Noninvasive PoC Anemia Detection Device

Team 11 - Final Report
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Abstract

Anemia, or iron deficiency of the hemoglobin in the blood, is a preventable disease that affects over two billion people worldwide, according to the World Health Organization (WHO). Diagnosis typically requires a visit to the nearest physician to get a blood test, which is costly, invasive, and inconvenient, especially to the many people in developing countries that are affected by this disease. We constructed an inexpensive, wearable, diagnostic device that was successfully able to distinguish between anemia and non-anemia between a small (n=2) cohort of patients with known anemia diagnoses.

Table of Contents

Introduction

Objective

The purpose of this project is to design and prototype a non-invasive point of care device for the detection of anemia. The minimum viable product will deliver two complete detection systems for data capture, a processing system for data analysis and detection, a power system for delivering the required capacity and charging needs, and a diagnosis indicator to relay the results to the testing administrator.

Background

Anemia is a condition that affects nearly 2 billion people, according to the WHO. Anemia is an entirely preventable disease, and once detected, the patient can take corrective action to restore their iron levels to a healthy state. According to Miller et al, the probability that you are affected by anemia increases five-fold in underdeveloped geographies [1]. Current non-invasive POC detection methods can be relatively expensive, and are difficult to move from place to place which makes them all the more inaccessible to the geographies that need it most. We propose to build a more portable and cost effective non-invasive anemia detection method by combining image and spectroscopy based detection methods in a wearable device that can be taken to regions without adequate medical facilities and used to help diagnose this preventable disease.

High-level Requirements

1. The device we build will be required to provide accurate binary diagnosis of anemia at least 9 times out of 10. To elaborate, this would require the system to perform at an accuracy of 90%, allowing for an error rate of 10%. Furthermore, the error rate includes errors caused by false positives and missed detections alike.

2. The device should be able to provide diagnosis based on data from both the oxygen level from a fingertip pulse oximeter[2], and the hemoglobin level based on RGB heuristics given by the pallor of the conjunctiva [3].

3. The device will deliver all 10 diagnoses on a single charge, and be able to deliver diagnoses even while charging.

Design

Block Diagram

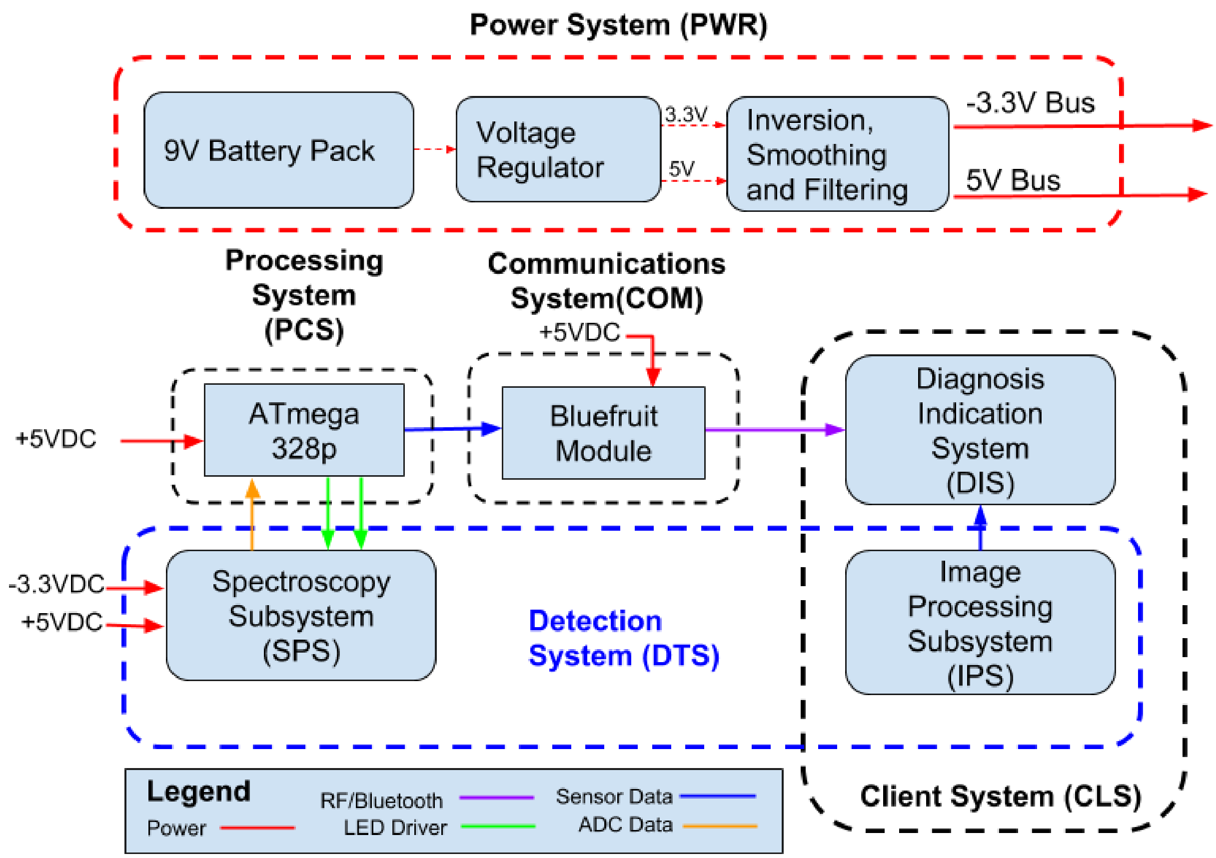

Figure 1: High level block diagram

The high level design shown in Figure 1 consists of the core modules required to power our detection, processing, and communications systems, as well as the core detection and processing systems required to implement our detection algorithm. The Client System is described later in this document as being a system implemented entirely in software, and run on an Android smartphone. The Processing System will consist of an ATMega328P processor and some simple signal processing required to implement the SpO2 detection algorithm required for the Pulse Oximetry data. Each component of the high-level block diagram is described in further detail below.

Power System (PWR)

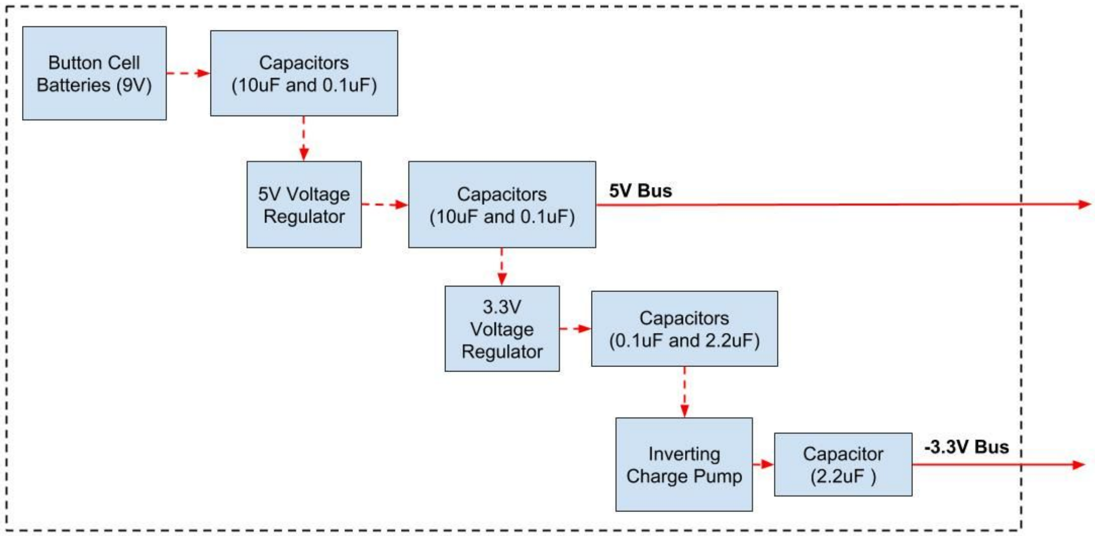

Figure 1: Block diagram of the power system

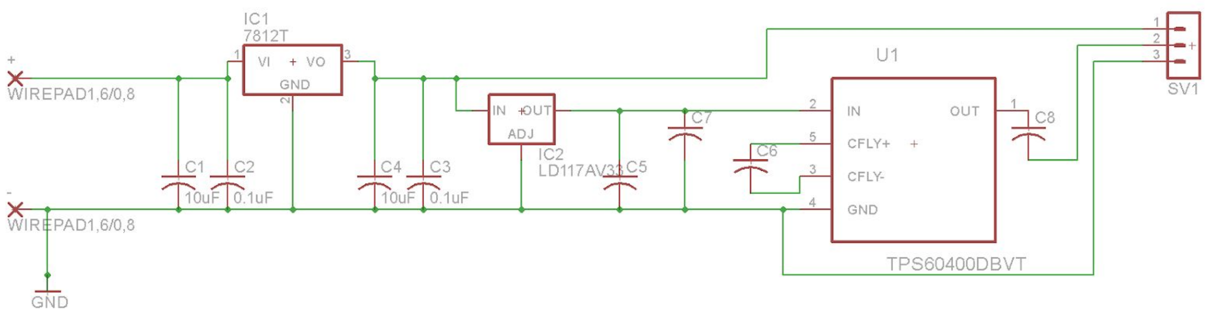

Figure 2: PCB Schematic for power board

The power system, depicted at a high level in Figure 1, will be used to first convert and then deliver power to all other subsystems, with the exception of the Client System (CLS), as it this system exists on a smartphone. A 9V battery is passed through to a linear regulator to create a 5V VCC rail. From here, it is passed on to a 3.3V linear regulator, and then inverted to -3.3V using an inverting charge pump. Each step of voltage conversion is flanked by a series of capacitors for smoothing and filtering. The final outputs of the power board are 5V, -3.3V, and ground. The topology is shown in Figure 2.

Originally, we had decided to use LIR2032 batteries to power this system, which is a rechargeable 3.6V button cell battery that is small and typical for portable applications such as ours.Unfortunately, the LIR2032 batteries only provided a more 15mA of current each, at 3.3V, which would require us to chain together several LIR2032 in series and then in parallel to properly feed the 5V rail and -3.3V rail. For this reason, we chose to use a 9V battery that provided more than the 100mA we needed, at a capacity of 400mAh.

Current Consumption

The overall power requirement of 100mA is calculated from observed values of current draw for the following subsystems detailed in Table 1. Original current consumption was made out to be around 200mA based on datasheet current consumption models. However, after testing each individual subsystem, a more realistic current consumption value maximum was 100mA.

Circuit	Components	Current Draw (mA)
Power system	9V Battery, Linear regulators, charge pump inverter, capacitors	10
LED Driver	Red LED, IR LED, Transistors, Resistors	25
Photodiode	OPT101, Resistor, capacitor	1
Spectroscopy-Filter and Amplifier	Resistors, capacitors, op-amp	5
Spectroscopy - Sample and Hold	Sample and Hold chip, resistors, capacitors	2
Processing	ATMega328P, resistors, Capacitors	25
Communications	Adafruit Bluetooth module	10
Total		78

Table 1: Current consumption upper bounds

$$78mA * 10\, seconds * 10\, runs = 2.16mAh \tag{1.1}$$

Equation 1.1: Energy Storage Capacity Requirement Calculation

The total power consumption is shown in Equation 1.1 and was calculated by multiplying the current consumption by the time it takes to make 10 diagnoses.

Processing System (PCS)

The Processing System (abbreviated PCS, seen at a high level in Figure 3) consists of the embedded processor, and the spectroscopy processing algorithm which will calculate the SpO2 from the spectroscopy data provided by the spectroscopy subsystem, as described more fully in [2].

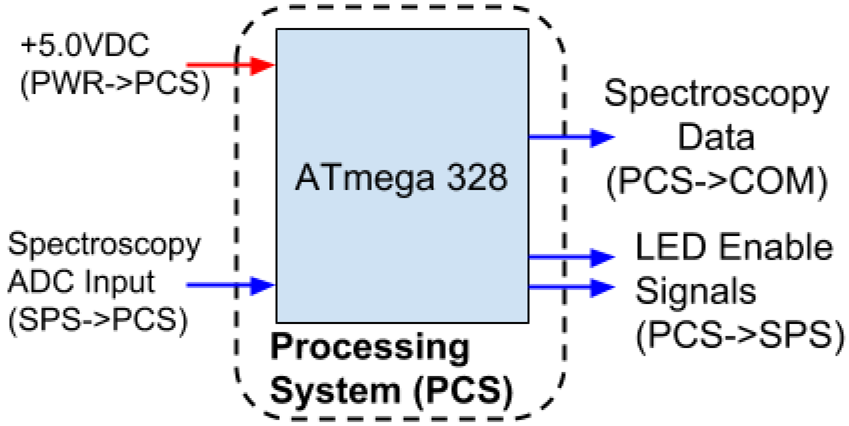

Figure 3: Block diagram of the processing system

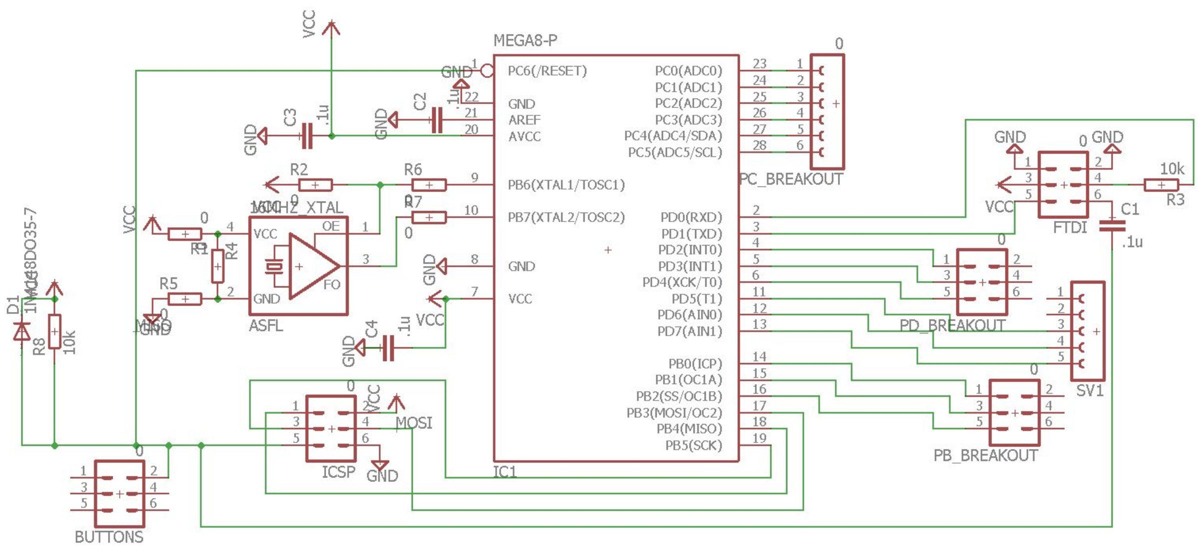

Figure 4: PCB Schematic for the Processing System

In designing the PCS, the most critical decision was which microprocessor to use. We evaluated the SAM D21, TI MSP430, ATmega 328P, and the dsPIC33F for the following constraints: cost, complexity to develop, availability of community resources, and physical package availability. The initial thought was to use the MSP430, as author JD had experience with this microcontroller from extracurricular activities, but it was decided against due to the lack of available high-level languages and steep initial learning curve. The SAM D21 was also considered, but decided against due to the higher cost of the development kit ($50 vs $20) in comparison with the remaining options, as well as the apparent lack of a DIP package for easy prototyping. This left the ATmega and the PIC, both of which have large communities with many resources for solving problems. We decided to use the ATmega, as our TA had the most experience with this processor, and the support for the Arduino language made it much easier to start development, as the low level registers and other embedded constructs are not strictly necessary to understand in order to create working code.

The PCS provides two major functions, spectroscopy data collection and transmission, and the timing system. As can be seen in Figure 4, the PCS has breakout pins exposed for its ADC pins, as well as for the FTDI, ICSP, and PWM pins. Through the ICSP and FTDI pins, we can flash the bootloader and load programs, respectively, which allows us to debug the code that is currently running on the microcontroller. In following a reference design provided in [11], we added breakouts for nearly ever pin, with capacitors to filter and isolate the VCC and GND lines, and a protection diode on the VCC line, which we ultimately decided not to use when a layout flaw was discovered that prevented it from providing any protection. The pins used are described further in Table 3.

The spectroscopy data was collected by simply reading the IR and red ADC pins, calculating the ratio of red to IR output using fixed-point arithmetic, and sending the calculated ratio into a lookup table as found in [13], which can be seen in Table 2. This data is then written over an emulated serial port to the communications system using the Arduino driver provided by Adafruit [14]. The lookup table is an approximation to Equation 2.2, and does not rely on extracting the AC component explicitly from the incoming signal.

The timing signals were generated using the built-in timers and PWM pins on the ATmega, and are discussed further in Appendix C.

Communications System (COM)

The communications system (abbreviated COM) will facilitate the transmission of pulse oximetry data obtained by the Spectroscopy Subsystem to the Client System, so it can be processed and shown by the Diagnosis Indication System. It functions by accepting serial data from the PCS, and transmitting it over Bluetooth to the CLS. As this project is not focused on exploring the challenges of designing and implementing communications systems, we elected for an all-in-one Bluetooth module from Adafruit called the Bluefruit. This module, which is centered around the MDBT40 BLE IC simplifies the interface with the PCS while also providing automated handshaking, GATT services, and receipt of Bluetooth data. We chose this module over our original selection, the PAN1740, as the PAN1740 required the use of the reflow oven in order to solder it, as well as pads with much tighter tolerances for the PCB. The high level block diagram is depicted in Figure 5, and a more detailed schematic can be found at [14].

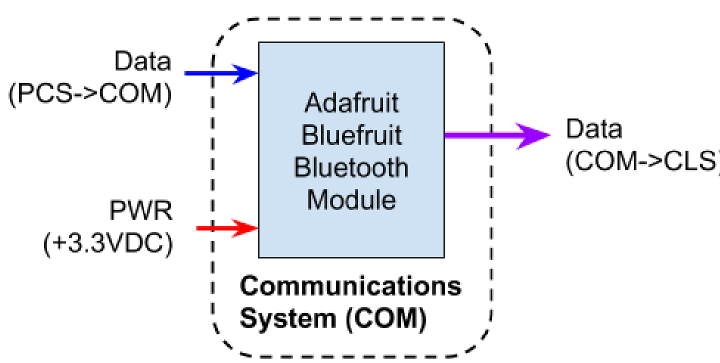

Figure 5: Block diagram of the communications system

Spectroscopy Subsystem (SPS)

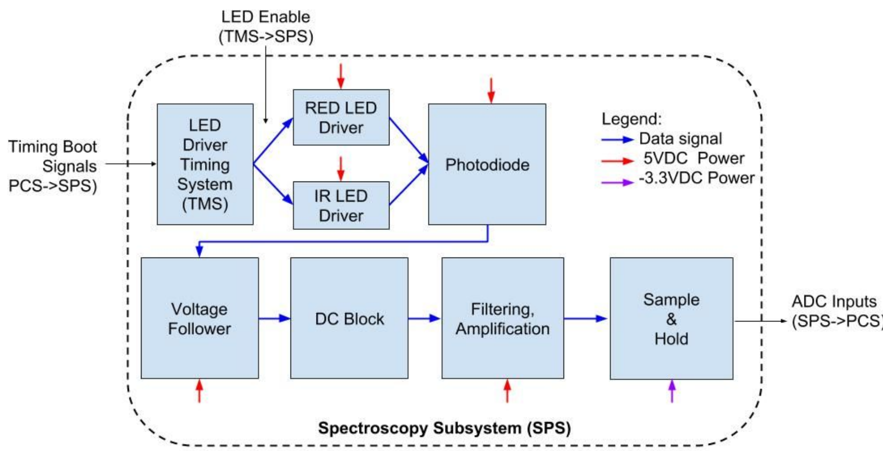

Figure 6: Block diagram of the spectroscopy subsystem

The Spectroscopy Subsystem (abbreviated SPS) is one of two subsystems that comprise our Detection System, the other being the Imaging System within the Client System. The high level layout of the SPS is shown in Figure 6. This system will excite the finger of the patient with red (660nm) and infrared (940nm) light on a 50% duty cycle, which will then be captured by a photodiode and filtered before being sent to the processing system for further refinement.

A schematic showing the individual circuit components in the spectroscopy system is shown in Figure 7.

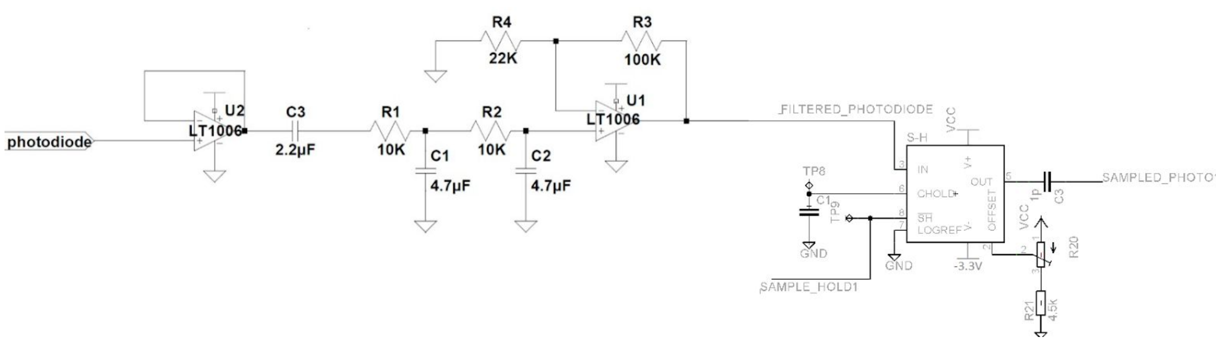

Figure 7: Circuit diagram for the spectroscopy system, including voltage follower, DC blocker, 2nd order RC filter, amplifier, and sample and hold IC.

We choose to implement the LED timing system using the PWM on the ATmega 328p (see Appendix C), as they provide sufficient drive levels and a high impedance as needed to drive the enable pins on the sample and hold and LED enable circuitry. The LED timing system signal is sent to the the base of a BJT, as shown in (19). This signal determines when to drive the Red and IR LEDs high and low.

As the LEDs are pulsed on and off, this light is absorbed through the user's finger and passed on to the photodiode, as represented in Figure 8.

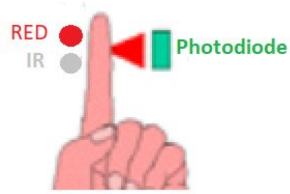

Figure 8: Pulse Oximeter Physical Usage; Finger is placed between RED/IR LEDs and the Photodiode

More specifically, when blood circulates through the finger, in accordance to the users heartbeat, the absorption of light through the finger's blood flow is then detected as a light signal through the photodiode on the other side of the finger [5]. The photodiode itself is configured to be highly sensitive as per [15], as physiological signals are rather small and hard to detect. The sensitivity can be configured by adjusting the values of c_{ext} and r_{ext} shown in Figure 9. This raw photodiode signal is then passed on to a voltage follower to boost current before entering the filtering and amplification stage.

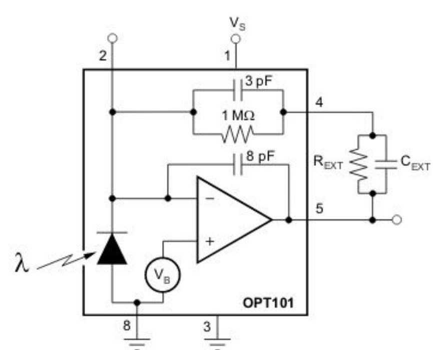

Figure 9: Photodiode Configuration used, with $R_{EXT} = 1M\Omega,\ C_{EXT} = 50pF$.

Then, DC bias in the signal is removed with the use of a 2.2uF capacitor. Then, it is processed through a second order RC low pass filter with $f_c = 3.38Hz$ as shown in Figure 7. This center frequency allows signals of under 180 BPM. Originally, it was our intent to use a second order active butterworth filter, with a design produced by Analog Devices' filter wizard[8]. However, after running a simulation of the suggested circuit in LTSpice, it was seen that the circuit did not provide the accurate filtering response suggested by the filter wizard output. Therefore, a passive second order filter was used. The frequency response can be seen in the bode plot presented in figure 10.

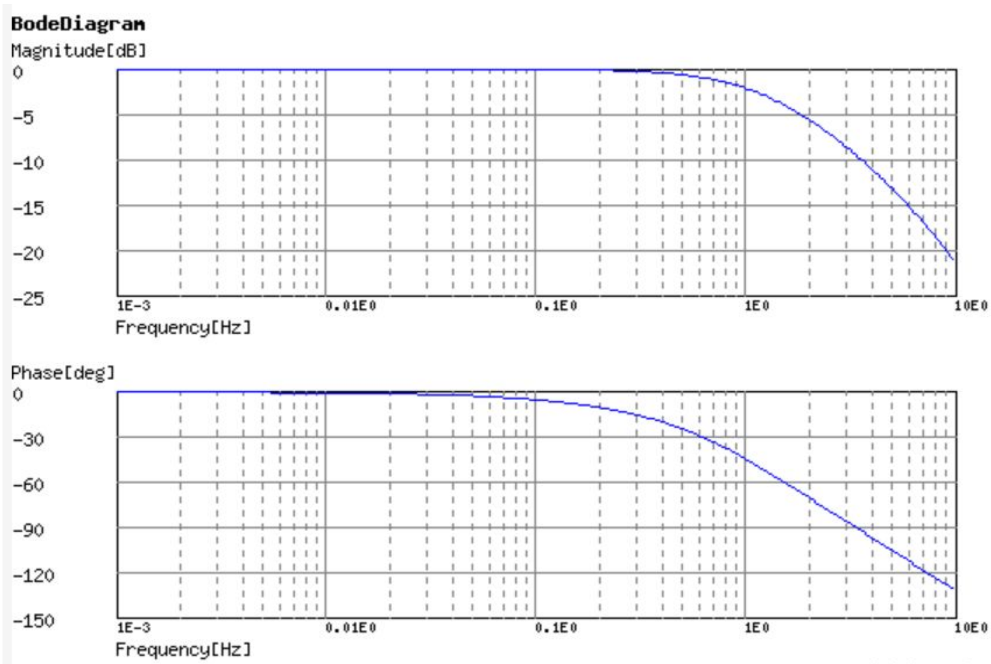

Figure 10: Magnitude and Phase Response of low pass filter

Once filtering happens, the signal is amplified with a gain of 5.5, achieved using a resistor ratio of 100k Ohm to 22k Ohm. This level of amplification was chosen based on the constraint that the input to the sample and hold circuit should fall within a 0-5V range, and preferable between 2V-5V for the cleanest sample and hold output. Because the amplifier injects DC bias, the signal at the output of the amplifier matched this requirement when a gain of 5.5 was applied. The amplified signal then is reconstructed by the aid of two separate sample and hold circuits. This complete flow of logic can be seen in the more detailed spectroscopy system block diagram in Figure 11.

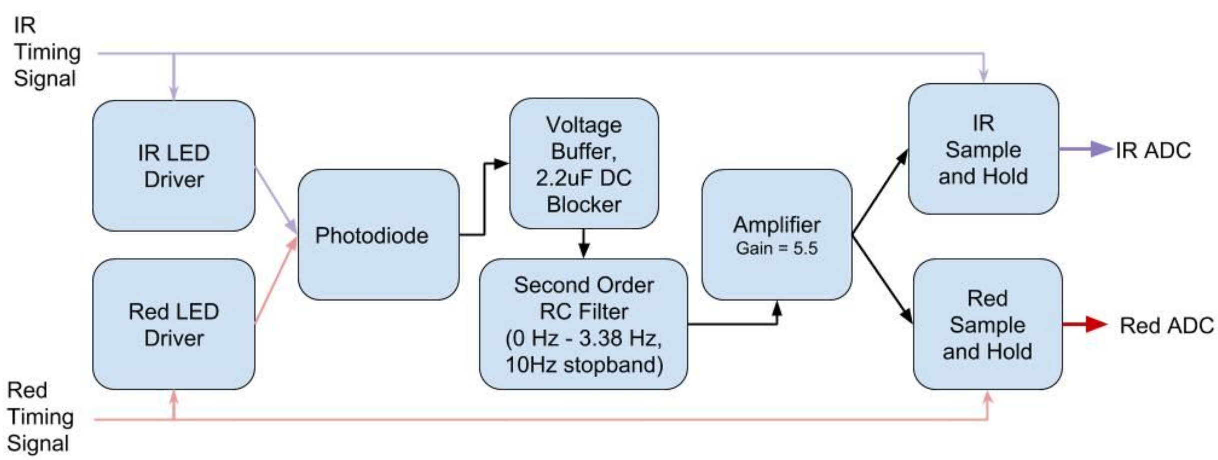

Figure 11: Detailed Spectroscopy System block diagram

Each sample and hold circuit is powered by a positive and negative voltage supply. As with all the other circuits, the positive rail is given by 5V DC. The negative voltage supply is powered by -3.3V, as is recommended by the datasheet to adequately perform the sample and hold operation on a signal between 2-5V (see Appendix E). The red sample and hold circuit will sample the signal when the red LED driver is on, and holds the last value recorded when the LED driver is off, because the sample and hold enable signal receives the same LED driver signal used to drive the red LED. This reconstruction is depicted in Figure 12. This will allow the output of the red sample and hold circuit to reconstruct just the red absorption signal that was passed through the spectroscopy system. Similarly, the IR sample and hold circuit also reconstructs the IR absorption signal. Finally, the reconstructed red and IR signals are sent to their respective ADC channels to be further processed.

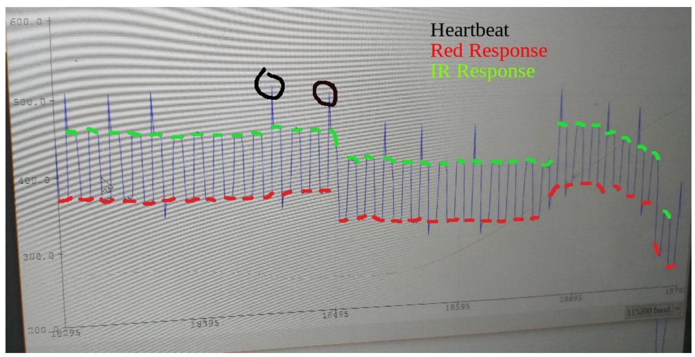

Figure 12: Signal from which the individual red and IR waveforms are recovered. Heartbeat is a nice bonus.

The design of our pulse oximetry system is heavily influenced by a reference design given in [6]. Once we sample the current from the photodiode, the equations for recovering the SpO2 are shown in (2.1) and (2.2). Equation 2.1 is the definition of SpO2, and (2.2) describes how to calculate a ratio that can be used to interpolate SpO2 using the total current I_{dc+ac} at wavelength $\lambda_1 = 660nm$ and $\lambda_2 = 940nm$, and the constant portion of the current at each wavelength I_{dc}. This yields the modulation ratio, R.

$$SpO_2 \equiv \frac{[HbO_2]}{[total\ haemaglobin]} \qquad (2.1)$$

Equation 2.1: Definition of SpO_2

$$R = \frac{\log_{10}((I_{dc+ac})/(I_{dc}))_{\lambda 1}}{\log_{10}((I_{dc+ac})/(I_{dc}))_{\lambda 2}} \qquad (2.2)$$

Equation 2.2: Modulation Ratio for recovering SpO_2. The λ_n implies a current observation at wavelength λ_n.

Once we calculate the modulation ratio R, which can be accomplished using a simple lookup table and linear interpolation between data samples, we can then apply another lookup using an empirical calibration curve already observed from laboratory instruments, shown in Figure 13.

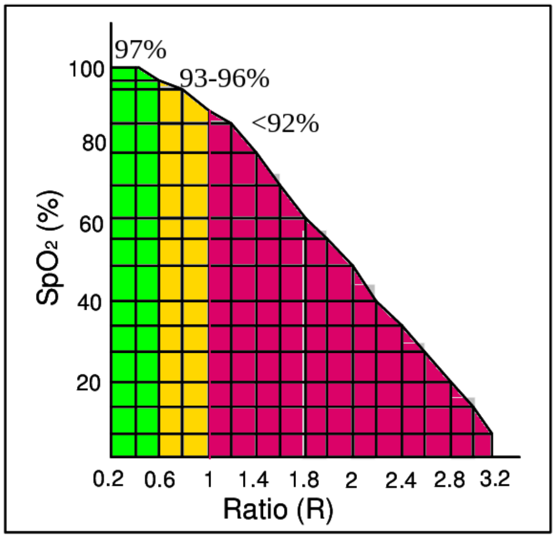

Figure 13: Modulation Ratio lookup curve

As represented by Figure 13, a modulation ratio of 1 or higher corresponds to a low SpO2 percentage, indicating that anemia could be present. Conversely, an absorption ratio of 0.6 or lower indicates a high SpO2 percentage, indicating that anemia is likely not present.

According to [6], the pulsatile amplitude of the heartbeat (which we aim to detect) is about 1% of the DC voltage. To ensure proper detection of minima and maxima, we need to resolve differences of half of that value, which equates to 0.5%. Our chosen processor has an ADC with 1024 distinct values, ranging from 0V to the supply voltage Vcc. To calculate the minimum detectable step voltage ΔV_{step}, we simply substitute our chosen supply voltage and divide through by the number of distinct values N, using Equation 3.1.

$$\Delta V_{step} = \frac{V_{cc}}{N} = \frac{5.0V}{1024} \approx 0.0048V \qquad (3.1)$$

Equation 3.1: Calculation of voltage step per bit of ADC resolution

To verify that our detectable step voltage is below what we want to detect, we must show that 0.5% of our chosen DC voltage is greater than the minimum step voltage, as seen in (3.2).

$$\Delta V_{step} < 0.005 \cdot 2V = 0.01V \rightarrow 0.0048V < 0.01V \checkmark \qquad (3.2)$$

Equation 3.2: Verification that resolution required will be realizable with our ADC.

From the minimum amplitude to the maximum amplitude, we will have the full 1% voltage change, implying we will have at least 5 and at most 7 different values on the ADC.

Client System (CLS)

The client system (abbreviated CLS) consists of the image capture, image processing, and diagnosis indication systems. It combines these systems through use of complex software systems that are exposed to the user via a smartphone application. A development version of the CLS is shown in Figure 14a. The purple circles will be used as a hint to the image processing algorithm as to where the upper and lower conjunctival regions exist, which reduces the complexity of the classification problem involved in identifying the regions automatically.

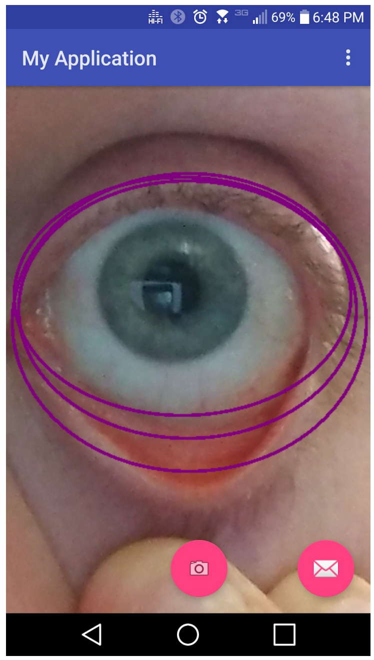

Figure 14a: Development version of Client System

Image Processing Subsystem (IPS)

The Imaging Processing Subsystem (abbreviated IPS) consists of the smartphone camera of the client system, and an image processing algorithm that will identify the redness of the conjunctiva to arrive at a partial diagnosis. As this system contains no hardware, it does not have a block diagram.

The ultimate goal is to calculate the difference in the redness of the two conjunctival regions below the eye. By employing a superpixel algorithm, we are able to more succinctly distinguish these regions, without having to employ more complex machine learning or feature detection techniques.

After creating a set of sufficiently large superpixels in the source image of the eye, the superpixels within the target region (seen as purple circles in Figure 14a) are assigned into different groups based on the region they occupy within the target region. If they fall within the largest circle and outside the smaller circle, they are classified as lower conjunctiva, and if they fall within the smaller circle only, they are classified as upper conjunctiva. The superpixels that fall without the conjunctival target region are thrown away.

The two groups of superpixels are then passed into a median filter, which returns the median color of each group. If the difference between these colors is sufficiently large, the diagnosis is given as a positive. Otherwise, the diagnosis is registered as being inconclusive.

The general flow of the algorithm is given in Figure 15. The superpixel algorithm employed is the one provided by OpenCV, shown in [9]. The output of this algorithm can be seen in Figure 14b, which shows the regions of the image that the superpixel algorithm segments the original image into. The difference in redness between the lower and upper conjunctival regions can be used to detect anemia, using thresholds that are calibrated to the current lighting conditions and image sensor used. OpenCV provides camera calibration APIs, which would be used at the outset to ensure a consistent

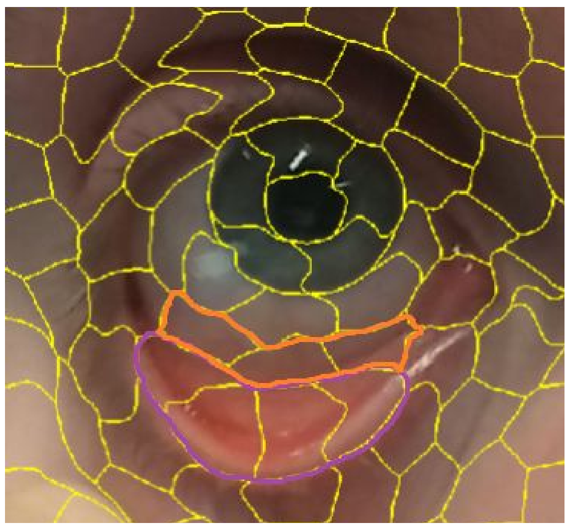

Figure 14b: Example segmentation of a human eye, depicting lower conjunctival regions (purple border), and upper conjunctival regions (orange border).

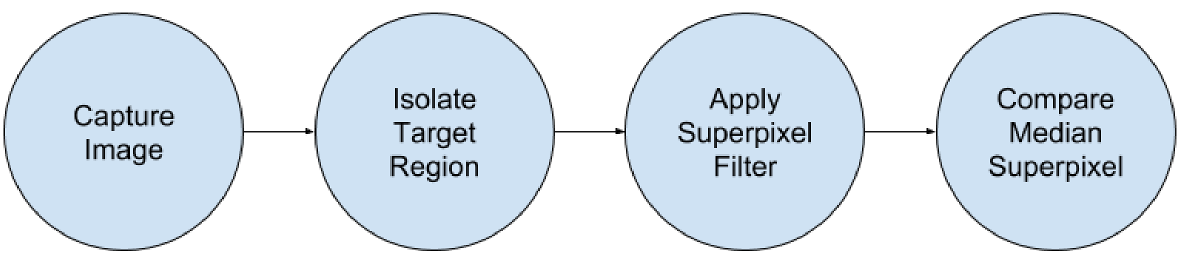

Figure 15: Image Processing Algorithm Flowchart

Verification and Validation

We verified the functionality of our timing system, seen in Figure 16.

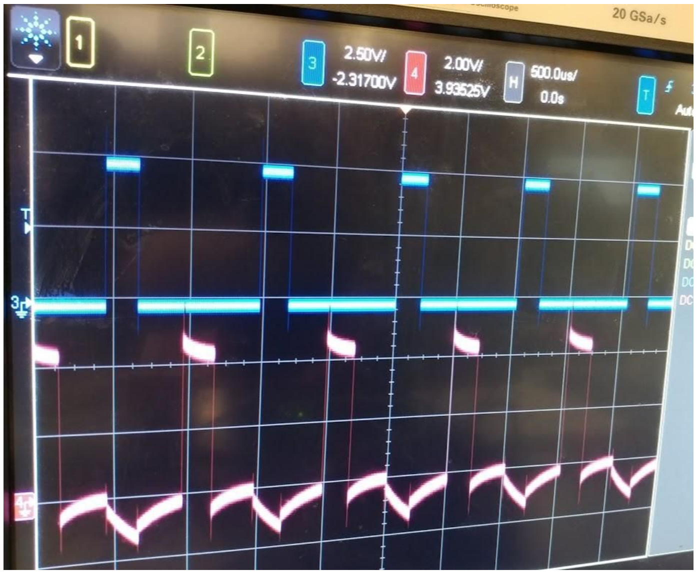

Figure 16: Verification of 20% Duty cycle, 5VPP+2.5VDC, with 180 degree phase between both timing signals. It was seen that the distortion in the second signal was due to the quality of the probe used.

We verified the sampling frequency of our ADC, seen in Figure 17.

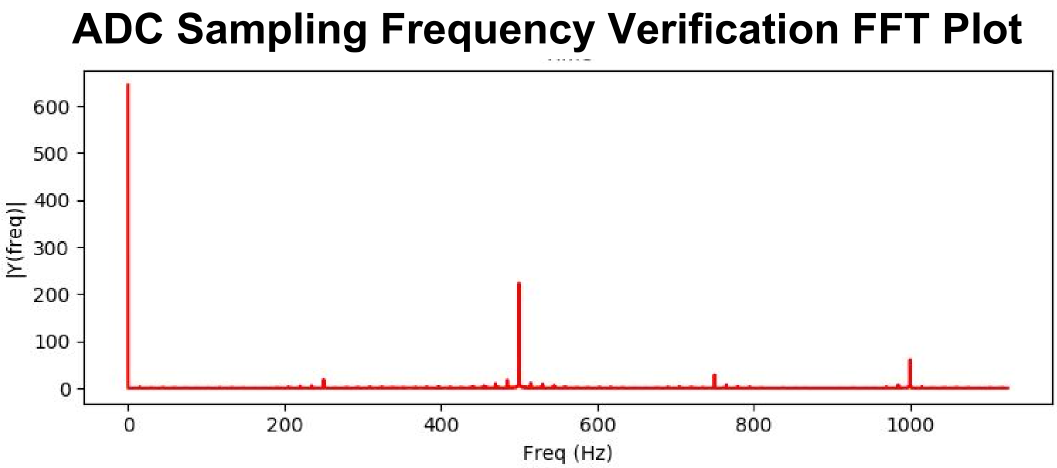

Figure 17: Verification of ADC Sample Rate: FFT of the sampled 500Hz 5VPP+2.5VDC waveform.

We verified the power, data rate, and communications requirements for the spectroscopy, processing, and communications systems by performing a fully closed loop test of our pulse oximeter with the CLS (components from Bluefruit LE Android application), seen in Figure 18.

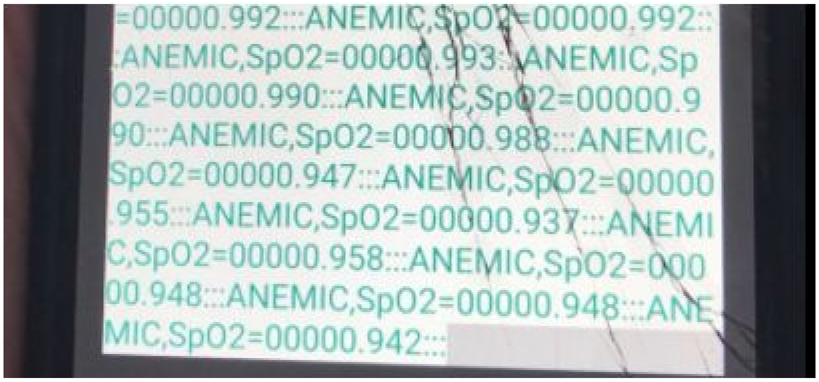

Figure 18: Verification that ADC data is processed, sent over serial line to communications system, and received by client system

We verified the functionality of the Power system’s voltage regulation and current capacity, seen in Table 4 and Table 5.

We verified the functionality of the low pass filter in the SPS, seen in Table 6.

Tolerance Analysis

We chose to use a two complete detection system because statistically, it will be more accurate than relying on any one method. According to a research study done with the NIH [3], examining the pallor of the conjunctiva can give you an indication of whether it is likely that a patient has anemia. More specifically, anemia can be defined as a hemoglobin content cutoff of under 110 g/L. The study then indicates that there is a likelihood ratio of 16.68 within a confidence interval of 95% that a patient has anemia (<110g/L) if pallor is present. In more simple terms, it is generally accepted that if a likelihood ratio of above 10 is present, then the effect can be considered to be present. Furthermore, the paper states that anemia can be diagnosed with the examination of conjunctival pallor with much greater likelihood if there is another indicator of low-hemoglobin anemia. For this reason, we have decided to use the pallor method in conjunction with checking SpO2 levels using a pulse oximeter. Ultimately, we hope to detect anemia correctly 9 times out of 10. Given the statistics presented by [3], we hope that we can achieve either 1 false positive or 1 missed detection, meaning one total incorrect diagnoses out of 10.

Risk Analysis

When creating devices used to assist in medical diagnoses, it is important to consider the ethical considerations of incorrect results. Assuming the device we build could be used in rural or remote developing areas, people who do receive a false positive might be forced to travel long distances before being able to speak with a medical professional about treating anemia. Similarly, failing to identify anemia could lead to malnutrition, and poor health. We understand the risks and stresses that a false diagnoses could have and therefore hope to mitigate this risk by providing a probability of anemia instead of a binary ‘yes’ or ‘no’, so that the final judgement call can be made by the medical professional and patient.

Cost Analysis

The total cost for this project is estimated to be $9103.10, with an estimated per-device production cost of $65.24, which is about 150% more expensive than we originally anticipated. Costs could be reduced by streamlining our design and producing at larger scales, with the expectation that they could hit our intended goal of $40/unit. For more information, see Appendix I.

Conclusions

Upon the completion of this semester, we had created a functional prototype of the anemia detection device outlined in this document. The hardware profile of this system was completely functional, but was very sensitive to ambient light and noise. An automatic gain control feedback loop could be implemented in the future to mitigate this issue. The software system contained a skeletal outline, and contained an app that could display results as well as a capturing screen that would allow the user to take a picture of their eye. The DIS was not completed, as it was deemed that the textual feedback given over Bluetooth was sufficient given the time constraints at the end of the semester. More work needs to be done to implement the image processing algorithm that provides a diagnosis based on conjunctival pallor. Upon testing our device with a sample size (n=2), the device reported the anemic partner to have be anemic with a mean absorption ratio of 0.95 , and the non-anemic partner to be non-anemic with a mean absorption ratio of 0.47. In our case, this diagnosis worked consistently and gave correct results 10 times. However, with a rather small sample size, and short testing period, more work needs to be done to establish whether the device was truly accurate or not, including much larger sample sizes from much broader demographics.

Ethics and Safety

The main purpose of this device is to diagnose an illness in a user or patient. The data processed through the device could be classified as medical data, and for that reason we hold ethics in safety in high regard.When working with others, our group will stand by the IEEE code of ethics[7], and follow the appropriate methods set out by the IRB if working directly with patient data. We will not falsify data or make claims about the effectiveness of our device that cannot be thoroughly backed up by the data we collect. We will always uphold the safety of our users and others who interact with our device at all times. We will continue to ensure our delivery and milestone estimates are accurate and supported by our individual progress.

Lastly, we promise to attribute any research or information taken from a source to the source itself, and never pass off the work as our own.

Appendix A: Abbreviations

Abbreviation	Meaning
AC	Alternating Current
ADC	Analog Digital Converter
BLE	Bluetooth Low Energy
CLS	Client System
COM	Communications System
CTS	Clear To Send
DAC	Digital Analog Converter
DIP	Dual in-line package
DIS	Diagnosis Indication System
DTS	Detection System
FTDI	Future Technology Devices International
FFT	Fast Fourier Transform
GND	Ground Plane, voltage reference
IC	Integrated Circuit
ICSP	In-Circuit Serial Programming
IEEE	Institute of Electrical and Electronics Engineers
IPS	Image Processing System
IR	Infrared light, which has a wavelength of 940nm for our purposes.
IRB	Institutional Review Board
LED	Light emitting diode
NIH	National Institutes of Health
PCB	Printed Circuit Board

PCS	Processing System
PPE	Personal Protective Equipment
PWM	Pulse Width Modulation
PWR	Power System
PoC/POC	Point-of-care
RX	Serial Receive
SI	Système Internationale
SpO2	Percent Saturation of Oxygen in blood
SPS	Spectroscopy System
TX	Serial Transmit
UART	Universal Asynchronous Receiver/Transmitter
VCC	Voltage at the Common Collector
VDC	Voltage Direct Current, eg the constant offset in an AC waveform
VPP	Voltage Peak-to-peak, in reference to AC waveforms
WHO	World Health Organization

Appendix B: Miscellaneous Tables

S.No	% SPO_2	RED/IR Calibrated
1.	90	0.143
2.	91	0.215
3.	92	0.292
4.	93	0.367
5.	94	0.441
6.	95	0.516
7.	96	0.591
8.	97	0.666
9.	98	0.741
10.	99	0.815
11.	100	0.891

Table 2: Lookup table used by the PCS in calculating the SpO2 ratio.

Function	Source/Destination	ATmega pin	Arduino pin
IR ADC	IR Sample and Hold	23	A0
Red ADC	Red Sample and Hold	24	A1
IR Timing Signal	IR LED Enable/Sample Enable	17	11
Red Timing Signal	Red LED Enable/Sample Enable	11	5
VCC	Power System	7	N/A
GND	Power System	8	N/A
Bluetooth TX	Communications System	16	10
Bluetooth RX	Communications System	15	9
Bluetooth CTS	Communications	17	8

	System		
Crystal Resonator +	External Oscillator	9	N/A
Crystal Resonator -	External Oscillator	10	N/A
Reset	Development Board	1	N/A
Serial RX	Development Board	2	N/A
Serial TX	Development Board	3	N/A

Table 3: Pin mappings used for the ATmega 328P

Appendix C: Timing System Implementation

The timing signals were generated by referencing the ATmega 328P datasheet [12], which we used to program the PWM pins to generate a 1kHz, 50% duty cycle, 5VPP+2.5VDC square wave using TIMER0 and TIMER2, the two 8-bit timers available in the ATmega 328P. We used Equation 4.1 to calculate the clock divider prescaling factor of 64.

$$f = f_0/(\tfrac{N}{T}) \qquad (4.1)$$

Equation 4.1: Calculation of clock divider to achieve given PWM frequency.

The factor f is calculated by taking the base clock frequency $f_0 = 16MHz$, and dividing by the base frequency of the signal you wish to generate. This frequency can be calculated by taking the number of states in your timer, $N = 2^8 = 256$, and dividing it by the period of your desired signal, $T = 1ms$. Substituting everything with SI units, we find that $f = 16000000/(256/.001) = 62.5$, which is closest to a prescaler of 64, and yields a base frequency of $f_b = 977\ Hz$ for our PWM. The duty cycle is achieved by setting the register OCR2A and OCR0B for timers 2 and 0, respectively, equal to the value $p(P, N)$ calculated by equation 4.2 as a function of the desired percentage P, and the number of states in the timer $N = 2^8 = 256$.

$$p(P, N) = N \cdot P/100 \qquad (4.2)$$

Equation 4.2: OCR Register setting for desired duty cycle percentage P.

Because we desired a 50% duty cycle, a value of $p = 128$ was selected for both. Finally, to achieve the 180 degree phase shift between the timers, we simply initialized one of them to be 0, and the other to be halfway along its count cycle, eg TCNT0 = 0 and TCNT2 = 128. Because they share a base clock and number of states, they roll over in their count at a perfect 180 degree phase offset. The signals resulting from the timing system can be seen in Figure 16.

Appendix D: Miscellaneous Schematics

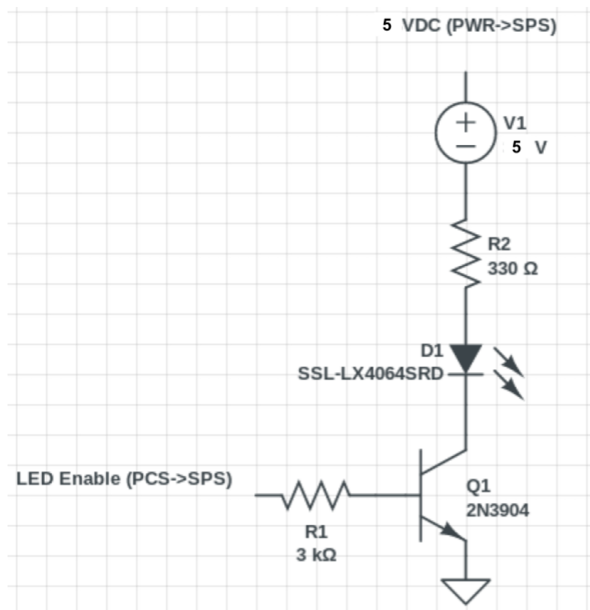

Figure 19: Simple LED Driver (660nm LED pictured).

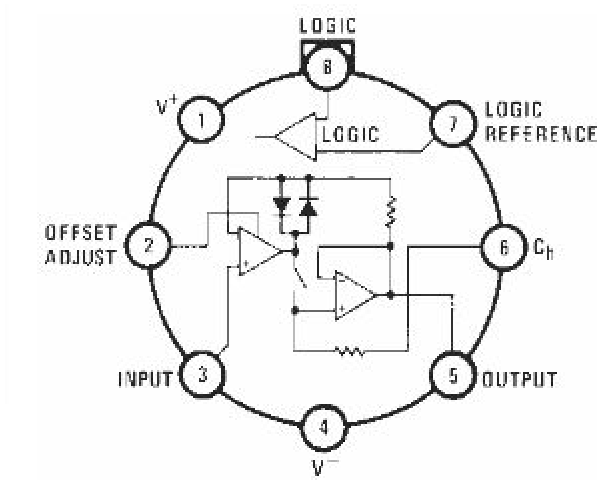

Figure 20: Sample/Hold Circuit. Enabled using the LED Enable. Two used in practice. Taken from [10]

Appendix E: Spectroscopy System Implementation

The -3.3V requirement can be seen in Figure 21, where -Vs is the value of the negative supply feed and Vs is the value of the positive supply feed, with Vin representing the allowed input voltages.

The following specifications apply for $-V_S + 3.5\ V \leq V_{IN} \leq +V_S - 3.5\ V$, $+V_S = +15\ V$, $-V_S = -15\ V$, $T_A = T_J = 25°C$, $C_h = 0.01\ \mu F$, $R_L = 10\ k\Omega$, LOGIC REFERENCE = 0 V, LOGIC HIGH = 2.5 V, LOGIC LOW = 0 V unless otherwise specified.

Figure 21: Requirement from which we derived the need for a -3.3V supply feed.

Another quirk we learned about was the requirement for a trimmer potentiometer in order to properly use the LT1006, which was instrumental in our amplifier. Details for this can be found in Note 3, Note 4, and Note 5 of the datasheet.

Appendix F: Processing System Implementation Notes

One key thing that we learned about the processing system that we did not have time to cover was that, when the development board is harnessed into the PCS, but unplugged from USB, the RESET pin is pulled low, so the PCS does not boot, even though it appears that it should be able to. The fix is to simply unplug the RESET harness when detaching the development board from the computer's USB port.

Appendix G: Requirements and Verification Table

Block	Requirement	Verification
Power System (13 pts)	Rechargeable battery pack must have minimum capacity of 20mAh of charge. (5 pts)	Discharge battery pack through 100kOhm resistance, measure current over time using multimeter to calculate overall energy storage.
	Power system should be able to supply sustained current of 100mA sustained and 125mA peak. (5 pts)	● Discharge battery into programmable load box drawing 100mA and 125mA. ● Add multimeter in current loop to verify draw on programmable load ● Optionally add 500 Ohm resistor in series, and measure the voltage drop with an oscilloscope to verify current
	5V and -3.3V outputs must be within a +/-10% tolerance after filtering and isolation. (3 pts)	Record waveforms for 10 minutes of 5V bus and -3.3V bus to make sure output voltage meets tolerance.
Processing System (16 pts)	The embedded processor must have an ADC that operates from 0 to 5VDC, +/-1%, with a resolution of better than 0.01V. (3 pts)	● Using a programmable load, set the voltage on an ADC pin to 0.1VDC, 1.1VDC, 2.1VDC, and 3.1VDC ● Increment the voltage in 10 steps of 0.01V for each voltage, and sample the ADC. ● Check that all samples differ by at least one unit on the ADC.
	The ADC must be capable of sampling at a frequency of at least 1kHz. (4 pts)	● Generate a 500Hz sinusoidal waveform, 5VPP, +2.5VDC offset on a function generator ● Sample sinusoid on the ADC for 1 minute. ● Send the samples on serial line to a computer ● Reconstruct the signal by running the samples through an FFT to ensure the 500Hz peak

		in the frequency spectrum.
	The embedded processor must be able to drive an LED by pulsing a DAC. (4 pts)	● Connect programmable output pin of microcontroller to gate of BJT in LED driver circuit ● Program the microcontroller to pulse the selected output pin at 1 Hz, 50% duty cycle, changing from 0VDC to 5VDC ● Observe flashing LED for 10 seconds using a stopwatch, and verify frequency.
	The embedded processor must be able to run on 5VDC, +/-10%. (1 pt)	● Connect embedded processor to 3.3VDC power supply ● Run LED driver verification to ensure proper functionality
	The embedded processor must have a UART to send spectroscopy data to the communications system. (5 pts)	● Send 1000 bytes to the ATmega UART, ● Increment all 1000 bytes within the ATmega, ● Send back the incremented bytes over UART ● Verify that all bytes were properly incremented, and thus properly received and re-transmitted.
Communications System (16 pts)	The communications system must be capable of running on 5V provided by the power system. (5 pts)	● Program the microcontroller to write data to the communications system serial port
	The communications system must be capable of transmitting at a rate of at least 9600 bits/sec, and support up to 115200 bits/sec. (5 pts)	Send data with baud rate set to 9600bps and then 115200bps.
	The communications system must consume no more than 40mA during transmission, and no more than 5mA during idle mode. (4 pts)	Record current waveform through bluetooth module during operation and ensure that peak current draw is less than 40mA. Record current waveform once again during idle mode and ensure that current draw is less than 5mA.

	The communications system must interface with the processing system over UART. (4 pts)	● Use the datasheet to write a serial console program for implementing the command grammar for the communications system selected. ● Connect to the communications system with a UART. ● Execute one transmit command over serial, and verify receipt on Bluetooth console.
Spectroscopy Subsystem (20 pts)	The bandpass filter must have a passband between 0.5Hz and 5Hz, corresponding to a passband bandwidth of 4.5Hz, +/-10%, with a 5Hz rolloff +/-10%, and mitigation of frequencies 3dB below the maximum signal amplitude at a stopband frequency of 5.5Hz +/- .5Hz. (4 pts)	● Using an oscilloscope, measure the magnitude response. ● Calculate the passband bandwidth, 3dB attenuation frequency, and rolloff frequency
	The photodiode must be capable of detecting both the red and infrared outputs of the two LEDs at the same sensitivity, to within 20% relative difference. (4 pts)	● Illuminate the photodiode with a monochrometer with a peak wavelength of between 600nm and 700nm, fixed output of 1mW ● Measure the current output of the photodiode and ensure it is in accordance with the provided datsheet[15]. ● Repeat test for monochrometer of peak wavelength between 900nm and 1000nm. ● Check that the two currents observed agree to within 20% tolerance
	The final output sent to the processing system must be between 0 and 5V. (4 pts)	● Pulse both LEDs at full brightness (1Khz, 5% duty cycle, 5VDC bias) for a period of 10 minutes and measure output waveform on oscilloscope. ● Collect voltage statistics and verify that the output voltage is between 0VDC and 5VDC over the entire test period.

	The spectroscopy subsystem must run on 5VDC. (4 pts)	• Power the spectroscopy system with 5V. • Repeat all verifications for spectroscopy subsystem. • After successful verification, repeat verifications using voltage of 5V • For each individual component in the spectroscopy system, verify through the datasheet that the chosen part can operate using 5VDC.
	The spectroscopy subsystem must output a signal which has a constant DC gain of 2V, +/-20%. (4 pts)	• Modulate the LED brightness with an automatic gain control (AGC) circuit. • Read output of spectroscopy subsystem on oscilloscope • Ensure that the DC offset of the pulsatile signal detected is always within 20% of 2V.
Client System (16 pts)	The client must support data transfer from the communications system. (5 pts)	The client system can transmit to and receive from the BLE radio employed by the communications system.
	The client must be capable of running the image processing subsystem. (5 pts)	Test the client system software against an Android phone.
	The client must be capable of displaying the final diagnosis. (6 pts)	The Android application shows the final diagnosis on the main screen.
Image Processing Subsystem (19 pts)	The image processing algorithm must feature some type of feature detection to identify different sections of the image. (6 pts)	Image processing algorithm detects the following features: 1. Conjunctiva 2. Eyeball 3. Periorbital (under eye) area
	The image processing algorithm must run on an Android device. (3 pts)	• Implement image processing algorithm • Execute image processing algorithm on Android device

	The image processing algorithm must use less than 250MB of RAM on the client. (3 pts)	• Record memory usage as image processing algorithm executes. • Compute statistics on usage and ensure it never exceeds 250MB
	The image processing algorithm must give a binary diagnosis (anemia/no anemia) in no more than 5s. (7 pts)	• Time image processing algorithm run time on Android phone. • Result of diagnosis should appear in a probabilistic metric: i.e. ‘green’ meaning it is highly probable for the patient to have anemia, or ‘red’ meaning it is highly improbable for the patient to have anemia where the individual accuracy of the the diagnosis being 90%..

Appendix H: Miscellaneous Verification Data

Input Voltage (V)	5V Output (V)	3.3V Output (V)	-3.3V Output (V)	Current Consumption (mA)
1.00	-0.05	-0.05	-0.24	0.1
2.00	-0.04	-0.04	-0.05	0.2
3.00	1.56	0.70	0.20	2.0
4.00	2.53	1.63	-0.04	4.0
5.00	3.50	2.61	-2.60	6.0
6.00	4.45	3.30	-3.26	8.0
7.00	5.01	3.29	-3.31	9.0
8.00	5.03	3.30	-3.27	9.0
9.00	5.02	3.30	-3.23	9.0

Table 4: Power System output verification

Load Current (mA)	Supplied Current - Base Current (mA)
25.0	27.4
50.0	45.4
75.0	78.4
100.0	93.4
125.0	127.4

Table 5: Power System current supply verification, 22.6mA base consumption with programmable load on top

Input Frequency (Hz)	Output Frequency (Hz)	Output Average (mV)	Output Peak-Peak (mV)	Attenuation from Maximum (dB)

0.5	0.50	513	1380	0.00
1.0	1.00	502	1240	-0.46
1.5	1.51	488	1050	-1.18
2.0	1.99	502	980	-1.48
2.5	2.56	519	980	-1.48
3.0	3.06	525	890	-1.90
3.5	3.49	525	800	-2.36
4.0	3.93	503	680	-3.07
5.0	5.20	499	620	-3.48
6.0	6.20	499	600	-3.62
7.0	2.31	499	540	-4.07
8.0	23.29	500	540	-4.07
9.0	22.88	499	510	-4.32
10.0	24.91	501	490	-4.50
15.0	1.01	499	460	-4.77
20.0	N/A	499	460	-4.77
25.0	2.52	499	430	-5.06
30.0	N/A	497	430	-5.06
40.0	N/A	499	430	-5.06

Table 6: Magnitude Response of Low-pass filter used in Spectroscopy System. The output frequency mismatching the input frequency is an indication of severe attenuation, and therefore, mixing with the noise floor.

Appendix I: Cost Analysis

Part Name	Part Description	Manufacturer	Quantity	Price per piece ($)
Arduino Development Board	Processor Development Kit	Arduino	1	17.32
ATmega328P	Processor	Atmel	3	2.50
ECS-160-20-3X-TR	16MHz Crystal Resonator	ECS Inc.	1	0.38
Surface Mount Passives	Resistors, capacitors	Various	1	68.32
LF398AN	Sample and Hold IC	Texas Instruments	5	2.72
OPT101	Photodiode	Texas Instruments	4	7.06
LT1006	Precision Single Supply Op-amp (filter, amplifier)	Linear Technologies	4	3.18
AD8031	Precision Op-amp (filter, unused)	Analog Devices	4	7.75
AS78L05ZTR-E1	5V Linear Regulator	Diodes Incorporated	5	0.35
LD11173v3	3.3V Linear Regulator	STMicroelectronics	10	0.47
LM2776DBVR	Inverting Charge Pump (-3.3V)	Texas Instruments	5	1.59
0.1in Header Pins	Breakout connections	Molex	100	0.05
Adafruit Bluefruit LE UART Friend	Bluetooth Module	Adafruit	1	18.20
ENW-89846A1KF	Bluetooth Module (unused)	Panasonic	1	14.51
LT6220	Precision Single Supply Op-amp (filter, unused)	Linear Technologies	4	2.99
LiCB CR2032 3V Lithium Battery	3.3V Button cell batteries (unused)	LiCB	10	0.70
CR2032 Battery holder	Power Supply Housing (unused)	X4-Tech	5	1.40
Duracell 9V Battery	9V Power Supply	Duracell	2	1.28
2 X 2 3/8 SOLDERABLE PERF BOARDS	Perf Boards	-	2	1.43

Hand Tools	Tweezers, Needle-nose Pliers	Various	1	11.28
0.1in Header Wire	Harness connection	Various	40	0.35
Printed Circuit Boards		PCB Way	25	5
Cost of Labor ($36/hr, 15 hours/week, 8 weeks)	Labor	See: Cover Page	1	8,640.00
Total:				**$9,103.10**

When prototyping, it is often common to order more parts than necessary and even leave parts unused either due to a design change or unforseen design constraint. Here, the cost of just the product itself is calculated, using only the parts that are truly needed to create a fully functional device:

Part Name	Part Description	Manufacturer	Qty	Price per piece ($)	Ttotal Cost ($)
ATmega328P	Processor	Atmel	1	2.50	2.50
ECS-160-20-3X-TR	16MHz Crystal Resonator	ECS Inc.	1	0.38	0.38
Surface Mount Passives	Resistors, capacitors	Various	1	68.32	6.83
LF398AN	Sample and Hold IC	Texas Instruments	1	2.72	2.72
OPT101	Photodiode	Texas Instruments	1	7.06	7.06
LT1006	Precision Single Supply Op-amp (filter, amplifier)	Linear Technologies	2	3.18	6.36
AS78L05ZTR-E1	5V Linear Regulator	Diodes Incorporated	1	0.35	0.35
LD11173v3	3.3V Linear Regulator	STMicroelectronics	1	0.47	0.47
LM2776DBVR	Inverting Charge Pump (-3.3V)	Texas Instruments	1	1.59	1.59
0.1in Header Pins	Breakout connections	Molex	50	0.05	2.50
Adafruit Bluefruit LE UART Friend	Bluetooth Module	Adafruit	1	18.20	18.20
Duracell 9V Battery	9V Power Supply	Duracell	1	1.28	1.28
Printed Circuit Boards		PCB Way	3	**5.00**	**15.00**
Total:				**65.24**	**65.24**

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