International Journal of
Science and Engineering Investigations vol. 9, issue 97, February 2020
Received on February 2, 2020 ISSN: 2251-8843

Bi-spectral Photoplethysmographic Non-invasive Device for Real-Time Monitoring of Blood Haemoglobin Level

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***Abstract*-**Anaemia results from the shortage of red blood cells (i.e. Haemoglobin) in the human body, which could lead to life-threatening health conditions. Conventionally, invasive methods are used for measuring the blood Haemoglobin Level. However, these have limitations, which include the infliction of needle pain on the patient during the collection of blood samples for tests, high risk of infections due to consistent prickling of the body tissue, and the overhead cost of repeating the test. Also, the invasive methods cannot offer real-time monitoring; hence making it inadequate for emergencies. To address these problems, we developed a bi-spectral Photoplethysmographic non-invasive device for real-time monitoring of blood haemoglobin level. In comparison with the traditional techniques, clinical applications were carried-out on 21 patients, to ascertain the performance of our device. Results show that our device performs accurately within an acceptable range of error.

***Keywords*-** *Haemoglobin, Anaemia, Near-infrared, Non-invasive, Photoplethysmographic, e-health*

I. INTRODUCTION

Anaemia has been classified as a major health challenge, especially in pregnant women because it exposes them to a higher risk of maternal mortality [1]. According to Alyson et al. [2], Anaemia could significantly increase the chance of neonatal mortality. Combating anaemia is, therefore, one of the tactics that should be employed in an attempt to reduce maternal and neonatal mortality. To effectively diagnose, treat and manage anaemia and other anaemia-related health problems, efficient diagnosis of the state of blood Haemoglobin (Hb) required. Also, the Hb level of a patient must be continually measured after a major surgery or during chemotherapy or radiotherapy (in the case of cancer patients), as low Hb levels could imply the shortage of blood or leukemia (a possible side effect of cancer treatment), which in turn can lead to other health complications. The Hb level is usually measured as part of the complete blood cell count. In general, it is a useful parameter for the diagnosis of various ailments.

According to Joseph *et al.* [3], traditional methods of determining haematological parameters such as oxygen saturation and Hb levels often involve the drawing of blood samples and the analyses of such samples in the haematology laboratory and are therefore classed of invasive diagnostic methods. Drawing of blood samples is a painful procedure that could also pose risks of sepsis and other blood infections. Haematological analyses of blood samples usually take lots of time and therefore, are unsuitable for emergency cases. Thus, repetitive and real-time determination of Hb level is almost impossible by these invasive methods. It is, therefore, pertinent that non-invasive methods of determining haematological parameters, which could also provide adequate means of record-keeping and data processing, be developed.

In the present paper, we propose a non-invasive transmittance photoplethysmographic (PPG) device for measuring blood Hb levels. The operation of this device is based on techniques in photo-spectroscopy.

II. LITERATURE REVIEW

The Hb is the predominant protein in red blood cells and is responsible for the transportation of mainly oxygen and carbon dioxide between lungs and tissues. Hb contains the heme group. The heme group allows the Hb molecule to bind oxygen because of the presence of the iron atom. The normal range of Hb concentration in blood is from 13.5 to 17 g/dl for males while it is 12 to 15 g/dl for females. Deviation from normal levels could be a disease or an indication of underlying conditions. Concentrations greater than the normal levels are termed polycythemia while concentrations lower than normal levels are termed anaemia [4]. To enhance the non-invasive measurement of haematological parameters of blood for the diagnosis of various human ailments, biomedical engineers are now exploiting the optical property of the Hb. Here, optical signatures such as the different transmission, absorption and reflection levels of light of different wavelengths by Hb products are considered. This novel approach has been applied in the design of various biomedical instruments that measure blood Hb levels in real-time. An important underlying principle of most of these devices is the Beer-Lambert law, which entails the theoretical basis for the photo-spectroscopic identification of molecular and crystalline structures [5].

The Beer-Lambert law is the linear relationship between absorbance and concentration of an absorbing species, and it

states that absorbance (A) is proportional to the concentration (c) of attenuating species in the material sample and the thickness (x) of the path through which the incident radiation travels as expressed in Eq.1.

$$A = \log_e\left(\frac{I_o}{I_t}\right) = \varepsilon C x \quad (1)$$

In Eq.1, I_o is the intensity of the incident radiation, I_t is the intensity of the emergent radiation while ε is the molar extinction coefficient. This equation relates the attenuation of light to the properties of the material medium through which the light travels. In simpler terms, we can say that the intensity of light varies exponentially with thickness. The Beer-Lambert law is also commonly applied to chemical analysis measurements and used in understanding attenuation in physical optics, for photons, neutrons or rarefied gases. In the present application, this law is applied to the determination of the blood Hb level.

The Hb is available in blood as various components such as Oxy-hemoglobin (HbO_2), Hemoglobin (Hb), Carboxy-hemoglobin (HbCO) and methemoglobin. Among these bio-molecules, HbO_2 and Hb are the main forms of Hb available in the blood. The other forms are available only in traces [4]. The Hb loosely amalgamates with oxygen in the lungs to form HbO_2. In this way, the ferrous iron in Hb is not oxidized but yet accommodates oxygen in a freely reversible reaction as shown in Eq2.

$$Hb + O_2 \rightleftarrows HbO_2 \quad (2)$$

HbO_2 is mainly available in arteries while Hb is mainly available in veins. In capillaries, both forms are equally available. For ascertaining the level of Hb in one's blood, the levels of HbO_2 and Hb in a particular volume of blood must be considered, as these forms are available together. The total availability of Hb in the blood is the combination of the availability of HbO_2 and Hb. For accurate determination of Hb level in the blood, it is necessary to measure the concentration of Hb as a mixture of HbO2 and Hb in a given volume of blood [4]. Evidence from photo-spectroscopic analysis reveals that HbO_2 and Hb have different absorption characteristics. The absorption, transmission, and scattering of light by HbO_2/Hb mixture depend on the wavelength of the light [6]. The most palpable differences between the absorption spectrum of HbO_2 and Hb are found between 550 to 800 nm. This phenomenon can be applied to develop oximetry based on the differential light absorption of oxygenated and deoxygenated blood. In the work Kumar and Ranganathan [6], this approach was applied in the development of a non-invasive PPG device for measuring the amount of light transmitted through the skin, tissues, and blood at the fingertip for estimation of Hb level in blood. However, the concentration of melanin in human skin varies. Melanin and haemoglobin mixture strongly absorb light in the ultraviolet (UV) and visible ranges, while they present low absorption in the Near-Infrared (NIR) range [7]. Almost complete absorption of light takes place up to a wavelength of 550 nm by HbO_2 and up to a wavelength of 700 nm by Hb. The light absorption is minimal at the wavelength of 603 nm for HbO_2. Hb and HbO_2 absorb an equal quantity of light at the wavelength of 805 nm; this wavelength is referred to as the isosbestic wavelength. These optical features are used in the estimation of Hb level using light sources [5].

Based on the above theory many researchers are currently developing non-invasive PPG technologies for measuring the concentration of HbO_2/Hb mixture in the blood to aid rapid diagnosis of different blood-related ailments. For example, Kumar and Ranganathan in [6], applied this principle in developing a PPG device which design consists of duo light sources of 740 nm and 805 nm respectively, and a photodetector. The emitted light is transmitted into the skin on the finger to emerge at the other side of the finger. The photodetector measures the intensity of light before and after it is transmitted through the finger. These data are fed to an embedded processor that uses a Beer-Lambert theory-based algorithm to calculate the blood Hb level of the patient. Similarly, Bhatia and Singh in [8], utilized the non-invasive technique based on the principles of pulse oximetry to develop a low-cost portable and user-friendly PPG device for monitoring Hb level in real-time. However, the PPG device that is developed in [6] and [8] respectively are susceptible to noise due to exposure to ambient light; this is because of their photo-spectroscopic probes (i.e. sensing parts) are poorly encapsulated external peripheral that extends out of the main instrumentation module.

In another related work, Butwick *et al.* [1] experimented to determine the accuracy of the Masimo Rainbow SET® Radical-7 Pulse CO-Oximeter for real-time measurement of Hb level in pregnant women undergoing Caesarean surgery. In their experiment, the Hb level of fifty patients undergoing Caesarean surgery was for monitoring for 48 hours after the surgery. Their result revealed that there is a need for the recalibration of their adopted device for improved accuracy and precision in an obstetric setting. Also, Timma *et al.* [9], performed a study that involved the development of a haemoglobin sensor system for online monitoring of Hb level in real-time. Their device consists of three LEDs, receivers, a microcontroller, and a wireless telemetric interface. Two of the three LEDs emit light in the spectral range of 600 to1000 nm (i.e. the therapeutic window region within which light absorption by the HbO_2/Hb mixture is dominant). The third LED emits an optical wavelength of 1300 nm that measures spectral absorption due to the blood plasma. Their measurements were correlated with a corresponding set of invasively measured values from Blood Gas Analysis (BGA). From this, they found a non-linear relationship between the blood Hb level measured by BGA and the calculated coefficients measured with their non-invasive sensor system.

In our development, we attempt to proffer technological solutions to the limitations of some of the aforementioned works. For instance, our design attempts to reduce the susceptibility of the spectroscopic probe to noise, as evident in [6] and [8], by ensuring that this optical probe is properly encapsulated from ambient light and located inside the main instrumentation module as a self-contained system. It is also evident that the analysis of [1] was based on a commercial PPG device manufactured by Masimo Corporation (Irvine Ca.) [10], and does not entail the development of a PPG device or an insight into the internal working of their adopted brand for

analysis so that a technical improvement may be proffered. In this light, we have developed our PPG device from scratch, starting from the underlying physics of photo-spectroscopy to the design of a software-based sensor system. Unlike the work of [9], we have restricted our device to probe within the therapeutic window region which only requires lights wavelengths in the red and NIR region of the electromagnetic spectrum to reduce non-linearity in measurement when compared with traditional methods. Therefore, our PPG device uses a bi-spectral probe in measuring the degree of light absorption by the HbO_2/Hb mixture alone. The detail on the account of this device is discussed in the remaining part of this paper.

III. MATERIALS AND METHODS

The working of our PPG device is based on the fact that there are significant absorption and transmission difference for light spectra in the red and NIR region between of HbO_2 and Hb in a given volume of blood. Here, the Beer-Lambert Law and techniques in absorption spectroscopy of light are applied to devising a mean by which the concentration of HbO_2/Hb mixture in blood could be measured in real-time. Using the relevant hardware components our PPG device is implemented as a programmed bi-spectral probing instrument.

After obtaining written institutional permission, this device was tested on 21 patients whose Hb levels have been measured invasively by traditional means. Data from both the invasive and non-invasive measurements were collected and statistically correlated on MATLAB to determine the accuracy and precision of the developed PPG device. The technical aspect of our work is discussed as follows.

A. System theory and modelling

The working of our photo-spectroscopic probe is modelled in Fig.1. This diagram is used in the derivation of mathematical equations and theories that describes this function.

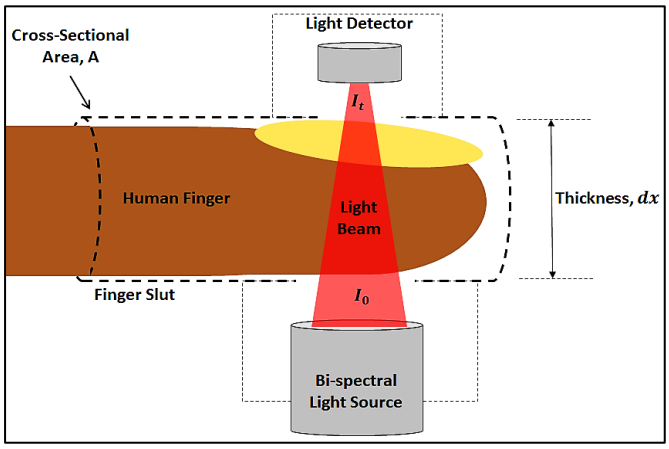

Figure 1. Diagrammatic model of the encapsulated photo-spectroscope in the PPG device

Here, a combined spectrum of consisting infrared and red incident light is transmitted through the finger with an average cross-sectional area, A and thickness dx. The intensity of this light spectrum is I_x and the number of irradiated HbO_2/Hb mixture is $CAdx$, where C is the concentration of blood HbO_2/Hb mixture. The total effective area of the HbO_2/Hb molecules present is $\sigma CAdx$, where σ denotes the effective cross-sectional area of each HbO_2 or Hb molecule. The probability that light is absorbed and transmitted across dx:

$$-\frac{dI_x}{I_x} = \frac{\sigma CA}{A}dx \tag{3}$$

In Eq.3, dI_x denotes the change in intensity across dx. By integrating both sides as follows:

$$-\int_{I_0}^{I_t}\frac{1}{I_x}dI_x = \int_0^x \sigma C dx$$

$$ln(I_0) - ln(I_t) = \sigma Cx$$

$$ln\left(\frac{I_0}{I_t}\right) = \sigma Cx \tag{4}$$

Where $I_0 > I_t$; hence by taking the exponent of both sides of Eq.4, as in:

$$e^{ln\left(\frac{I_0}{I_t}\right)} = e^{\sigma Cx}$$

We have:

$$\frac{I_0}{I_t} = e^{\sigma Cx}$$

So that:

$$I_t = \frac{I_0}{e^{\sigma Cx}} \tag{5}$$

For $\mu = \sigma C$, where μ is called the linear attenuation coefficient and is measured in c/m; then:

$$I_t = \frac{I_0}{e^{\mu x}} \tag{6}$$

From Eq.6, it is deduced that the intensity of light passing through the blood decreases exponentially with thickness. As μ is a function of wavelength so also is the Beer-Lambert Law. Hence;

$$I_t(\lambda) = \frac{I_0(\lambda)}{e^{\mu(\lambda)x}} \tag{7}$$

Based on Eq.4; we have:

$$A = log_e\left(\frac{I_0(\lambda)}{I_t(\lambda)}\right) \tag{8}$$

By substituting $\frac{I_0(\lambda)}{e^{\mu(\lambda)x}}$ in Eq.7 for $I_t(\lambda)$ in Eq.8, we have:

$$A = log_e\left(\frac{I_0(\lambda)}{I_0(\lambda)e^{-\mu(\lambda)x}}\right)$$

$$A = log_e\left(e^{\mu(\lambda)x}\right)$$

By the law of logarithm;

$$A = \mu(\lambda)x log_e(e) = 1.0\mu(\lambda)x \tag{9}$$

Hence $\varepsilon = \sigma$;

$$\therefore A = log_e\left(\frac{I_0(\lambda)}{I_t(\lambda)}\right) = \varepsilon C x \quad (10)$$

The derivation of Eq.10 is the proof of the Beer-Lambert formula in Eq.1. Being that our work is concerned with the estimation of the concentration of blood HbO_2/Hb mixture concentration; then:

$$C = \frac{A}{\varepsilon x} = \frac{log_e\left(\frac{I_0(\lambda)}{I_t(\lambda)}\right)}{\varepsilon x} \quad (11)$$

Our estimated value of $\varepsilon x = 0.013$; therefore:

$$C = \frac{log(I_0) - log(I_t)}{0.013} \quad (12)$$

In the design of our PPG device, I_0 and I_t are the measured variables, ε and x are constants while C is the unknown variable.

B. System design and implementation

An Arduino based hardware-software solution was developed to implement the above modelling of our PPG device. This includes the built-in bi-spectral photo-spectroscopic sensor Fig.2. Here a mixed spectrum source consisting of Red light and infrared of 740 nm and 805 nm respectively wavelengths is produced using a red LED and an IR-LED, respectively. During setup (i.e. recalibration routine) which only occurs once each the system is switched on, before the insertion of a finger into the PPG device, the initial value of light intensity is measured and stored as $I_0(\lambda)$ in the memory. Five seconds, later after which the finger may be inserted into the PPG device, the latter value of light intensity is continually measured and stored as $I_t(\lambda)$ in the memory. This in effect, also compensates for the various environmental and ambient influences on the accuracy of our PPG device.

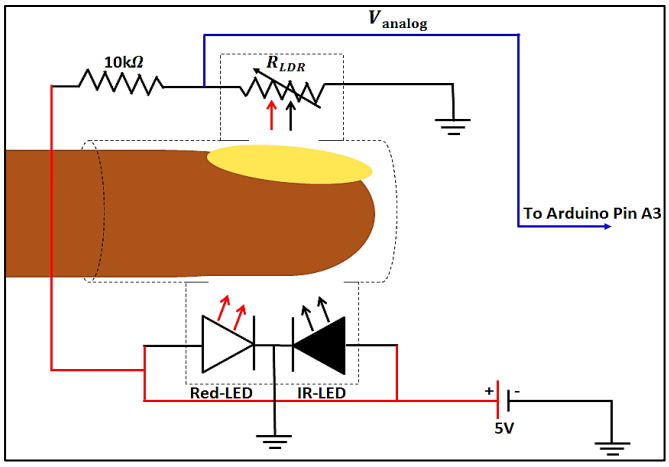

Figure 2. Design of the bi-spectral photo-spectroscopic sensor

A Light Dependent Resistor (LDR) is used for implementing the photo-sensing circuit. Here the LDR is connected with a 10Ω resistor to form a 5V powered potential divider as shown in Fig.2. The analog output voltage, V_{analog} of this circuit is expressed as:

$$V_{\text{analog}} = 5 \times \frac{R_{LDR}}{10 + R_{LDR}} \quad (13)$$

The value of V_{analog} is applied to the analog pin-A3 of the Arduino microcontroller. The value of R_{LDR} varies directly as light intensity so that V_{analog} is inversely proportional to light intensity as determined by Eq.13. This implies that the value of V_{analog} is higher at lower light intensity (i.e. when the absorbance, A due to high Hb-level is large) and vice versa. The value of V_{analog} is automatically scaled in the microcontroller to vary between 0-1023 at an Analog-to-Digital Conversion (ADC) Resolution of 0.0048828125 to generate an analog LDR_{value}. This is mathematically related to V_{analog} by Eq.14.

$$V_{\text{analog}} = LDR_{value} \times 0.0048828125 \quad (14)$$

The value of light intensity is generally expressed in Eq.15.

$$I = \left(\frac{250}{V_{analog}}\right) - 50 \quad (15)$$

Hence the value of the light intensities: I_0 and I_t are expressed in Eq.16 and Eq.17 respectively.

$$I_0 = \left(\frac{250}{V_0}\right) - 50 \quad (16)$$

$$I_t = \left(\frac{250}{V_t}\right) - 50 \quad (17)$$

As mentioned earlier, the value of I_0 is calculated and stored in the memory as a constant during setup while that of I_t is calculated continuously and stored as a variable after every system recalibration. These values are entered into Eq.12 for the computation of the concentration of blood HbO_2/Hb mixture. Therefore, the electrical form of Eq.12 is expressed as Eq.18.

$$C = \frac{log\left(\left(\frac{250}{V_0}\right) - 50\right) - log\left(\left(\frac{250}{V_t}\right) - 50\right)}{0.013} \quad (18)$$

The structure and circuitry design of the implementing hardware is shown in Fig.3. This comprises three major parts: the photo-spectroscopic sensor, the display unit and the Arduino microcontroller (running the system software). The formula in Eq.I8 is implemented as software codes written in the Arduino-C programming language. This program is embedded in the Atmel Atmega328 Microcontroller at the heart of the Arduino board. The physical implementation of this system is depicted in Fig.4. This system was extensively tested for accuracy, precision, and consistency, and it is performing as expected.

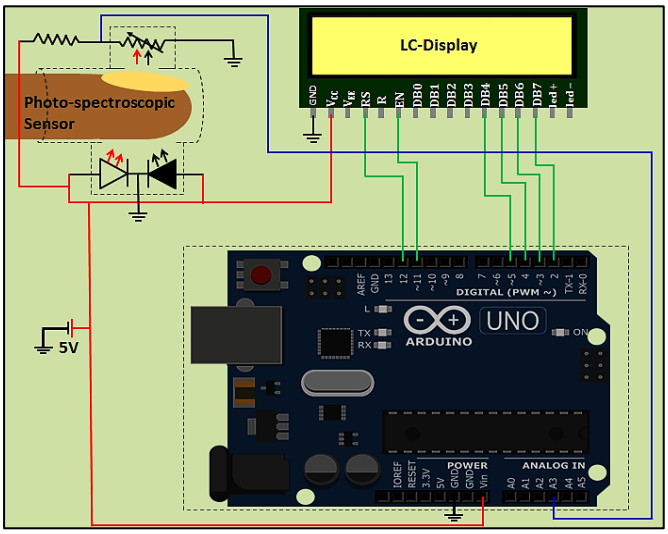

Figure 3. Hardware structure and circuit design

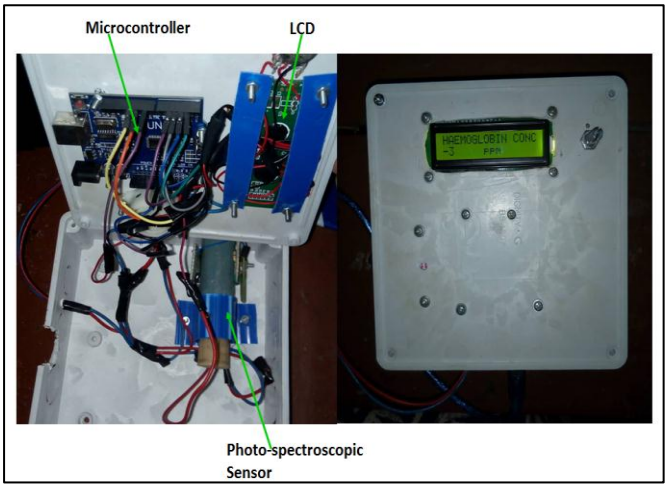

Figure 4. The complete PPG Sensing device

IV. RESULTS AND DISCUSSION

A. *Results and discussion*

To determine the accuracy and real-world applicability of the PPG device, it was deployed to undergo clinical trial; where it was used to measure the blood HbO_2/Hb level of 21 patients in parallel with the conventional spun hematocrit method – an invasive technique. Data from these tests are presented in Table 1. Shown in Fig.5 is the graphical analysis of these data. An error of 0.3493 g/dl and an accuracy of 65.07% was obtained. This shows a quasi-linear relationship between the measurements from our non-invasive device and the invasive technique. Our device was also used to determine whether patients are anaemic or not. Out of 15 anaemic subjects, the device was able to correctly identified 14 of them to be anaemic patients with an accuracy of 93.3%. This experimental procedure was also repeated in two more hospitals, to ensure the consistency in measurement by our device with changing ambience and environmental factors. Thus, our device has performed within an acceptable range of error.

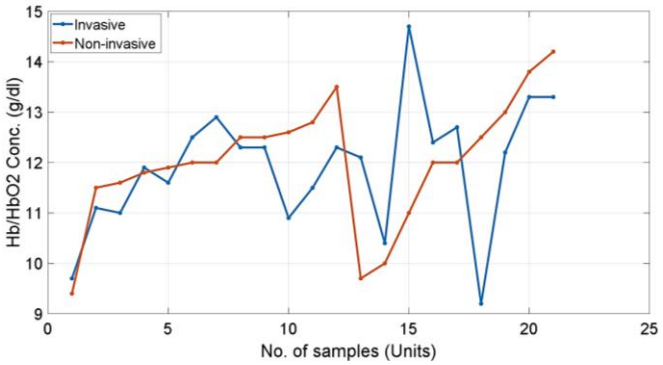

Figure 5. Plot of invasive versus non-invasive measurements

TABLE I. INVASIVE AND NON-INVASIVE MEASUREMENTS FROM THE CLINICAL TRIAL OF THE PPG DEVICE

S/N	Invasive (g/dl)	Non-invasive (g/dl)	Error (g/dl)	Percentage error (%)	Percentage accuracy (%)	Sex
1	9.7	9.4	0.3	3.09	96.91	F
2	11.1	11.5	0.4	3.60	96.40	F
3	11	11.6	0.6	5.45	94.55	F
4	11.9	11.8	0.1	0.84	99.16	F
5	11.6	11.9	0.3	2.59	97.41	F
6	12.5	12	0.5	4.00	96.00	F
7	12.9	12	0.9	6.98	93.02	F
8	12.3	12.5	0.2	1.63	98.37	F
9	12.3	12.5	0.2	1.63	98.37	F
10	10.9	12.6	1.7	15.60	84.40	F
11	11.5	12.8	1.3	11.30	88.70	F
12	12.3	13.5	1.2	9.76	90.24	F
13	12.1	9.7	2.4	19.83	80.17	M
14	10.4	10	0.4	3.85	96.15	M
15	14.7	11	3.7	25.17	74.83	M
16	12.4	12	0.4	3.23	96.77	M
17	12.7	12	0.7	5.51	94.49	M
18	9.2	12.5	3.3	35.87	64.13	M
19	12.2	13	0.8	6.56	93.44	M
20	13.3	13.8	0.5	3.76	96.24	M
21	13.3	14.2	0.9	6.77	93.23	M

V. CONCLUSION

We have developed a device for measuring blood haemoglobin level, based on the theory that there is significant absorption and transmission difference for light in the red and NIR region of the electromagnetic spectra by HbO2/Hb mixture in a given volume of blood. This device is capable of

non-invasive measurement of blood haemoglobin level. Thus, we offer an effective technological means for real-time diagnosis of anaemia/anaemia-related health emergencies.

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How to Cite this Article:

Olakanmi, O., Benyeogor, M., Alabi, H. & Kumar, S. (2020) Bi-spectral Photoplethysmographic Non-invasive Device for Real-Time Monitoring of Blood Haemoglobin Level. International Journal of Science and Engineering Investigations (IJSEI), 9(97), 17-22. http://www.ijsei.com/papers/ijsei-99720-03.pdf