak-to-peak voltage of 2.96V and is virtually noise free. This approximately 3V output matches the 1000 gain from 3mV as well. This test displays all the main capabilities that the device seeks to attain. The gain is applied correctly, with appropriate filtering to not have the signal degrade. There is no saturation in the output signal and the waveform is well shaped, showing good noise handling and design integrity. Furthermore, the output can handle inputs of that magnitude and is sensitive to the minute changes in the signal amplitude across time. These results, obtained after rigorous testing and careful iterative design as described, demonstrate the desired functionality.

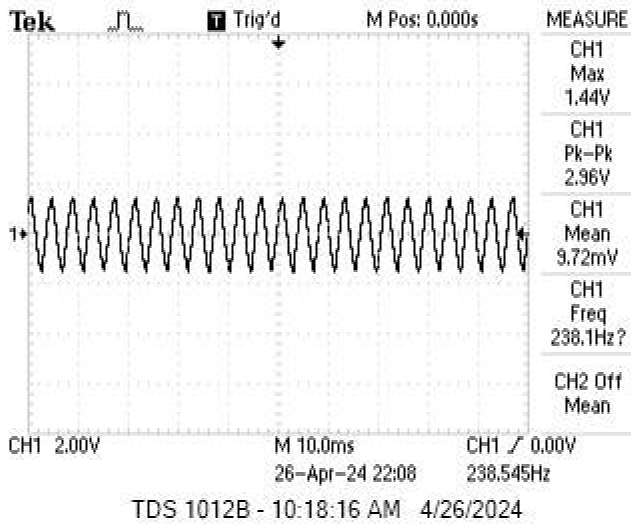

Figure 4: Test Outputs from Breadboard Device (Gain 1000)

Subsequently, with the success of those benchmark tests, testing on real action potentials was conducted. By connecting electrodes to Professor Bruce Land in an ECG setup, the input testbench as detailed earlier was dismantled. Figure 5 shows the findings of this experiment. These three waveforms are of the circuit set to 1000 gain, showing a 1-1.5V output signal approximately. These also show different time subsets of the signal, magnified for viewing ease. These waveforms display well formed action potentials, undeniably recognizable as ECG recording. The steady rate of each action potential display demonstrates a heart rate. Noise is apparent between the signals, but the action potentials themselves are very well defined with no degradation apparent in the signal. This test is indicative of all the prior conclusions and highlights the efficacy of the device with how well formed and distinguishable the action potentials are. Altogether, this is an exceptional result that well matches our desired results and exceeds expectations of efficacy on certain fronts.

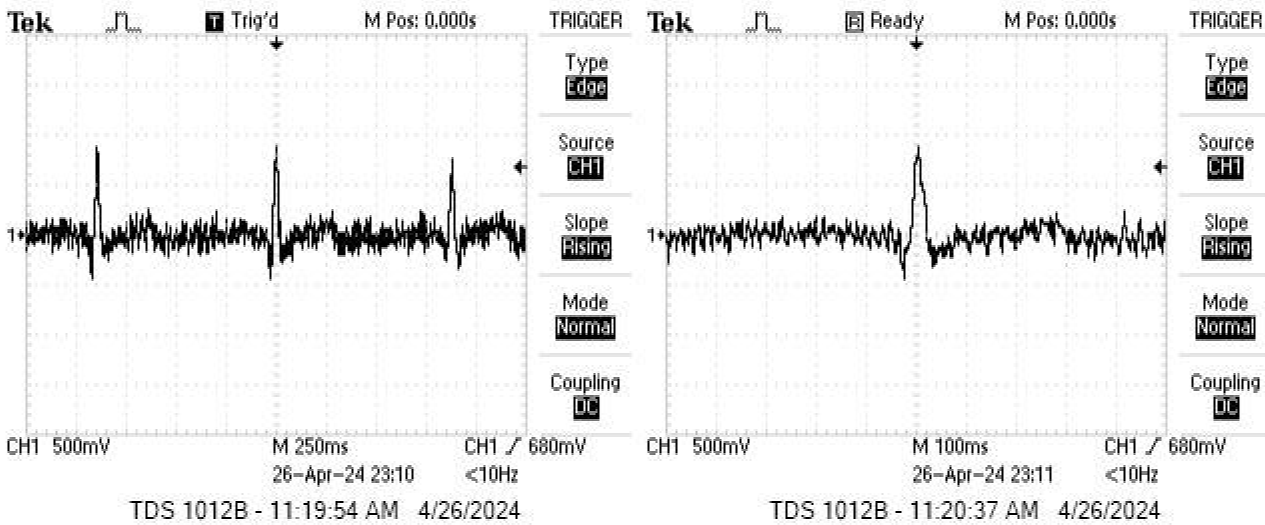

Figure 5: Outputs of ECG input (Left 250ms slice, Right 100ms slice)

Points of note include, that this ECG testing was done in an extremely noisy environment, in close proximity of power lines and currents. In a more ideal biological lab environment, like the neurophysiology lab in Comstock Hall run by Professor Bruce Johnson, these noise elements would not be present and an even better result would be observable. Along the same line, time willing more testing of different varieties would have been done. A PCB had been developed as seen in Figure 6, however this was fabricated relatively late. Doing testing on a PCB would significantly reduce noise elements from crosstalk apparent in breadboard design, even with careful breadboard design. Additionally, testing on biological specimens common in laboratory environments, like crawfish tails, would be the next step. Allowing biology students, as the intended users of the device, to test on their samples would be ideal to also gauge the accessibility of the device.

Regardless, the success of the current testing goes to show the efficacy of the device, and further testing using a PCB in a biological laboratory would only make the environment more ideal for handling the signals. Therefore, one can only expect better results compared to the benchmark tests done in nonideal conditions on nonideal hardware.

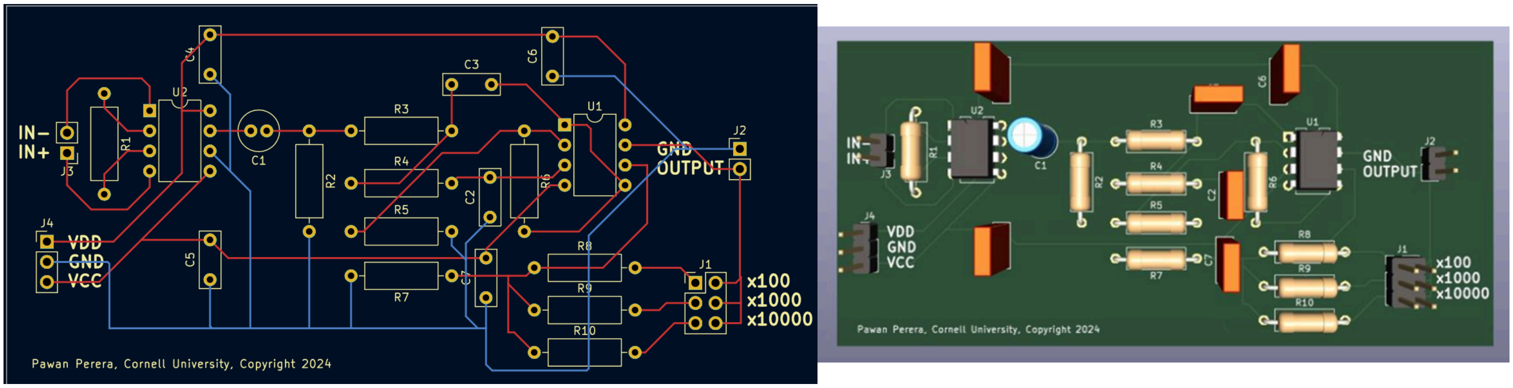

Figure 6: PCB Layout

Conclusion

Overall, the developed device met the requirements and produce marked results, a great success. The testing produced very well defined action potentials and showed noise suppression elements. Furthermore, auxiliary implements like battery charging and bluetooth output were added later for even more added accessibility. Ultimately several pitfalls during the design process were encountered. Most of these were overcome with insightful design decisions, however in hindsight, some possible improvements were highlighted. Having the frequency range be tunable, bluetooth output from the device, and additional gain stages for better gain/bandwidth trade off would be logical next steps for future iterations. This is important to mention, especially the tunable frequency, as when juxtaposed with the current results, shows how this already great outcome can achieve even more precision.

Furthermore, time limitations did reduce the amount of development capability that could have offered even more fidelity to the project. With the finalized PCB design, testing on this implement would inexorably show better results than a noisy breadboard apparatus. Furthermore, exposing this device to biology students would have offered valuable insight as a developer of the device. Additional features such as device housing and ergonomic considerations could have been done as well.

Despite those shortcomings, this project exceeded expectations on many fronts and provided and altogether successful solution to the initial problem. As detailed, the device performs exceptionally well in detecting action potentials using extracellular voltage recording, even in noisy environments. Most notably the finalized price point is well under $50. This is a stark improvement to the commercial devices that perform similarly, but with an approximate $1000 cost per channel. As the main objective to distinguish this device from competitors, this device accomplishes this splendidly. Altogether, the insights gained during this design process as well as the overall efficacy of the finalized design, demonstrate a novel solution to the extracellular voltage recording problem and its particular costliness.