Noninvasive PoC Anemia Detection Device

Team 11 - Design Document
ECE 445 Spring 2018

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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

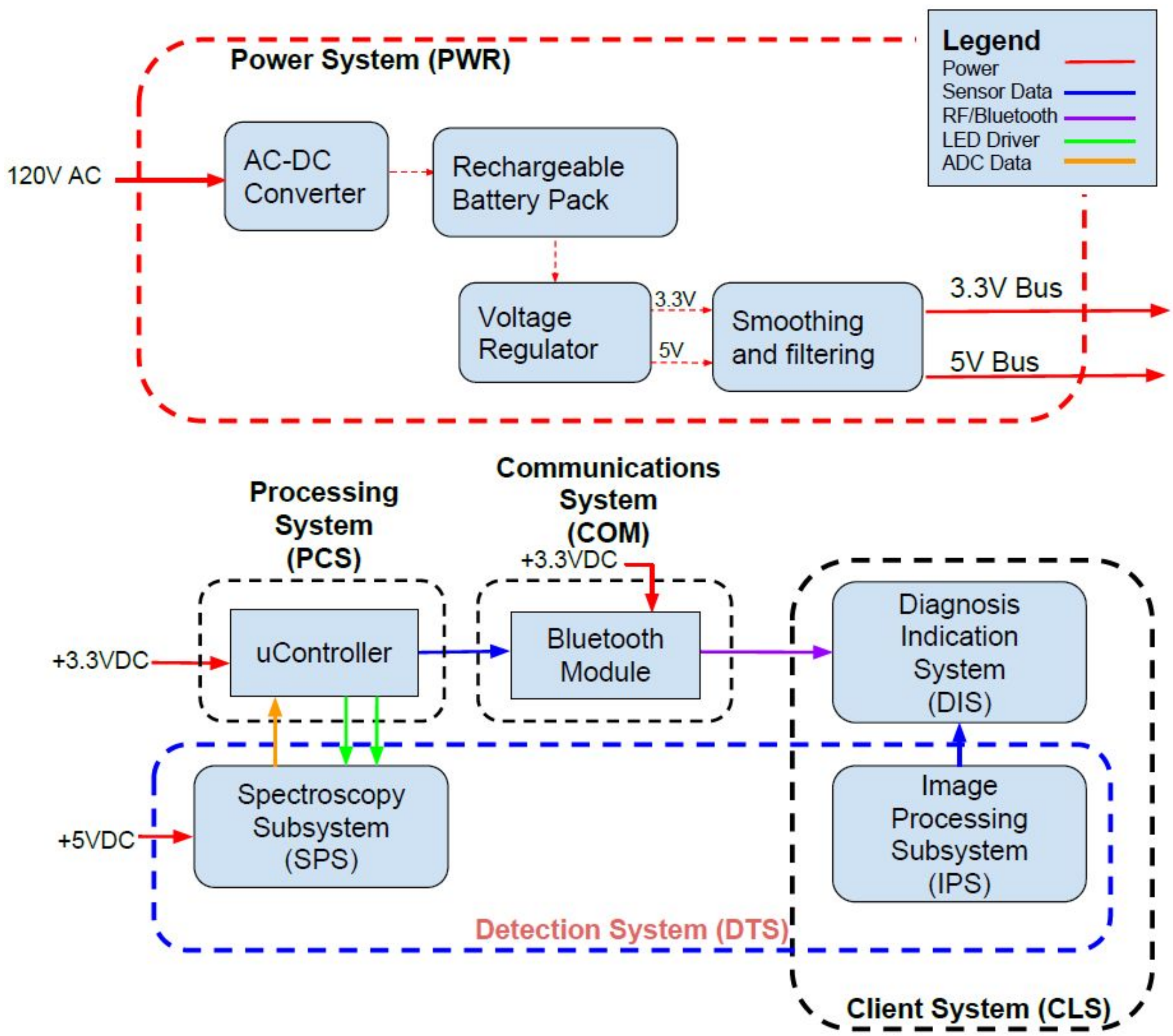

Figure 1: High level block diagram

The high level design shown 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 undecided embedded processor and some simple DSP required to implement the SpO2 detection algorithm required for the Pulse Oximetry data.

Power System (PWR)

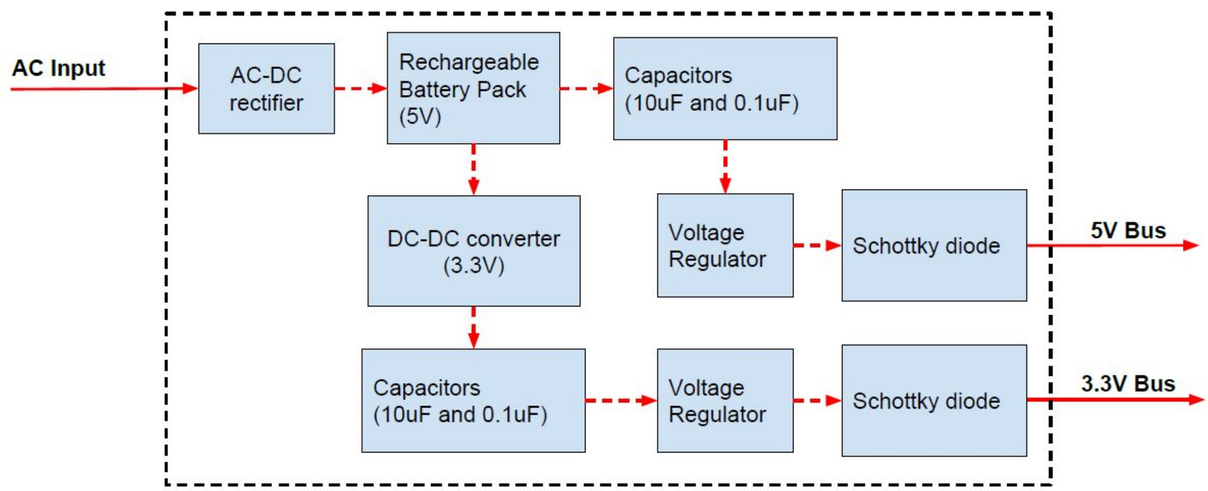

Figure 2: Block diagram of the power system

The power system will be used to first convert and then deliver power to all other subsystems, with the exception of the CLS. It will first convert 120V AC power to 5V DC. This low voltage line will then be used to deliver charge to the local battery. From 5V given by the rechargeable battery, two individual low voltage DC lines will feed the rest of the circuit. The first line will remain at 5V and the second will be stepped down to 3.3V using a DC-DC converter. Both lines will go through a bypass capacitor, decoupling capacitor, and voltage regulator to smooth out signal and manage the power needs of downstream instruments. Lastly, for protection and isolation, the the 5V and 3.3V lines will go through a schottky diode before providing power to other subsystems. It is our intention to use an off the shelf system that contains a rechargeable battery and AC-DC conversion. From there, the rest of the power system can be custom designed.

Current Consumption

We assume the following current consumption from each component:

Subcircuit	qty	Part Name	Supply Feed	Current consumption (total)
Timing Circuit	2	555 Timer	5V	30mA
Photodiodes	1	Monolithic Photodiode	3.3V	15mA (Isc)
	1	Red LED (660nm)	3.3V	20mA
	1	IR LED (940nm)	3.3V	20mA
	2	Transistor	3.3V	2mA
Sample & Hold	1	Transistor	3.3V	2mA
	1	OpAmp	5V	520uA
DC,Filtering,Amplifying	1	BandPass OpAmp	5V	.9mA
	1	Amplifier	5V	520uA
	1	Ref OpAmp	3.3V	750uA
Bluetooth	1	BLE Module	5V	4.9mA
Embedded Processor	1	ATMega	3.3V	0.2mA
		Passives		5mA
Total Current Consumption				**101mA**
3.3V Branch				60mA
5V Branch				41mA

Total power consumption:
101mA * 10 seconds * 10 runs = 2.81mAh

Processing System (PCS)

The Processing System (abbreviated PCS) 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].

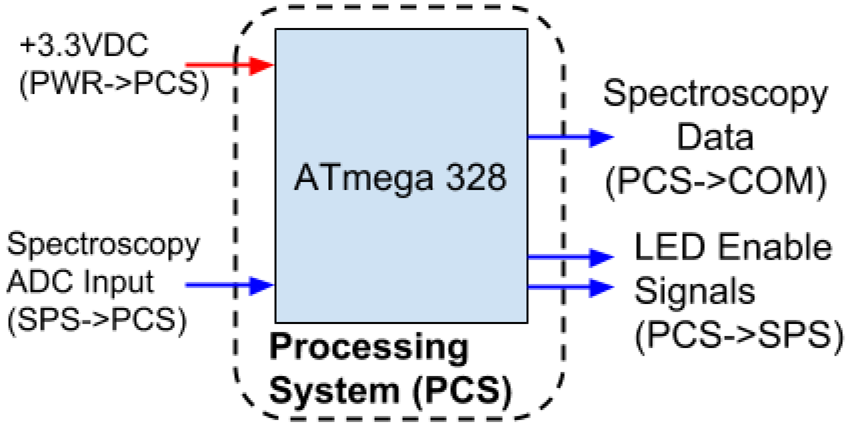

Figure 3: Block diagram of the processing system

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.

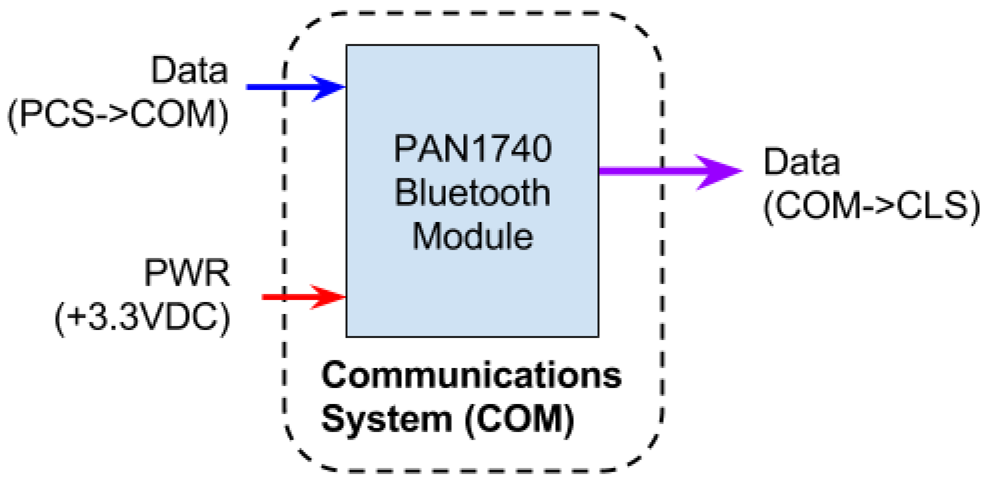

Figure 4: Block diagram of the communications system

Spectroscopy Subsystem (SPS)

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. It 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. 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:

$$SpO_2 \equiv \frac{[HbO_2]}{[total\ haemaglobin]}$$

Equation 1: Equation for recovering SpO_2

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

Equation 2: Modulation Ratio for recovering SpO_2. The λ_n implies a current observation at wavelength λ_n.

Once we calculate the modulation ratio, 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:

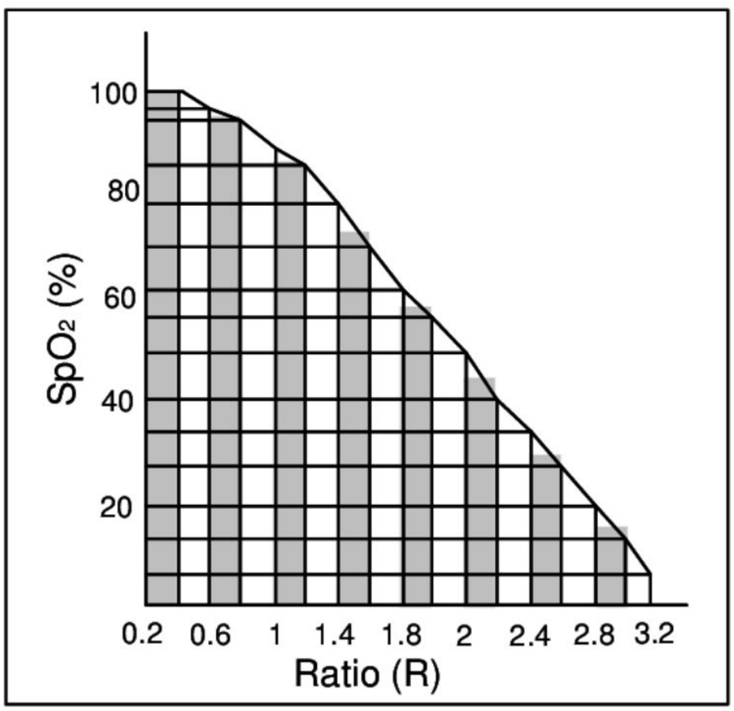

Figure 5a: Modulation Ratio lookup curve

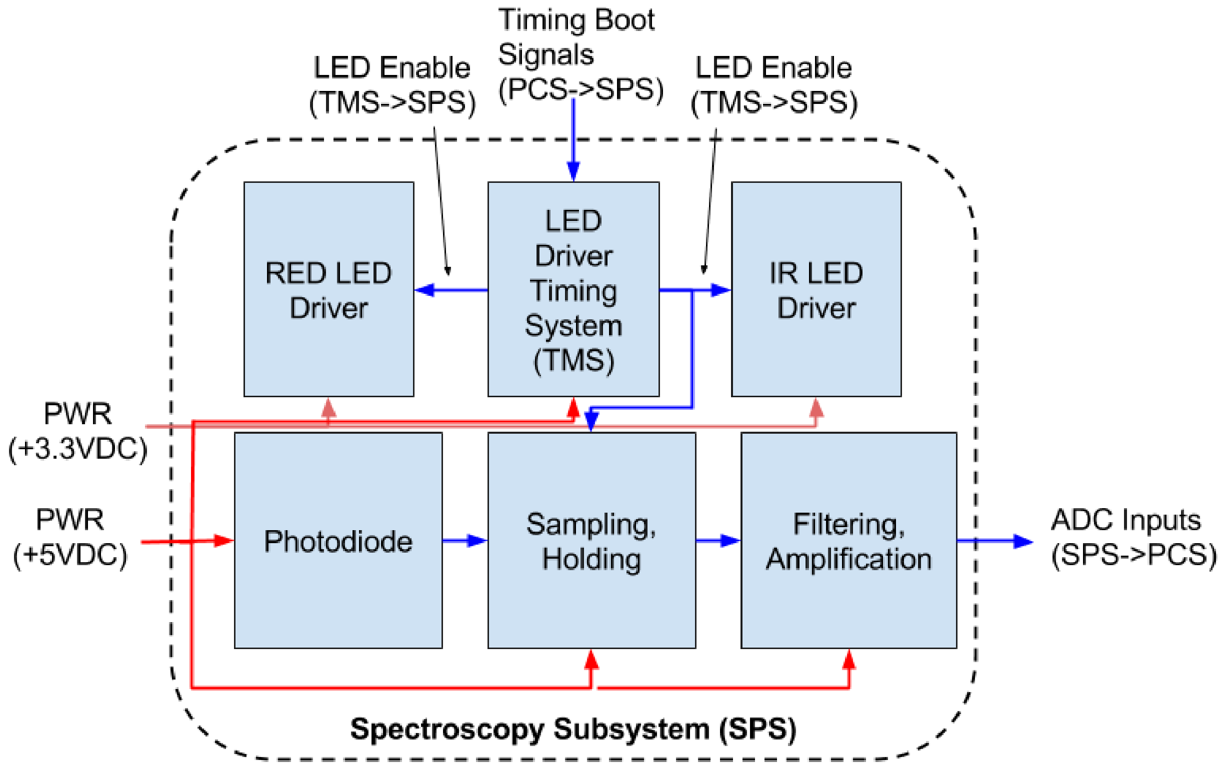

Figure 5b: Block diagram of the spectroscopy subsystem

We choose to add a series of hardware timers (based on the 555 design) to more tightly control the sequencing and timing of the pulses. We also introduce an analog sampler that is tied to this timing circuit in order to ensure that there are no timing issues in processing the ADC input. Using an analog sampler, we can ensure that what the ADC samples is the data we want, and not the data from a different channel.

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, or 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.

$$\Delta V_{step} = \frac{V_{cc}}{N} = \frac{3.3V}{1024} \approx 0.0032V$$

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:

$$\Delta V_{step} < 0.005 \cdot 2V = 0.01V \rightarrow 0.0032V < 0.01V \checkmark$$

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.

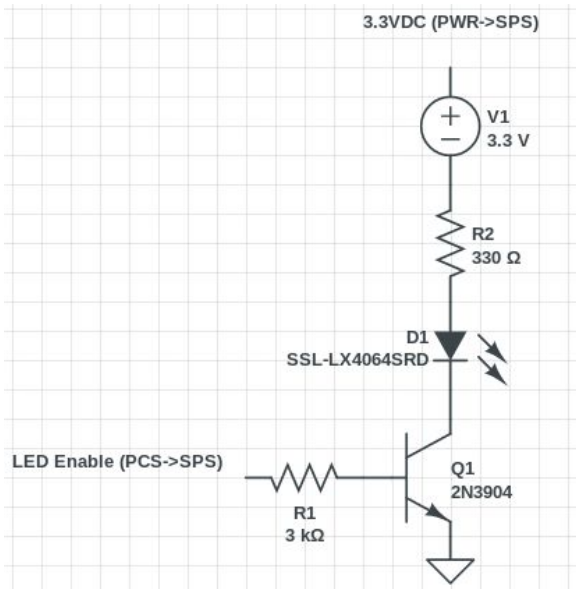

Figure 6: Simple LED Driver (660nm LED pictured). The Enable signal comes from the TMS, not the PCS

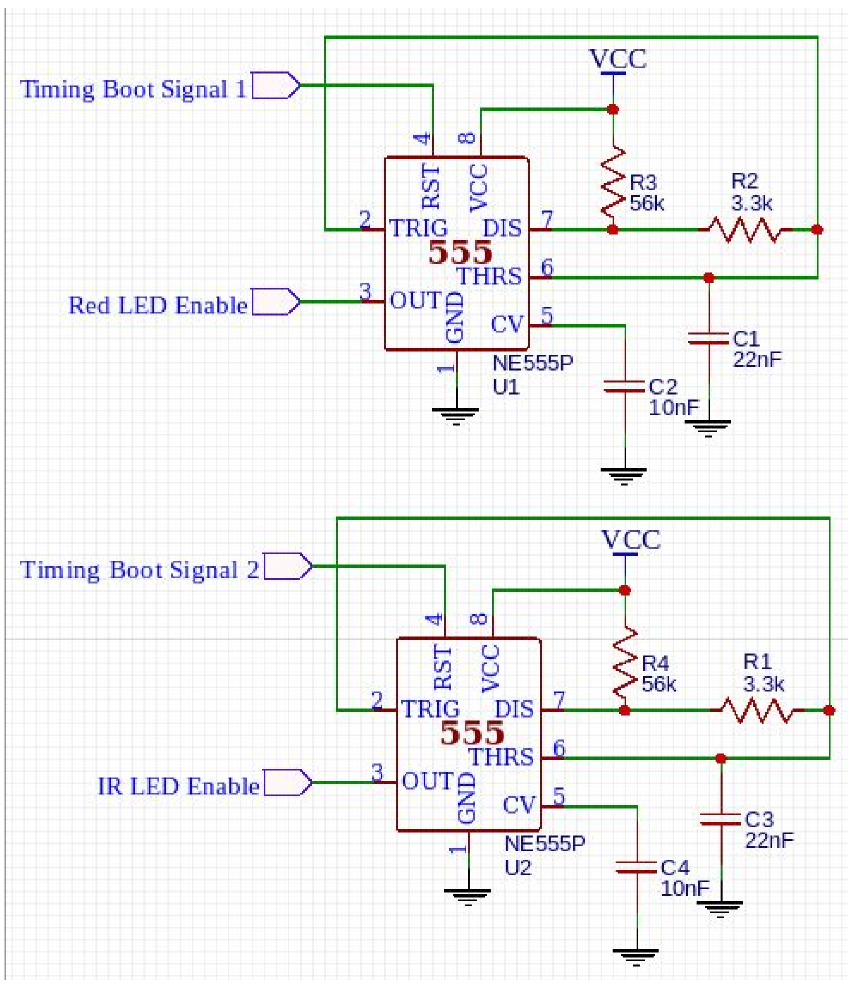

Figure 7: LED Timing Circuit (50us pulse, 1ms period)

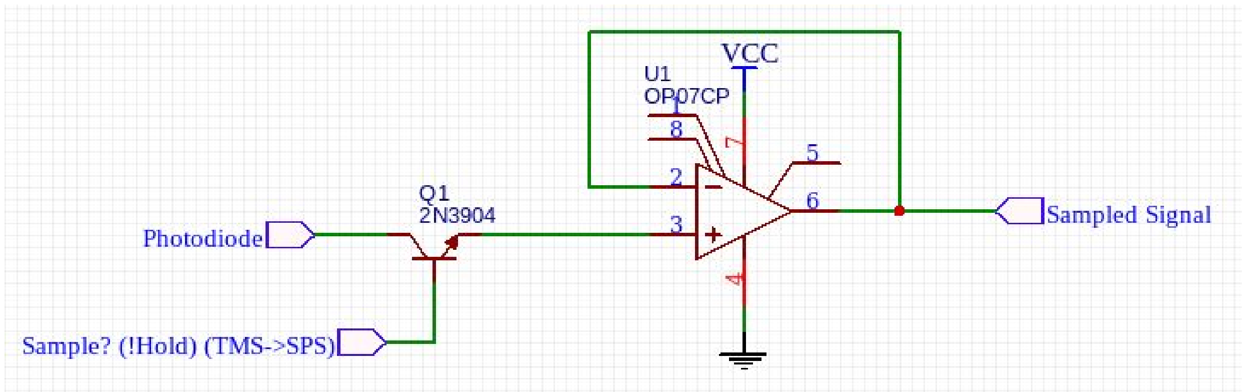

Figure 8: Sample/Hold Circuit. Enabled using the LED Enable. Two used in practice.

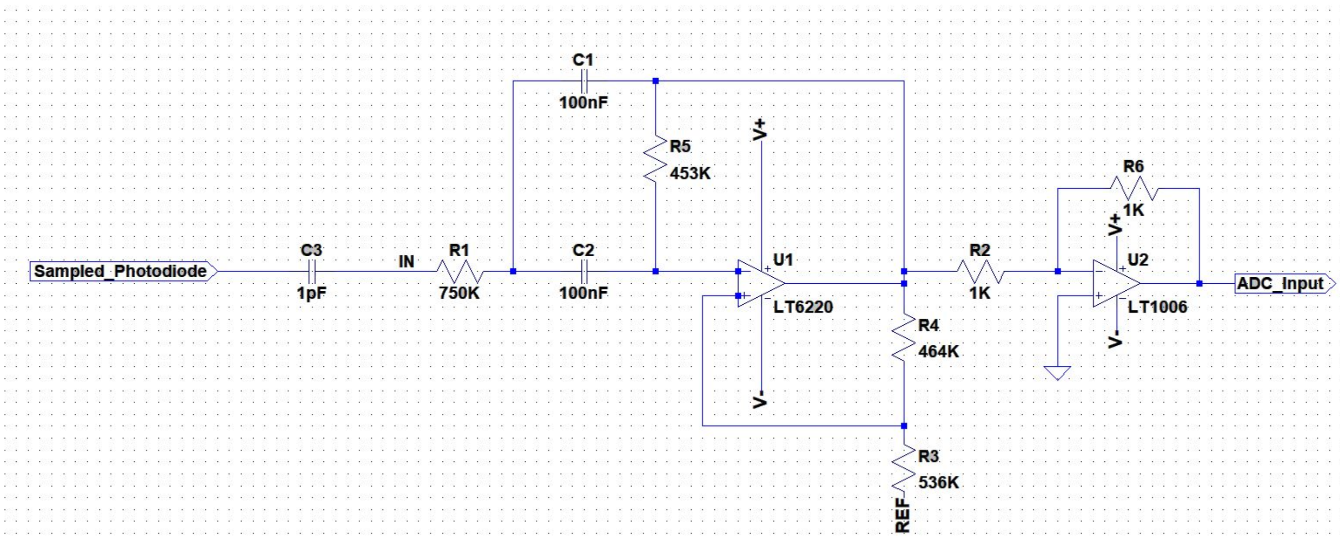

Figure 9a: DC Blocking, Active Bandpass Filtering, and Amplification.
*note: V+ = +3.3V and V- = 0V

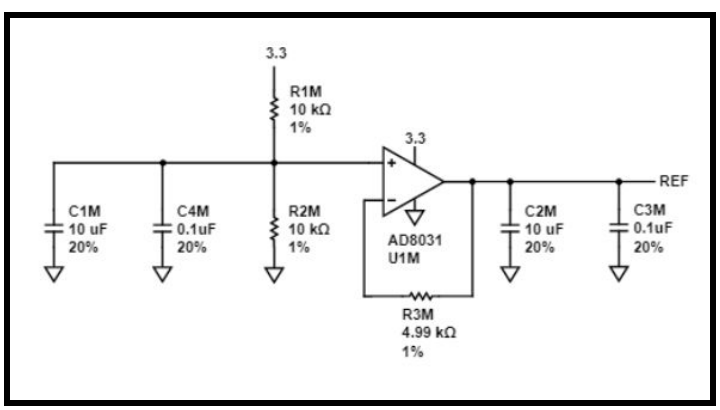

Figure 9b: Active Bandpass Filtering and reference voltage generation

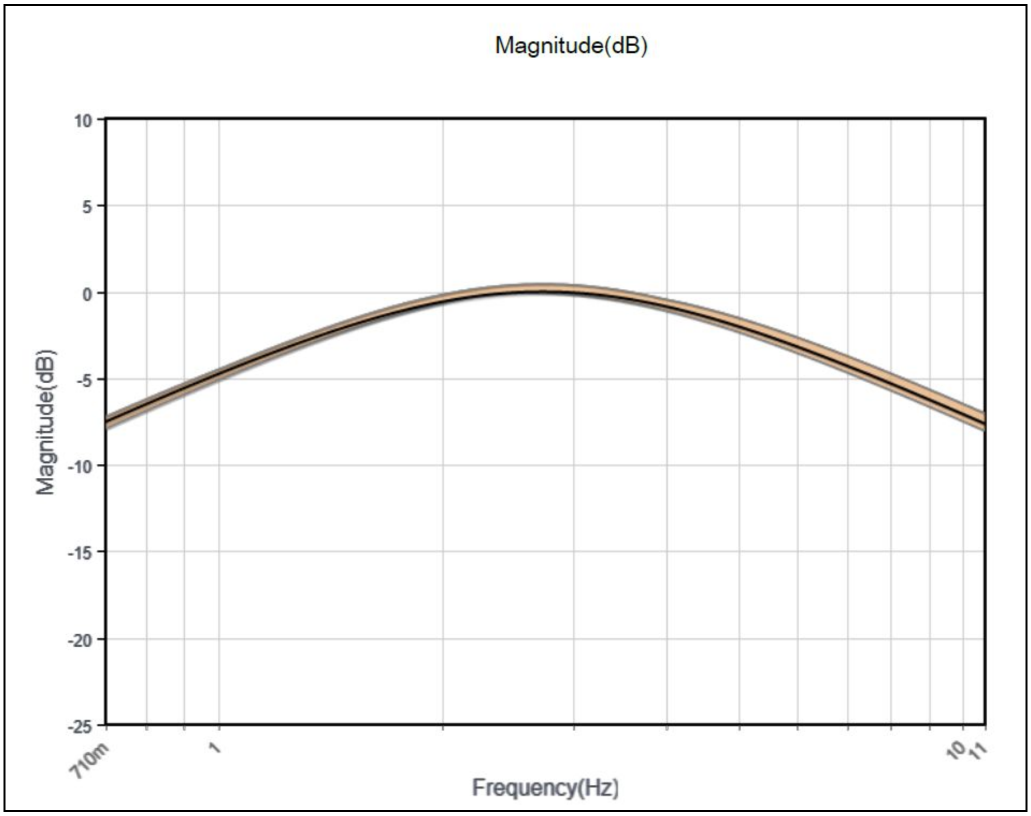

Figure 9c: Frequency response of active bandpass filter.

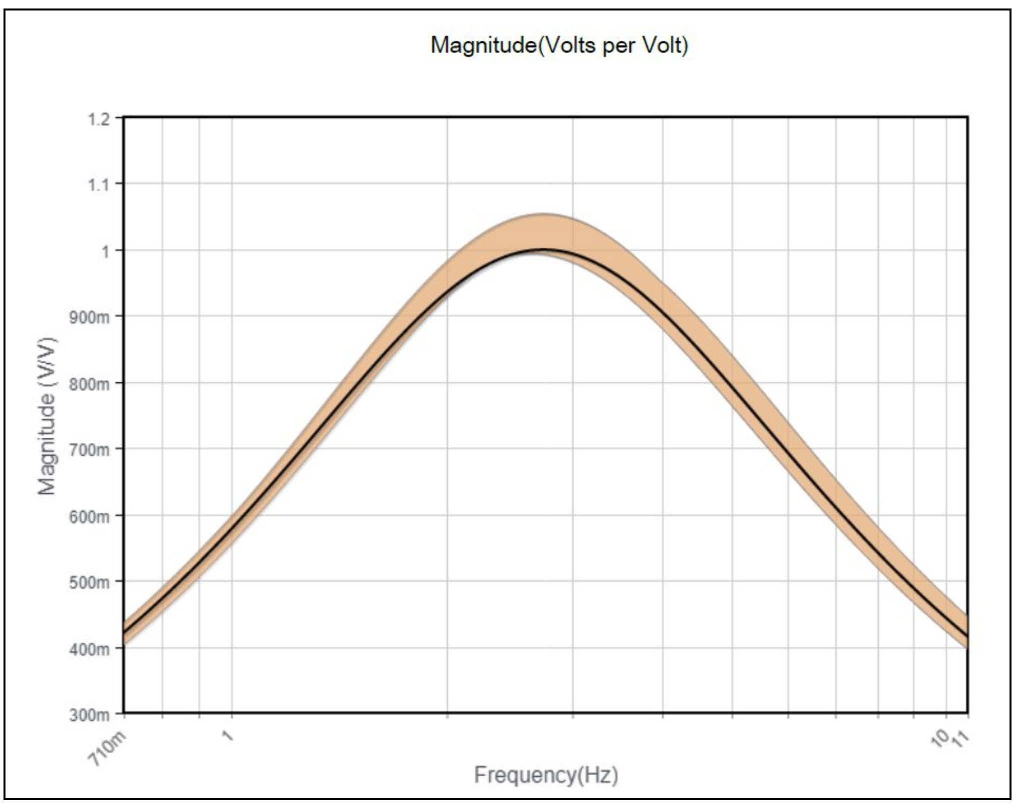

FIgure 9d: Magnitude of signal from active bandpass filter

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. The block diagram shown in the High Level Block Diagram is sufficient to show the function of this 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.

Diagnosis Indication System (DIS)

The Diagnosis Indication System is where the user will read out their final diagnosis. This diagnosis will be implemented in software and shown through an Android application. As this system contains no hardware, it does not have a block diagram. We have designed a mockup of the Android application used to host the Diagnosis Indication System.

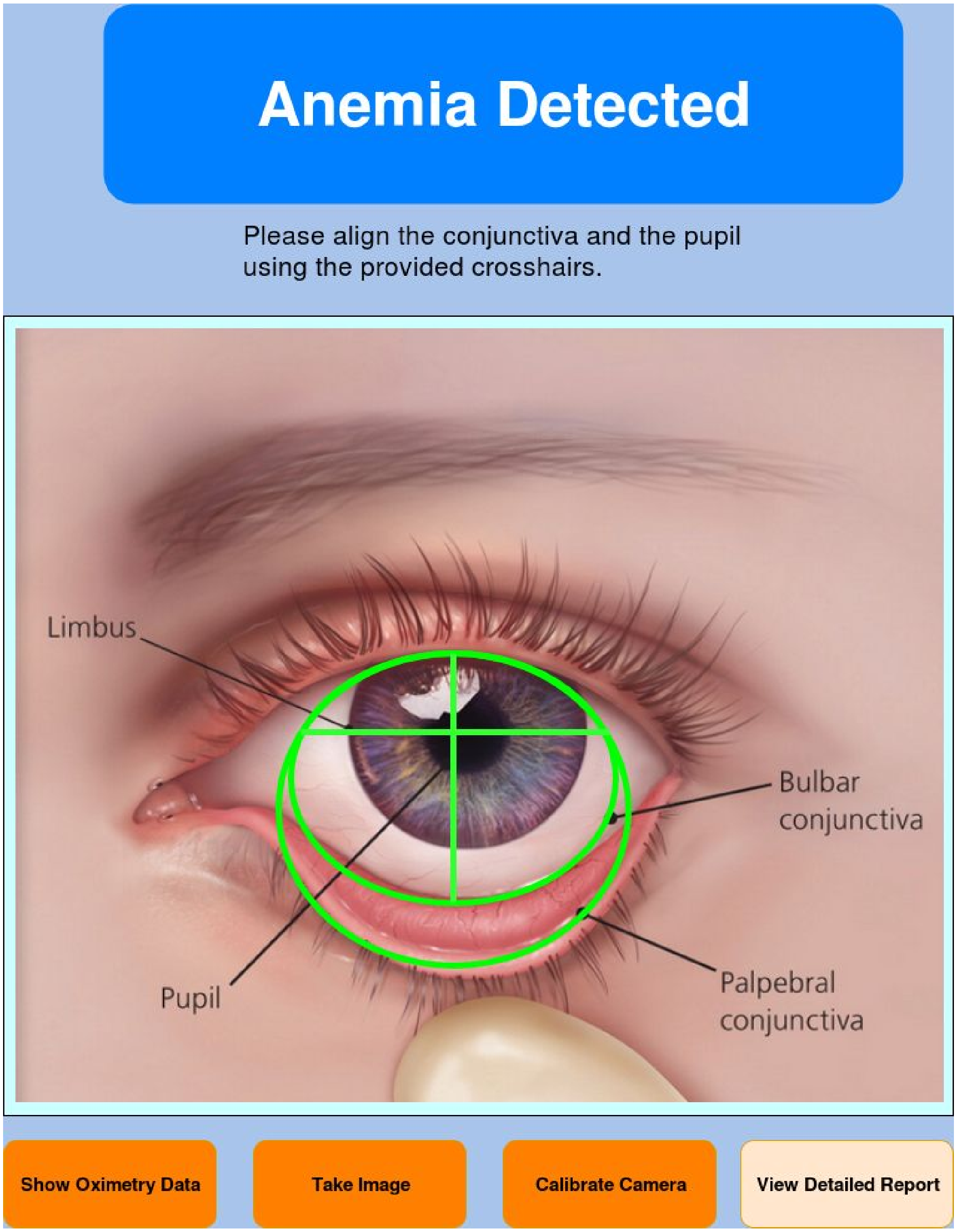

Figure 10: Mockup of Android application

External to these requirements, we may extend the Diagnosis Indication System to do the following:

- Show measured SpO2 from the SPS
- Show EI value from the conjunctiva image

Requirements and Verification

Block	Requirement	Verification
Power System	Rechargeable battery pack must have minimum capacity of 20mAh of charge.	Discharge battery pack through 100kOhm resistance, measure current over time using multimeter to calculate overall energy storage.
	Power system should be able to supply current of 150mA sustained and 200mA peak.	● Discharge battery into programmable load box drawing 150mA and 200mA. ● 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 +/-1% tolerance after filtering and isolation.	Record waveforms for 10 minutes of 5V bus and 3.3V bus to make sure output voltage meets tolerance.
Processing System	The embedded processor must have an ADC that operates from 0 to 3.3VDC, +/-1%, with a resolution of better than 0.005V.	● 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 0.005V 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.	● Generate a 500Hz sinusoidal waveform, 3.3VPP, +1.65VDC 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.	• 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 3.3VDC • Observe flashing LED for 10 seconds using a stopwatch, and verify frequency.
	The embedded processor must be able to run on 3.3VDC, +/-10%.	• 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.	• 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	The communications system must be capable of running on 3.3V provided by the power system.	• 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.	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 200uA during idle mode.	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 200uA.

	The communications system must interface with the processing system over UART.	● 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	The bandpass filter must have a passband between 0.5Hz and 5Hz, corresponding to a passband bandwidth of 4.5Hz, +/-10%, with a 0.25Hz rolloff +/-10%, and mitigation of frequencies 3dB below the maximum signal amplitude at a stopband frequency of 5.5Hz +/- .25Hz.	● 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.	● 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 ● 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 3.3V.	● Pulse both LEDs at full brightness (1Khz, 5% duty cycle, 3.3VDC 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 3.3VDC over the entire test period.

	The spectroscopy subsystem must run on 5VDC and 3.3VDC.	• Power the spectroscopy system with 5V. • Repeat all verifications for spectroscopy subsystem. • After successful verification, repeat verifications using voltage of 3.3V • For each individual component in the spectroscopy system, verify through the datasheet that the chosen part can operate using either 3.3VDC or 5VDC.
	The spectroscopy subsystem must output a signal which has a constant DC gain of 2V, +/- 20%.	• 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	The client must support data transfer from the communications system.	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.	Test the client system software against an Android phone.
	The client must be capable of displaying the final diagnosis.	The Android application shows the final diagnosis on the main screen.
Image Processing Subsystem	The image processing algorithm must feature some type of feature detection to identify different sections of the image.	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.	• 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.	● 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.	● 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%..

Tolerance Analysis

Heartbeat detection plays a critical role in the implementation of a pulse oximeter, as it is the ratio of the amplitude of the heartbeat signals at different frequencies which provides our system with the estimation of oxygen saturation. As such, we choose to put a particular focus on ensuring this critical system is realizable within the specifications we set forth in the Requirements sections of this document.

Our intention is to hone in on frequencies shown by the pulsatile signal relating to heartbeat and blood flow. These frequencies fall between 0.5Hz and 5Hz, so we chose to use a 2nd order butterworth filter centered at 2.75Hz. The filter has a passband bandwidth of 4.5Hz, +/-10%, with a 0.25Hz rolloff +/-10%, and mitigates frequencies 3db below the maximum signal amplitude at a stopband frequency of 5.5Hz +/- .25Hz. Using the Analog Devices Filter Design tool [8], we created a second order Butterworth Filter which satisfies all of these requirements, while being realizable with parts of the following tolerances:

Capacitor	5%
Resistor	1%
Inductor	5%
Op Amp Gain-Bandwidth Product	20%

Risk Analysis

The block that poses the greatest risk to the completion of our project is the Client System. The client system contains an as-yet unspecified image processing algorithm that will need to provide feature detection, classification, and diagnosis capabilities. To mitigate this risk, we will be scoping the features of the image processing algorithm such that the identification of the features of the image is part of the image capture itself, so as to decrease the complexity in the most complicated portion of the algorithm. One potential manifestation of this is using an image template that all images must conform to, such that features exist in a known location of the image. 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.

Schedule

Week 1 (1/15):
- Brainstorm

Week 2 (1/22):
- Revision of Idea
- Decide Between Project Ideas (Jeremy, Mythri)

Week 3 (1/29):
- Project Approval

Week 4 (2/5):
- Proposal Document

Week 5 (2/12):
- Complete Spectroscopy System Design (Jeremy)
- Complete Power System Design (Mythri)
- Eagle Assignment (Jeremy, Mythri)

Week 6 (2/19):
- Finalize Part Selection (Jeremy, Mythri)
- Design Document
  - Statistical Analysis (Mythri)
  - Spectroscopy System Tolerance Analysis (Jeremy)

Week 7 (2/26):
- Design Review
- Order Parts (Mythri, Jeremy)
- Verify Power System (Mythri)
- Complete Client System Core Design (Jeremy)

Week 8 (3/5):
- Build and Unit Test DIP Prototype Systems
  - Spectroscopy System (Jeremy, Mythri)
    - Butterworth Filter (Mythri)
    - Photodiode (Jeremy)
    - LED Drivers (Jeremy)
    - 555 Timing (Mythri)
  - Power System (Mythri)
  - Processing System (Jeremy)
  - Communications System (Jeremy)
- Begin PCB Layout (Mythri, Jeremy)
  - Component Placement
  - Preliminary Routing

Week 9 (3/12):
- Implement Spectroscopy Calculation Algorithm (Jeremy)
- Characterize and Validate Spectroscopy Timing System (Mythri)
- Implement Serial Communications with Processing System (Jeremy)
- Finish PCB Layout (Jeremy, Mythri)
  - Finalized Routing
  - Test Point Placement
  - Processor Flashing Pin Placement
- PCBWay Orders

Week 10 (3/19):
- Spring Break

Week 11 (3/26):
- Repeat Validations of Individual Systems (Jeremy, Mythri)
- Create Barebones Android Application (Jeremy)
- Evaluate and Plan PCB Fixes

Week 12 (4/2):
- Final PCB Assembly (Mythri)
- Final Spectroscopy system assembly (Jeremy)
- Off-bench Testing with Power Supply (Mythri)

Week 13 (4/9):

Add Bluetooth Interface to Client System (Jeremy)
Implement Superpixel Anemia Detection algorithm (Jeremy)
Compute Anemia Likelihood (Jeremy)
Wristband Interface Construction (Mythri)
Extended Charge Cycling (Mythri)
Full System Test (Mythri, Jeremy)

Week 14 (4/16):
Add Image Calibration (Jeremy)
Complete User Interface (Jeremy)
Final Hardware Assembly (Mythri, Jeremy)
Prepare slides for final demo (Mythri, Jeremy)
Week 15 (4/23):
Final Demo (Mythri, Jeremy)
Week 16 (4/30):
Final Paper (Mythri, Jeremy)

Cost Analysis

Part Name	Price (1pc)
555 Timer	$ 0.41
Monolithic Photodiode	$ 7.35
Red LED (660nm)	$ 0.49
IR LED (940nm)	$ 0.29
Transistor	$ 0.80
Transistor	$ 0.40
OpAmp	$ 3.90
BandPass OpAmp	$ 3.56
Amplifier	$ 3.90
Ref OpAmp	$ 3.17
BLE Module	$ 15.25
ATMega	$ 2.20

Passives	$ -
Batteries	$ 3.20
PCB	$ 10.00
Fabric for wristband	$ 10.00
Pulse Oximeter Casing	$ 7.00
Cost of Labor ($36/hr, 15 hours/week, 8 weeks)	$ 8,640.00
Total:	**$ 8,711.92**

Ethics and Safety

Both ethics and safety are of great importance to us while pursuing this project.

Because we will be working with a 120V AC line and stepping it down to a lower DC voltages, we will be sure to abide by the following safety precautions when working in lab. First and foremost, we will always be aware of any damaged or frayed equipment, and work without bringing food or water into a lab setting. When testing, we can take precaution by placing one hand on our back or in our pocket to prevent a closed loop current passing through the body. Additionally, using proper grounding methods, working with a partner, and wearing PPE will ensure that any safety risk regarding electrical shock is minimized.

In addition to safety, our group will also hold ethics in high regard as this project may require us to work with medical/patient data. 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.

References

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3685880/
[2] https://www.nxp.com/docs/en/application-note/AN4327.pdf
[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1497067/
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