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Non-Invasive Optical Biosensing: A Hybrid Nirs–Ppg Approach For Blood Parameter Estimation

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Abstract: Haemoglobin, oxygen, platelets, red and white blood cells, and plasma are some important parameters of blood. As haemoglobin carries oxygen from the lungs to the body and returns carbon dioxide to the lungs, haemoglobin and oxygen saturation are very important. Their levels are important for the diagnosis of number of diseases. Haemoglobin concentration is currently determined via invasive blood sample, which is unsuitable for real-time patient monitoring during crises due to its inconvenience and analysis delays. In this study, we have used Photoplethysmography (PPG) and Near-infrared spectroscopy (NIRS) to measure blood haemoglobin and Oxygen saturation level non-invasively. Here we have developed multi wavelength photometric system containing LED's of different wavelength (550, 660, 810, 940 nm) and photo detector. Signal from the sensor system is given to the microcontroller for the further processing and displays using LCD display. In this study we take 25 volunteers of different age group that are suggested for Complete blood count or Haemoglobin test by the doctor or medical practitioner. Proposed non-invasive haemoglobin measurement have significant positive linear association with a correlation coefficient of r is 0.9318 (ρ <0.0001) with mean bias of 0.5280 g/dL and limits of agreement (95%) ranging from -0.6391 to +1.6951 g/dL as compared to invasive standard laboratory method. In case of Oxygen saturation correlation values of r is 0.6123 (ρ <0.0001) with mean bias of 0.3200% with 95% LoA ranging from -1.440% to +2.0840%.

Index Terms - Haemoglobin, oxygen saturation, non-invasive, Near-infrared spectroscopy, photophethysmography

I. INTRODUCTION

Haemoglobin, oxygen, WBC, RBC, platelets, and plasma are among the various components that make up blood [1]. The 4 protein molecules that make up haemoglobin are known as globulin chains, and globulin chain has a crucial centre structure known as the haem molecule [2]. A metal protein called haemoglobin is found in blood plasma's red blood cells [3]. Haemoglobin, the main constituents of human blood which carries oxygen from the lungs to other parts of the body and carbon dioxide from other parts of the body back to the lungs. Based on a patient's health situation, haemoglobin levels help medical practitioner to diagnose various diseases. The measurement of haemoglobin (Hb) concentration, which is usually performed as part of a complete blood count (CBC), is one of the most widely used blood tests. A lower than normal haemoglobin level can be caused by various types of anemia, bleeding, erythropoietin deficiency (from kidney disease), lead poisoning, malnourishment, iron, folate, vitamin B12, and vitamin B6 nutritional deficiencies, over hydration, and red blood cell destruction due to transfusion reaction. Higher haemoglobin levels can be caused by congenital heart disease, corpulmonale, pulmonary fibrosis, polycythemia vera, and increased red blood cells from excess erythropoietin. Iron deficiency anemia (IDA) is the most common kind of anemia among Asians (UNICEF 2004) [4]. The amount of haemoglobin in the blood is determined via a haemoglobin test. This information can be used to diagnose and track polycythemia vera (high hemoglobin level) and anemia (low hemoglobin level) [5].

Currently, invasive methods that include taking the patient's blood and analyzing it are used to measure haemoglobin and oxygen saturation concentration. Apart from the inconvenience of drawing blood, this method's disadvantage is the delay between blood collection and analysis, which makes it unable to monitor patients in real time during emergencies and accidental situations [6][7]. The amount of haemoglobin is measured when drawn blood sample is subjected to chemical analysis. This process requires an experience paramedical staff to take a blood sample, a lab technician to perform the chemical analysis in conjunction with a pathologist to interpret and verified results [3][8]. One of the invasive procedures is the complete blood count (CBC), which looks at the blood component in the tube to determine the amount of haemoglobin in the blood. Biosensors are one method of measuring haemoglobin levels [9]. Haemoglobin levels have been assessed in many regions using the Sahli method, the filter paper test, or the pallor test [10]. Other methods for figuring out how much haemoglobin is in a person's blood include the Lovibond type comparator method, the centrifuge method, and the copper sulfate method. Grey wedge photometer, cyanmethemoglobin, and hemocue methods. In these procedures, a patient's blood is drawn and their haemoglobin levels are assessed using a variety of instruments and reagents [10]. Cyanmethemoglobin, which has a maximum absorption at 540 nm wavelength, is produced by chemically altering haemoglobin in the hemoglobinocyanide process. The haemoglobin concentration is the result of the absorption process [2].

Non-invasive measurement method is better than these invasive methods. Additionally, it facilitates real-time data monitoring, allowing for prompt clinical responses to the recorded data. Since it was found that near-infrared light could insert into biological tissues to a considerable depth, near-infrared spectroscopy and photoplethysmography has evolved into a non-invasive method for biomedical sensing and clinical diagnostics [2][6][7][11][12]. Thermography, Ultrasound, Magnetic resonance imaging (MRI), and X-rays are examples of non-invasive medical diagnostic techniques that have greatly reduced patient risk and enhanced our comprehension of how the body works. The benefits of non-invasive procedures include the absence of scars or incisions, a shorter healing period, a lower risk of infection, bleeding, or the need for blood transfusions, and a quicker return to normal work [13]. Numerous non-invasive techniques have been used for the estimation of blood parameters as a pathogenic advancement, including imaging, spectro-photometry, opto-acoustic spectroscopy, transmission spectroscopy, and reflection spectroscopy [14][15].

II. MATERIALS AND METHODS

Proposed system uses Photoplethysmography (PPG) and Near-infrared spectroscopy (NIRS) to measure the amount of haemoglobin and oxygen saturation in the blood sample. Multiple LEDs, an optical detector, a signal conditioning unit, a microcontroller, and a display unit are additional components of the system. Following figure 1 show the block diagram of proposed system.

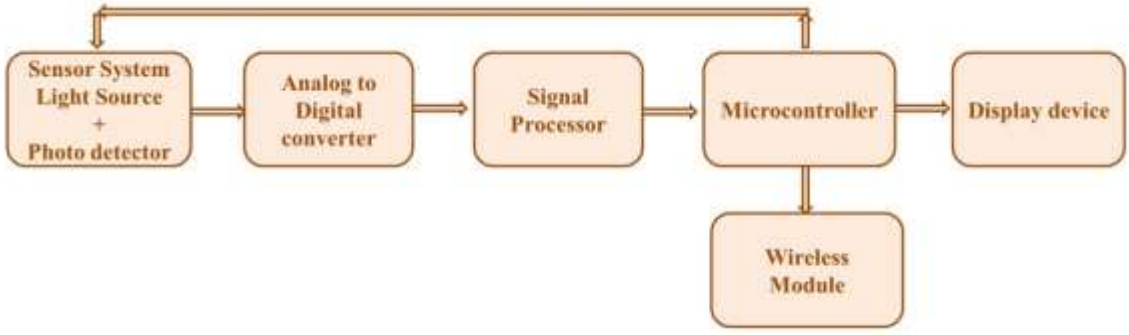

Figure 1 Block diagram of proposed system

The basic principle of haemoglobin and oxygen measurement is that light is absorbed and transmitted differentially in the visible and near-infrared areas by blood plasma, oxygenated haemoglobin, and deoxygenated haemoglobin. Absorption and dispersion are caused by haemoglobin in blood and tissue in the finger, respectively. To measure blood haemoglobin and blood oxygen saturation non-invasively, we have studied LEDs such as Kingbright APT2012SGC/APT2012CGCK (550 nm), Kingbright AA3021LSYSK/J3-TR (590 nm), Kingbright APTR3216SRCPRV (640 nm), Lumex Opto/Components Inc. SML-LX15SRC-TR (660 nm), Vishay Semiconductor VSMY98145DS (810 nm), Kingbright APT2012F3C (940 nm) to transmit light with proper intensity and wavelength.

The optical detector picks up light that has been transmitted through the fingertip. Here, optical detectors like PIN photodiode SFH2201, VEMD55A0C, TEFD4300, RDB-C152SM, OPT101 Monolithic

Photodiode, and Trans-impedance Amplifier were studied. Here, light intensity is detected based on haemoglobin and oxygen saturation level using the photoplethysmography and near-infrared spectroscopy approach. The signal conditioning system receives the detector's output and performs all required modifications, including signal attenuation, signal amplification, signal filtering, etc. The microcontroller unit receives the signal conditioning system's output and processes it before sending it to the display unit. The value of haemoglobin (g/dL) and oxygen saturation (%) measurements will be shown on the display device.

Proposed system uses fingertip sensor that consists of finger clip containing four LEDs of different wavelength such as 550, 660, 810 and 940 nm with photo detector encapsulate in it. Index finger is placed in the sensor system and the output signal is given to the microcontroller for the signal conditioning and further processing. We have used Arduino uno board having ATmega328P microcontroller with six analog input ports with a resolution of 10 bit ADC and 32 KB of flash memory. Processed signal is given to the 16x2 LCD display system which displays the value of blood haemoglobin and blood oxygen saturation. Further ESP32 microcontroller board also assisted with the system for the Wifi and Bluetooth features for the IoT applications and long distance data transmission. Following figure 2 shows interfacing of sensor system with Arduino Uno and LCD display.

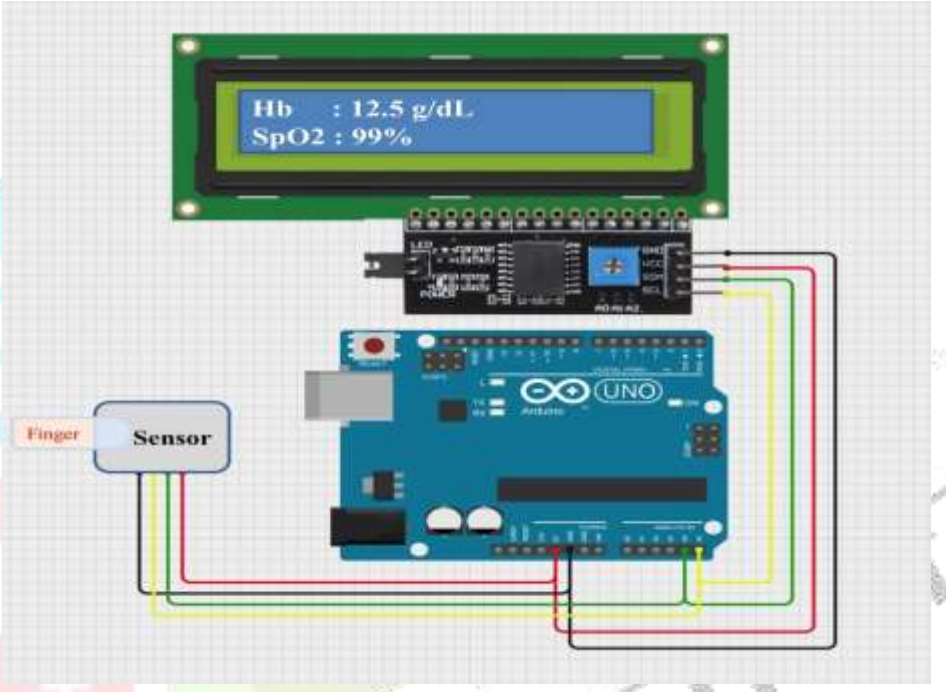

Figure 2: Interfacing of sensor system with Arduino uno and LCD display

In this study, Oxygen saturation is the proportion of haemoglobin that is connected to oxygen, which has an immediate impact on the optical properties. Haemoglobin's optical coefficient defines how it absorbs and scatters light. The main optical coefficients for haemoglobin are the anisotropy factor (g), absorption coefficient (μa), and scattering coefficient (μs). These coefficients depend on the oxygenation state (oxygen saturation) and are very wavelength-dependent.

The modified Beer-Lambert Law (MBLL) and optical sensors are used to assess haemoglobin content noninvasively. For photoplethysmography (PPG) and near-infrared spectroscopy (NIRS) in biological tissue, the conventional Beer-Lambert Law is adjusted to account for scattering, path length variation, and baseline shifts.

The MBLL, which is supplied by, connects changes in tissue absorption to changes in measured optical intensity.

$$A = \log (I0/ I) = \varepsilon cl + G \quad (1)$$

Where:
A is absorbance,
ε is the molar extinction coefficient of haemoglobin,
c is the haemoglobin concentration,
l is the differential path length factor (accounts for scattering),
G is a geometry-dependent baseline term.

In order to assess haemoglobin noninvasively, light is passed through the fingertip at four different wavelengths (such as 550, 660, 810, and 940 nm) and its intensities are measured. The MBLL is used to extract variations in haemoglobin-related absorbance by comparing signals at the chosen wavelengths.
The AC component (produced from pulsatile arterial blood) is analyzed after being extracted from the raw signal. MBLL can be used to calculate relative changes in concentration. For absolute values, calibration is done using reference methods like the laboratory method or cyanmethaemoglobin. MBLL can be used to calculate relative changes in concentration. For absolute values, calibration is done using reference methods like the laboratory method or cyanmethaemoglobin.

$$\Delta A\lambda = \text{Ɛ}HbO_2, \lambda\Delta\,[HbO_2]DPF\lambda + \text{Ɛ}Hb, \lambda\Delta\,[HbO_2]DPF\lambda + \text{Ɛ}COHb, \lambda\Delta\,[COHb]DPF\lambda + \text{Ɛ}MetHb, \lambda\Delta[MetHb]DPF\lambda \quad (2)$$

Where,
ΔAλ – Absorbance at differential wavelengths
εHbO2, λ – extinction coefficient of oxygenated haemoglobin at particular wavelength
εHb, λ – extinction coefficient of deoxygenated haemoglobin at particular wavelength
εCoHb, λ – extinction coefficient of carboxyhaemoglobin at particular wavelength
εMetHb, λ – extinction coefficient of methaemoglobin at particular wavelength
DPFλ is the differential path length factor at wavelength λ.

The ratio of oxyhaemoglobin concentration to total haemoglobin concentration is known as oxygen saturation (SpO2).

$$SpO2 = \frac{(HbO2)}{([HbO2] + [Hb])} \quad (3)$$

Where,
SpO_2 is blood Oxygen saturation,
HbO_2 is Oxygenated haemoglobin,
Hb is deoxygenated haemoglobin

III. RESULT AND DISCUSSION

Here we take 25 volunteers of different age group between 20 to 70 years with different sex. Volunteers are suggested for the complete blood count (CBC) or Haemoglobin test by the doctor or medical practitioner are only taken as the part of this study.

Table 1: Following table shows the result of non-invasive haemoglobin measurement using proposed system in comparison with invasive (laboratory) test.

Volunteer	Invasive Haemoglobin (in g/dL)	Non-invasive Haemoglobin (in g/dL)	Error (%)
1.	13.5	14.4	-6.67
2.	14.3	15.2	-6.29
3.	13.8	12.9	6.52
4.	14.9	15.5	-4.03
5.	14.4	15.3	-6.25
6.	12.3	13.5	-9.76
7.	11.7	12.5	-6.84
8.	16.5	15.9	3.64
9.	11.8	12.4	-5.08
10.	15.5	15.1	2.58
11.	16.2	17	-4.94
12.	13.5	14.6	-8.15
13.	13.7	14.5	-5.84
14.	13.8	14.4	-4.35
15.	11.9	12.8	-7.56
16.	13	14.1	-8.46
17.	12.2	13.1	-7.38
18.	15.6	16.2	-3.85
19.	14.9	15.6	-4.70

20.	11.5	12.3	-6.96
21.	14.1	13.6	3.55
22.	11.5	11	4.35
23.	13.8	14.3	-3.62
24.	12.9	13.5	-4.65
25.	9.9	10.7	-8.08

Haemoglobin readings comparing invasive (reference) and non-invasive techniques are shown in Table 1 along with computed errors shown as percentages. There is some variation in errors, ranging from -9.76% to +6.52%, but overall there is close agreement across the 25 matched readings in the sample. Strong association and acceptable bias for clinical validation are confirmed by statistical analysis. Graphical representation of given data is as shown in figure 3.

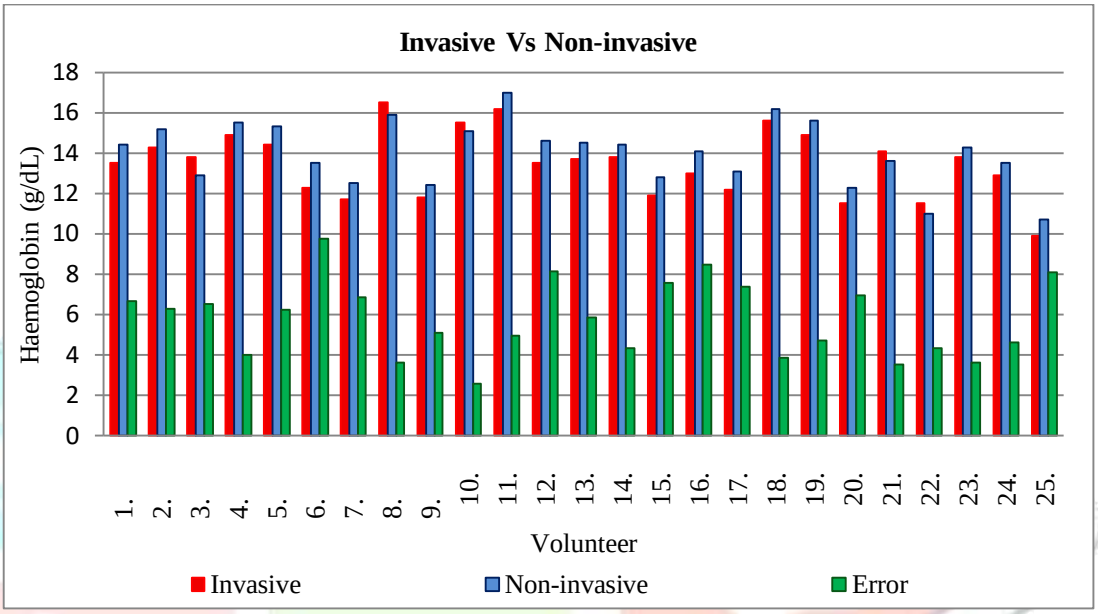

Figure 3 Comparison between invasive and non-invasive reading with error value of haemoglobin

The average invasive Haemoglobin is 13.35 g/dL, but the average non-invasive Hb is 13.88 g/dL, resulting in a mean error of -4.69%. The standard deviation (SD) of errors is 5.25%, and 72% of readings had absolute errors of less than 7%. This indicates high precision in the majority of situations, but outliers like -9.76% point to motion artifacts or the need for calibration. A substantial positive linear link between invasive and non-invasive hemoglobin readings is shown by the Pearson correlation coefficient (r), which is 0.9318 with $p < 0.0001$. The non-invasive approach's dependability for monitoring trends in clinical settings is supported by this high r value.

Bland-Altman shows a standard deviation of 0.5955 g/dL and a mean bias of 0.5280 g/dL (non-invasive overestimates slightly). 95% of differences lie within ±1.70 g/dL, which is clinically acceptable for hemoglobin monitoring according to ISO 81060-2 recommendations. However, calibration could further tighten limits. The 95% limits of agreement cover -0.6391 to 1.6951 g/dL.

Table 2: Following table shows the result of non-invasive oxygen saturation measurement using proposed system in comparison with invasive (laboratory) test.

Sr. No.	Invasive oxygen saturation (in %)	Non-invasive oxygen saturation (in %)	Error (%)
1.	99	100	-1.01
2.	98	97	1.02
3.	98	99	-1.02
4.	98	99	-1.02
5.	97	98	-1.03
6.	98	98	0.00
7.	99	100	-1.01
8.	99	98	1.01
9.	98	97	1.02
10.	98	98	0.00
11.	99	98	1.01
12.	98	99	-1.02
13.	98	97	1.02
14.	97	98	-1.03
15.	99	100	-1.01
16.	98	99	-1.02
17.	99	100	-1.01
18.	97	98	-1.03
19.	98	99	-1.02
20.	98	98	0.00
21.	97	98	-1.03
22.	97	98	-1.03
23.	97	96	1.03
24.	98	99	-1.02
25.	97	96	1.03

The non-invasive system closely matches invasive SpO_2, with modest percentage errors and a moderate linear correlation, according to the oxygen saturation values in Table 2. The agreement is clinically acceptable. Paired invasive and non-invasive oxygen saturation readings, which are typically between 96 and 100%, indicating a population that is normoxic and has a restricted physiological distribution. Several measurements indicate 0% error, while the equivalent error column (invasive − non-invasive,%) spans about from −1.03% to +1.03%. Graphical representation of non-invasive value for oxygen saturation in comparison with invasive value with error (%) is as shown in figure 4.

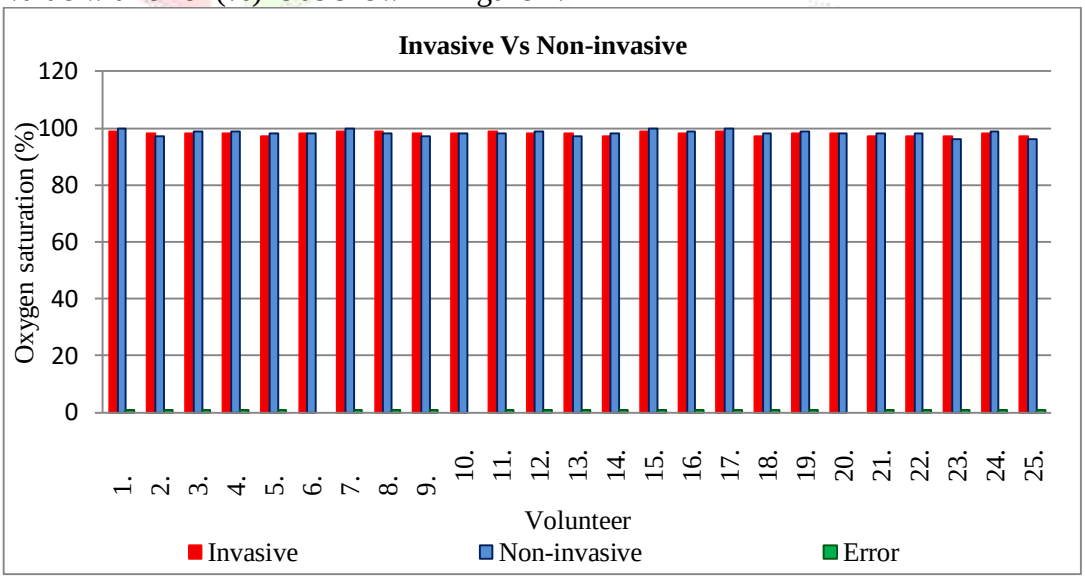

Figure 4: Comparison between invasive and non-invasive value with error (%) of oxygen saturation

For oxygen saturation, Pearson correlation coefficient is given as r = 0.6123 with p = 0.0011. Invasive and non-invasive SpO_2 tend to rise and fall simultaneously, although there is a discernible scatter around the regression line, according to this r value, which indicates a moderately positive linear association. Bland-Altman analysis yields a mean bias of 0.3200% and a standard deviation of 0.9000%. 95% of non-invasive measurements lie within around ±2% of the invasive reference, according to the 95% limits of agreement, which range from −1.4440% to 2.0840%.

IV. CONCLUSION

Most clinical and validation investigations indicate that contemporary noninvasive haemoglobin and oxygen saturation devices are appealing for screening, trend monitoring, and application in resource-constrained situations since they are rapid, easy to use, and painless. When exact haemoglobin and Oxygen saturation levels are required, they are still not a complete substitute for laboratory hematology analyzers. Despite the following significant limitations, confirmatory blood tests are recommended for final diagnosis and treatment decisions: wide limits of agreement, susceptibility to motion, effects of perfusion and skin pigmentation, and lower accuracy at very low or very high hemoglobin levels. High Pearson correlation and appropriate Bland-Altman agreement limits indicate the non-invasive hemoglobin measurement system's great clinical validity when compared to invasive reference standards.

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