Noninvasive Hemoglobin Screening Device

Engineering World Health Design Competition Submission

Problem Definition

One of the biggest health issues facing developing countries is anemia, which is defined as a deficiency of red blood cells which are made primarily of a protein called hemoglobin. In Asia and Africa, the most prevalent type of anemia is iron deficiency anemia. Iron-deficiency anemia can be caused by blood loss, pregnancy, lack of iron in the diet, or an inability to absorb iron. These problems are difficult to resolve because the people affected are losing iron faster than they can consume food containing iron.

The Free Burma Rangers (FBR) are an organization for humanitarian service in high conflict regions such as Myanmar, formerly Burma. The Free Burma Rangers supply teams which provide emergency medical care, food, and shelter to those in need. One condition that affects the population that the FBR interacts with is anemia. Because hemoglobin levels are indicative of anemia, which can cause serious health concerns, it is important to have a device which can screen hemoglobin levels of many people over a short period of time.

Impact in Developing World

Currently, the FBR use a method called the Hemoglobin Color Scale, a simple and inexpensive test requiring a drop of blood, which can be used by non-health professionals in isolated areas. This device is only 80% accurate, meaning that 20% of the time the device yields an inaccurate reading. The FBR workers need a simple but more accurate device to measure hemoglobin that does not use expensive reagents or machinery. The device would have to be low cost and durable to withstand the climate of Myanmar.

Described in this paper is a non-invasive hemoglobin measurement device. This technology promises to be low-cost, more sustainable, and matching or exceeding accuracy to the current test used by the FBR. The current method used is invasive and not completely reliable. Although some noninvasive methods of hemoglobin measurement exist, they are prohibitively expensive and not sustainable in a harsh environment. The non-invasive method eliminates the concern for open infection and use of consumables, as well as providing an opportunity for increased reliability and sustainability.

Required Performance Specifications

In order to effectively perform the hemoglobin screen in the context for which it is designed, this device must be cost effective, accurate, rugged, dust proof, and waterproof. It must be hand-held, less than five pounds in weight, and smaller than ten inches in length. This technology is designed to be operated by untrained workers in the developing world to assist with detecting, processing, and quantifying levels of hemoglobin in erythrocytes by utilizing the principle of photoplethysmography (PPG) and Beer-Lambert's Law.

Implementation of Prototype

Two PPG signals must be obtained before hemoglobin levels can be determined. To obtain these signals, the team chose the Covidien DS100A Nellcor Oximax SPO_2 Sensor. This is a pulse oximeter finger clip that contains a red LED for one signal, an IR LED for the other signal, and a photodiode. The LEDs are shined through the finger, and the light detected by the photodiode on the other side produces a current. The desired PPG signals must be measured as a voltage. To accomplish this, a transimpedance amplifier was constructed using a MCP6004 quad-op-amp chip and a 180kΩ resistor connected between the negative input and the output.

From here, the signals must be filtered to remove any noise or frequencies outside of the range of 0.5 to 3.4 Hz, which is a common frequency range for a PPG signal. The filter circuit has two stages. The first contains a passive high-pass filter and an active low-pass filter with a gain of 48 that also uses the MCP6004 chip. The second filter stage is the same as the first but having two stages makes the signal's transition band narrower, removing additional unnecessary frequencies [See **Appendix A** for Filter Circuit Schematic]. The signal then goes to another op-amp in the MCP6004 configured as a non-inverting buffer with unity gain. This circuit was obtained through the work on "Easy PPG" by Embedded Lab [See **Appendix H** for References]. The output provides the required PPG signals.

The device uses a Raspberry Pi 3 Model A+, an ADS1015 analog to digital converter, and an MCP4725 digital to analog converter [See **Appendix B** for Block Diagram]. These components are used to receive the PPG signals, make the required calculations, and output the patient's hemoglobin level. These results are displayed on a SparkFun 16x2 SerLCD screen, and the data is stored on a 32GB micro SD card. The device is powered by a 5V 4000mAh battery pack made by VGE [See **Appendix C** for Schematic]. All components are sealed inside a 3D printed case designed by the team, which features waterproof buttons, switches, and connectors [See **Appendix D** for Case Drawings].

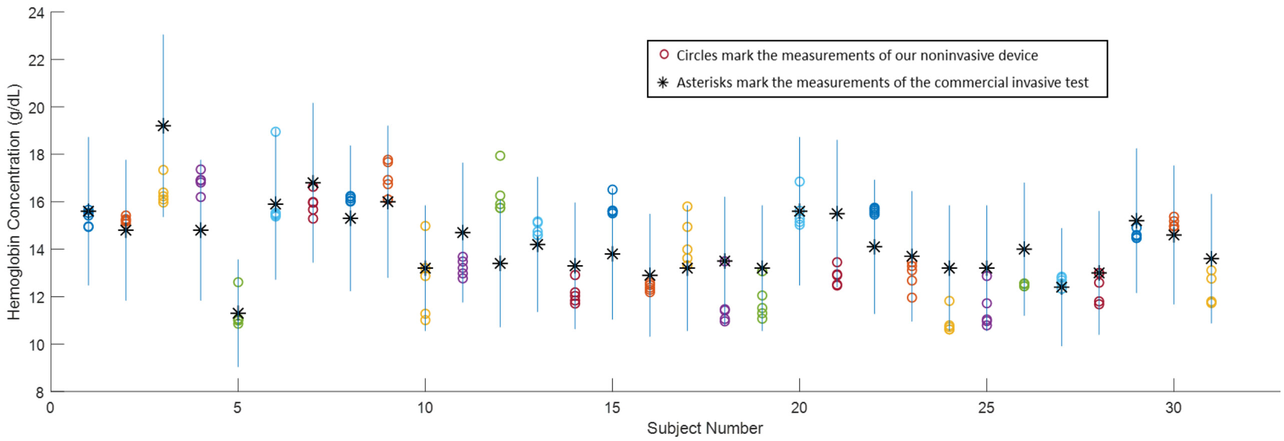
The hemoglobin concentration level is calculated using the principles of photoplethysmography and Beer Lambert's Law. Photoplethysmography is an optical technique for measuring volume changes in the blood. Beer Lambert's Law states that the amount of absorbance by a substance is directly proportional to the product of path length travelled by light through the substance, extinction coefficients, and concentration of the substance. Using this knowledge and several assumptions, the concentration of hemoglobin in the blood can be calculated. The calculations were performed in Python 3 on the Raspberry Pi. This method of calculating hemoglobin has been attempted and published previously [See **Appendix H** for References]. The equations for path length, oxygen saturation, and total hemoglobin concentration have been adapted from the previous published works [See **Appendix E** for Calculation Flow Chart].

The prototype meets the given specifications in size and weight. The device weighs 1.58 pounds and measures 7.96 x 3.75 x 2.51 inches.

Proof of Performance

Accuracy

Thirty-two subjects have been tested with this device. Each subject was tested five times with this device and once with an invasive test (AimStrip Hemoglobin meter). The results are shown in the figure below.



Asterisks mark the measurements of the commercial invasive test and circles mark the measurements of the noninvasive device. The vertical bars represent 80% accuracy to the commercial point of care device.

It is of note that the point of care test used as "standard" was neither entirely accurate nor precise. The invasive standard had an average deviation of 0.575 g/dL. A more accurate standard would be the results from a hematology laboratory where a blood sample is taken and tested by a medical professional for its hemoglobin concentration.

Percent accuracy was calculated as

$$\%\ Accuracy = 100 - \left|\frac{Hb_{actual} - Hb_{measured}}{Hb_{actual}} * 100\right|$$

where Hb_{actual} is the measurement from the commercial invasive test and $Hb_{measured}$ is the measurement from this device. The accuracy of this device for 32 subjects with five tests for each was 91.5% accurate to the invasive standard.

Precision
The average deviation was calculated as

$$Average\ deviation = \frac{\sum|Hb_{measured} - \mu_{Hb}|}{n_{trials}}$$

where μ_{Hb} is the mean of the measured hemoglobin values measured among five trials and n_{trials} is five. The average deviation is 0.415 g/dL.

The standard deviation was calculated as

$$\sigma = \sqrt{\frac{\sum(x-\mu)^2}{n\cdot 1}}$$

The average standard deviation for this data is 0.556 g/dL with a mean of 14.01 g/dL.

Reusable and Non-Consumable
This device can be used repeatedly without the necessity of consumables such as needles and test strips. The devices currently used in the target market (Myanmar and clinics elsewhere in the developing world) are invasive tests which are one-time use and require multiple consumables.

Non-invasive
This device uses light-based sensing and Beer-Lambert's law to measure hemoglobin concentration in the blood. Oxyhemoglobin absorbs more infrared light than red light and deoxyhemoglobin absorbs more infrared light. When the red and infrared lights are shone through the finger, the photodiode receiving the unabsorbed light yields a photoplethysmographic wave which represents absorbance. Absorbance, along with oxygen saturation, extinction coefficients, oxygen saturation, and light path length is used to calculate a total concentration of hemoglobin.

Fast Reading
After the user begins the test, the infrared light shines for thirty seconds and then turns off. Then the red light shines for thirty seconds. Including user operation, initialization, and computation, the entire test takes one minute and thirty seconds.

Water, drop, and dust resistant
The electronic components of the device are designed to be potted in epoxy resin. This process fills the entire electronic assembly with epoxy which ensures resistance to shock and vibration as well as

protects the sensitive electronic components from moisture and corrosion. The electronics potting makes the device resistant to drops and water resistant so that it is submersible under water up to 1 meter for 30 minutes.

Cost
The cost of the prototype is $439.76; however, the technology can be manufactured at $112.29 per unit when more than 1,500 units are produced [See **Appendix F** for Cost Breakdown].

Business Plan

Market
This technology will be marketed to international charities focused on medical care.

Funding
This technology will be initially funded by outside sources-- National Science Foundation research grants and several angel investors. The technology will be sustainable with sales after the sale of 1,500 units.

Sales
The devices will be sold to international charities at 150% of manufacturing costs, which are estimated at $112.29 per unit. The 50% margin accounts for labor and overhead costs.

Manufacturing
This technology contains two major components, the printed circuit board (PCB) and a housing unit, which would need custom manufacturing. All other components are commercially available and would only need to be purchased for final assembly. The housing unit for the device would be injection molded low density polyethylene (LDPE). LDPE is a lightweight impact resistant plastic often used in medical laboratory equipment. Estimated production cost of 10,000 housing units is $13.51 per unit and $135,100 total.

The PCB would contain the analog-digital converters, filters, and control circuit. Estimated production cost of 10,000 units is $3.30 per unit and $33,000 total. Both the housing unit and the PCB will be manufactured in China. China has many plastic molding facilities as well as PCB manufacturers.

Final assembly of the device will take place within a developing country in order to help promote the economy of the country through job growth. This would also keep the manufacturing of the device lower which in turn could lower the final cost of this device. Levels of inspection occur after obtainment of parts, shipment of parts, and assembly. The inspection includes rigorous tests to ensure quality and performance specifications.

Distribution

This technology will be distributed to Myanmar, to meet the initial motivation for this device-- the needs of the Free Burma Rangers. This device could also be distributed to developing countries across the world. Parts will be transported by ship out of the global port in China from there they will be transported to the assembly locations by local couriers.

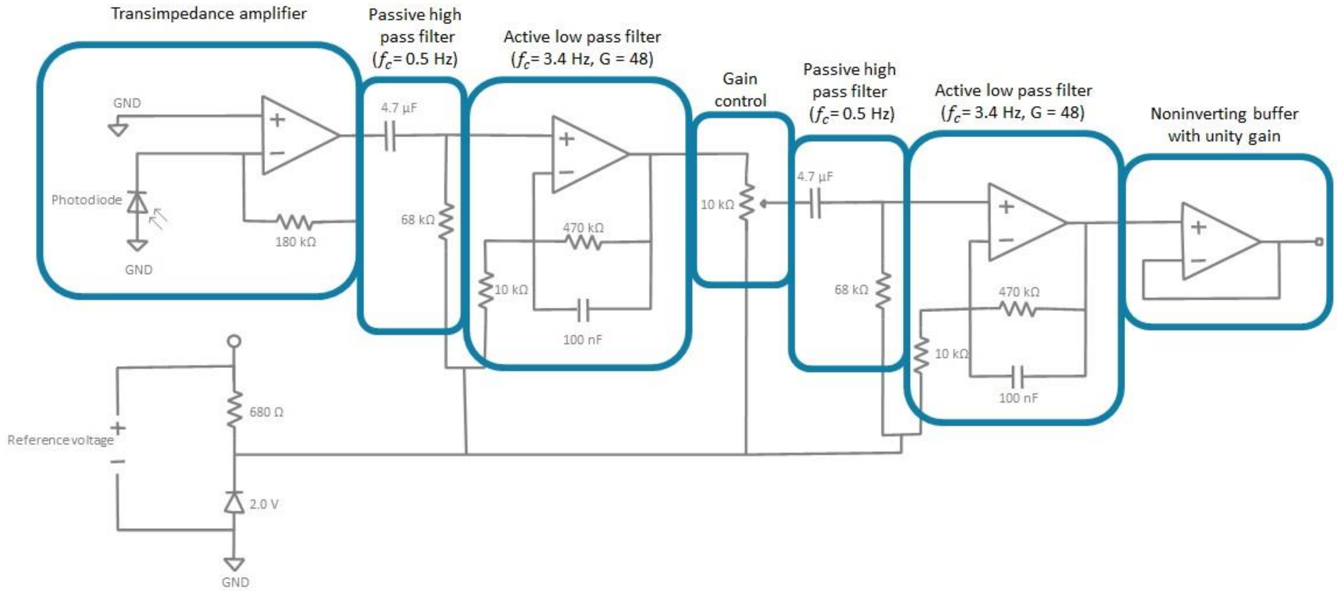
With the help of charities and Non-Government Organizations (NGO) which have connections to local clinics, the device can be distributed and administered there. Partnerships will be established with the charities to implement a training program in which locals can be equipped to use and maintain the device effectively.

Regulation/Patent

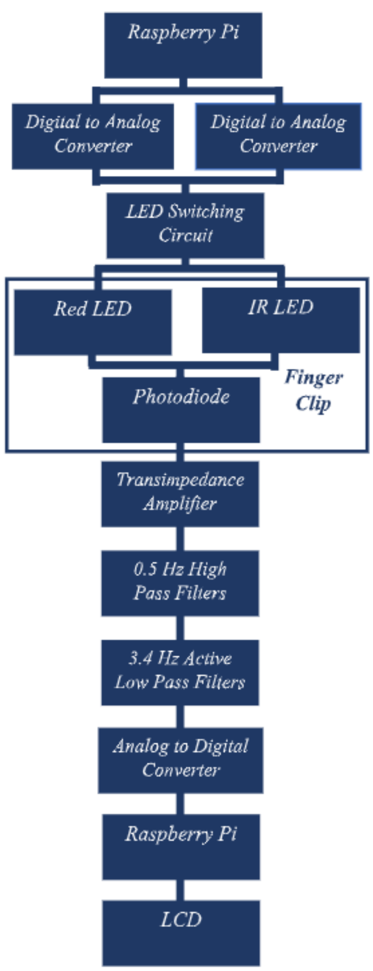
To ensure the accuracy and safety of this device it would need to be certified by the FDA. The FDA is the most common regulatory agency of medical devices and is accepted in most of the world. The intellectual property used to develop this technology was published in a journal for the Institute of Electrical and Electronic Engineers (IEEE).

Appendices

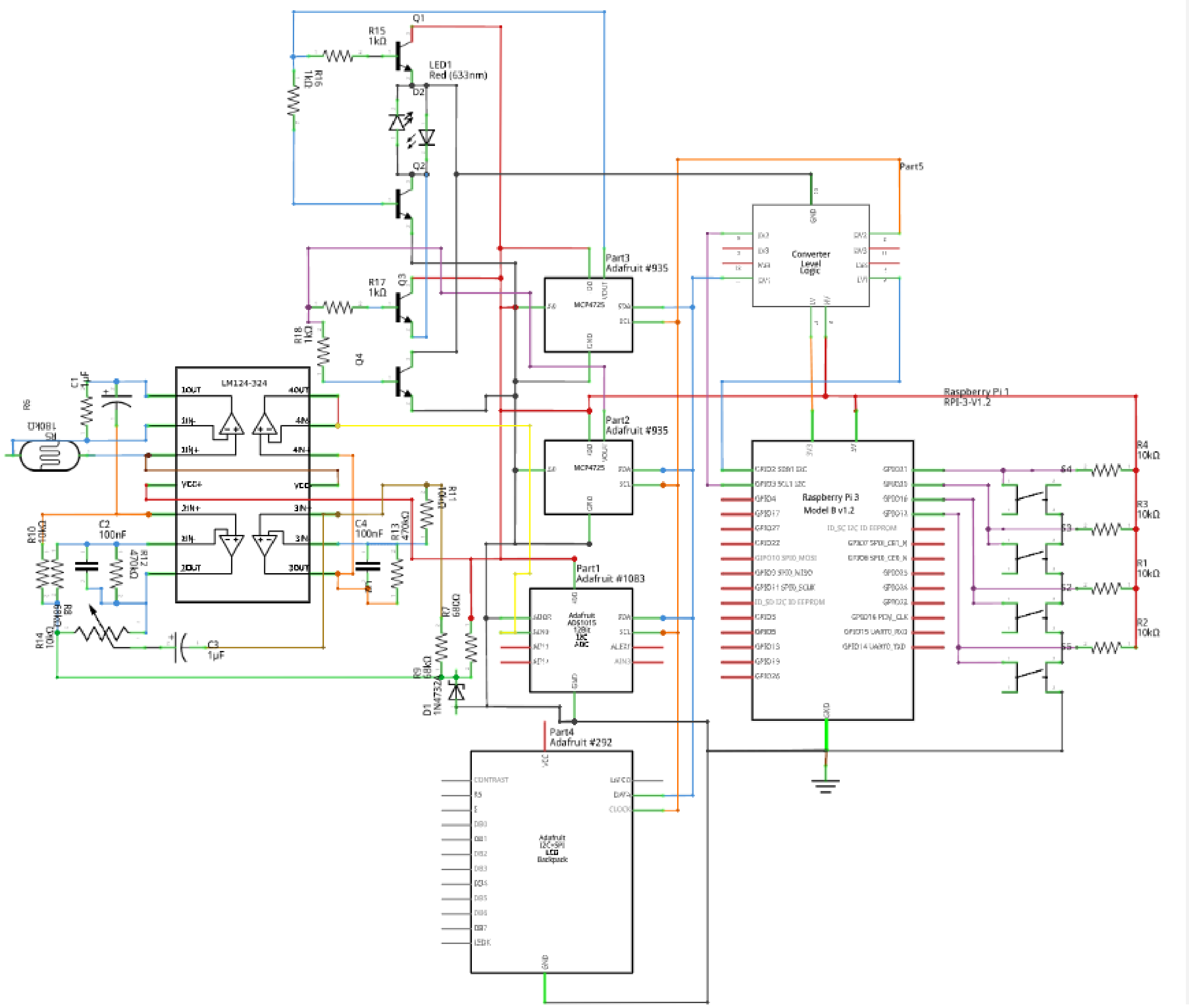
Appendix A – Filter Circuit Schematic



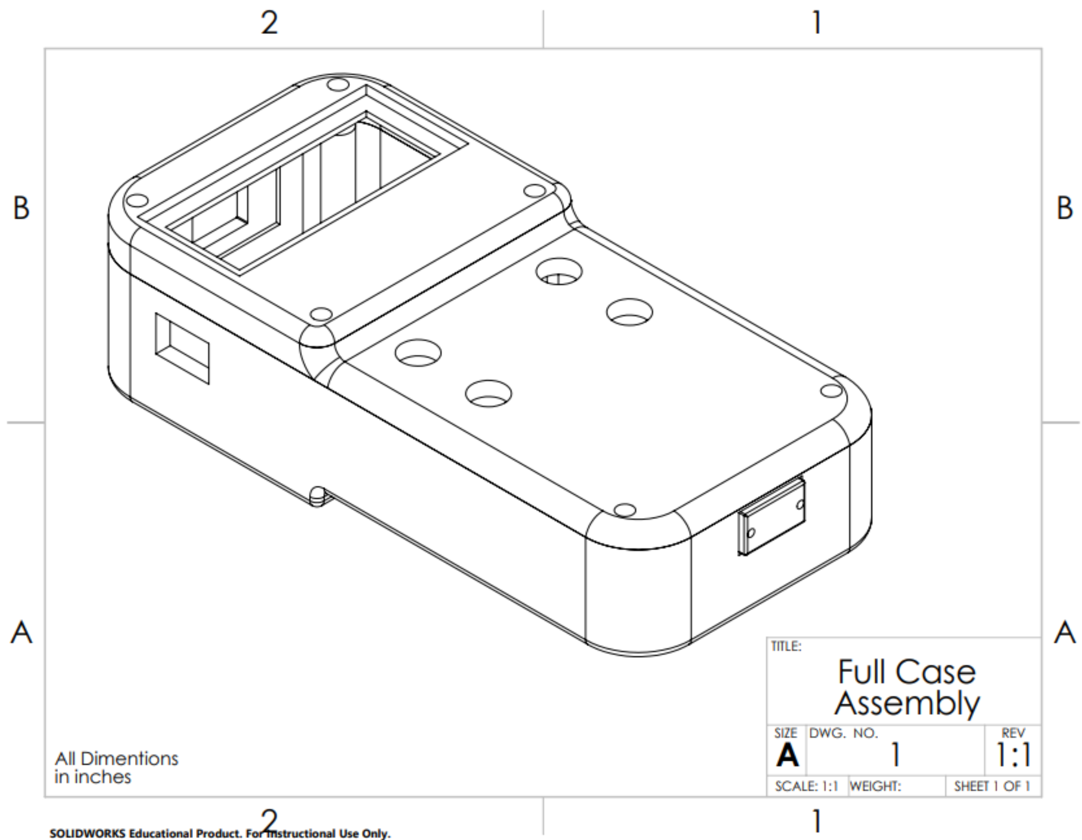
Appendix B– Hardware Block Diagram

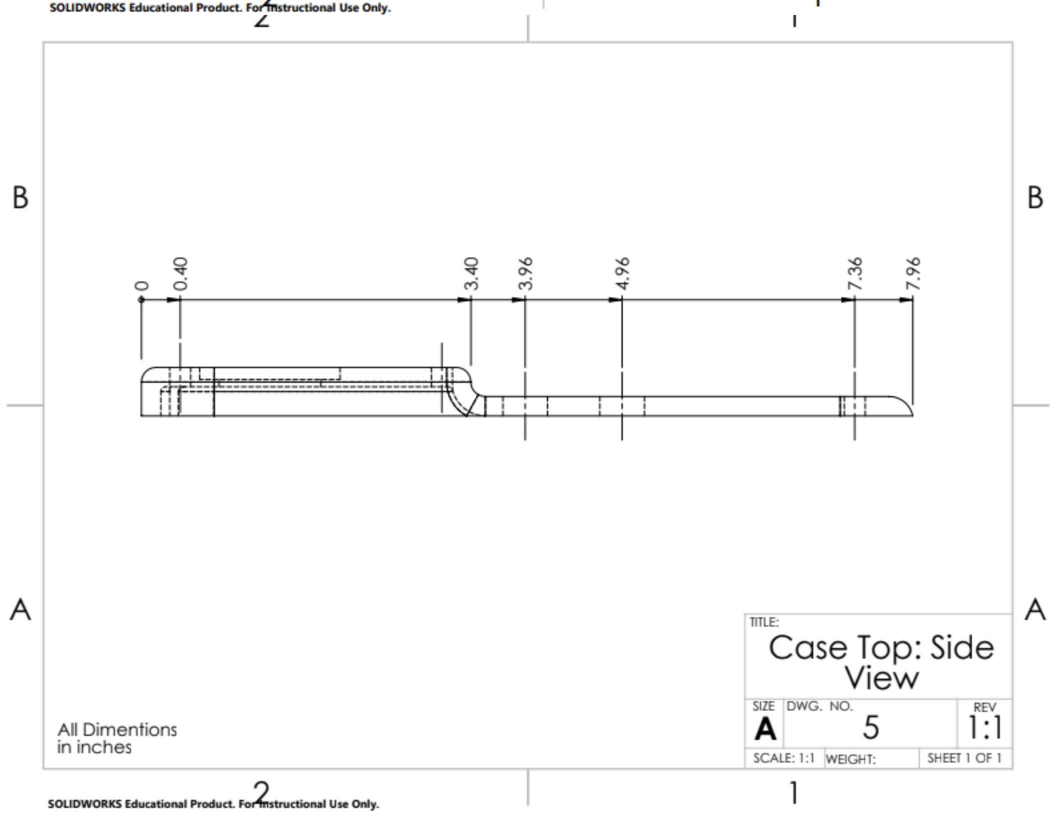


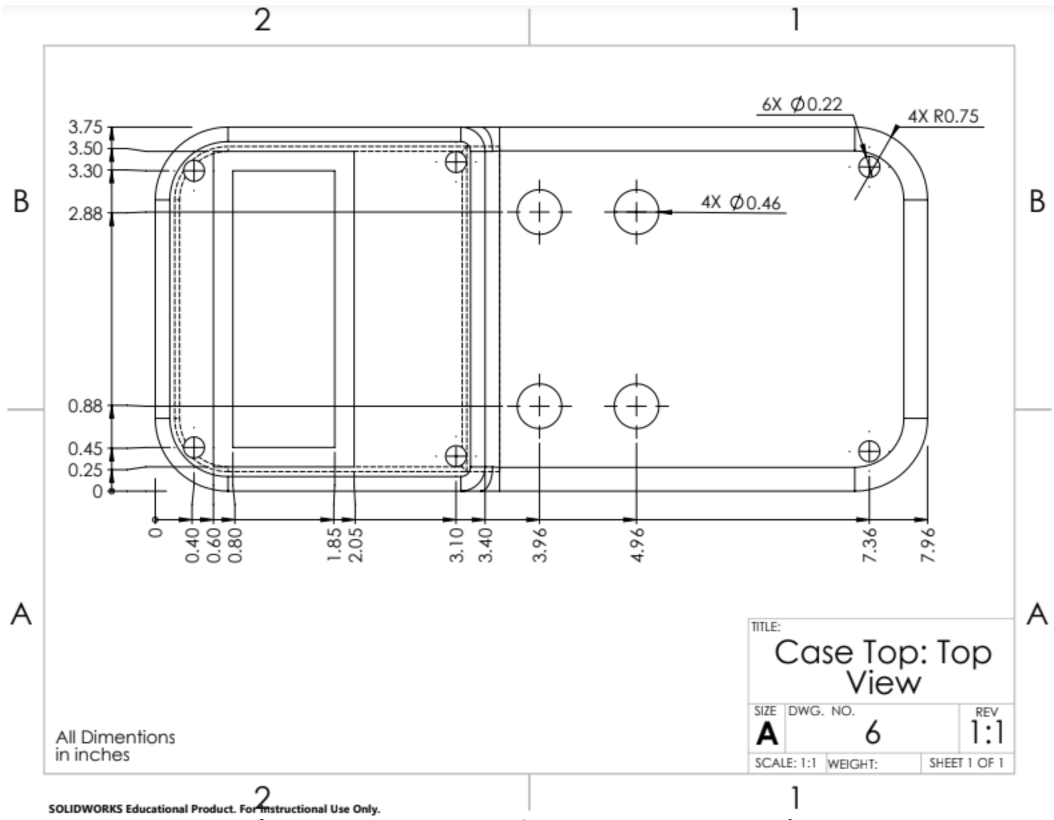
Appendix C – Complete Schematic

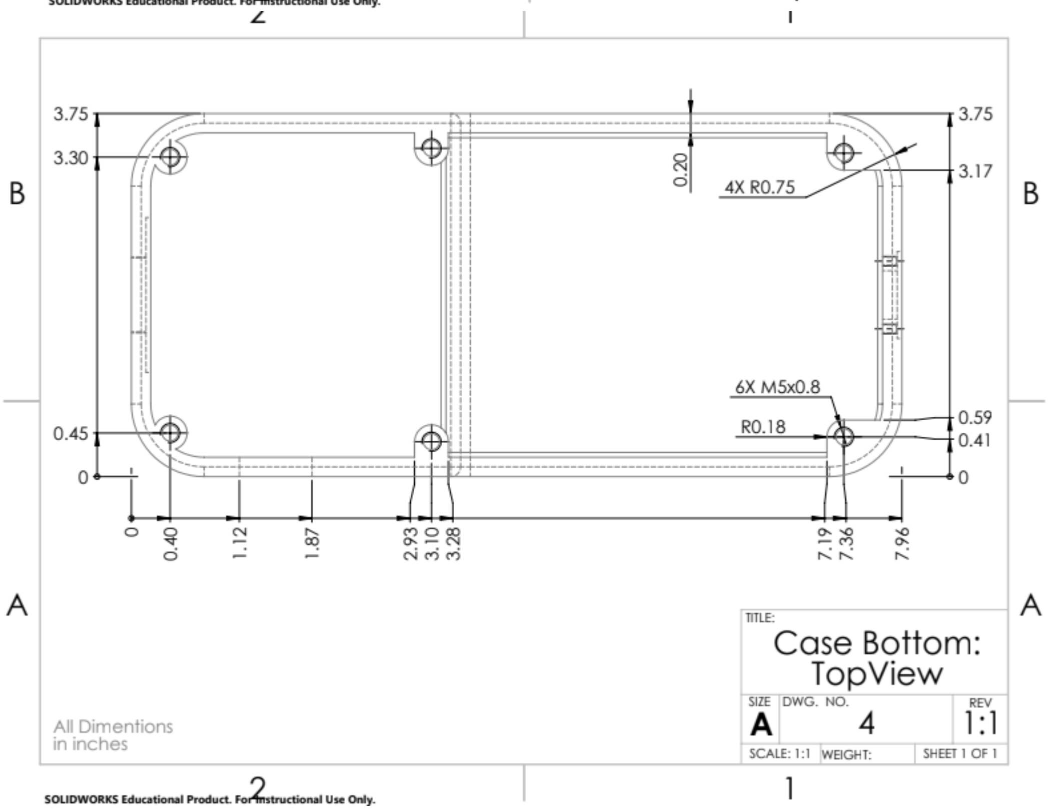


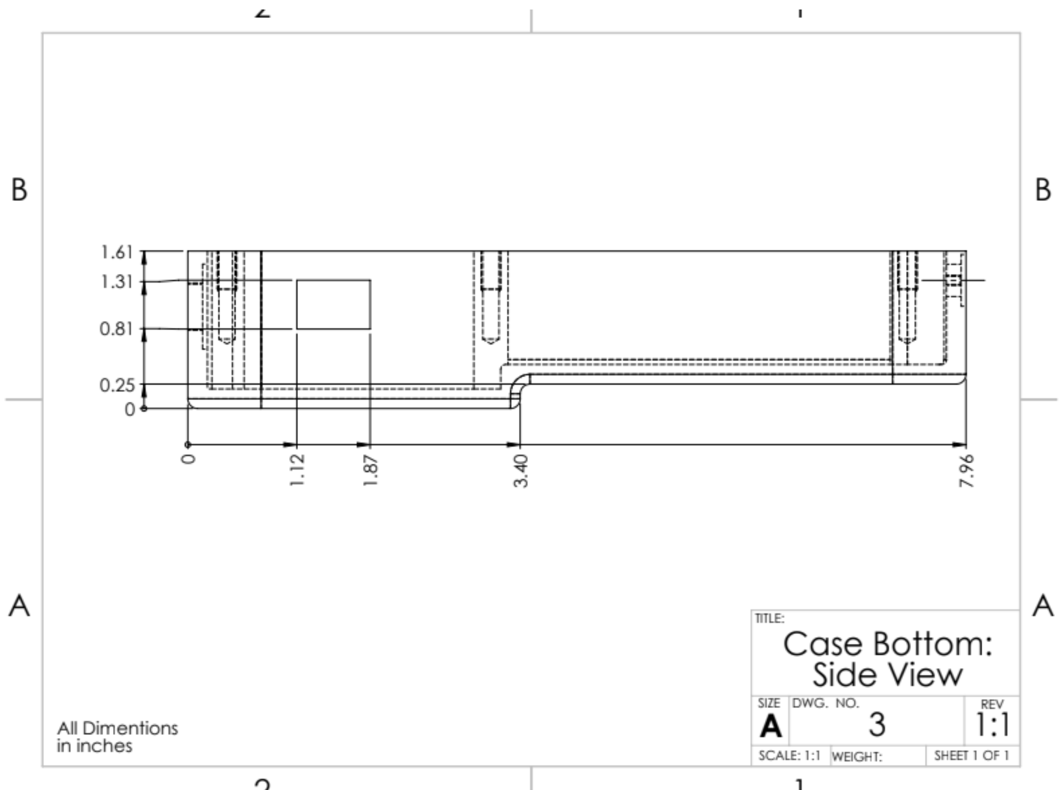
Appendix D – Case Drawings



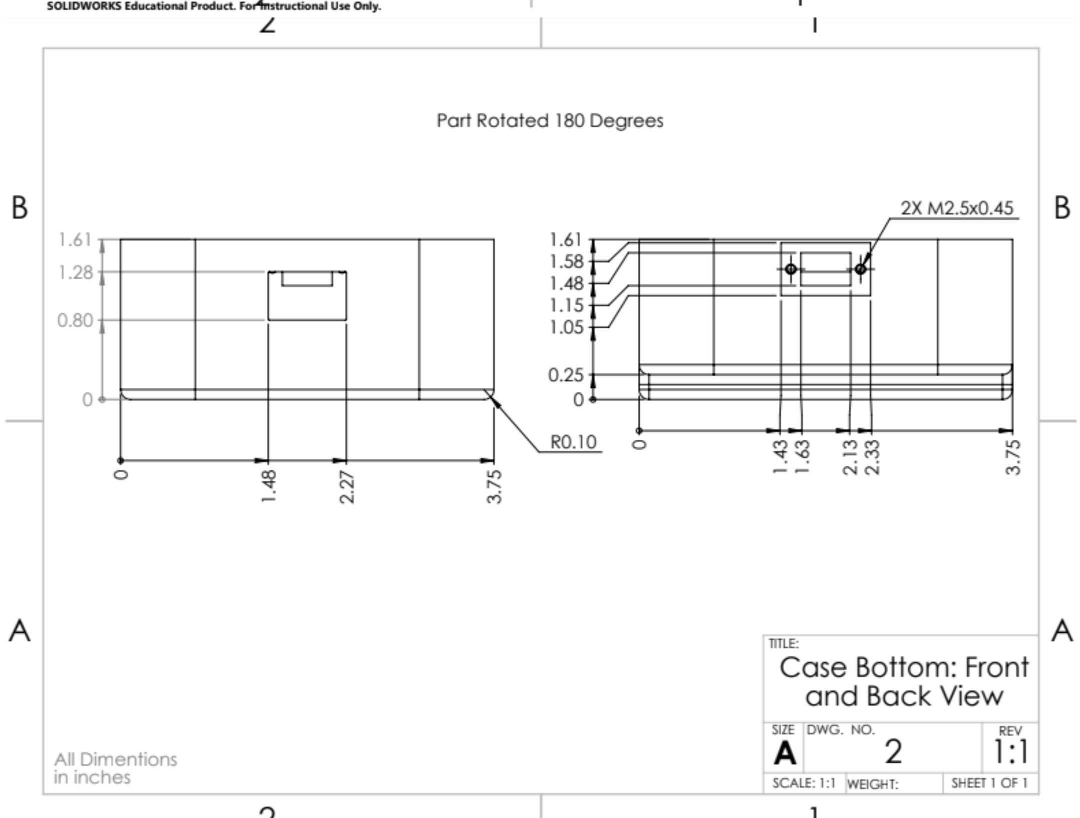



6X Ø0.22
4X R0.75
4X Ø0.46
3.75
3.50
3.30
2.88
0.88
0.45
0.25
0
0
0.40
0.60
0.80
1.85
2.05
3.10
3.40
3.96
4.96
7.36
7.96
TITLE:
Case Top: Top View
SIZE A
DWG. NO. 6
REV 1:1
SCALE: 1:1
WEIGHT:
SHEET 1 OF 1
All Dimentions in inches
SOLIDWORKS Educational Product. For Instructional Use Only.


3.75
3.30
0.45
0
0.20
4X R0.75
3.75
3.17
6X M5x0.8
R0.18
0.59
0.41
0
0
0.40
1.12
1.87
2.93
3.10
3.28
7.19
7.36
7.96
TITLE:
Case Bottom: TopView
SIZE A
DWG. NO. 4
REV 1:1
SCALE: 1:1
WEIGHT:
SHEET 1 OF 1
All Dimentions in inches
SOLIDWORKS Educational Product. For Instructional Use Only.

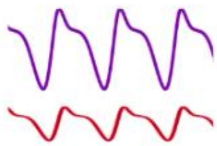


2
1
B
B
1.61
1.31
0.81
0.25
0
0
1.12
1.87
3.40
7.96
A
A
TITLE:
Case Bottom:
Side View
SIZE
A
DWG. NO.
3
REV
1:1
SCALE: 1:1
WEIGHT:
SHEET 1 OF 1
All Dimentions
in inches
2
1



2
1
Part Rotated 180 Degrees
B
B
2X M2.5x0.45
1.61
1.28
0.80
0
0
1.48
2.27
3.75
R0.10
1.61
1.58
1.48
1.15
1.05
0.25
0
0
1.43
1.63
2.13
2.33
3.75
A
A
TITLE:
Case Bottom: Front
and Back View
SIZE
A
DWG. NO.
2
REV
1:1
SCALE: 1:1
WEIGHT:
SHEET 1 OF 1
All Dimentions
in inches
2
1

Appendix E – Calculation Flow Chart



Infrared and red PPG signals are acquired for approximately 30 seconds

$$A_R = Amplitude\ Red$$
$$A_{IR} = Amplitude\ Infrared$$

Amplitudes of the infrared and red PPG signals are calculated excluding extremes and averages

$$DC_R = DC\ Level\ of\ Red$$
$$DC_{IR} = DC\ Level\ of\ Infrared$$

DC level of infrared and red PPG waves are calculated

$$V_R = \frac{A_R}{DC_R}$$
$$V_{IR} = \frac{A_{IR}}{DC_{IR}}$$

Signals are normalized by diving each signal by its corresponding DC component

$$R = \frac{V_{IR}}{V_R}$$

Ratio of ratios is calculated by diving the normalized signals

$$SpO_2 = \frac{\varepsilon_R - \varepsilon_{IR} \cdot R}{\varepsilon_R - \varepsilon_{RO} + \left(\varepsilon_{IRO} - \varepsilon_{IR}\right) \cdot R}$$

Oxygen saturation is calculated using the ratio of ratios and the extinction coefficients of hemoglobin

$$T_f = -0.00031 + .03642 \cdot V_{IR}$$
$$T_f = -0.001641 + 0.0495421 \cdot V_{IR}$$

Path length of light is calculated separately for male and female subjects

$$Hb = \frac{V_{IR}}{\left(\varepsilon_{IR} + \left(1 - SpO_2\right) + \varepsilon_{IRO} \cdot SpO_2\right) \cdot T_f}$$

Hemoglobin concentration is calculated using the prominence of the normalized infrared PPG signal, path length, and oxygen saturation

Appendix F – Cost Breakdown

Item	Price per unit	Price in Bulk	Quantity	Price	Bulk Price
Nellcor Ocimax Reusable SpO2 Sensor	$ 75.00	$ 20.00	$ 1.00	$ 75.00	$ 20.00
Battery	$ 25.95	$ 14.00	$ 1.00	$ 25.95	$ 14.00
Raspberry Pi Model 3 A+	$ 25.00	$ 10.00	$ 1.00	$ 25.00	$ 10.00
DAC	$ 4.95	$ 3.00	$ 2.00	$ 9.90	$ 6.00
ADC	$ 9.95	$ 7.00	$ 1.00	$ 9.95	$ 7.00
Push Buttons	$ 0.73	$ 0.50	$ 4.00	$ 2.92	$ 2.00
32GB Memory Card	$ 9.98	$ 2.00	$ 1.00	$ 9.98	$ 2.00
Rocker Switch	$ 2.00	$ 0.20	$ 1.00	$ 2.00	$ 0.20
LCD Screen	$ 19.95	$ 16.00	$ 1.00	$ 19.95	$ 16.00
Case	$ 233.31	$ 13.28	$ 1.00	$ 233.31	$ 13.28
Potting	$ 0.11	$ 0.11	$ 64.00	$ 6.91	$ 6.91
Logic Level Converter	$ 2.00	$ 0.60	$ 1.00	$ 2.00	$ 0.60
Op AMP	$ 0.89	$ 0.30	$ 1.00	$ 0.89	$ 0.30
PCB	$ 16.00	$ 14.00	$ 1.00	$ 16.00	$ 14.00
				Total Price	**Total Bulk Price**
				$ 439.76	$ 112.29

Appendix G – Device Photo

Appendix H – References

Chugh, S. (2015). Non Invasive Hemoglobin Monitoring Device. *IEEE*.

EASY PULSE SENSOR (VERSION 1.1) OVERVIEW (PART 1). (2013, April 20). Retrieved from Embedded Lab: http://embedded-lab.com/blog/easy-pulse-version-1-1-sensor-overview-part-1/

Lopez, S. (2012). Pulse Oximeter Fundamentals and Design. *NXP Semiconductors*.

Meinke, M. F. (2006). Model function to calculate the refractive index of native hemoglobin in the wavelength range of 250 –1100 nm dependent on concentration. *Applied Optics*.

W.G. Zijistra, A. B.-v. (1991). Absorption Spectra of Human Fetal and Adult Oxyhemoglobin, De-Oxyhemoglobin,. *Clinical Chemistry*.