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The Blood Hemoglobin Sensor Based On $(Ba,Sr)TiO_3$ Films: The Performance Evaluation and Data Analysis

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ABSTRACT

The information of blood hemoglobin level is very important for human health. Normal hemoglobin levels for men are in the range of 14-18.5 g/dL, and for women in the range of 12-16.5 g/dL. A hemoglobin level below the normal range indicates an anemia problem which could be fatal for human's health. To detect the blood hemoglobin level, optical sensors must respond to the light within the range of 250-900 nm wavelength. In this paper we report the performance of Barium Titanate and Strontium Titanate $(Ba,Sr)TiO_3$ films which are capable of detecting the blood hemoglobin level in the spectrum range of 380-780 nm. The performance of $(Ba,Sr)TiO_3$ then compared with FDS100 standard sensor. The LED in this study, as a light source, has a wavelength of 545 nm and 570 nm. The $(Ba,Sr)TiO_3$ film, LED and artificial blood samples were placed in a container and integrated with other electronic devices. The hemoglobin $(Ba,Sr)TiO_3$ measurement data obtained was then processed using a machine learning method (linear regresion algorithm) and compared with the actual hemoglobin value from artificial blood. The evaluation of data measurement using linear regresion showed that $BaTiO_3$ has more accuracy (84.83%) as compared to $SrTiO_3$ (82.95%). This result is in accordance with the result from the optical and electrical properties, where a small band gap energy and a small resistance produce better optical and electrical properties resulting in a higher level of accuracy.

Keywords: $BaTiO_3$, haemoglobin, linear regresion, machine learning, sensors, $SrTiO_3$

1. INTRODUCTION

Determination of hemoglobin level plays an important role in evaluating various diseases, such as anemia [1] , polycythemia vera [2], and hematuria [3]. The fast and accurate detection of hemoglobin level to determine the health conditions of the patient is needed for critical conditions, such as before surgery, or before blood transfusion [4], [5]. According to [6], the blood hemoglobin level can be detected at 250 – 900 nm electromagnetic's wavelength using an appropriate sensor and device.

Sensor which is applicable in that wavelength includes FD11A, FDS025, FDS015, and the most widely used is FDS100. In this study, the FDS100 sensor was used as a control (or comparator) for our synthesized sensors. Other materials that have potential as optical detector in that range are Barium Titanate and Strontium Titanate (in this case abbreviated to $(Ba,Sr)TiO_3$) which can detect light at wavelength of 380-780 nm. The $(Ba,Sr)TiO_3$ sensor can be modified by changing its composition which is very beneficial. The $BaTiO_3$, which is a ferroelectric material, has a polarization phenomenon associated with an increase in the light sensitivity of the device [7]. Several studies have also shown that $BaTiO_3$ can be applied to optical devices such as solar cells, light sensor, photocatalytic sensors, and photodetectors [8]–[11]. $SrTiO_3$ has a high storage capacity, good chemical and thermal stability, and good mechanical strength. In addition, it has paraelectric properties which can turn into ferroelectric at high temperatures [12]. The optical properties of $(Ba,Sr)TiO_3$ which has a small energy bandgap and has good sensitivity in the visible region will be useful for detecting hemoglobin level.

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In this research, the (Ba,Sr)TiO_3 film were synthesized using chemical solution deposition (CSD) method and applied to AuIDE (Gold Interdigital Electrode) platform to build the optical sensor for hemoglobin measurement. The measurement system include the sensor, signal amplification unit, analog to digital converter, microcontroler, and specific LEDs as the light sources. The LED that was used as a light source must also have the appropriate wavelength to detect blood hemoglobin level as suggested by [13]. Thus, several criteria for determining the wavelength in measuring blood hemoglobin levels include the location of the absorbance peak of C=O functional group, high Pearson correlation, and the wavelengths above 500 nm to avoiding melanin's absorption which could interfere with the blood hemoglobin level detection process. According to Pearson correlation value, the wavelength that is highly correlated with hemoglobin is above 500 nm. Melanin in human skin has a high absorption area in the UV to visible light region, with a peak at 335 nm, and will decrease as the wavelength increases[14]. Based on those criteria, the selected wavelengths are 545 and 570 nm.

The use of machine learning in determining the hemoglobin level have been done by many researchers worldwide, such as [15]–[18]. The use of machine learning method allows the detection of blood hemoglobin level to become more accurate as more data is processed and analysed. In this paper, the blood hemoglobin's level measurement from (Ba,Sr)TiO_3 sensor were compared to the results from FDS100 sensor. The results then analysed using linear regresion algorithm to evaluate the performance and the potential of the (Ba,Sr)TiO_3 film in detecting the hemoglobin's level.

2. MATERIAL AND METHODS

Hemoglobin has the C=O functional group as one of its structural constituents as shown in Figure 1. This research begins by making (Ba,Sr)TiO_3 using the Chemical Solution Deposition method. This research begins by making BST using the CSD method. The solution was prepared by mixing the ingredients (Barium titanate [$BaTiO_3$] and Strontium titanate [$SrTiO_3$]) with 2-methoxyethanol solvent. All ingredients were mixed and stirred using a magnetic stirrer and magnetic bar to obtain a homogeneous solution with a rotational speed of 8000 rpm within 60 minutes [13].

Then the film growth was carried out by dripping the stirred (Ba,Sr)TiO_3 solution using a magnetic stirrer on the surface of the active part of the AuIDE substrate as shown in Figure 2. The next process is the annealing process using a furnace with the Muffle Furnace Fila brand which is set at a speed of 1.67 ^{0}C/minute until it reaches a temperature of 250 ^{0}C, then the temperature is held for 1 hour, after that the temperature is decreased until it reaches room temperature. Three samples were made for each $BaTiO_3$ and $SrTiO_3$ for further hemoglobin measurements.

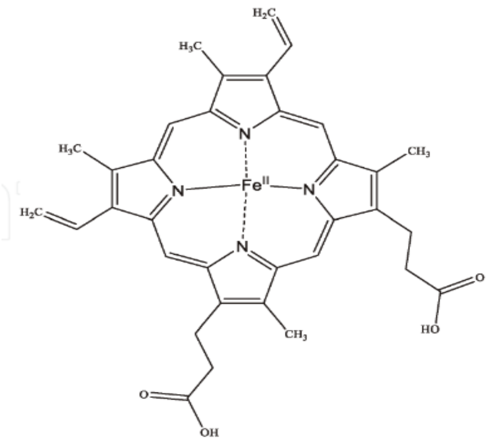
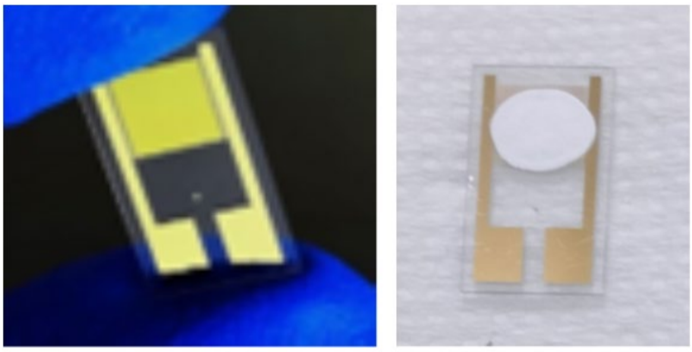


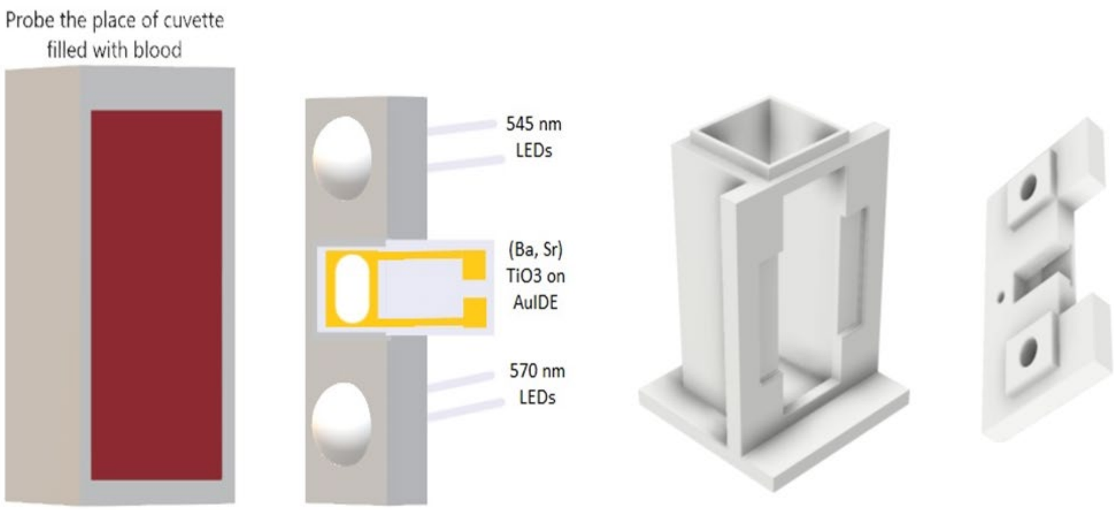
Figure 1. Hemoglobin structure [19].



(a) (b)

Figure 2. AuIDE substrate (a) Before (Ba,Sr)TiO_3 dripping, and (b) after (Ba,Sr)TiO_3 dripping.

LED, cuvette and (Ba,Sr)TiO_3 were placed in a probe. This probe was designed by taking into account the shape of the sensor (Ba,Sr)TiO_3, the wavelength of LED used (545 nm and 570 nm), and the cuvette where the blood sample was placed (Figure 3). The probe was made of filament (PLA/Polylactic Acid) and printed using a 3D printer.



(a) (b)

Figure 3. (a) Probe design for (Ba,Sr)TiO_3, (b) The print-ready probe.

The electronic circuits in the probe consist of several segments: the LED circuit, the sensor circuit, and the amplifier circuit which is mounted on the PCB board. The three circuits will be interconnected with the Raspberry Pi and ADS1115 connectors. Figure 4 shows the circuit scheme used in this study. The LED section is connected to the 3 GPIO (general purpose input/output) pins on the Raspberry Pi. GPIO pin 20 is connected to the 545 nm LED, GPIO pin 21 is connected to the 570 nm LED. In the sensor circuit, the sensor section was connected to the 5 V Raspberry Pi pin as the voltage source. The $(Ba,Sr)TiO_3$ sensor has two contact pins connected by a cathode and anode. While the FDS100 sensor has three pins. The first pin functions as the sensor output pin and is connected to the anode, the second pin is connected to the Raspberry Pi ground, and the third pin is connected to the cathode and the sensor voltage that obtained from a 5 V source. The Raspberry Pi does not have an analog reading pin, so the ADS1115 circuit was added which in this study was used as an ADC (Analog to Digital Converter).

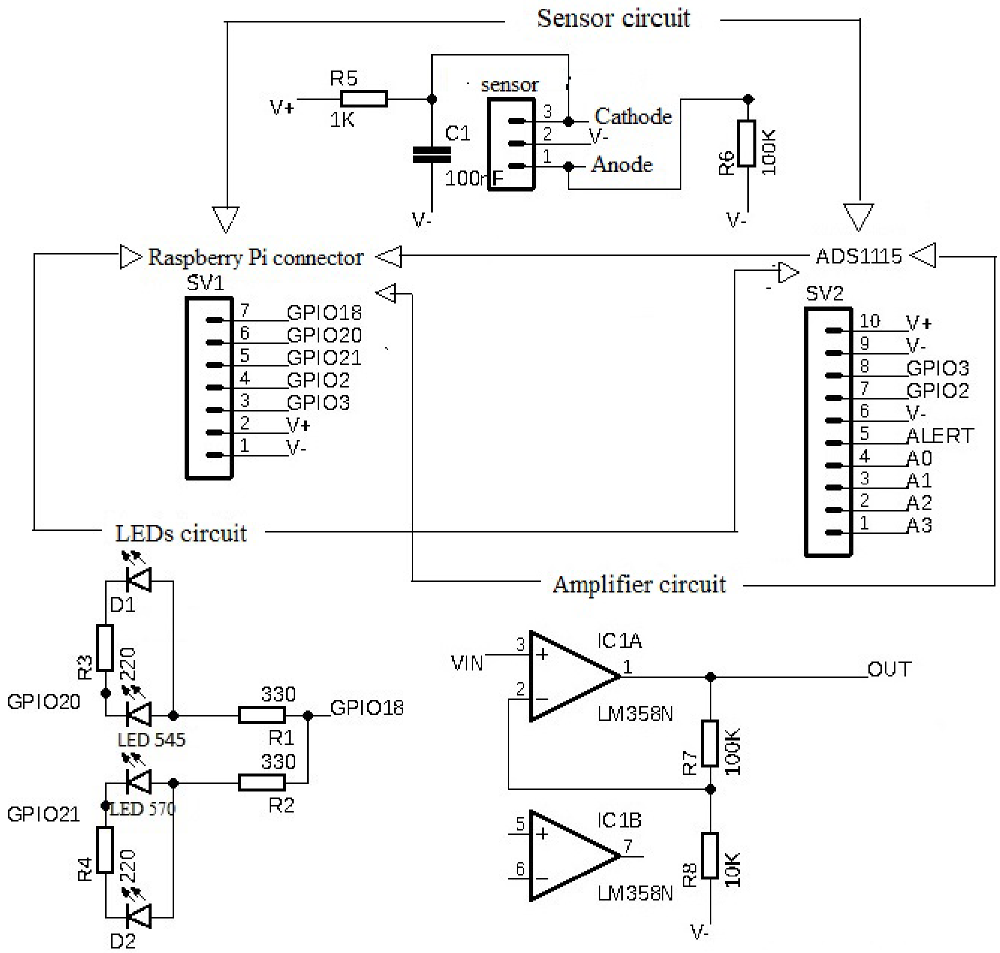


Figure 4. Electronic circuit scheme.

Detection of blood hemoglobin level is carried out in a probe containing a cuvette, LED, and sensor. As much as 1.2 cc of blood sample from BioRad MeterTrax was put into the cuvette, and placed inside the probe. The blood haemoglobin samples used in this study were varied into 10 levels (from 8.4 gr/dL to 17.7 g/dL), each with three repetitions. The blood samples were measured using the synthesized $(Ba,Sr)TiO_3$ film and also using the FDS100 sensor (by Thorlabs Company). The LED will emit light towards the blood sample, the light will then be reflected and captured by the sensor so that the reflectance value of hemoglobin was obtained (Figure 5). The reflectance data then converted to digital signal and sent to Raspberry Pi for further analysis.

The detection of each blood sample was carried out 5 times. Reflectance intensity is processed using a linear regression algorithm to obtain results for detecting blood hemoglobin levels [20]. The results of this detection will be processed to obtain predicted hemoglobin values, accuracy, and precision [21] from the (Ba,Sr)TiO_3 sensor and the FDS100 sensor. Accuracy is a measure that shows the degree of closeness of the analyst's results to the control values. While, precision is a measure that shows the degree of conformity in repeated measurements, so that if the same value is obtained from repeated measurements, it can be said that the precision is high. After that, the detection results from the synthesized (Ba,Sr)TiO_3 sensor will be compared to the results from the FDS100 sensor.

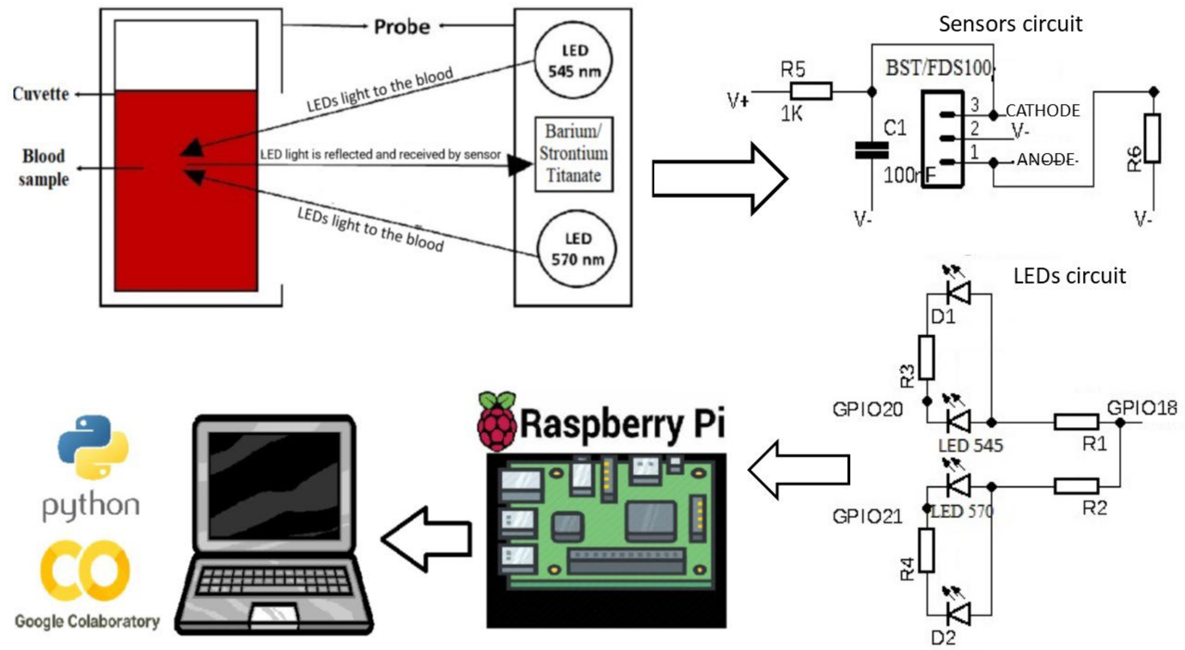


Figure 5. Blood Hemoglobin level measurement scheme.

3. RESULTS AND DISCUSSION

There are six sensors (three $BaTiO_3$ and three $SrTiO_3$) that will be tested and compared with the reflectance data from FDS100. For each sensor and hemoglobin levels (10 variations of hemoglobin levels from artificial blood), five measurements of optical reflectance were recorded. In total there are 300 data will be analised. Of this 300 data, 80% will be trained (240 data) while 20% (60 data) will be tested and compared with 50 controlled data from FDS100 sensor. The linear regression algorithm was used in the Google Colaboratory environment to produce some coefficients (*a*, *b*, *c*, *d*, *e*, *f*, *g*) for calculating the best prediction on hemoglobin levels. The results of linear regression approach give us the equation to calculate the hemoglobin level:

$$y = a + bx_1 + cx_2 + dx_3 + ex_4 + fx_5 + gx_6 \quad (1)$$

a = 22.63841 e = 0.004667 b = 0.005395
f = -0.00901 c = 0.007521 g = -0.00272 d = -0.00372

The results were shown in Table 1. It appears that the hemoglobin value obtained by the (Ba,Sr)TiO_3 varies but not too far from the actual value detected from the FDS100 sensor. Since a gold metal facilitates the transport of charge carriers, the combination of (Ba,Sr)TiO_3 with gold will create a metal-semiconductor structure known as the Schottky diode. The Schottky diode will produce high current when it is forward biased [22], this will make it easier for (Ba,Sr)TiO_3 to respond and performs the detection.

Table 1 Hemoglobin level of each sensor along with its accuracy and precision

Control level (g/dL)	FDS100 level (g/dL)	Prediction hemoglobin value of (Ba,Sr)TiO_3 (g/dL)					
		$BaTiO_3$ sample number			$SrTiO_3$ sample number		
		1	2	3	1	2	3
17.70	18.43	16.03	15.46	16.47	16.54	15.47	15.61
16.00	14.56	14.47	13.35	11.93	15.06	14.36	12.91
15.70	15.19	14.78	15.31	16.54	17.10	13.88	14.86
15.00	15.47	16.93	14.20	15.50	14.33	17.01	17.09
12.70	12.37	13.73	10.69	11.24	11.53	14.46	12.12
11.00	10.42	10.90	9.75	10.49	13.59	11.72	13.08
10.40	11.28	10.55	13.22	13.26	13.12	12.25	11.08
9.70	9.10	12.07	10.50	11.65	10.60	13.77	11.67
9.30	9.84	11.10	11.39	11.29	13.47	12.72	13.07
8.40	9.41	10.69	10.12	10.82	10.23	12.32	9.85
Accuracy (%)	90.97	84.83	84.37	83.93	82.93	81.92	82.63
Precision (%)	93.10	92.43	92.27	92.65	92.85	92.31	90.12

It was found that when hemoglobin level are above 11 g/dL, the predictions of haemoglobin level from (Ba,Sr)TiO_3 is quite accurate and not far from the reference's value (the hemoglobin level of the control). For hemoglobin levels below 10 g/dl, the predictions of hemoglobin levels from (Ba,Sr)TiO_3 is a bit off from the actual hemoglobin value. So, It can be stated that (Ba,Sr)TiO_3 can detect blood hemoglobin levels pretty well in the normal range (12-17 g/dl) which correspond to lower level condition of anemia (10-12 g/dl), but probably inadequate for severe anemia condition (lower than 10 g/dl).

The accuracy and precision of (Ba,Sr)TiO_3 sensor is above 80% for accuracy, and above 90% for precision. This result confirms the benefit of linear regression algorithm in data analysis to produce an accurate prediction of hemoglobin level [15], [18], [23]–[26]. However, the value is still lower than the accuracy and precision of the FDS100 (commercial sensor), with a difference of 6-8 % of the accuracy of the FDS100 sensor, and the precision of (Ba,Sr)TiO_3 lower 0.2-2.9% than the FDS100. The best measurement of $BaTiO_3$ shows accuracy of 84.83% as compared to 82.95% for $SrTiO_3$. The best precision measurement for $BaTiO_3$ is 92.65%, while for $SrTiO_3$ is 92.85%.

The accuracy of $BaTiO_3$ is better than $SrTiO_3$ with a difference of 1-2%. It caused by differences in the structure (phase) of crystals between $BaTiO_3$ and $SrTiO_3$. $BaTiO_3$ is a ferroelectric that has a tetragonal crystal structure. In $SrTiO_3$, the Sr atoms replace Ba atoms occupy 8 tetragonal vertex causes shrinkage of the tetragonal structure and makes space for Ti (4+) ions to make shifts limited. Also, this replacement play a role in increasing curie temperature [27]. When the temperature is above the Curie temperature, the $SrTiO_3$ crystal structure has shrunk [28]. The increase in temperature above the curie point also causes $SrTiO_3$ has a phase transition from ferroelectric to paralectric [12] so that the hysteresis curve changes. This is one of the factors that causes accuracy and precision of $BaTiO_3$ better than $SrTiO_3$.

Considering that research on the application of $(Ba,Sr)TiO_3$ on AuIDE substrates made using the CSD method as a detector of hemoglobin levels was the first to be conducted, it can be said that $(Ba,Sr)TiO_3$ has great potential, as seen from the results obtained. Although it cannot be denied that there are still many aspects that need to be improved to make this device feasible and useful.

4. CONCLUSION

$(Ba,Sr)TiO_3$ films above the AuIDE substrate were used as a light sensor to detect blood hemoglobin levels using 545 nm and 570 nm LEDs as light sources. The hemoglobin's level obtained from $(Ba,Sr)TiO_3$ were compared to FDS100's data and processed using a linear regression algorithm. Based on the data, it appears that $BaTiO_3$ is better than $SrTiO_3$ in detecting the blood hemoglobin levels which might come from the difference phase and crystal (and electronic) structure of those materials. In general, the accuracy and precision of $(Ba,Sr)TiO_3$ based sensors in detecting blood hemoglobin levels is pretty good and it has potential to be developed as a blood hemoglobin level detector. There is still plenty of room for improvement to maximize the $(Ba,Sr)TiO_3$'s performance to become a reliable device.

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