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Blood glucose prediction using non-invasive optical system based on photoplethysmography

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ABSTRACT

Several people must frequently evaluate their blood glucose since it is an important indicator of health problems mainly diabetes. Different medical systems are commercialized to measure blood glucose levels; some are invasive others are noninvasive. The main purpose of this article is to develop a non-invasive device for measuring blood glucose levels based on the detection and analysis of the photoplethysmogram signal. The developed systems include an optical sensor to detect the photoplethysmography (PPG) signal, digitalizing and acquiring boards to a computer and a software program to process and analyze the digitalized PPG signal regarding some features extracted from its waveform. These features are the systolic amplitude Sa and the b/a amplitude ratio in the second derivative PPG (SDPPG) waveform. An invasive glucometer is also used along with the Sa and b/a ratio determined from the developed system to generate a calibration model which is used to deduce blood glucose level (BGL) values. The result showed that the calibration model using the b/a ratio is more accurate for non-invasive blood level measurement then that of Sa with a difference in glucose estimation around 2 mg/dl and with the correlation coefficient (R2) of the glucose level prediction between 0.8904 and 0.9775.

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1. INTRODUCTION

The human body uses glucose as a significant source of energy. To carry out daily tasks, the body needs blood glucose levels in the normal range (80 to 150 mg/dl) [1]. However, a higher or lower glucose level could result in a number of internal complications. In addition, the vital hormone insulin is produced by the body as a result of eating. Generally high blood glucose concentration is possible if the creation of α cells is greater as compared to that of the β cells. Because of this condition, enough insulin is not secreted in the body for glucose consumption. This condition makes mention a diabetes mellitus [2]. Diabetes is an incurable illness in which the body is unable to maintain blood glucose levels within the normal range (5 to 8 milmol/l) [3]. The International Diabetes Federation (IDF) estimates that 387 million people will have diabetes by 2035 [4]. The diabetes conduct to different health problems, e.g. cardiovascular diseases, atherosclerosis problems, chronic renal disease (CKD), nervous system diseases, foot amputation due to ulceration, and early death [5]. Since most commercially available glucose tests are now uncomfortable and carry a risk of infection, invasive measurement techniques have been used the most frequently worldwide [6]. Nevertheless, numerous commercial devices for continuous blood glucose monitoring utilize electrochemical

sensors [7]. Which present a high response for glucose detection in blood [8]. For pricking the blood, the lancets are used in the primary stage for blood glucose monitoring for many commercial devices available in the market [9]. As a result of taking blood samples from the fingertip more than twice a day for frequent monitoring, the practice of repeated measurement is quite painful [10]. For decades, different non-invasive methods are effective substitutes for these invasive methods because patients will find it more convenient, pleasant, and affordable. There are numerous noninvasive methods for measuring blood glucose that have been proposed [11].

Chu *et al.* [12] developed a computational model based on energy conservation principles, integrating physiological data like heart rate, oxygen saturation, and blood flow velocity. They also devised a hardware system for data collection, including a dual-wavelength photoplethysmography (PPG) acquisition setup. Habbu *et al.* [13] introduced a neural network model using single pulse analysis and frequency-time features from PPG signals. Satter *et al.* [14] utilized wrist PPG signals to estimate blood glucose level (BGL), focusing on waveform-based features like pulsatile part (AC) and steady part (DC) ratio and features derived from empirical mode decomposition (EMD). Additionally, a study in [15] proposed a non-invasive method to estimate HbA1c using PPG signals with two wavelengths. These approaches demonstrate the ongoing effort to develop non-invasive techniques for glucose monitoring.

In this paper we develop a new system measuring a glucose level in non-invasive way. The PPG technique is used for this purpose. This technology is simple, low-cost, and has already been effectively applied to the detection of oxygen saturation and pulsation rate on various wearable devices [12]. A PPG system utilizes light to evaluate changes in blood circulation volume by measuring the absorption of light in the tissue. It is observed that some wavelengths of light's absorption and reflectance are sensitive to the body's hemodynamic characteristics, which are closely tied to the condition of the cardiovascular system, while it is well known that blood glucose levels, which may be immediately measured as pulse morphological profiles, have a long-term impact on the cardiovascular system [16]. For that reason, establishing a link between PPG pulse shape and blood glucose levels may offer a useful means of noninvasively predicting blood glucose levels.

The main goal of our works is to replace the conventional invasive-glucose measurement with our proposed non-invasive glucose monitoring device. Due to the device's inexpensive price, many individuals can utilize it. Additionally, it is quite simple to use and ought to easily fit the majority of patients' fingers. The rest of this paper is first concerned with a brief description of the glucose measurement principle. This is followed by the presentation of the hardware system which developed to detect the PPG signals on different subjects. Then the developed software is detailed. Finally, in the last section, an analysis of the PPG and second derivative PPG (SDPPG) parameter variations according to glucose measurement are presented and discussed before a conclusion is given.

2. MATERIAL AND METHODS

The suggested design and the method of execution are described in detail in this section. The entire procedure is separated into three steps: hardware development; invasive data collection; software development. Each step is crucial for the successful completion of the project.

2.1. Hardware development

The PPG signal is detected by using the easy pulse shield as shown in Figure 1. It is a pulse sensor developed by ARDUINO which was designed to illustrate the principle of photoplethysmography (PPG) as a non-invasive optical technique for detecting cardio-vascular pulse wave from a fingertip. The easy pulse operates using transmission mode. Within the sensor casing, an infrared (IR) LED and a photodetector are positioned on opposite sides, facing each other. The choice of an IR LED is based on the fact that glucose, being a type of monosaccharide with the chemical formula $C_6H_{12}O_6$, exhibits various near-infrared (NIR) absorption peaks at specific wavelengths (940, 970, 1408, 1688, 1925, 2261, and 2326 nm). However, at 940nm, the interference of optical signals by other blood components such as water, platelets, and red blood cells is minimal. This allows for optimal depth of penetration and accurate prediction of glucose levels [17].

2.2. Invasive data collection

To develop the calibration model of our developed systems, we used Diagno-Check Sens glucose meter D3DL661938 as shown in Figure 2 [18]. This was used, using clinically recommended approach, to measure simultaneously with the developed system the blood glucose level in milimole per liter. Figure 3 illustrates the block diagram of our proposed system to measure blood glucose level.

Figure 1. Easy pulse shield

Figure 2. Diagno-Check Sens glucose meter

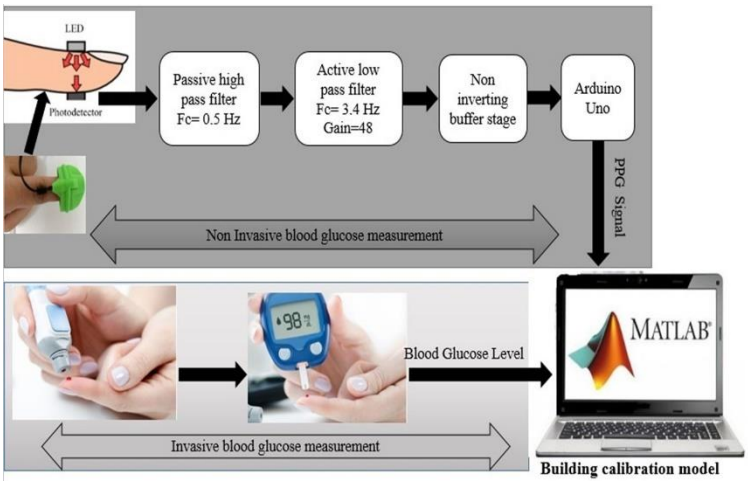


Figure 3. The block diagram of our proposed system to measure blood glucose level

2.3. Software development

2.3.1. PPG features extraction

In order to detect the systolic amplitude of the PPG signal, the peak finder function in MATLAB [19] is adapted to identified peaks and valley for each pulse in PPG signal as shown in Figure 4(a), Figure 4 (b) using a user-defined magnitude threshold, this function quickly locates local peaks or valleys (local extrema) in a noisy vector. It then determines if each peak is significantly greater (or smaller) than the data around it. In our system, the threshold value is fixed empirically. Whereas peaks systolic was denoted as "Ps" and valley point was denoted as "Pd". The systolic amplitude Sa is obtained using (2),

$$Sa = Ps - Pd \tag{2}$$

Following the automated application of our MATLAB-developed algorithm, systolic amplitudes were obtained for 10 pulses, the second derivative of PPG, the SDPPG signal is generated using the diff () function in the MATLAB Software. The obtained signal SDPPG contain 5 waves called a, b, c, d, and e. In our work b/a ratio is derived using (3). One should know that the amplitude of b and that of a are obtained using the peak function finder as shown in Figures 5(a), (b), and (c).

$$b/a = amplitude(b)/amplitude(a) \tag{3}$$

2.3.2. Regression mode

After denoising the PPG signal using finite impulsion response filter. PPG features were detected. A regression model between the data extracted from the PPG and original values of blood glucose was constructed. This process is illustrated in Figure 6.

Previous studies have noted significant differences in the characteristics of photoplethysmography (PPG) waveforms between healthy individuals and those with diabetes. Nirala *et al.* [20] highlighted the first and second eigenvalues derived from the first derivative of the PPG signal as key features for identifying type 2 diabetes mellitus (T2DM). Furthermore, research [21] has shown that elevated glucose levels in the

blood alter the shape of the PPG signal, which can be used to estimate blood glucose levels indirectly. However, the systolic amplitude and b/a ratio are obtained from the peaks of PPG and SDPPG data, due to the significance of its pulsatile components in reflecting variations in the blood flow inside arteries, these characteristics are provided. Diabetes impacts blood volumetric changes via altering blood propagation. The accumulation of atherosclerosis and diabetes in the arteries is assumed to be the origin of this condition. Changes in blood circulation cause the morphology of PPG to become rounder as a result, diabetes alters the artery wall's elasticity, which is thought to change the PPG's morphology [22]. Through this work two PPG indices are exanimated, systolic amplitude Sa and b/a ratio are obtained from ten PPG and SDPPG recording for the same subject. In the first step these derived values of Sa and the b/a ration are set in two vectors (4) and (5) whereas the invasive BGL simultaneously measured values are set in another vector (6). In second step the most accurate linear regression models that depict the change in systolic amplitude are then selected. Equation (7) and b/a ratio (8) with BGL are determined.

$$Xsa = [X(1).....X(10)] \tag{4}$$

$$X'b/a = [X'(1).....X'(10)] \tag{5}$$

$$Y = [Y'(1).....Y'(10)] \tag{6}$$

With Xsa is systolic amplitude vector, $X'b/a$ is b/a ratio vector, and Y is blood glucose level vector.

The equations (7) and (8) represent the linear regression model.

$$Y = aXsa + b \tag{7}$$

$$Y' = a'X'_{\frac{b}{a}} + b' \tag{8}$$

With Y is the estimated value of blood glucose concentration from systolic amplitude in PPG signal and Y' is the estimated value blood glucose concentration from b/a ratio feature in SDPPG signal. The a, a', b, and b' are the regression coefficients.

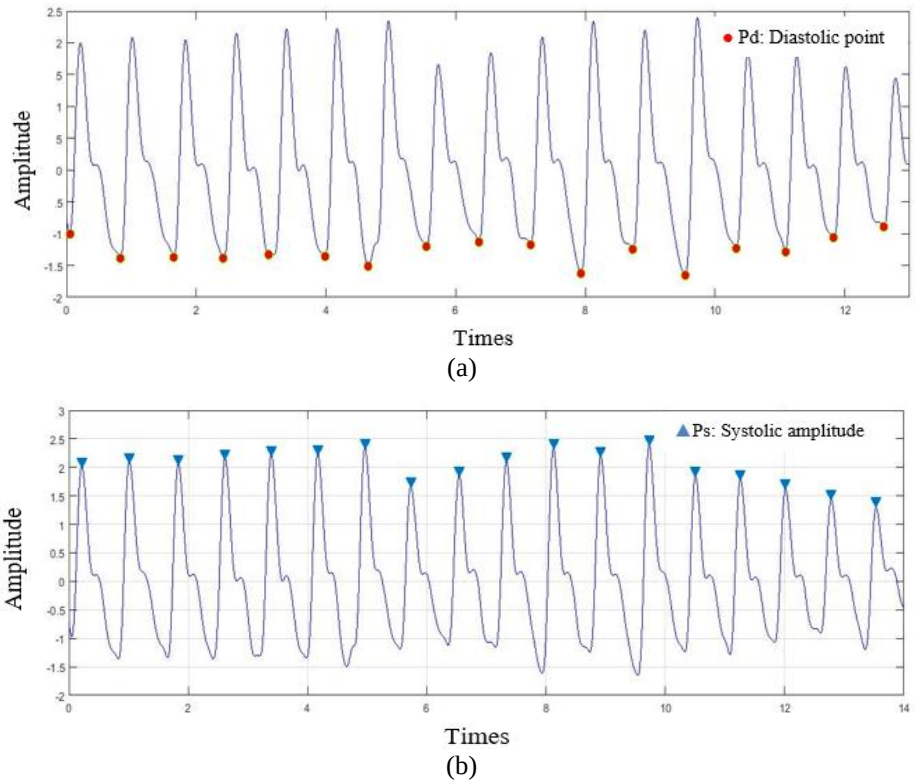


Figure 4. The identification peaks and valley in PPG signal: (a) systolic amplitude in PPG signal and (b) valley point in PPG signal

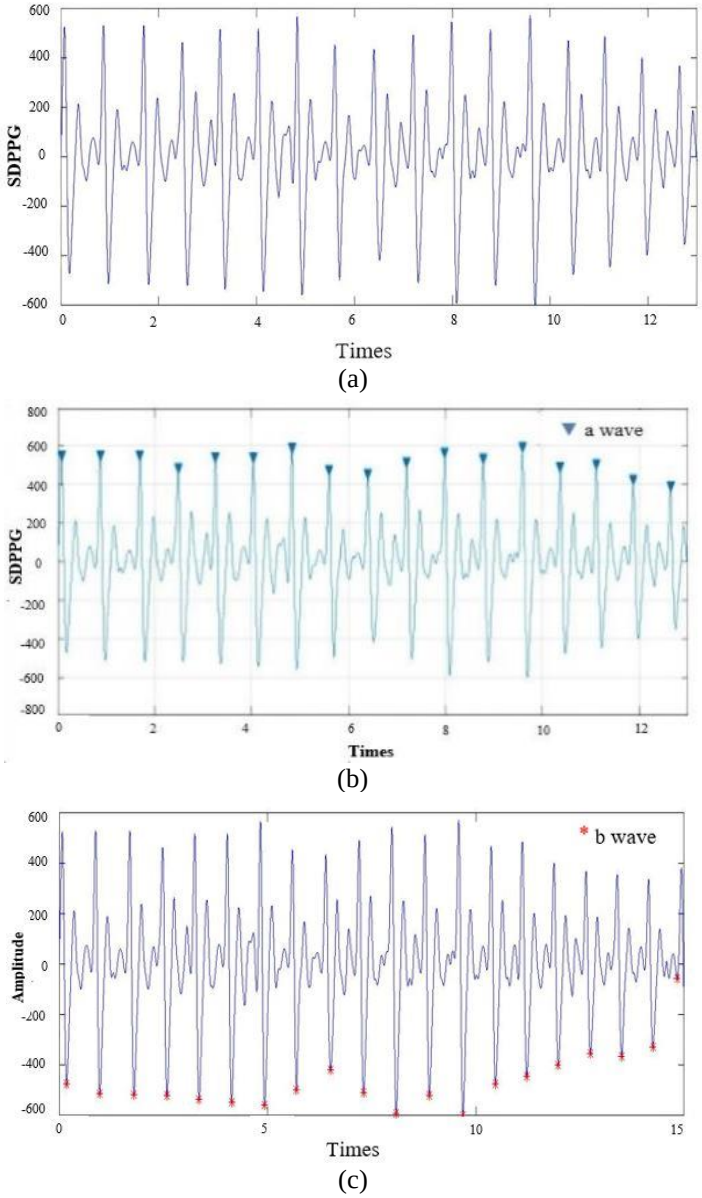


Figure 5. The detection of different waves in second derivative of PPG signal: (a) second derivative of PPG signal (SDPPG), (b) '*b*' wave detection in SDPPG, and (c) '*a*' wave detection in SDPPG

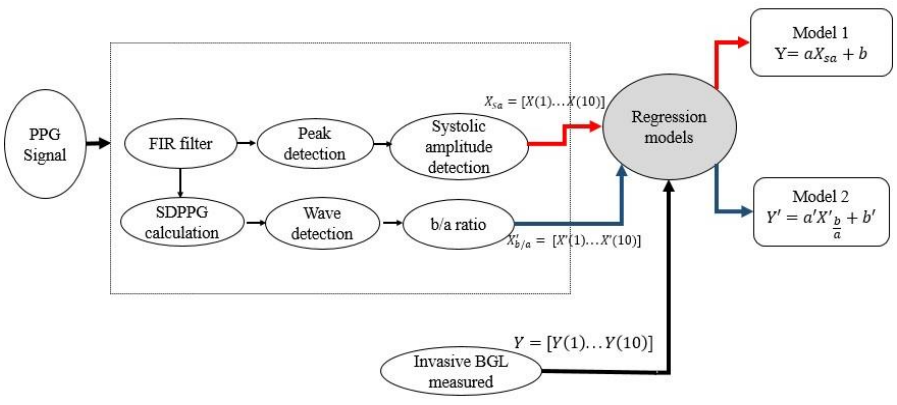


Figure 6. The building process of our calibration model

2.4. The measurement protocol

In this this study, we recruited 10 males healthy subjects, These participants, who ranged in age from 20 to 38, were all in good physical health overall and agreed in writing to participate in the study. However, the blood glucose level will be checked at several moments throughout the duration of many days, both before and after meals, which will result in varying quantities of sugar levels in the blood.

3. RESULTS AND DISCUSSION

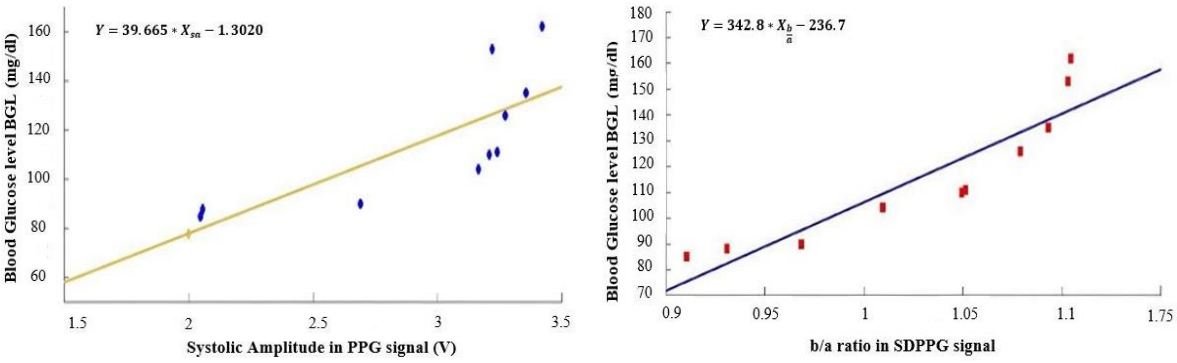
In this study, several measures were made to build our regression model in order to predict the BGL using a noninvasive PPG sensor. Using a group of ten male volunteers across a range of ages, the proposed system was assessed. Following system calibration, the performance of the non-invasive blood glucose measurement system was evaluated using the validation data sets for each individual. Figures 7(a) and (b) present an example of regression analysis for a subject, demonstrating that both Sa and the b/a ratio PPG features increase as the actual blood glucose level (BGL) rises. After the system was fully calibrated, validation data sets for each subject were used to evaluate the performance of the measurement model. The proposed non-invasive glucose sensor prototype's performance is evaluated using correlation coefficients (R^2), root mean squares error (RMSE) and Pearson's r correlation coefficient.

$$R^2 = 1 - \frac{\sum(X_v - Y_v)^2}{\sum(X_v - Y')^2} \tag{9}$$

$$RMSE = \sqrt{\frac{\sum(X_v - Y_v)^2}{n}} \tag{10}$$

$$r = \frac{\sum(X_v - X')(Y_v - Y')}{\sqrt{\sum(X_v - X')^2 \sum(Y_v - Y')^2}} \tag{11}$$

where X_v is the predicted blood glucose level, Y_v is the real GCB reading, Y' is the mean of real GCB reading, and X' is the mean of predicted blood glucose level.



(a) (b)

Figure 7. The regression models between BGL and PPG signal features: (a) The regression models between BGL and systolic amplitude in PPG signal, (b) The regression models between BGL and b/a ratio in SDPPG

Table 1 resumes the obtained results of BGL, from commercially invasive glucometer and our non-invasive PPG system using Sa ratio feature. According to the research of [11], [23] relating non-invasive BGL analysis, We can verify the accuracy of the predict non-invasive BG value obtained results. In fact, based on this research and the object on which the measurements were taken, we discover that, the mean value of the correlation coefficients (R^2) is: 0.8037. and Pearson's r coefficient is: 0.98. It is evident that there is a strong correlation between the BGL measurement using invasive device, and the BGL measurement using noninvasive PPG sensor according to Sa feature. Through this study, we used also the b/a ratio in the PPG signal to predict BGL to further evaluate the link between the commercially available invasive glucometer and our suggested non-invasive PPG sensor. Table 2 resumes the obtained results of BGL, from commercially invasive glucometer and our non-invasive PPG system using b/a ratio feature.

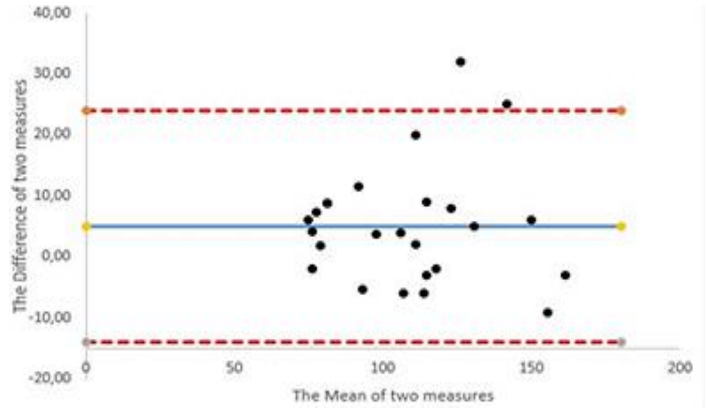
From Table 2 we can notice that there is a strong correlation between the blood glucose level measurement using invasive device, and the predict blood glucose level using noninvasive PPG sensor according to the b/a ratio. Based on our research and the specific subject of our measurements, we found that the average correlation coefficient (R^2) is 0.9314, and Pearson's r coefficient is: 0.99. To further assess the agreement between blood glucose levels (BGL) measured using an invasive device and our developed system, we conducted a Bland-Altman analysis as shown in Figure 8(a) and (b).

Table 1. Summarizes the BGL values of both a commercially available invasive glucometer and our proposed non-invasive PPG sensor using the systolic amplitude (Sa) feature

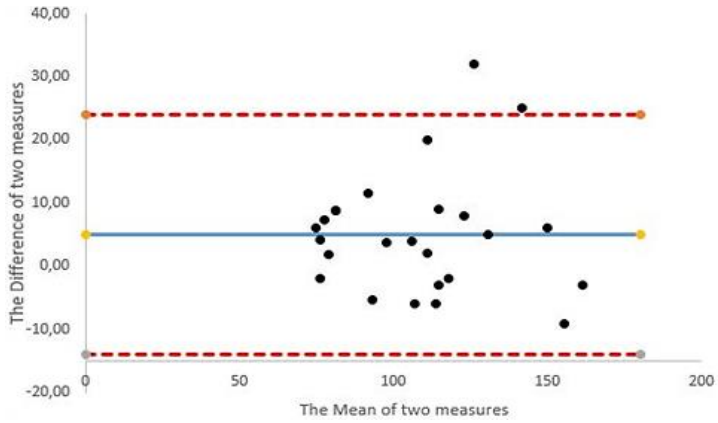
Subject	1	2	3	4	5
BGL using invasive glucometer (mg/dl)	100	106	105	110.6	107.6
BGL using noninvasive PPG sensor (mg/dl)	119.16	111.12	109.36	108.98	105.97
Correlation (R^2)	0.6356	0.89	0.7637	0.8552	0.8743
RMSE (mg/dl)	20.24	5.83	4.61	2.4	7.03
Pearson's r correlation coefficient	0.98	0.95	0.99	0.99	0.99

Table 2. Results from our suggested non-invasive PPG sensor using b/a feature and those from a currently available invasive glucometer

Subject	1	2	3	4	5
BGL using invasive glucometer (mg/dl)	100	106	105	110.6	107.6
BGL using noninvasive PPG sensor (mg/dl)	107.2	102	104.88	110.14	108.8
Correlation (R^2)	0.9069	0.9692	0.9117	**0.9775**	0.8904
RMSE (mg/dl)	6.08	3.94	1.28	1.59	4.52
Pearson's r correlation coefficient	0.99	0.993	0.998	0.999	0.992



(a)



(b)

Figure 8. Bland-Altman plots for predicted values and reference values (a) using systolic amplitude in PPG signal and (b) using b/a in SDPPG

In this figure, the blue line represents the mean difference (d) between the two sets of measurements: the predicted glucose values from our method and the glucose values obtained using the invasive device. The red lines represent the range of $d \pm 1.96$ times the standard deviation (std). The Bland-Altman plot illustrates that the mean difference (d) between the two measurement sets is consistently close to zero in all cases, which is highly favorable. Consequently, beyond the correlation coefficient, we can confidently conclude that our proposed method yields reliable predictions for BGL, as supported by the Bland-Altman analysis. According to the results obtained in this work and comparing to others works, we can verify that the suggested method is accurate. Table 3 synthesize a comparison of the suggested system and some of the other proposed systems in the domain scientific literature.

The difference value of BGL between invasive systems and the non-invasive systems is lower than most of the proposed systems in the domain scientific literature whereas the correlation coefficient is greater. This proves an amelioration in the precision of the results due to our developed individual calibration model for each subject independently of the others. This approach mitigates the challenges arising from inter-individual variability in PPG measurements. Factors such as finger circumference, skin roughness leading to light scattering, variations in body fluid concentration, interference from other biological constituents, skin tone, and motion artifacts can significantly influence PPG readings. By tailoring regression models to each individual, we address these challenges effectively, ensuring more accurate and reliable blood glucose predictions. This individualized approach enhances the precision of non-invasive glucose monitoring, providing personalized insights into glucose dynamics while minimizing the impact of confounding factors inherent in PPG measurements. The study carried out in this work was on 10 subjects; however, in the future scope we envisage to add more subjects to the experiment to generalize these obtained results.

Table 3. Comparisons between the systems we've proposed and those that have been put out in the relevant scientific literature

Works in the domain	Techniques used				
	Spectroscopy technique	Subjects	Wavelength (nm)	PPG features extraction	R^2
Rachim and Chung [23]	Not mentioned	12	530,660,850,950	01	0.85
Ogunsanya and Daramola [24]	Transmission/GSM module	40	1550	01	0.95
Qawqzeh *et al.* [22].	Transmission	587	950	03	0.70
Al-dhaheri *et al.* [25]	Transmission	10	940	01	0.839
Jain, Joshi, and Mohanty [16]	Absorption and reflectance	97	940	01	0.900
Our proposed method	Transmission	10	940	02	0.9775

4. CONCLUSION

In this work, an infrared optical sensor is developed to non-invasive measurement of blood glucose level. This was accomplished using software programs which were developed to first process the photoplethysmogram signal and then extract two important features from PPG signal morphology. To model the link between PPG signals and BGL, a linear regression model was developed. The obtained result on the different tests applied on different subjects show that there is a strong correlation between the commercial glucometer measurements and our proposed system measurements. Similarly; according to obtained results and compared with other studies, we can confirm the feasibility of using our developed infrared optical sensor like a non-invasive blood glucose measurement technique. In the future, we intend to expand the number of participants in our studies. And also, we envisage to test more PPG features with different regression models to increase the performance of our non-invasive glucometer.

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