Finger Plethysmograph to Measure Blood Resistivity

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Abstract

Impedance plethysmography can be used to measure arterial volume change that occurs with propagation of the blood pressure pulse in a limb segment. For this measurement, we assume a constant value of blood resistivity. However, blood resistivity may change under both physiological and pathological conditions. Use of an impedance plethysmograph on a finger immersed in a saline filled beaker may yield a method for determining this change in blood resistivity. This may develop into a method that diabetics can use to measure glucose levels noninvasively. The goal of our project is to design a finger plethysmograph to measure blood resistivity.

Table of Contents

Problem Statement

Our goal is to design a finger plethysmograph to measure blood resistivity. In order to accomplish this, we will need to design and build a data acquisition device to acquire the signal from the finger. The device should mechanically immobilize the test subjects' finger such that motion artifacts are kept to a minimum. This device should be able to detect the electrical potential (voltage) change across the finger so that the change in resistance may be determined. It should be able to detect the velocity-dependent change in blood resistivity due to arterial blood pulsations.

In addition, we will need to build an electrical circuit to perform signal processing and analysis. This circuit should be capable of rectifying the alternating current (AC) signal from the finger data acquisition device and modulate it into a direct current (DC) signal to be analyzed. The circuit should be capable of discerning or visually displaying the voltage changes caused by correlated changes in blood resistivity. As an added feature, this circuit may contain an automatic reset function capable of adjusting one of the differential amplifier inputs to that of the output from the data acquisition (finger holder) device. This will allow the device to easily accommodate fingers having different electrical resistances and will prevent having to manually adjust voltages using a potentiometer to match independences with each new test subject or finger position.

Background Information

Diabetes

Diabetes is a disease characterized by the body's inability to manage glucose levels. It is a chronic condition caused by the pancreas's lack of ability to produce enough insulin or the

failure of the body to effectively use the insulin produced. Individuals with type 1 diabetes produce little to no insulin and as a result need to self-administer doses of insulin on a daily basis. People with type 2 diabetes cannot use insulin effectively. The condition is usually treated through lifestyle changes and if necessary, oral drugs [1] (WHO 2008). Regardless of type, however, it is important for all diabetics to closely monitor their blood glucose concentration.

The prevalence of diabetes is astounding. In the United States alone there are 17.9 million diagnosed cases of diabetes, and it is estimated that there are an additional 5.7 million undiagnosed individuals living with the disease [2]. The disease is also on the rise. Over the last three years, the number of diagnosed individuals has risen 13.5 percent. In addition, the American Diabetes Association projects 57 million people as pre-diabetic. Globally, occurrence rates of diabetes are even higher; at least 171 million people worldwide have diabetes [1].

As a result, the economic burdens of diabetes are substantial. In the US, the total estimated costs of diabetes in 2007 include $116 billion in excess medical expenditures and an additional $58 billion in reduced national productivity [3]. The indirect costs of diabetes that affect productivity include increased work absenteeism, reduced productivity while at work, unemployment from disease-related disability, and lost productive capacity due to early mortality. As highlighted by the large number of individuals living with the disease as well as the large associated economic burdens, there are exceptionally strong motivations (both moral and financial) to perform research in the area of diabetes treatment and monitoring. Thus, an improved method for diabetics to monitor their blood sugar is highly desired.

Electrical Theory

Four electrode impedance plethysmography uses two electrodes to pass current through the finger and two electrodes to measure the voltage output across the finger. For this project, the finger will be inserted downward into a tube similar to that shown in **Figure 1.** The electrode at the top, near the base of the finger, is the current input. The electrode at the bottom acts as the ground where the current exits the system. The two center electrodes measure the voltage across the middle section of the finger. By passing current through the finger (which provides resistance), the resulting voltage drop can be measured across these electrodes [4].
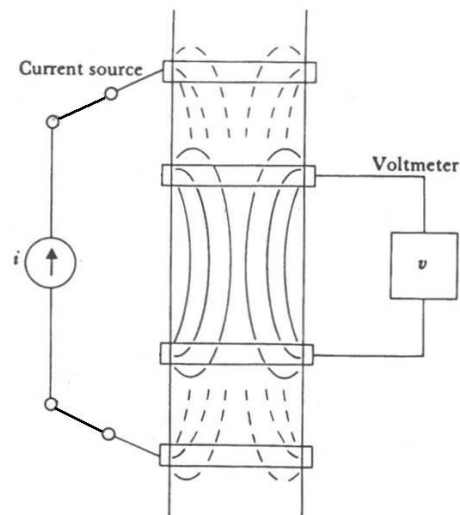

Figure 1: Four electrode impedance plethysmography [4]

The voltage measurements obtained will vary depending upon physiological changes in the blood and due to the blood pulse itself. It is expected that these measurements will be small. In order to observe and analyze the signal, the wires from the middle electrodes are connected to a circuit where the signal will be amplified and processed. Finally, the voltage output can be used to calculate the impedance and resistivity of the blood in the finger. It is thought that the resistivity can be correlated with different blood compositions.

Biological Theory

During high blood flow, such as when the blood pulses through the finger, the red blood cells (RBCs) align as shown in **Figure 2**. When current passes through in this situation, it meets less resistance compared to when there is lower blood flow. During lower blood flow as shown on the right of **Figure 2**, the RBCs tend to clump together or misalign. In this situation, the current has a more difficult time passing through the blood and as a result the impedance increases. It is this electrical impedance and consequent resistivity change that is of interest to be quantified.
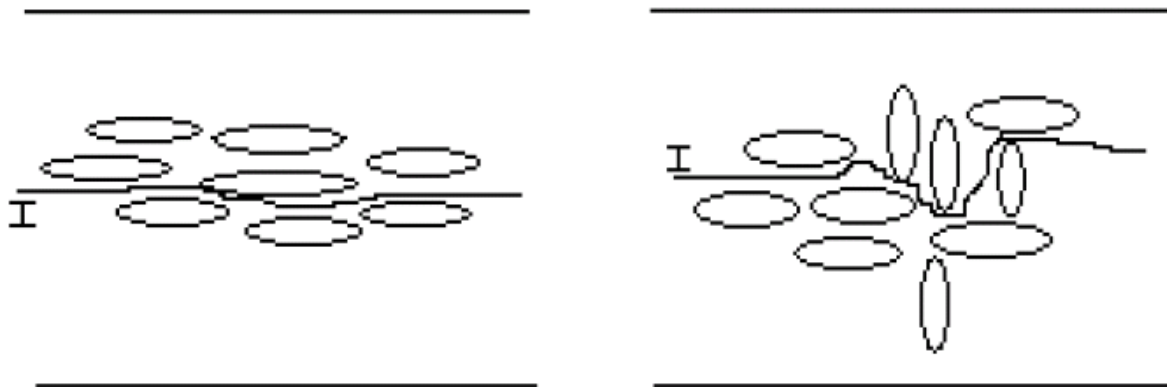

Figure 2: RBC alignment during high blood flow (left) and low blood flow (right)

It is hypothesized that the resistivity of blood will change with differing blood glucose levels. Higher levels of glucose in the blood would result in greater clumping of the RBCs and a higher resistivity. One of the goals is to be able to correlate these different impedance and resistivity measurements with varying glucose levels [5].

The arterial change in volume of the blood vessel during a pulse also has to be taken into account. If the finger is surrounded by isotonic saline (0.9% NaCl), the saline acts to cancel any signal generated by the volume change. During a pulse, an amount of saline equal to that of the

pulse volume is displaced in the finger holder. The saline produces a signal that is equal and opposite to that of the signal from the volume change of the blood vessel. Thus, the signal generated from the actual volume change of the vessel doesn't interfere with the small change in resistivity trying to be obtained [6].

Current Devices

Current blood glucose monitors require a small sample of the patient's blood in order to determine glucose levels. This usually needs to be attained through a painful, self-induced finger prick using a lancet. The blood sample is then placed on a test strip where it interacts with chemicals. The strip is inserted into the blood glucose meter and provides an electronic pulse to the meter depending on the reaction. The meter then provides a digital readout of the amount of glucose in the blood. An

Figure 3: Accu-Chek kit with glucose meter, test strips, lancet, and carrying case [7]

example product is the Accu-Chek kit shown in **Figure 3**. Other test strips change color and come with corresponding indexes that give a range of glucose levels depending on the composition of the blood [8]. This method may not be as accurate as the digital readout, but both still require a blood sample. Because of the associated inconvenience and pain of these methods, a simpler, more user-friendly non-invasive method is desired.

Design Constraints

Note: For a precise list of design constraints please see the attached PDS appendix

As with any biomedical device with a patient-electrical interface, the primary design constraint is safety. Electricity is only being applied across the finger, so there is no direct threat of current exposure to the heart. Extra precautions should still be taken, however, to ensure the patient is not exposed to excessive current. First, the electrical circuit going to and from the finger electrode device must be electrically isolated from the rest of the circuit, so any possibility of exposing the patient to 120V, 60Hz wall voltage is eliminated. Furthermore, the prototype must be completely electrically insulated. This will prevent another point of electrical contact being made with the patient, creating another route for current. The prototype must meet all Institutional Review Board (IRB) requirements so that it may be used in clinical studies.

Current home blood glucose meters' test results are considered 'accurate' if they fall within ±20% of an accepted laboratory derived reference result [11]. Although this seems like a high margin of error, our design is by definition going to be less accurate than current invasive methods, so exceeding their accuracy is unlikely. Errors resulting from motion artifacts should be reduced by firmly restraining the finger and employing an automatic reset function.

The device is being designed for a clinical testing environment. Accordingly it should be easily operated by a trained medical professional. It must be designed ergonomically so the user does not experience any discomfort. Finally the device must be aesthetically pleasing with a professional and non-intimidating appearance.

Human Factors

Ergonomics will play a crucial role in the design of our plethysmograph this semester on a variety of levels, including those specified by Professor Martin of safety, comfort, ease of use, productivity and performance, and aesthetics.

Because the plethysmograph has the potential to be used as a non-invasive device for measuring blood-glucose levels, it is imperative that it is simple and intuitive. Many individuals ranging from children to elderly would likely use this device to monitor their glucose levels and therefore it should be user-friendly. Additionally, because these individuals will have varying physical strengths, mental abilities, and perceptiveness, its use should be very straightforward with a simple set of instructions to ensure that all ages that need to use the device are capable.

The plethysmograph should perform effectively in all settings in order to accurately reflect actual blood-glucose levels. Because varying demographics will have different skin and blood properties, as well as varying nutritional intakes, there are a variety of factors that can potentially affect the blood resistivity properties. Therefore, we will have to take this into consideration in order to ensure our design can either be calibrated to obtain accurate results or will relay accurate results for a variety of patients. Also, patients from these various backgrounds will also have different physical attributes (finger size) that will affect our ability to acquire a signal. We must ensure that our housing that holds the saline solution is adjustable to prevent blood flow from being cut off from the finger, prevent the finger from translating excessively, and allow for current to flow through the solution. Therefore, we will either have to design a flexible membrane or allow the user to manually adjust the location of the electrodes to achieve maximal readings.

Finally, we have to develop a way to convert waveform signals into a reading that can be easily interpreted by a user. Currently, the pulse of bloodflow through the finger is recorded as a change in voltage on an oscilloscope. Because this signal doesn't mean anything to a common user, we must develop a way to convert the waveform into a numerical reading that reflects actual glucose levels.

As can be seen, human factors engineering will play a huge part in our design process and we will have to determine the most effective way for our design to be safe, comfortable, easy to use and interpret readings, perform reliably, and be aesthetically pleasing. While achieving perfect ratings in each of these categories is unlikely, we will have to make trade-offs to achieve the maximum device performance while also achieving easy levels of usability.

Previous Semester - Final Design
Finger Stabilizer

The final design (**Figure 4**) uses two elastomeric foam cuffs to stabilize the proximal and distal ends of the finger. These cuffs accommodate a wide range of finger tip and base sizes. This design allows for the ability to perfectly match the restraint size to the subject's finger size.

The foam came as a 6' cylinder with 5/8'' inner diameter and a ½'' wall. Three cylinder sections were attached to the tube: one section at the bottom to stabilize the finger tip, one stabilizing the proximal interphalangeal joint, and the other at the top opening of the tube to stabilize the proximal phalange. The proximal phalange tubing inner diameter was increased to 3/4'' because of the gradual thickening of the finger.
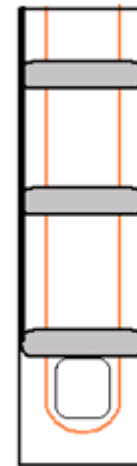

Figure 4: Final finger-holder with three elastomeric foam cuffs.

The outer shell of the finger stabilizer was cut to be 4.5'' long and constructed out of 1.5'' Sch. 40 PVC. The length of the tube was overestimated due to the fact that most anthropometric data used measurements from the metacarpophalangeal joint to the tip of the index finger. This data does not help determine an acceptable length due to the interference of the interdigit webbing when the finger is inserted. The foam stabilization at the finger tip also took this variation into account, being 1" long and placed 2.5" from the top of the receptacle. This ensured that a finger of length 3.5" and greater, measured from the metacarpophalangeal joint, would contact all three foam inserts.

The electrodes were made from tin defibrillator electrodes. Each electrode was .5" wide and 5" long, enough to completely wrap the inner circumference of the tube. The electrodes were spaced in the tube such that the current ground electrode was at the bottom of the tube and the current input electrode was directly underneath the first foam stabilizer. The top voltage electrode was placed directly below the current input electrode. The bottom voltage electrode was placed immediately under the proximal interphalangeal joint-stabilizing foam. The ground electrode was modified from the original ring to a circular plate measuring 1" in diameter and attached perpendicularly to the long axis of the tube. Each electrode had a wire soldered to it, which was run up the inner wall of the tube to exit out the top. The bottom of the tube was sealed with a 1.5" Sch. 40 PVC end cap.
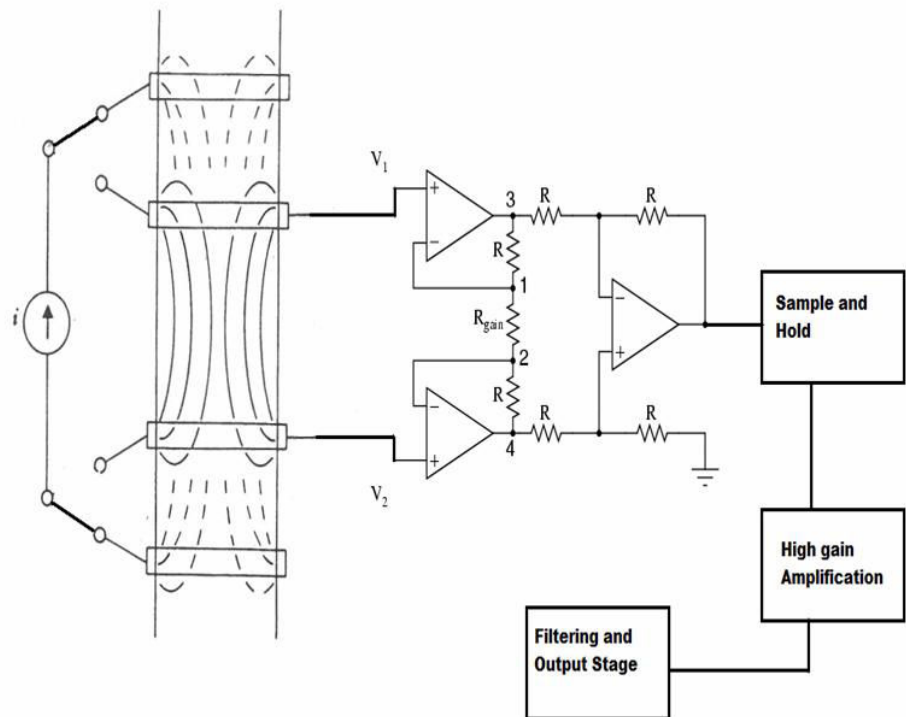
Circuitry

The voltage signals from across the finger are expected to be very small and could be buried within a substantial amount of noise. Because of this, a circuit must be designed that both amplifies the small voltage difference across the finger and filters out any noise that corrupts the signal. The extremely small nature of the signals being measured results in the need for high gain

amplification. Because of this high gain, any movement of the finger would saturate the amplifiers. The sensitivity of the measurements requires the need for an automatic reset and sample and hold circuit. The signals being measured have a substantial amount of common interference that does not need to be amplified. To focus solely on the changing signal, a differential amplifier must be used.

All of these requirements were factored into the preliminary design of our circuit (**Figure 5**). The circuit has an instrumentation amplifier that acts as a preamp to amplify the changing voltage across the finger. This is then sent through a sample and hold circuit [9]. The sample and hold circuit automatically resets the output once it moves outside a preset voltage window (**Figure 6**). This allows for the circuit to reset once the high gain amplification stage saturates. The exact requirements for the filter must be determined after data collection. It is necessary to assess the sources of noise and interference in order to be able to accurately design the filters. For this reason the filters are left unspecified.

Figure 5: Block diagram showing instrumentation amplifier connections to the plethysmograph and signal cascade through the rest of the circuit [4]
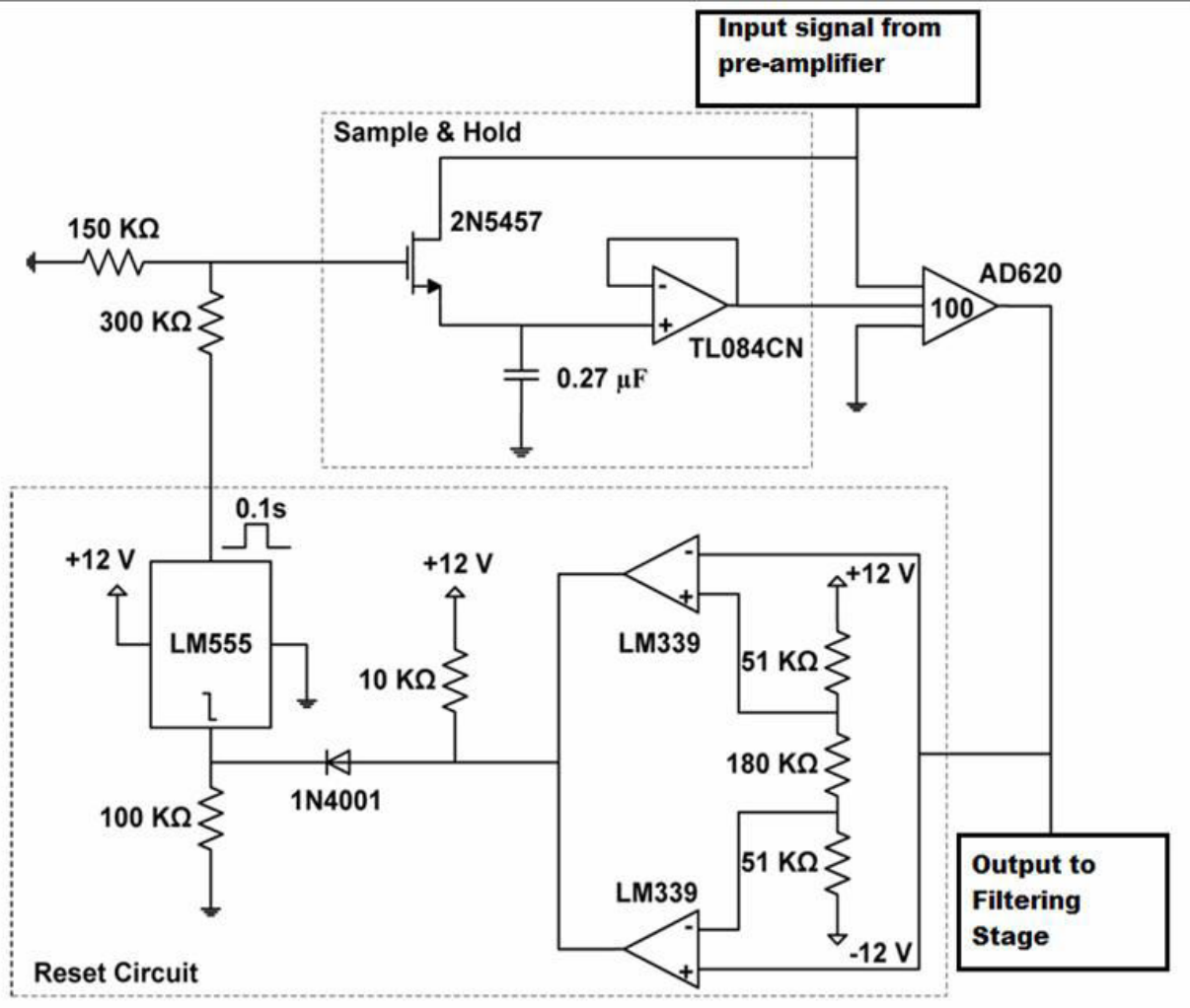
Figure 6: Circuit diagram of the sample and hold circuit used to reset the circuit during saturation [9]

The current input into the receptacle must be chosen so that it can pass safely through the tissue without causing discomfort, but still encounter some resistance such that a potential difference can occur across the finger (**Figure 7**). A current ranging from 1-10 mA at 50-100 kHz [10] should provide a safe current that will not harm the test subject, yet still allow for an adequate voltage drop to appear across the finger. The exact current value will change between subjects due to variations in body resistance.
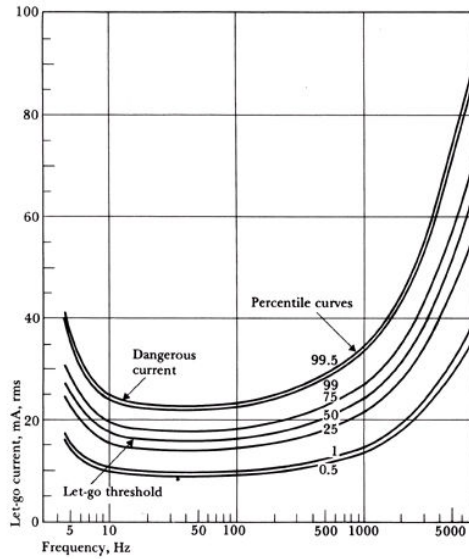
Figure 7: A plot of let go current versus frequency. As the current frequency is increased the affect it has on the muscles and tissues of the body decreases [4]

The final circuit design consists of six modules that have been designed specifically to measure the signals from the finger restraint. These six modules are differential pre-amplification, rectification, sample and hold, automatic reset, high gain differential amplification, and filtering and signal processing (**Figure 8**).
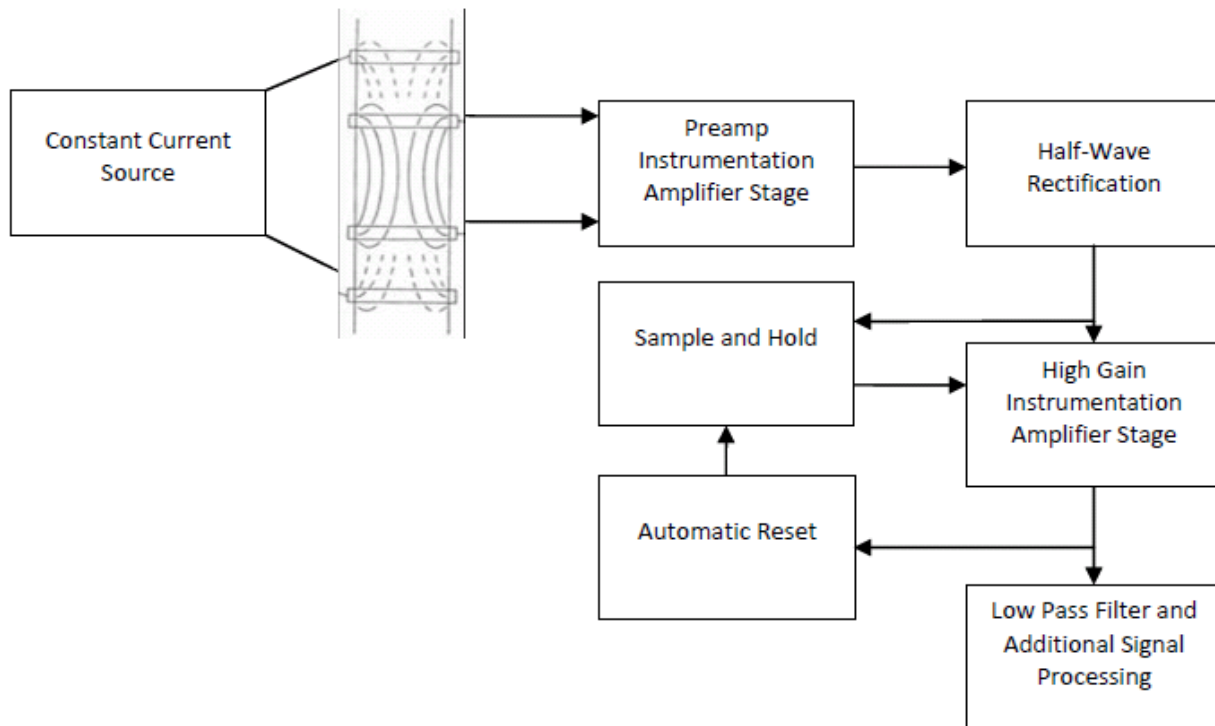

Figure 8: Block diagram showing the constant current source, electrode configuration and signal pathway

Both differential amplifiers are AD620 instrumentation amplifiers. These amplifiers were chosen due to the fact that the gain could be altered with a single resistor. The gain of the preamp was set at 19 V/V while the high gain amp was set for a gain of 100 V/V. The preamp gain was set high so that the incoming signal would be amplified enough to exceed the forward voltage requirement of the rectifying diode.

The rectifying stage uses a 1N4001 diode to create a half-wave rectifier with a ripple voltage to peak voltage ratio of 0.01. The rectification stage was added to strip the envelope off the high frequency input signal. The resulting DC signal would contain the low frequency changes in voltage that are to be amplified further.

The sample and hold circuit consists of a 2N5457 n-type enhancement MOSFET and a TL084CN op-amp. The MOSFET operated as a voltage controlled switch which would close when the output exceeded ±9 volts. This would cause an electrolytic capacitor to charge to the voltage sampled from the rectifier output. This capacitor would then hold this voltage at the high gain amplifiers inverting input. This allowed for the high gain amplifier output to be reset back to zero. The TL084CN op-amp acted as a buffer with very high input impedance to slow down the capacitors rate of discharge.

The reset circuit consisted of a window comparator with a window set at ±9 volts. LM339 comparators were used to construct the window. When the output voltage exceeds +9 volts or drops below -9 volts the comparator output is -12 volts. This causes the 555 timer to output a voltage pulse with amplitude of 8 volts and duration 0.1 seconds. This pulse turns on the MOSFET and enables it to sample the rectifier output. Once the MOSFET samples, the output is returned to within the comparator window.

The filtering and data processing stages have not been completely designed at this time.

Further research and testing is needed to determine what filtering needs to be done to the signal. As of now a low pass filter is the only filter in the circuit. This low pass filter has a 10 Hz cutoff so that it attenuates any high frequency noise. This cutoff was also chosen because the voltage pulses are expected to be at a frequency of 1-2 Hz, so anything above this is not wanted. Additional filtering and signal processing will need to be determined at a later date. Each section of the circuit was tested to ensure accuracy before the final testing was completed.

Results

Upon testing of the device, a pulsatile waveform from the heartbeat was not immediately apparent. As previously stated, the pulsatile waveform from blood flow in the arteries will be very small with respect to the total impedance value of the finger. Further data analysis will be required therefore, to isolate the signal of interest. The output of the system was tested with and without the presence of pulsatile blood flow (**Figure 12**). Blood flow was stopped by occluding the brachial artery of the subject for a short period of time. A Pulsar 6i signal generator was used to input a 10 kHz, 0.9 mA square wave signal to the outer electrodes of the finger device. An oscilloscope was used to sample the data and record it to a disk for transfer onto a computer. To make the signal more legible, the line averaging function of Excel was used (averaged across 30 lines). Although the non-occluded graph seems slightly more pulsatile, there appears to be little significant difference between the two graphs. If the heart is approximated to pulse at a frequency of around 1 Hz, the space between pulses should be around 1 second. As originally expected, further signal analysis is required to isolate the signal of interest.
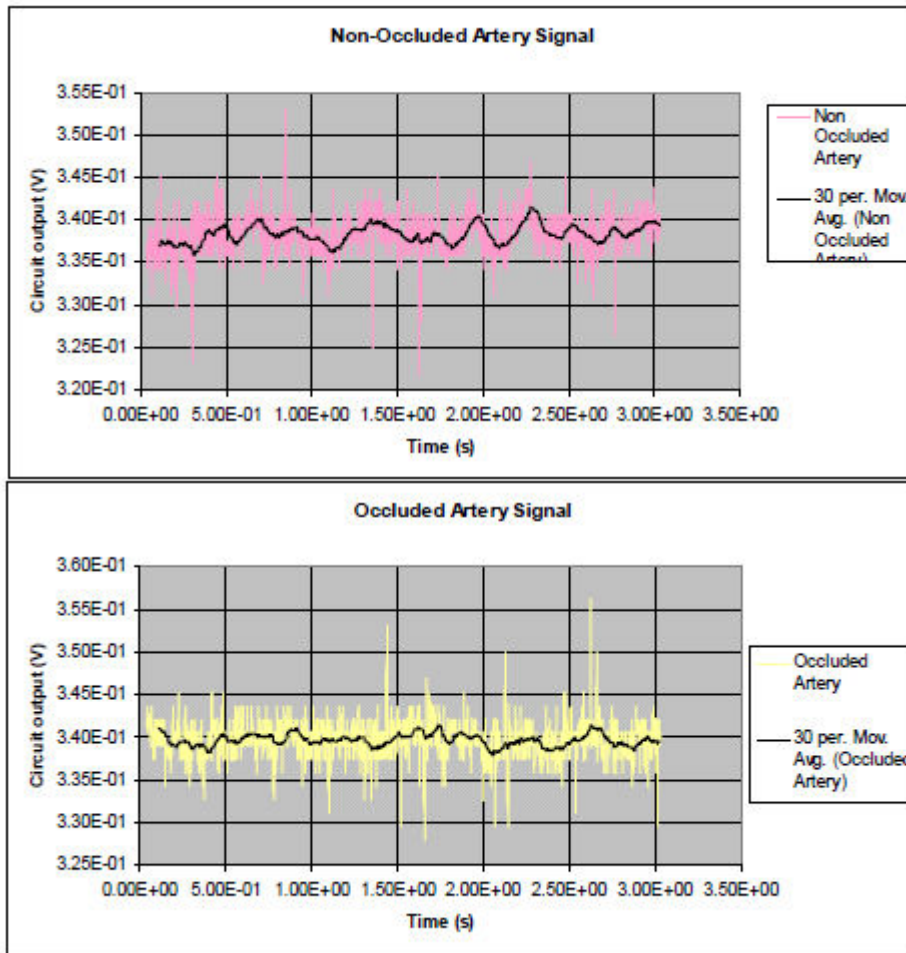
Figure 12: Graph shows output plethysmograph with artery occluded (bottom) and not occluded (top). Occluding artery will eliminate the change in impedance caused by blood flow. Black line shows line averaging over 30 time points

Current Design
Circuitry

   To limit the amount of variable affecting the data acquisition process, focus was directed towards finalizing the circuit design. This way once the circuit was finished, all efforts could be turned to redesigning and testing the finger-holder. Several modifications to the circuit were made to both increases accuracy and performance.

   One of the major problems last semester with the circuit's performance was the presence of a large repeating peak with gradual decrease before the peak started again. This interference was not seen after the first amplifier stage but was very prevalent after the 100 V/V gain amplifier. This artifact was determined to be the ripple voltage of the half-wave rectifier.

Initially the ratio of ripple voltage to peak voltage was .01V/V. This was achieved with a 100KΩ resistor and a 0.1µF electrolytic capacitor. To decrease the ripple voltage to a small enough value so that amplified peaks wouldn't interfere with the data collection. This was done by increasing the value of the capacitor to 10µF. This provided a ripple to peak ratio of .1V/mV. This small ripple, when amplified by 100 by the differential amplifier, led to only a .01V/V gain, which was small enough not to interfere with our signal.

The current finger holder design requires a constant current generator to provide a current through the finger so that a voltage can be detected. Last semester a Pulsar 6i stimulator/pulse generator was used as our constant current source. This system worked for preliminary testing, but was not appropriate to use as a permanent solution. The generator provided a pulse train, and wasn't a true AC signal, which we believed was necessary. The pulse train does not operate at a pure frequency like a sine wave does, and the additional higher frequency harmonics of the square wave could interfere with our data collection. This is especially true for when we conduct impedance versus frequency testing. To solve this problem a simple constant current source was developed (**Appendix A**). The current source consisted of an LM741 op-amp with a 1.2KΩ resistor at the inverting terminal. The finger holder could then be placed within the negative feedback loop of the op-amp. This would provide a constant AC current proportional to the AC voltage signal provided by the signal generator. In the future an oscillator would replace the signal generator in providing the appropriate voltage and frequency.

One key aspect of our circuit is the sample-and-hold and automatic reset circuit. To ensure accurate differential amplification of the changing signal, the sample and hold circuit must not allow any change in the voltage being held at the capacitor until the amplified signal trips the reset. While analyzing the circuit it was seen that the sample-and-hold may not be

holding the voltage constant between resets. After careful analysis, we have determined that the transistor may not be operating in the correct region to ensure reliable switching. Additional analysis must be made to correct this problem.

Circuit Testing

When attached to the finger holder, the circuit must detect a very small change in voltage and rectify, amplify and filter that signal so that it can be analyzed. To determine if our circuit was sensitive enough to detect the small change in voltage due to the resistance change in the blood we designed a resistive model of the finger (**Figure 13**). By using this model we could observe how the circuit would behave when presented with a signal believed to be similar to that obtained by the finger holder. It was established in past studies that the change in resistance would be approximately one part in a thousand. To do this we estimated the resistance of the blood in the finger to be 660Ω-cm. This was reinforced by research showing that average blood resistivity to be $\sim151\Omega$-cm [12]. By choosing a total resistance of 660Ω this estimated the finger length of 4.4cm.
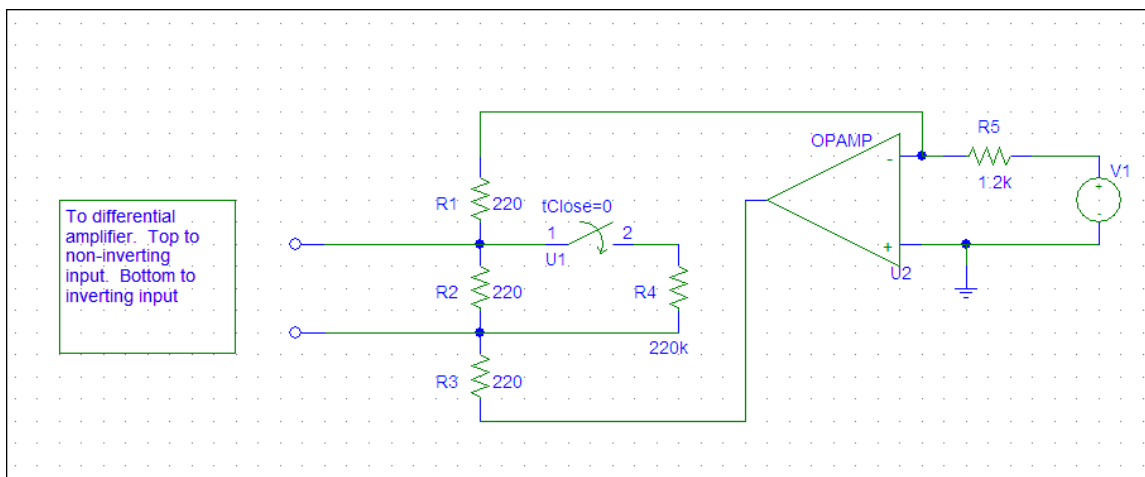

Figure 13: Schematic of the circuit used to model the resistance changes in the finger.

The model was building using three 220Ω resistors in series. To simulate a 1 in 1000 change in resistance, a $220k\Omega$ resistor was added in parallel to R2 (**Figure 13**). The change in

resistance was controlled with a momentary on – off switch. The voltage change across R2 was the input to the first amplifier stage of the circuit.

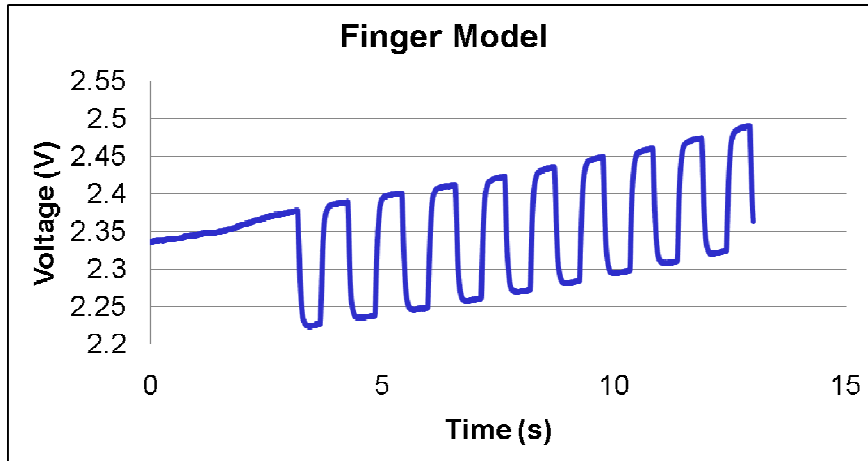Using this model, we were able to fine tune the circuit to determine what range of AC current was appropriate to achieve a significant voltage change at the output. It was found that an AC voltage of 1.1Vp-p at 10kHz provided a perceivable signal at the output of the circuit. The

Figure 14: Voltage signal result from testing with the finger model.

voltage change 0.15 Vp-p (**Figure 14**). One observation made during this testing was that when the switch was depressed for a long period the lower voltage drifted back towards the baseline. When the switch was released, the voltage jumped above the baseline and drifted down towards the baseline. We believe this observation can be attributed to the sample-and-hold circuit not operating correctly, but more tests are needed to determine this for sure. Another possible explanation for this could be the slow leakage of charge by the holding capacitor C1 (**Appendix A**).

Finger Holder

The past design is insufficient to detect the small signal changes. Because the finger stabilizer has a 1.5" inner diameter, there is a significant volume of saline solution between the finger and electrodes; the fingers that we tested had 0.5" diameters, and therefore there is at least

0.25" between the finger and electrodes. Current follows the path of least resistance, and because the saline solution is in closer proximity to the tin electrodes, current created will tend to flow through the solution. In order to address this, we acquired a 1" inner diameter PVC pipe and fabricated a finger holder with less separation between finger and electrodes in order to force more current through the finger. In doing so, were ableto detect a voltage drop across the finger and to detect pulsatile blood flow signals from the finger. The other aspect in changing the finger stabilizer was improving patient usability and improving the ergonomic aspects. This was done by an armrest.

Previously, the finger stabilizer is free-standing. The patient must either hold the finger stabilizer with their other hand or awkwardly rest the stabilizer on a surface. Both of these situations are problematic. First, the patient is placed in an uncomfortable position while utilizing the device. Second, because the patient often has to utilize both hands to stabilize the device, they are unable to use their free hand to manipulate other portions of the circuit/display. Third, because the device is free-standing, the patient will likely be unable to hold the device perfectly still and will introduce additional motion artifacts into the signal. By adding an arm-rest with a holder for the finger stabilizer, the patient was able to comfortably rest their arm, insert their finger at the appropriate angle, and use their free hand for other manipulations of the device.

Testing

In this study we focused on identifying a pulsatile signal caused by the varying impedance from blood flow. Signals were acquired for 10-30 seconds from the impedance plethysmograph, as well as a commercial pulse oximeter, (fig. 15). In order to reduce uncontrolled variables, the same 22 year old male subject was used in all studies. Measurements were recorded using NI Elvis digital interface breadboard and custom LabView software. The

pulse oximeter serves as a positive control in identifying the pulsatile signal from the heart beat. This signal helps identify the frequency of the heart beat in the spectral domain. The output signals from the finger plethysmograph and the pulse oximeter appear to have an aligned periodicity (fig. 15, fig. 7). This alignment is further analyzed by using a Fourier transform to view the signals in the frequency domain (fig. 16, fig. 19). The highlighted region (~.9 Hz or 54 BPM) of the spectral graph of fig. 16 shows an alignment of frequencies of the plethysmograph with pulse oximeter signals. The presence of a corresponding spectral peak to the pulse oximeter may signify a periodic component from the heart beat present in the plethysmograph signal. Frequency components from 0.5 -1.5 Hz were amplified by a factor of 3 and frequency components from 0-0.4 Hz were attenuated by a factor of 10 in order to clarify the signal of interest (fig. 17). The filtered signal further makes a correlation apparent between the periodicity of the pulse oximeter and plethysmograph signals.

A negative control was conducted in which the change in impedance from blood flow was removed from the plethysmograph signal by occluding the subject's brachial artery. Identical frequency analysis and filtering was performed on the negative control signals (fig. 18, fig. 19, fig. 20). In the frequency domain, there is a noticeable lack of a periodicity in plethysmograph signal. Futhermore, there is no significant peak in the expected 1 Hz range of the frequency domain signal (fig. 19).
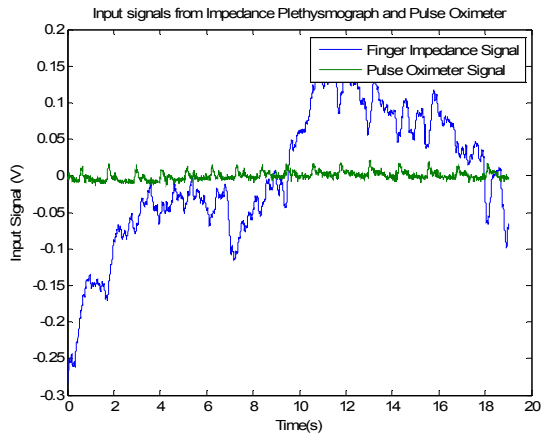
Fig. 15. Non-occluded raw data. Output from our finger plethysmograph and a pulse oximeter (positive control signal). Signals were sampled at 1kHZ. Both signals were normalized to zero.
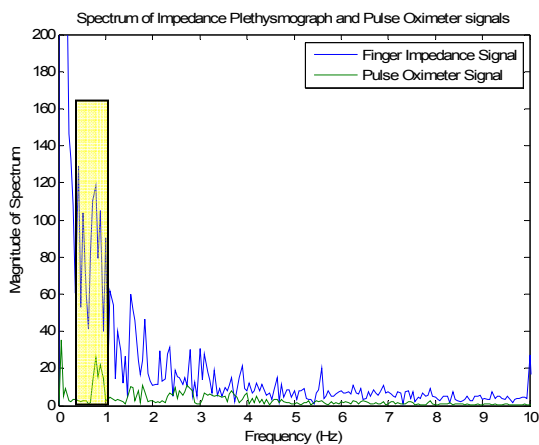

Fig. 16. Non-occluded spectrum. Spectrum of the signal (DC components of both spectrum are eliminated in the adjusted signal). There are two peaks aligned at ~1 that is likely cause by heart beat.
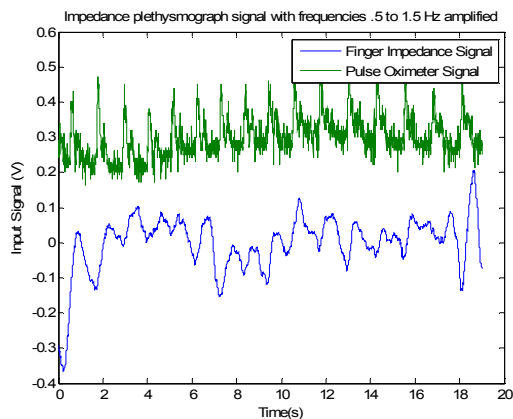

Fig. 17. Non-occluded filtered signal. The signal is boosted from 0.8-1.5 Hz frequencies by a factor of 3. Low frequency signals < |.2 Hz| are attenuated by a factor of 10. Heart beats appear apparent in both.

Occluded Artery Input signals from Impedance Plethysmograph and Pulse Oximeter
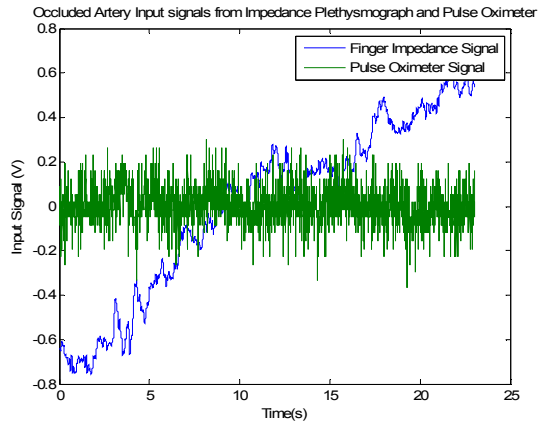
Fig. 18. Occluded raw data. Output from our finger plethysmograph and a pulse oximeter. Signals were sampled at 1kHZ. Both signals were normalized to zero.

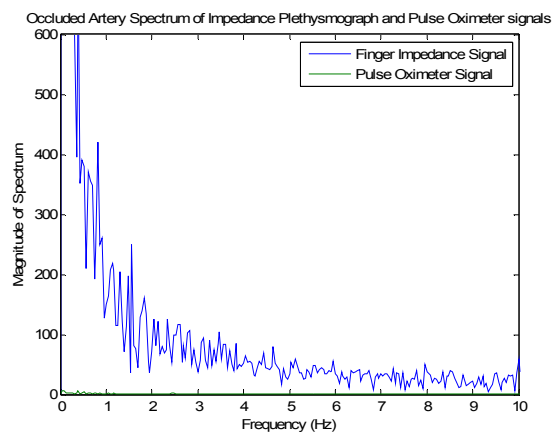Occluded Artery Spectrum of Impedance Plethysmograph and Pulse Oximeter signals

Fig. 19. Occluded spectrum. Spectrum of the signal (DC components of both spectrum are eliminated in the adjusted signal

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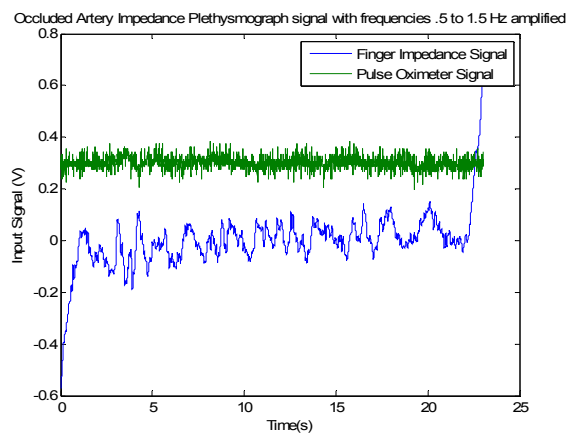Occluded Artery Impedance Plethysmograph signal with frequencies .5 to 1.5 Hz amplified

Fig. 20. Occluded filtered signal. Filtered output from our finger plethysmograph and a pulse oximeter

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Results and Discussion

From testing the finger model, it was shown that the circuit built could effectively amplify and rectify a changing voltage caused by a $1/1000\Omega$ resistance change. When the switch of the finger model was depressed, a 200mV voltage change resulted. This voltage change, while relatively small, is large enough to be accurately measured and studied. These tests confirmed that the circuit was functioning as predicted and that it could be used in conjunction with the plethysmograph. As noted above, the output had a 20mV/sec drift. This drift was the result of the sample and hold capacitor leaking charge slowly through the op-amp buffer. As of now this drift does not interfere with the data collection, but for future use in glucose measurement this drift will need to be minimized or eliminated.

Testing was performed on both generations of the finger holder prototype. The results from the tests done on the first generation (figures omitted) showed that a larger amount of current (5mA) was needed to produce a measurable signal. However, this signal revealed very little correlation to the pulse oximeter signal. When the same tests were performed on the second generation finger holder, a much smaller current (2.58mA) was needed to produce a sensitive and measurable signal. The difference was attributed to the idea that a majority of the current supplied to the electrodes did not pass through the finger, but instead passed through the saline surrounding the finger. The first generation finger holder used a larger diameter tube of 1.5''as compared to the 1'' diameter of the second generation. The use of a smaller diameter tube focused more of the current through the finger due to the smaller volume of saline. One drawback, that must be investigated, is the affect of the saline decrease on the devices ability to cancel out signals developed by the volume dependant resistance changes.

The second generation finger holder provided the best results during testing. The raw data from the device showed a correlation between the low dips and the peaks of the pulse

oximeter signal. This decrease in voltage with each heart beat matches the results observed with the finger model. This correlation validated the results gathered from the finger holder testing. The results from the brachial artery occlusion tests showed that when the blood flow was stopped with an inflated blood pressure cuff the correlating peaks and troughs between the pulse oximeter and plethysmograph signal disappeared. This further supports the claim that the troughs present in the non-occluded test are caused by the changing resistance of the vessel with each pulse of blood.

One aspect of the design was not tested during these trials, this being weather the saline had done an efficient job canceling out the volume dependent resistance changes. Because of this we are unable to state that the changes in voltage reported are caused solely by the hypothesized blood cell orientation and clumping, but most likely a combination of this and blood vessel volume changes. Additional testing is needed to discern between these two sources of resistance change.

From the testing done on the circuit and finger model prototypes it has been shown that impedance plethysmography of the finger may be a method for determining resistance changes in the blood. The results from these trials show that the current design is adequate enough to detect the change in resistance in the finger when the heart pumps blood through it; however additional improvements and testing are necessary to focus in on the resistance change due to blood cell alignment. Once this is done clinical trials can be performed to determine if the blood resistivity can be used to determine a persons blood glucose levels.

Future Work
Clinical Studies

Several areas of improvement are required on the prototype to make it an effective testing tool as a plethysmograph for blood resistivity, including building an optimal finger holder and defining the correct current amplitude and frequency. Once optimized, the device can begin clinical trials to determine whether a correlation between glucose levels and blood resistivity exists. The next step in that process is obtaining IRB approval, by proving that our device is safe and reliable so that we and our clients can test on human subjects. At the end of this study, it will hopefully be determined whether there is a correlation between glucose levels and blood resistivity. Further testing may also be conducted to determine whether other physiological factors of blood resistivity (such as protein composition) can also be measured with this device.

Conclusion

In the United States, over 17.9 million are afflicted with diabetes, with over $116 billion dollars being spent annually in diabetes related treatment. The development of a non-invasive system to measure glucose could improve the life of diabetic patients by allowing them to comfortably and painlessly measure their blood sugar. Impedance plethysmography of the finger can be used to measure blood resistivity, which may correlate to blood glucose levels and other physiological metrics. The semester's prototype with the changes described in the report, we believe, gave us a working prototype capable of measure the impedance of a finger. With a working prototype, our clients should be able to study the change in impedance from pulsatile blood flow in order to run clinical studies to correlate blood resistivity with glucose levels.

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Appendix A - Circuit

Schematic of the circuit used to amplify, rectify and filter the signal received from the finger holder. This schematic also shows how the sample and hold circuit is incorporated.
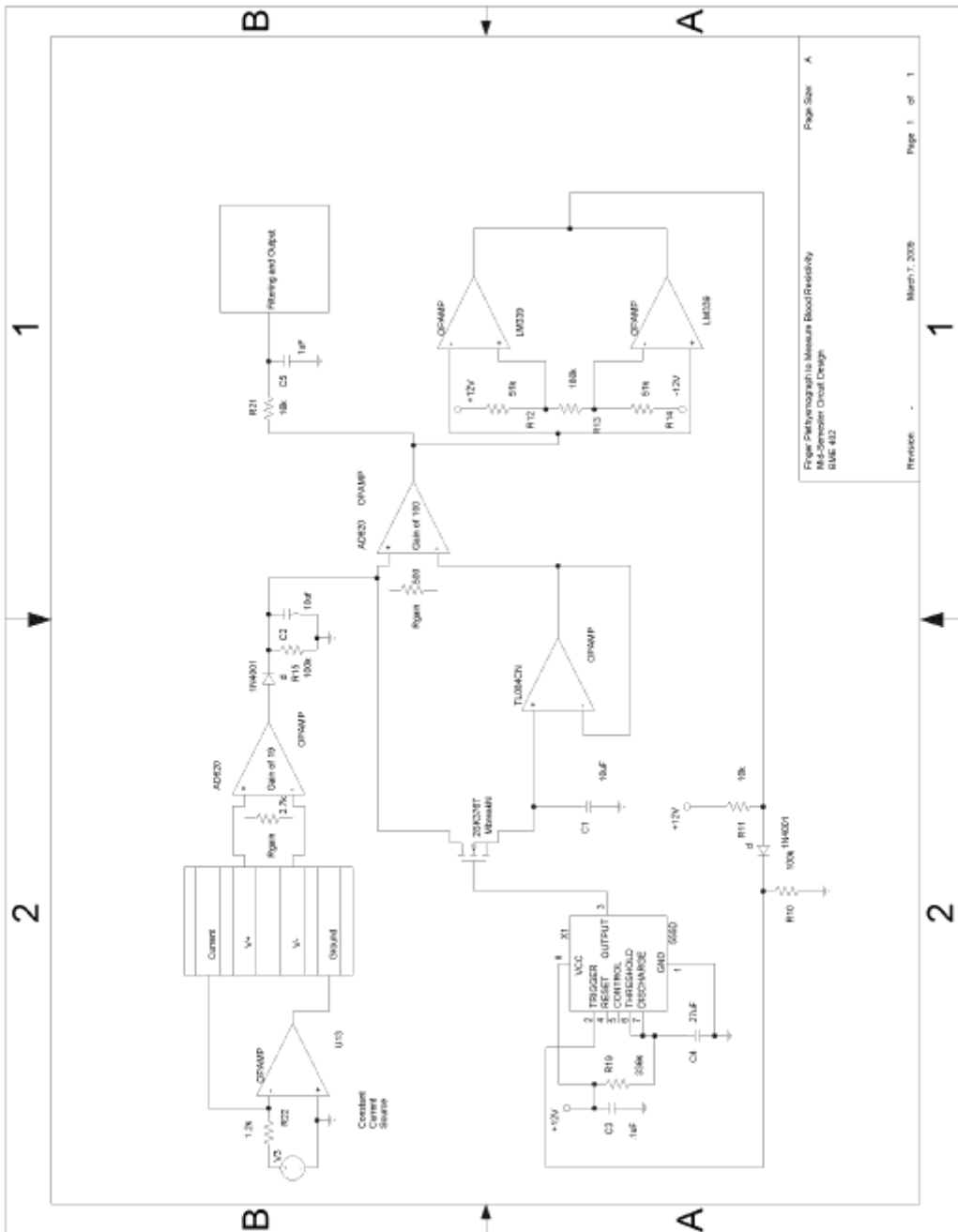
Appendix B – Product Design Specifications

A Finger Plethysmograph to Measure Blood Resistivity

Team Members: Tim Balgemann, Sarah Offutt, Lucas Vitzthum, Josh White

Function: Our goal is to design a finger plethysmograph to measure blood resistivity. Impedance plethysmography may be used to measure arterial flow change that occurs with propagation of the blood pressure pulse in a limb segment. For this measurement, we assume a constant value of blood resistivity that will change under dynamic and static conditions. However, blood resistivity and flow conditions may change under both physiological and pathological conditions. Use of an impedance plethysmograph on a finger immersed in a saltfilled beaker may yield a simple method for determining blood resistivity. This may develop into a method that diabetics can use to measure glucose level noninvasively.

Client requirements: **(itemize what you have learned from the client about his / her needs):** Briefly describe, in bullet form, the client needs and responses to your questions.
- The device must observe the change in impedance caused by pulsatile blood flow
- The device must meet all Institutional Review Board (IRB) requirements, so that it may be used in a clinical trial.
- The device should employ an automatic reset function to compensate for motion artifacts.

Design requirements: This device description should be followed by list of all relevant constraints, with the following list serving as a guideline. (Note: include only those relevant to your project):

1. **Physical and Operational Characteristics**
   a. *Performance requirements*: Initially, this device is intended to be used in a clinical research setting. Accordingly, it must be intuitive and easy to use for a trained medical professional. The data output must be reliable, and easy to read with a user friendly interface.

   b. *Safety*: The device will be designed so that the electricity used will not cause any harm to the user. Electrical exposure is limited to the finger, so no current should ever flow through the heart. The American Heart Association recommends that no more than 10 μA RMS current be applied across the chest. Because our device exceeds this limit, it is important that the device is thoroughly electrically insulated such that no alternative current route is made through the body. (www.americanheart.org) . Proper labeling must be used to ensure the patients and clinicians are aware of the dangers

involved with applying an electrical current to the body. The safety standards employed in this device should meet Institutional Review Board's regulations.

c. *Accuracy and Reliability*: Current home blood glucose meters' test results are considered 'accurate' if they falls within +/–20% of an accepted reference result, usually a lab test[1]. Although this seems like a high margin of error, our design is by definition going to be less accurate than current blood drawing methods, so exceeding their accuracy is unlikely. To compensate for motion artifacts, the device should use an automatic reset function.

d. *Life in Service*: The device should be operable for a period of up to 6 months or until the completion of the necessary testing and evaluation of the prototype can be completed. The device should be able to provide consistent results over an entire research trial with run times of up to 5 consecutive hours. The device should be able to withstand minor physical impact such as being dropped from a height of 1 meter.

e. *Shelf Life*: The device should be able to withstand a shelf life of up to 3 years if kept in a 10-35º C low humidity environment. The saline solution should be made fresh daily to prevent changes in salinity from evaporation.

f. *Operating Environment*: This device will be used in a clinical and laboratory setting. It will likely be in a controlled temperature, humidity and light environment. The lab will most likely have other instrumentation instruments, so the device will likely be subjected to electrical interference. This device should employ some means of reducing electromagnetic interference to the signal.

g. *Ergonomics*: The device must be able to accept a wide range of finger sizes, while minimizing finger mobility. The user must be able to easily insert their finger into the device with their finger and fore arm comfortably yet firmly restrained.

h. *Size*: The devices size must be such so that it doesn't interfere with the positioning of the finger and it can't hinder the data collection, but size is not a critical design constraint in this clinical setting

i. *Weight*: The prototype designed for clinical setting does not need to be overly light. It must be under 25 pounds so any personal can move it without assistance.

j. *Materials*: Materials must be corrosion resistant, as they will be exposed to a saline solution for an extend period of time. All non electrical components must be insulating, so that no other points of electrical contact are made with the body.

k. *Aesthetics*: Color, shape, form, texture of finish should look professional yet non intimidating to ensure both physicians and patients feel comfortable with the device.

2. **Production Characteristics**
    a. *Quantity*: We will initially construct 2-3 devices to be used in research.

    b. *Target Product Cost*: The current device is being designed for a research environment where low cost is not a high priority.

3. **Miscellaneous**
    a. *Standards and Specifications*: Must meet all Institutional Review Board Requirements for clinical trials. Exact specifications can be found at http://www.grad.wisc.edu/research/hrpp/hsirbs/hs.ForIRBMembers.html .

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