CMBES/SCGB

2018 ACCES23-CMBEC41

Joint Conference
Charlottetown PEI
May 8-11, 2018

DEVELOPMENT OF A NON-INVASIVE POINT-OF-CARE HEMATOCRIT SENSOR FOR ANEMIA DETECTION

Haley Butler[1], Wyatt MacNevin[1], Emad Naseri[1], Jordan Torrealba[1], Nadja Bressan[1], Gulrose Jiwani[2], Ali Ahmadi[1]

[1]School of Sustainable Design Engineering, University of Prince Edward Island, 550 University Avenue, Charlottetown, Canada

[2]Faculty of Nursing, University of Prince Edward Island, 550 University Avenue, Charlottetown, Canada

ABSTRACT

Anemia, a condition characterized by insufficient oxygen delivery to cells and tissues within the body, affects approximately a third of the world's population. Causes of anemia can be attributed to malnutrition, low erythropoietin production, kidney disease, and forms of cancer. Current tests for anemia involve invasive blood sampling and costly diagnostic procedures to produce results. Through the development of a portable non-invasive hematocrit sensor to aid in the diagnosis of anemia at the point-of-care, detection and treatment of anemia can be improved. Using the variance of absorption of IR and red light of oxygenated hemoglobin (HbO2) and deoxygenated hemoglobin (Hb) a portable sensor was designed and created to determine oxygen saturation – the most reliable method of anemia detection.

INTRODUCTION

Anemia is a condition characterized by insufficient oxygen delivery to cells and tissues within the body required to sufficiently reach metabolic and physiological needs [1]. Anemia can be caused by inadequate red blood cell (RBC) volume, inadequate oxygen-carrying capacity, increases in blood acidity, or insufficient levels of iron or ferritin in the blood [2][3]. Anemia, when undetected, has been shown to contribute to significant health consequences, including pregnancy complications and disorders, physical and cognitive development disorders, increased risk of morbidity, weakness, fatigue, and dizziness [4]. Causes for anemia have been researched to include lower erythropoietin production, kidney disease, cancer (including chemotherapy side-effects), and severe malnutrition – which serves as a leading cause for anemia, particularly in developing countries with reduced food security [5][6][7]. In developing countries, with high rates of malnutrition and poor access to medical and diagnostics services, a portable, low-cost, point-of-care sensor for detecting anemia could aid in improving diagnosis and care.

Traditional methods for detection of anemia involve an invasive approach requiring blood sampling and subsequent lab-based testing of hemoglobin concentration, hematocrit volume, and complete blood count (CBC) [4][8][9]. These procedures require access to diagnostic facilities and can be greatly time intensive with a substantial cost. Recent developments in this field have been made to increase both the portability and non-invasiveness of these sensors through using microfluidic-based sampling methods [10], optical attenuation methods [11], or light scattering-based measurement methods [12] [13]. Although these developments have greatly improved the approaches for the detection and diagnosis of anemia, there still exists a need for improvement in long-term user monitoring and size and cost reduction. Additionally, to improve the functionality of the point-of-care device in developing countries, there exists a need for improvements in the sensor's design

in order to improve the integration of the device into the environment of its use.

To attempt to address these areas of technical improvements, an optical attenuation-based hematocrit sensor was designed and preliminary testing was performed. LED and IR light sources and detectors were implemented into the design to facilitate a non-invasive measurement modality through interactions between oxygenated and deoxygenated hemoglobin and the specific wavelengths of light. The sensor was embedded within a custom index finger mount attached to a microcontroller. Bluetooth was used in the design to enable data to be sent wirelessly to accommodate for clinical use in circumstances where there is limited access to electronics and technology. A display screen is currently being developed for the device.

This paper will present the sensing methodology used in the design of the point-of-care hematocrit sensor, the sensor design, preliminary testing results, and identified areas of improvement.

THEORY

Anemia can be diagnosed on the basis of oxygen deficiency. Iron deficiency anemia is a common type of anemia due to insufficient iron to produce hemoglobin. The optical properties of hemoglobin are used to develop the basis of the measurement system and sensor development. The main forms of hemoglobin in the blood are oxyhemoglobin (HbO2) and hemoglobin (Hb), where hemoglobin binds oxygen in the lungs to form oxyhemoglobin [14]. These molecules have different associative absorption properties dependent on the wavelength of light used. Appreciable variances in absorption occur between 550-1000nm, thus if wavelengths of transmitted light are detected through the finger, the differences in attenuation can be used to determine oxygenated hemoglobin and hematocrit concentration in the blood. For this study, 650nm and 950nm were used to elicit differentiable readings (Figure 1).

METHODOLOGY

A portable hematocrit sensor was developed based on measuring the variance in absorbance of LED and IR light through blood by measuring the attenuation of signals through the right index finger. By analysis of the ratio of LED and

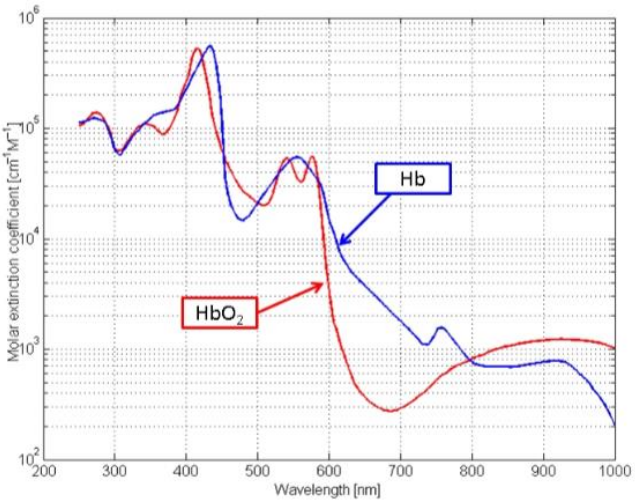

Fig. 1: Hb and HbO2 Absorbance for Different Wavelengths of Light [14]

IR signals, hematocrit and blood oxygenation can be determined. An overview of the measurement principle can be seen in (Figure 2).

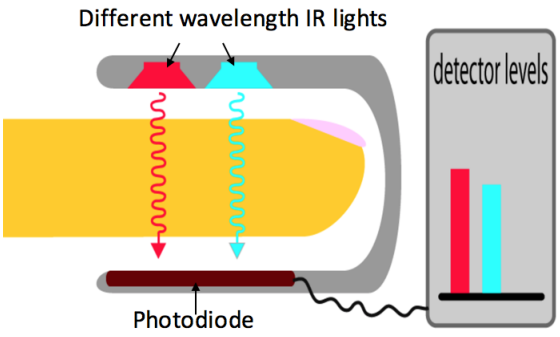

Fig. 2: Overview of Operation Principle Using IR and Red Light [13]

To contain the LED and IR lights and the associated detectors, a finger clamp was designed and 3D printed using ABS material. This finger clamp is adjustable to accommodate a range of finger sizes to improve the functionality of the device. As this device was designed as an initial proof of concept, further

designs will involve integrating the electronics and microcontroller into the finger clamp to produce a stand-alone measurement system. IR and LED light is transmitted from the source, through the inserted finger – where it interacts with and is absorbed by Hb and HbO2 molecules, and the attenuated signal is received by IR and red photodiodes. The detected signals are then transmitted to a microcontroller (Smraza UNO R3 Board ATMEGA328P) for signal processing. A custom code was developed to convert these signals into IR and red light values which are displayed to the user. The values are then compared using the following formulae:

$$A_R = \log (I_0/I)$$

Using this formula to determine the absorbance of the light, a ratio between the red absorbance and IR absorbance can be measured knowing the known wavelength of both sources before attenuation. This ratio is then correlated to a known hematocrit level and is used to determine the relative ratio of oxygenated and deoxygenated hemoglobin in the blood – indicating the oxygen saturation of the blood. From the oxygen saturation, anemia could be detected in individuals using the system in a portable and non-invasive manner. An overview of the materials used in the design of the portable sensor is shown in (Table 1).

Table 1: Overview of Design Components for Sensor

Part	Cost
Smraza UNO R3 Board ATMEGA328P	$14.99
IR LED	$0.98
Red LED	$2.76
Photodiode IR	$2.51
Photodiode Red	$2.07
Resistor Kit 47-8.2K 1/20W	$12.12
Striveday 24AWG 1007 Copper Wire Electric wire kit	$19.99
Elmer's Epoxy	$6.48
LMC6062 Precision Op Amp	$2.50

RESULTS AND DISCUSSION

A prototype was developed using the breadboard diagram (Figure 3). The LED and IR sources and IR and LED photodiodes were soldered to 24 AWG braided core wires and connected to the microcontroller. SMD components were used due to availability. A precision op-amp, LMC 6062, was used for signal amplification, in the following circuit diagram (Figure 4). This represents amplifying the photodiode signal 10x, from 200-300mV to 2-3V. Software was developed using the Arduino IDE to convert these data over serial into more meaningful absorbance data.

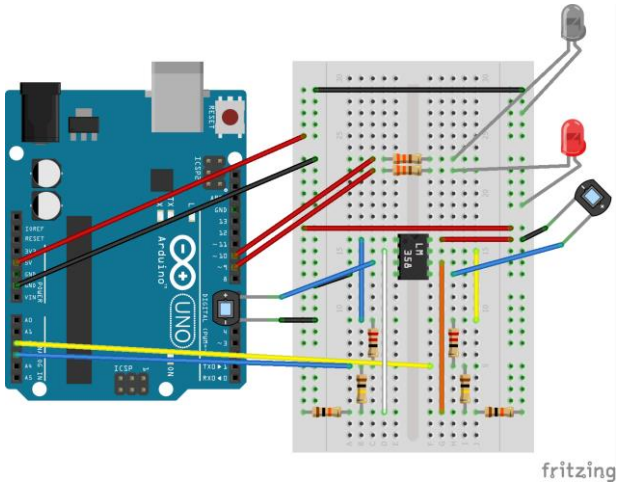

Fig. 3: Breadboard Diagram for Sensor Design (fritzing)

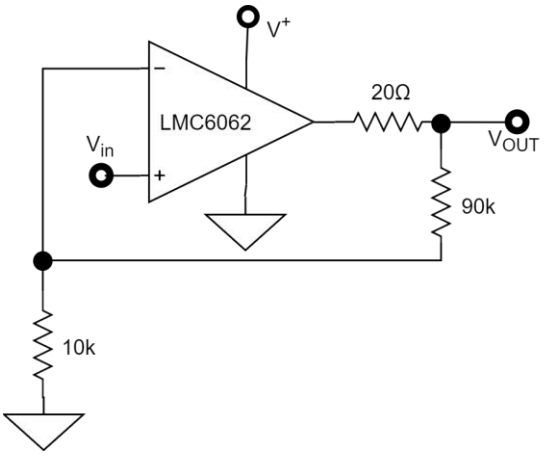

Fig. 4: LMC6062 10x Amplification Circuit Diagram

From there, the circuit could be tested, verified, and then remade in a more permanent configuration. A 5cm x 7cm perfboard was used to solder the THT resistors; 2x10Ω in series, 6x15k in series, and 1x10k, and op-amp. The leads to the LEDs and Photodiodes were then soldered onto this board, and the necessary Arduino connections (+5V, GND, 10, 11, A0, A1) made. This current prototype can be seen in Figure 5. Modifications have since been made to block ambient light entering, and infrared and red from leaving the sensor body.

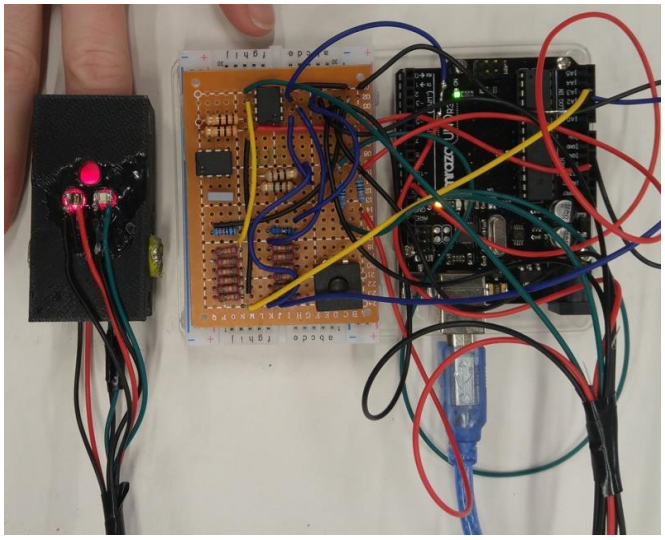

Fig. 5: Initial Hematocrit Sensor Prototype

The preliminary results from the prototype can be seen in the following table.

Table 2: Preliminary Results

	Subject 1	Subject 2	Subject 3	Subject 4
R_2	460	453	453	385
IR_2	545	520	518	472
A_R	0.151	0.158	0.158	0.229
A_{IR}	0.107	0.128	0.130	0.170
A_R/A_{IR}	1.411	1.230	1.220	1.350
A_R/A_{IR} corrected	0.470	0.410	0.407	0.450

The R/IR absorbance values can then be related to the SpO2 levels for the individual. The relationship of the values can be seen in Figure 6.

From this it is apparent that all the subjects have between 95% and 100% blood oxygen saturation. For a healthy individual the SpO_2 percentage should be between 94%-100%. If saturation levels fall below 90%, supplementary oxygen should be administered [15].

The system was calibrated using an existing pulse oximeter. The existing unit was tested on the same subjects and using the data a correction value was determined. This value was 1/3 the A_R/A_{IR}.

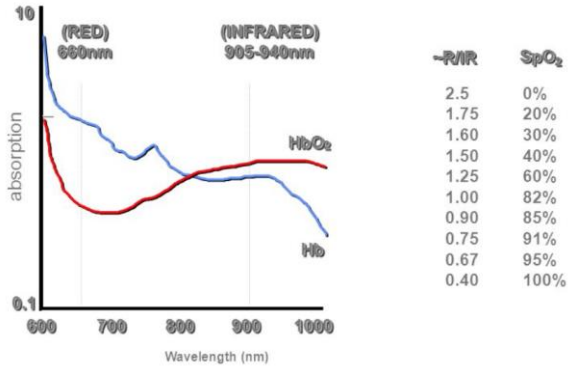

Fig. 6: R/IR correlation to SpO_2

Moving forward, further testing will be required to validate the design and the measuring ability of the sensor as it relates to hematocrit, oxygenated blood, and deoxygenated blood. To improve the functionality of the design, the electrical components and the microcontroller will be reduced in size and cost and integrated further into the body of the finger clamp. Bluetooth compatibility will be added to enable communication of the data to nearby mobile-devices or computers located at the point-or-care. To enable improved user-interactions, an LED display and interface will be added within the top portion of the finger clamp unit. This addition will allow users to quickly measure and read oxygenation levels to determine anemia in patients on location. The mobile-phone application will need to be further developed to possess Bluetooth capabilities and the general design of the app will need to improve in terms of user-interface options, connectivity, and display. Furthermore, as there exists great value in directly identifying anemia stemming from iron deficiency – particularly in developing countries where over-supplementing is performed during childbirth, carrying its own

adverse side-effects – the sensor will be further correlated to detect iron levels based on oxygenation of the blood. This improvement will be performed through direct testing and correlation or through identifying a wavelength of light that is attenuated directly through interactions with iron in the blood.

CONCLUSION

After performing testing and analysis on the prototype it was determined that it can detect hemoglobin results accurately. From this, a lack of saturated oxyhemoglobin, hypoxemia, can be detected. Knowing an individual has hypoxemia can allow fast diagnosis for health conditions, such as anemia. Moving forward, a non-invasive method for detecting iron will be explored and integrated into the existing design. This will enable accurate detection of anemia without the need of blood sampling. Other areas of improvement include app development, size reduction of the circuit board, and correlation of results with blood iron and ferritin levels. With these improvements, the technology has the ability to reduce the cost, skill and time required to detect iron deficiency anemia around the world.

REFERENCES

[1] W. H. Organization, "Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity," *VMNIS| Vitamin and Mineral Nutrition Information System,* pp. 1-6, 2011.

[2] L. Gotloib, D. Silverberg, R. Fudin and A. Shostak, "Iron Deficiency is a Common Cause of Anemia in Chronic Kidney Disease and can often be Corrected with Intravenous Iron," *Journal of Nephrology,* vol. 19, no. 2, pp. 161-167, 2006.

[3] P. R. Dallman, R. Yip and C. Johnson, "Prevalence and Causes of Anemia in the United States, 1976 to 1980," *The American Journal of Clinical Nutrition,* vol. 39, no. 3, pp. 437-445, 1984.

[4] B. De Benoist, E. McLean, I. Egli and M. E. Cogswell, "Worldwide Prevalence of Anaemia 1993-2005: WHO Global Database on Anaemia," WHO, Geneva, 2008.

[5] N. Thakur, J. Chandra, H. Pemde and V. Singh, "Anemia in Severe Acute Malnutrition," *Nutrition,* vol. 30, pp. 440-442, 2014.

[6] M. Dicato, L. Plawny and M. Diederich, "Anemia in Cancer," *Annals of Oncology,* vol. 21, no. 7, pp. 167-172, 2010.

[7] K. Knight, S. Wade and L. Balduccu, "Prevalence and Outcomes of Anemia in Cancer: a Systematic Review of the Literature," *The American Journal of Medicine,* vol. 116, no. 7, pp. 11-26, 2004.

[8] C. Ullrich, A. Wu and C. Armsby, "Screening Healthy Infants for Iron Deficiency Using Reticulocyte Hemoglobin Content," *The Journal of the American Medical Association,* vol. 294, no. 8, pp. 924-930, 2005.

[9] A. Gomez-Simon, L. Navarro-Nunez and E. Perez-Ceballos, "Evaluation of Four Rapid Methods for Hemoglobin Screening of Whole Blood Donors in Mobile Collection Screening," *Transfusion and Apheresis Science,* vol. 36, no. 3, pp. 235-242, 2007.

[10] J. Hennek, A. Kumar, A. Wiltschko, M. Patton and G. M. Whitesides, "Diagnosis of Iron Deficiency Anemia Using Density Based Fractionation of Red Blood Cells," *Lab on a Chip,* vol. 16, pp. 3929-3939, 2016.

[11] J. L. Nirupa and V. Kumar, "Non-Invasive Measurement of Hemoglobin Content in Blood," *Medical Measurements and Applications, 2014 IEEE International Symposium ,* 2014.

[12] K. Abhishek, A. Saxena and R. Sonkar, "Non-Invasive Measurement of Heart Rate and Hemoglobin Concentration Level Through Fingertip," *2015 International Symposium on Signal Processing, Informatics, Communication and Energy Systems,* 2015.

[13] Punter-Villagrasa, J. Cid and P. Miribel-Catala, "An Instantaneous Low-Cost Point-of-Care Anemia Detection Device," *Sensors,* vol. 15, pp. 4564-4577, 2015.

[14] G. Kumar and J. Schmitt, "Optimum Wavelengths for Measurement of Blood Hemoglobin Concentration and Tissue Hydration by NIR Spectrophotometry," *Proc. SPIE 2678, Optical Diagnostics of Living Cells and Biofluids,* 1996.