

Experimental blood glucose estimation from photoplethysmography recordings on distal finger phalange

Estimación experimental de glucose en sangre a partir de registros de fotopletismografía no invasiva en dedo

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Resumen

La concentración de glucosa en sangre contiene información sobre la salud y calidad de vida de una persona. La presencia de altas concentraciones de glucosa en el torrente sanguíneo indica un mal funcionamiento del sistema humano. Actualmente, existe un método de prueba aceptable para estimar el nivel de glucosa; consiste en sacar una muestra de sangre del dedo con un pinchazo utilizando un alfiler o lanceta. Sin embargo, esta muestra presenta algunas desventajas o problemas asociados, tales como infecciones, estrés emocional y problemas de coagulación, típicos en pacientes que viven con diabetes. Por lo tanto, en este estudio se analiza la fotopletismografía reflectiva (PPG, por sus siglas en inglés), técnica no invasiva basada en una fuente de luz y un fotodetector capaz de medir la cantidad de luz que refleja el cuerpo humano a través de la piel. Particularmente, se construyen dos fotodetectores capaces de medir los niveles de glucosa en sangre basados en los diodos emisores de luz infrarroja LTE-302 y COM-09349, en combinación con el fotodetector FDS-100. Además, se realiza el diseño de la circuitería necesaria para la adquisición y acondicionamiento de las señales muestreadas. El sistema de sensado es validado a través de un conjunto de mediciones realizadas a tres voluntarios, dos hombres y una mujer, de diferentes edades. Las mediciones de cada sensor se comparan con un glucómetro comercial, el One Touch Select Plus Flex, obteniendo error aproximado de 14 % para el primer sensor y 7.9 % para el segundo sensor; sin embargo, la desviación de las mediciones se encuentra dentro de especificación de la norma NORM ISO 15197:2013. Concluyendo que, la técnica de PPG reflexiva podría ser utilizada como un método no invasivo para estimar el nivel de glucosa en sangre en el cuerpo humano.

Palabras clave: Fotopletismografía, infrarrojo-cercano, interfase, glucosa.

Abstract

Blood glucose concentration shows the quality and health of an individual. High glucose levels in the blood flow indicate atypical behavior of the human system. Currently, there is an acceptable test method to estimate glucose level; it consists in taking out a blood sample by the finger with a pin prick. However, the blood sample test has some disadvantages because it can produce some non-desired issues, such as infections, especially a typical case in people living with diabetes. Therefore, this work is motivated by applying reflective Photoplethysmography (PPG), a non-invasive technique based on a light source and a photodetector near the human body's skin. In this case, we propose two different blood glucose sensors using the infrared diodes LTE-302 and COM-09349 with a photodetector FDS-100. It is worth noting that both designs have multiple development stages, and all of them are self-designed and validated through various test samples with three healthy volunteers, one woman and two men. The results present an error of about 14 % for the first sensor, while for the second sensor is about 7.9 %. Moreover, the sensor measurements are compared against a commercial glucometer, the One Touch Select Plus Flex, and the specifications of the NORM ISO 15197:2013 standard. Finally, the reflective PPG technique could be applied as a non-invasive method to estimate the blood glucose level in the human body.

Keywords: Photoplethysmography, near-infrared, interphase, glucose.

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Historial del manuscrito: recibido el 18/10/2022, última versión-revisada recibida el 18/10/2022, aceptado el 08/11/2022, publicado el 11/11/2022. **DOI:** <https://doi.org/10.29057/icbi.v10iEspecial5.10074>



1. Introduction

Diabetes is a chronic degenerative disease increasing worldwide daily (Sun *et al.*, 2022). This disease is considered a heterogenic metabolic disorder. Moreover, it results from the inaction of insulin by the pancreas endocrine malfunction, consequently losing the sensibility of the tissues to insulin because of a sustained state of hyperglycemia.

According to the National Health and Nutritional Study (ENSANUT), 2016; in Mexico, the total prevalence of diabetes was about 13.7 % (9.5% diagnosed while 4.1% were non-diagnosed); where diagnosed patients present a glycemetic disorder. Patients diagnosed with this disorder commonly live in marginal regions and, in some cases, are self-medicated with homemade treatments. Those patients being cared for by social security services improve their glycemetic control (Basto-Abreu *et al.*, 2022). In 2020, ENSANUT estimated that diabetes prevalence would increase in the following years (Basto-Abreu *et al.*, 2021); aging is one of the main reasons for this increase, and meal habits play an essential role in the evolution of diabetes. In Mexico, the total caloric intake commonly comes from discretionary foods such as sugary drinks and non-essential high-caloric foods instead of legumes, fruits, and vegetables, combined with obesity and poor exercise, which boosts diabetes development. Moreover, from 2000 to 2018, diabetes prevalence rates increased by about 46 %, highlighting women and individuals over 50. Therefore, Mexico is still in a deep diabetogenic environment, and it is suitable to expect that diabetes prevalence will increase over the years, being a challenge for both early detection and diagnosis in the control of this disease.

Developing a non-invasive glucometer is an essential strategy that can improve a patient's quality of life with this suffering (Covarrubias *et al.*, 2022). In Chincoya *et al.*, (2021) a glucose estimator is designed and developed based on photoplethysmography (PPG) working around 870 nm; however, the authors do not give details about the base model applied to the glucose estimation in mg/dL. Also, another non-invasive method exists to get such parameters; an example is spectroscopy, as reported in (Briseño *et al.*, 2021). Nowadays, there is available the non-invasive glucometer FreeStyle (Alba, 2008). Nonetheless, Schwarz *et al.*, (2021) suggest that it is necessary to investigate more details about this device. Specifically, exactness and precision, focusing on the emerging methodologies and a most significant diabetic sample population, as well as a broader range of glucose level estimation, to study the exactness and precision for glucose concentration below 70 mg/dL, including level-1 and level-2 of hypoglycemia. Furthermore, evaluate its ability to measure glucose levels over 300 mg/dL and quick concentration level changes needed for clinical diagnosis. It is crucial to note that all the available devices must satisfy the international norm (ISO) 15197:2015 (Pleus *et al.*, 2021, and Kim *et al.*, 2021), which establishes the minimum criteria for a glucometer to achieve a minimum acceptable accuracy.

Body PPG allows the measurement of volumes, capacities, and resistances of different body organs, including the lungs and the vascular system (Inés de Mir Messa *et al.*, 2015). Photoplethysmography uses the absorption or reflection of a specific wavelength produced by the other functional groups found in the tissues, commonly used to know the heart rate, oxygen saturation, and oxygenation index in the tissues (Chincoya *et al.*, 2021).

In this work, we develop a non-invasive blood glucose level device based on PPG signals to estimate blood glucose concentration in the human body. The complete system consists of two infrared diodes, one photodetector, a National Instrument board for data acquisition, and electronic circuitry for signal conditioning. The proposal can estimate blood glucose levels accurately, avoiding painful methods commonly used to control blood glucose levels. The device can calculate the glucose level by combining PPG signals and the reflected light from blood vessels through the skin. Moreover, we located the overall system in a black box, measuring the glucose concentration through a filtering glass window, avoiding environmental noises, such as natural and artificial light.

The organization of this paper is as follows. Section 2 describes the materials, the method, and the conceptualization of the sensor development. Section 3 describes the validation process for the system. Further, in Section 4, we show results and measurements. Finally, Section 5 presents the conclusions of this research.

2. Materials and methods

The device's design is based on the application of PPG to detect volume variation in the bloodstream. This process starts with an infrared light emitting from a light emitting diode (LED), then the light goes through the skin, and the light reflected by blood vessels is captured by a photodetector. Further, the photodetector signal is filtered and converted to a digital signal. Finally, the digital signal is processed to estimate the final glucose concentration, dividing the complete estimation process into five main stages, from its detection until the display of the glucose level. Figure 1 shows each phase of glucose detection and estimating level, describing the overall system as follows:

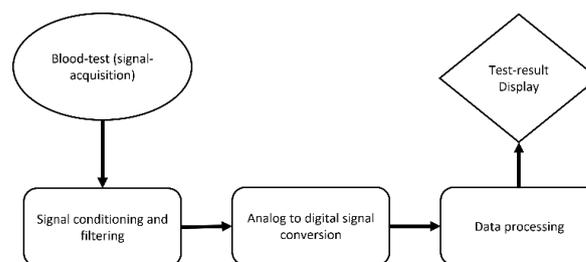


Figure 1: Block diagram of the stages implemented in the measurement and glucose estimation process.

2.1. Sensing

The sensing stage comprises two infrared diodes, classified within the near-infrared range (NIR), and an FDS-100 photodiode. As part of the design, we develop two sensing devices. The first uses the diode COM-09349 (Sensor-1), while the second uses the diode LTE-302 (Sensor-2); each device has two diodes, either COM-09349 or LTE-302, placed on each side of the FDS-100 photodiode. Figure 2 depicts the two sensing systems; the difference between both sensors is the light source at different wavelengths. Figure 2a shows the sensor implementation at 950 nm; meanwhile, Figure 2b shows the 940 nm sensor. In this case, we decided to place two NIRs because, in reflective PPG, the skin absorbs more than 90% of

the light emitted and only reflects 10 % from the body's skin (Shelley *et al.*, 2001). The sensitive interval of the photodiode FDS-100 is about 350 nm to 1100 nm and is resistant to visible light interference (Liu & Zhang, 2021).

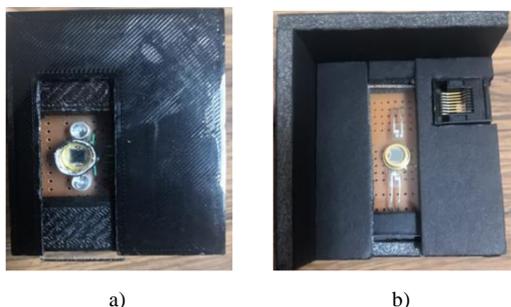


Figure 2: Electronic circuit breadboard implementation highlighting principal modules.

The photodiodes are connected in photovoltaic mode, producing a potential difference proportional to the incident light illuminance. In this case, the light beams come reflected from the finger. Figure 3 depicts the overall system configuration and its operational mode.

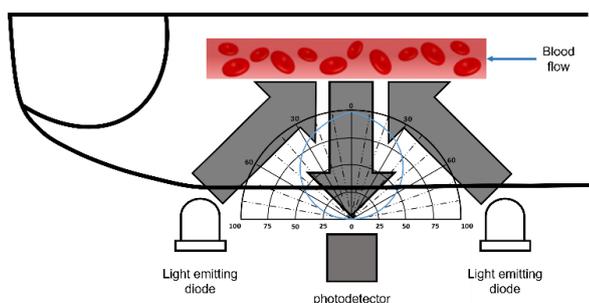


Figure 3: Sensor arrangement, two infrared emitters, one photodetector in the measurement position.

2.2. Signal conditioning and filtering

According to Bruen *et al.*, (2017), glucose levels in the blood may change in 10 min. Tang *et al.*, (2020) report changes in glucose levels in the blood are delayed by 4 to 10 min to the interstitial fluid. There are reports of a time lag between glucose changes after a meal is about 5 to 25 minutes (Siegmund *et al.*, 2017). The glucose changes in the blood over a relatively long time; considering this, the signal from the PPG device should be sampled at a rate as fast as 0.0083 S/s. At this rate, avoiding aliasing demands a steep slope at the filter transition band. Hence, we propose to oversample at a rate of 500 S/s. After being amplified, the signal from the sensor is pass-band filtered from 0.5 Hz to 5 Hz. Therefore, Figure 4 shows the electronic circuit implementation, highlighting the principal modules.

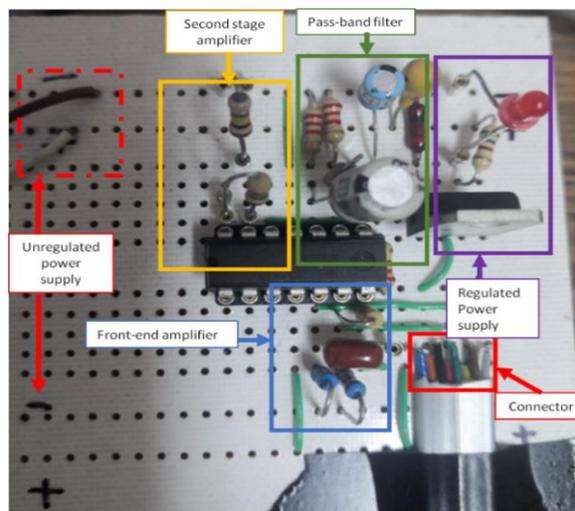


Figure 4: Electronic circuit breadboard implementation highlighting principal modules.

2.3. Signal digitalization

The recording instrument uses a commercial data acquisition system (DAQ), the National Instruments NI USB-6211, configured to a dynamic range between -5 V to 5 V with DC coupling. Then the recording system achieves a sensibility of $76.29\mu\text{V}@16\text{bits}$. Finally, the input configuration is reference single-ended (RSE).

2.4. Data processing

The recording instrument has a GUI for easy and informative recordings; it includes an indicator where it is possible to observe the waveform of the current recording. Figure 5 shows the glucose estimation device, the sensor array, signal conditioning, and the recording system.

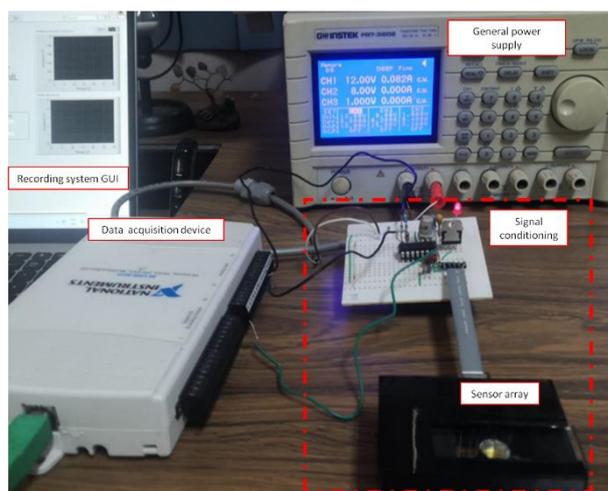


Figure 5: Glucose estimation device, system setup.

Figure 6 depicts the reconstruction of data stored corresponding to the unfiltered sensor output. The cardiac rhythm is visible; variation in the pulse amplitudes suggests different amounts of light absorbance through the variable mass of the finger due to the bloodstream. Moreover, this figure shows the blood glucose dynamical behavior of the three

individuals. It is worth mentioning that even though all the individuals are healthy, the data acquisition levels show differences in the bloodstream dynamic, associating these differences with the human inability to control glucose levels due to the age of individuals.

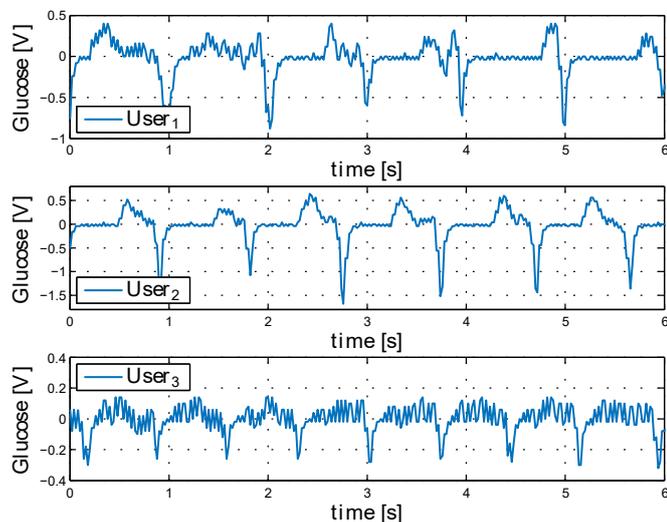


Figure 6: Reconstruction of the sensor unfiltered data.

Figure 7 shows the reconstruction of the data stored corresponding to the filtered sensor output. Focusing on the variability produced by the concentration of different blood components, cardiac rhythm is still visible. From that data, it is hard to differentiate blood components without further concentration information. In consideration, it is paramount to perform glucose concentration estimations with a certified device during every signal recording session. After filtering, the signal only has the direct current component to characterize the sensor and correlate a voltage value with its corresponding glucose level by a mathematical function.

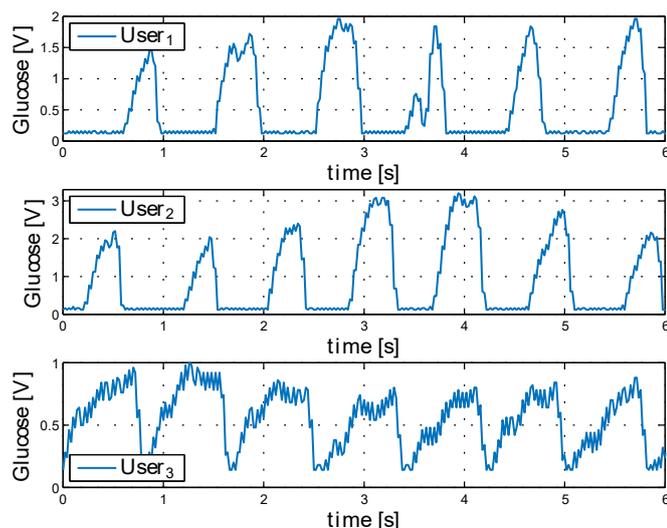


Figure 7: Reconstruction of the sensor filtered data.

2.5. Data processing

Finally, we obtained the system's transfer function using the recorded data and a modeling process based on regression,

computing the estimated glucose concentration by the GUI algorithm in the recording system. The transducing function that correlates voltage level with its corresponding glucose level is not part of this work; however, the computing procedure can be seen in the author's previous work (Vázquez et al., 2022). The algorithm takes the voltage signal to calculate the final glucose level, diagnose the patient according to the diabetes stages, and record it. Figure 8 depicts an example of the final-recording system GUI user's panel.

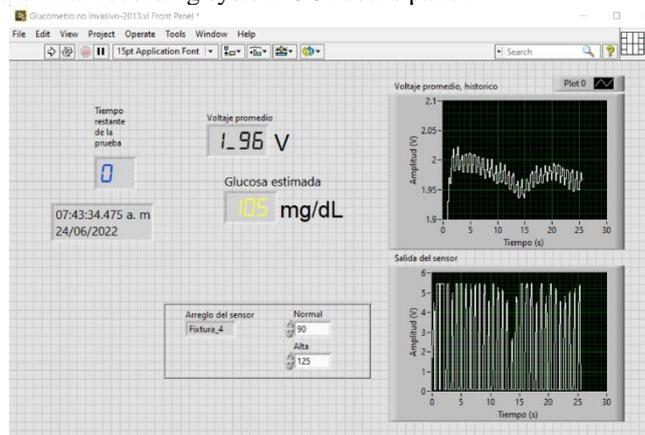


Figure 8: Recording system GUI.

3. Validation

The system's validation consists of three healthy volunteers, two men, and one woman, from different ages. Their ages are 22, 36, and 58 years old, respectively. The results of the glucose estimations are contrasted against the One touch Select Plus Flex glucometer, a commercial device based on an invasive method. According to its specifications, it meets the ISO 15197:2013 standard. The importance of this standard and the European version EN ISO 15197:2015 is the establishment of rules about the acceptable performance of blood glucose monitoring devices. The standard states that readings from the device shall fall within ± 15 mg/dL of the average values measured with the comparison method for blood glucose concentrations < 100 mg/dL and within $\pm 15\%$ for blood glucose concentrations ≥ 100 mg/dL for at least 95% of the system's results (Breitenbeck et al., 2017).

4. Results

The testing protocol involves applying photoplethysmography to measure and record the blood glucose concentration in the early morning after an overnight fast and repeating it for five consecutive days. The recording software reads the volunteers' glucose signals to define the glucose concentration level; they then measure it using the One Touch Select Plus Flex. Table 1 concentrates the results of three measures for both devices belonging to each subject. As seen from Table 1, Sensor-2 seems to be better than Sensor-1, being an error of about 7.9 % and about 14 %, respectively. However, this is a partial conclusion because the error computed is the deviation of each sensor compared with the One Touch Select Plus Flex measures; nonetheless, they all accomplish the NORM ISO 15197:2013. Therefore, there is necessary to achieve more assessments to define precision and

exactness because all commercial devices present variability in their measurements, even though they exhibit consistency and cope with the ISO 15197:2013 standard.

Table 1: Glucose concentration from two subjects in three different tests.

Subject	<i>Invasive glucometer: One Touch Select Plus Flex</i>	<i>Sensor-1</i>	<i>Sensor-2</i>	% Error <i>Sensor 1</i>	% Error <i>Sensor 2</i>
	(mg/dL)	(mg/dL)	(mg/dL)		
1	95	85	90	10.53	5.26
1	99	73	113	26.26	14.14
1	91	88	100	3.30	9.89
2	94	83	92	11.70	2.13
2	96	77	105	19.79	9.38
2	103	90	110	12.62	6.80

5. Conclusions

Blood glucose levels are commonly measured by invasive methods, causing pain to those living with this disease. PPG signals are a feasible technique able to estimate hemodynamic features in the time domain; however, blood glucose levels by PPG signals still to be an open field of study. In this work, the implementation of a device able to estimate glucose concentration in blood using a non-invasive method has been demonstrated. Two different devices are designed; the sensor with 950 nm produces a small average error in its estimations compared to the 940 nm sensor; according to the ISO 15197:201 standard, the results are acceptable. Nonetheless, more experimentation is needed to have conclusive results.

Acknowledgment

This work is partially supported by Tecnológico Nacional de México/ IT Tijuana grants 13486.21-P, “Sincronización de sistemas para el monitoreo y control de la diabetes mellitus tipo 1”.

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