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Comparative Analysis of Near-Infrared Light Absorption in Glucose and Blood Component Solutions With and Without 1 MHz Ultrasound Enhancement

Puteri Eyriena Maysara Yazit[a], Muhamad Amin Abd Wahab[a,*], Mohamad Ikhwan Jamaludin[a], Mohamad Ikhwan Kori[a], Muhammad Faiz Md Shakhih[a], Azli Yahya[a], Nasrul Humaimi Mahmood[a] and Awais Gul Airij[b]

[a]*Faculty of Electrical Engineering, Universiti Teknologi Malaysia, 81310 Johor Bahru, Malaysia*
[b]*Dawood University of Engineering and Technology, Karachi, Pakistan*
**Corresponding author. E-mail: muhamadamin.abdwahab@utm.my*

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ABSTRACT

Diabetes is a global health issue that affects approximately 537 million people. The prevalence of diabetes is projected to reach 783 million by 2045. Invasive glucometers and patch sensors provide effective management through continuous monitoring, but these devices are inconvenient and lead to poor compliance. Alternative methods such as non-invasive near-infrared (NIR) monitoring offer continuous monitoring, but these devices are also often vulnerable to ambient light interference and absorption by substances such as ascorbic acid. Recent studies have shown that ultrasound can enhance optical interactions and increase measurement sensitivity in complex fluids. In this study, a proof-of-concept system combining 1 MHz ultrasound with a 940 nm NIR LED-photodiode circuit was developed. Ultrasound-assisted glucose detection was evaluated under controlled fluid-solution conditions at glucose concentrations ranging from 0 to 300 mg/dL. To assess selectivity, samples were tested with and without 30 mg/dL ascorbic acid under ultrasound and non-ultrasound conditions. The results showed that ultrasound increased the sensitivity from 113 $\mu V/(mg{\cdot}dL^{-1})$ to 124 $\mu V/(mg{\cdot}dL^{-1})$ in glucose-only samples and from 71 $\mu V/(mg{\cdot}dL^{-1})$ to 74 $\mu V/(mg{\cdot}dL^{-1})$ in glucose-ascorbic acid samples. The result corresponds to an increase in sensitivity improvement from 7.37% to 19.60%. Ultrasound also improved linearity (R^2) and reduced Root Mean Square Error (RMSE) across all test conditions, indicating improved consistency. In terms of selectivity, the measurement remained high (>98%), with voltage differences below 2% between glucose-only and glucose-ascorbic acid samples. This confirms the minimal influence of external factors under the tested conditions. Overall, these findings indicate that combining ultrasound and NIR for glucose detection can improve the sensitivity and reliability of the signals in water-based glucose solutions. Further validation, such as using tissue-mimicking phantoms and in vivo studies, is required before this approach can be considered for non-invasive glucose monitoring applications.

Keywords: *Non-invasive glucose monitoring; NIR spectroscopy; Ultrasound; Diabetes*

1. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder defined by high blood glucose levels. The main cause is decreased insulin secretion [1]. In 2019, diabetes contributed to 1.5 million deaths worldwide and is expected to increase to 783 million cases by 2045 [2]. To reduce complications and monitor the disease, accurate and continuous glucose monitoring plays a crucial role. Conventional monitoring, such as glucometers and sensor patches, whether invasive or minimally invasive, causes discomfort and carries a risk of infection, especially in high-risk groups [3]. Due to these problems, there is a growing demand for alternative non-invasive glucose monitoring devices that can ensure patient comfort and improve quality of life [4].

Among the new non-invasive methods, near-infrared (NIR) spectroscopy has shown potential for detecting glucose by analysing light absorption in biological tissues. However, despite this method showing good potential, the technology is limited by the detection of weak glucose signals and interference from other absorbers, such as air, haemoglobin, and other substances in the blood [5, 6]. In addition, environmental variables such as ambient light and temperature changes affect the signal-to-noise ratio (SNR) and this can lead to a reduction in the accuracy of the measurement [7]. The presence of absorbing molecules such as lactate and ascorbate can cause additional spectral overlap, thereby reducing the selectivity of the measured readings [8, 9].

Recent studies show that ultrasound can enhance the optical properties of biological tissues and improve the performance of NIR-based glucose monitoring. In these studies, ultrasound can reduce light scattering and increase light penetration. In addition, acoustically modulating the target area with ultrasound significantly improves spatial resolution and overall signal strength [10, 11]. This combined approach between ultrasound and NIR has been explored through various mechanisms. One study that used 40 kHz ultrasound to induce molecular aggregation reported more effective glucose detection with infrared light [5]. In addition, more advanced systems use “ultrasound tagging of light,” in which focused ultrasound locates the optical signal deep within the tissue. One such system, NIRLUS®, has demonstrated high clinical accuracy in healthy subjects. Additionally, the measurement accuracy achieves a mean absolute relative difference (MARD) of

10.7% relative to the gold-standard laboratory reference [12]. In addition, ultrasound-modulated optical sensing (UOS), which combines ultrasound with a 1645 nm laser, focuses the optical signal in a 20 mm-thick phantom, achieving an MARD of 26.6% [13]. Ultrasound has also been shown to improve the accuracy of glucose estimates derived from physiological signals such as photoplethysmography (PPG)-based Perfusion Index [14].

Based on previous studies, this paper investigates whether combining a 1 MHz ultrasound with a 940 nm NIR system can improve the accuracy and selectivity of glucose detection in solution. The analysis focuses on the photodiode voltage response in glucose solutions alone and in glucose solutions mixed with ascorbic acid, under conditions with and without ultrasound. The concentration of ascorbic acid is fixed at 30 mg/dL. While the glucose concentration ranges from 0 to 300 mg/dL. This ascorbic acid level was chosen based on previous studies in which ascorbic acid concentration significantly affected glucometer readings [9]. Sensitivity and selectivity were used to assess whether ultrasound can improve the photodiode voltage response to glucose, thereby supporting a more reliable approach to non-invasive glucose monitoring.

For the NIR system, the 940 nm wavelength was chosen because previous studies have shown that it provides a strong correlation with glucose absorption ($R^2 \approx 0.99$) and is less affected by water interference than the 800 nm or 950 nm wavelengths [15]. For the ultrasound wave, the 1 MHz frequency was chosen based on previous findings that this frequency value increases the optical modulation depth by approximately 2.5× while ensuring stable propagation in aqueous media [11, 15]. Based on this information, the combination of the 940 nm NIR wavelength and 1 MHz ultrasound is used to investigate the effectiveness of glucose detection in solution.

2. MATERIALS AND METHODS

2.1. NIR Circuit Design and Experimental Setup

The NIR sensor system was developed using a Vishay VSLY5940 940-nm NIR LED as the light source. The system was powered by a 5 V supply in series with a current limiting resistor. To detect the emitted NIR light, a Hamamatsu S1223 silicon photodiode was used at the receiver. In addition, the photodiode output was also amplified using an LM358 operational amplifier (Op-Amp) configured in a non-inverting configuration and powered by a dual ±9 V power supply. The amplified analog signal produced by the photodiode was recorded using the analog input of an Arduino Uno microcontroller and visualized using Better Serial Plotter software. For the ultrasound system, a pair of Olympus A102S 1 MHz surface-contact transducers was used, with one serving as the transmitter (Tx) and the other as the receiver (Rx). Tx was driven by a 5077PR pulse/receiver at 400 V and 20 dB, and the Rx output was observed via a Tektronix TBS1062 digital oscilloscope. During measurement, the glucose sample is placed in a borosilicate beaker.

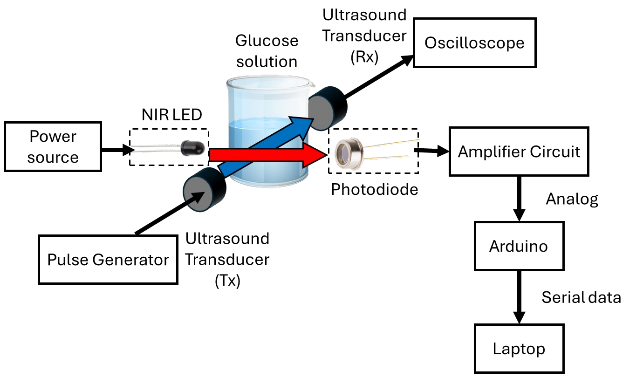

Figure 1 Experimental setup of the integration of the 940 nm NIR system with 1 MHz contact ultrasound. Red arrows indicate the propagation direction of NIR light, while blue arrows represent the direction of ultrasound wave transmission.

For the experimental setup, the NIR LED and photodiode were positioned facing each other to ensure light transmission through the solution in the beaker. At the same time, the ultrasound Tx and Rx were aligned on opposite sides of the beaker to ensure that both light and sound waves pass through the sample perpendicularly, reducing interference. All tests were conducted in a dark, enclosed room to avoid interference from external light [14]. Figure 1 shows a simplified experimental setup of the overall system. Photodiode voltage readings were taken at 30-second intervals and repeated ten times for each concentration. The data were averaged and filtered using a five-point moving average filter and analyzed using MATLAB software.

2.2. Glucose Solution Preparation

The glucose solution was prepared by dissolving anhydrous D-glucose ($C_6H_{12}O_6$) in distilled water. The glucose solution was prepared at concentrations of 0, 50, 100, 150, 200, 250, and 300 mg/dL, according to the relationship in Equation 1 [16]. Note: 1 deciliter (dL) equals 100 milliliters (mL).

$$Concentration, \rho i = \frac{Glucose\ powder\ (mg)}{Distilled\ water\ (dL)} \quad (1)$$

The 0 mg/dL solution served as a reference. For selectivity analysis, a 30 mg/dL ascorbic acid solution was prepared by dissolving 30 mg of L-(+)-ascorbic acid in 100 mL of distilled water. Then, 0.15 mL of ascorbic acid solution was added to each glucose concentration to simulate the presence of foreign substances in the glucose solution just like in blood. All prepared solutions were stored in sealed vials. This was to ensure consistency and prevent contamination during measurement. These samples were then used in the sensitivity and selectivity evaluation.

2.3. Circuit Functionality Test

Before the actual experimental measurements were performed, the NIR detection system was tested. The evaluation method was to align the LED and photodiode and vary the distance between them from 0 to 10 cm. During this test, no obstacles are placed between the LED and the photodiode. For each distance, the voltage readings are recorded continuously for 30 seconds, and the procedure is repeated 3 times to ensure consistent measurements. The resulting data is plotted as a graph of voltage versus distance. The purpose of this test is to verify the expected signal attenuation behavior and ensure proper alignment and response of the optical system.

Not only that, but the ultrasound system was also tested by sending and receiving ultrasonic signals across the same distance, but with a beaker containing a solution placed between Tx and Rx. The received waveform was monitored using a digital oscilloscope. The purpose of this test was to ensure that the ultrasound waves penetrated the beaker containing the solution.

2.4. Sensitivity and Selectivity analysis

This sensitivity and selectivity analysis focused solely on the photodiode voltage response to varying glucose concentrations under the conditions of glucose solution alone and glucose solutions mixed with ascorbic acid, both with and without ultrasound. Sensitivity was assessed by correlating glucose concentration with voltage using three metrics: coefficient of determination (R^2), root mean square error (RMSE), and average slope (sensitivity). The slope, which represents the rate of change in voltage per mg/dL of glucose, was calculated using the point-to-point slope method (Equation 2) [17,18],

$$Sensitivity = \frac{1}{n}\sum_{i=2}^{n}\left|\frac{V_i - V_{i-1}}{G_i - G_{i-1}}\right| \tag{2}$$

where V_i and V_{i-1} represented the consecutive voltage readings, G_i and G_{i-1} were the corresponding glucose concentrations, and n was the number of data points used. Interpretation of the strength of correlation for the Pearson correlation coefficient follows the scale defined in previous research [19]. The percentage increase in sensitivity attributable to the presence of ultrasound was determined using Equation 3.

$$Percentage\ increase\ (\%) = \frac{S_{WU} - S_{WoU}}{S_{WoU}} \times 100 \tag{3}$$

Where S_{WU} is the sensitivity with ultrasound, and S_{WoU} is the sensitivity without ultrasound. In addition, selectivity was assessed by comparing the voltage responses of solutions with and without ascorbic acid under both ultrasound and no ultrasound conditions. The purpose is to determine whether ultrasound can enhance the system's ability to distinguish glucose from external substances such as ascorbic acid. Selectivity was measured using Equation 4, both at individual concentrations and by comparing average slopes.

$$Selectivity(\%) = \frac{Glucose+acid\ detected}{Glucose\ detected} \times 100 \tag{4}$$

3. RESULTS AND DISCUSSION

3.1. NIR Circuit Functionality Test and Ultrasound Transmission

The NIR circuit functionality test was conducted in a dark environment (lights off) to evaluate the signal between the NIR LED and the photodiode at distances of 0- 10 cm. The voltage results show a decreasing trend, with a reading of 4.903 V at 0 cm and 2.11 V at 10 cm. As shown in Figure 2, the optimal operating range is clearly identified between 0 and 2 cm, where the signal strength remains consistent. Beyond 3 cm, a significant voltage drop can be observed. This indicates a significant decrease in detection capability for distances of 3 cm and above. Based on this observation, the effective NIR detection range is estimated to be approximately 0 to 3 cm. This result agrees with the behavior shown in a previous study [20], which showed an optimal range of up to 2 cm. The slightly different results may be due to differences in circuit sensitivity, emitter-detector alignment, or optical path configuration between the systems. For ultrasound transmission, the Tx and Rx are placed facing each other with a beaker containing a distilled water solution placed between them.

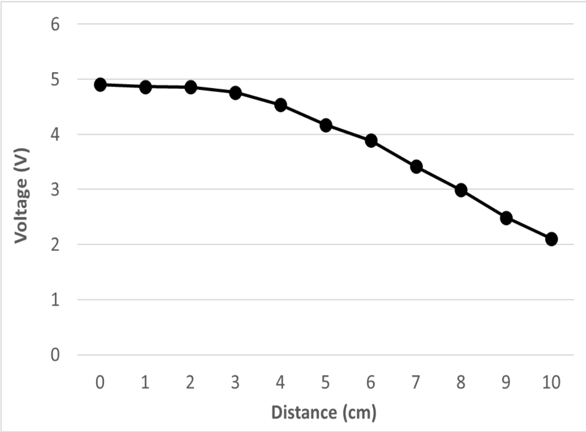

Figure 2. Voltage responses at varying distances between the 940 nm NIR LED and photodiode without a sample.

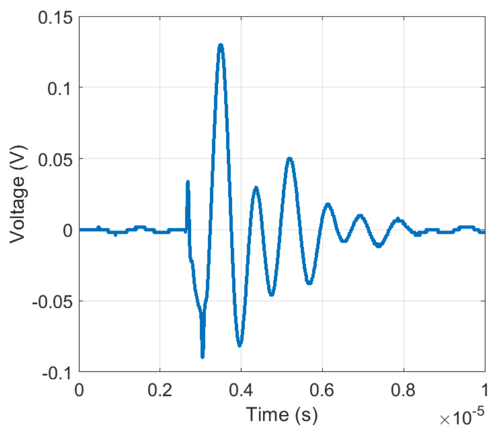

Figure 3. Ultrasound waveform captured during propagation through solution, confirming stable transmission.

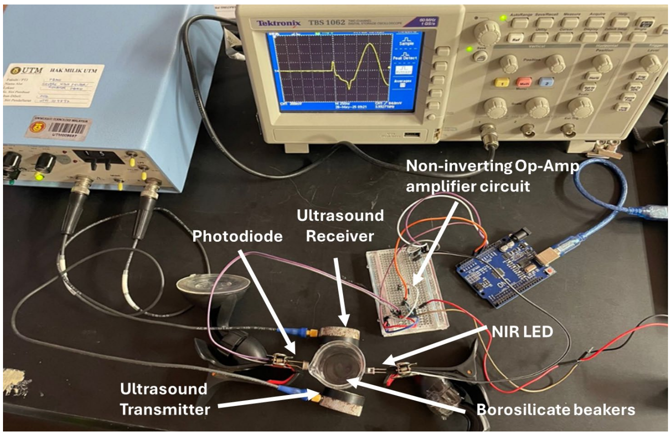

Figure 4. Integration of the NIR circuit with the 1 MHz ultrasound transmission system.

The receiver's successful detection of the signal confirms that the ultrasound wave propagated through the solution, as shown in Figure 3. Figure 4 shows the experimental setup used in the study, and all measurements are taken in a dark environment.

3.2. NIR Measurement Response for Glucose and Glucose + Ascorbic Acid with and Without Ultrasound

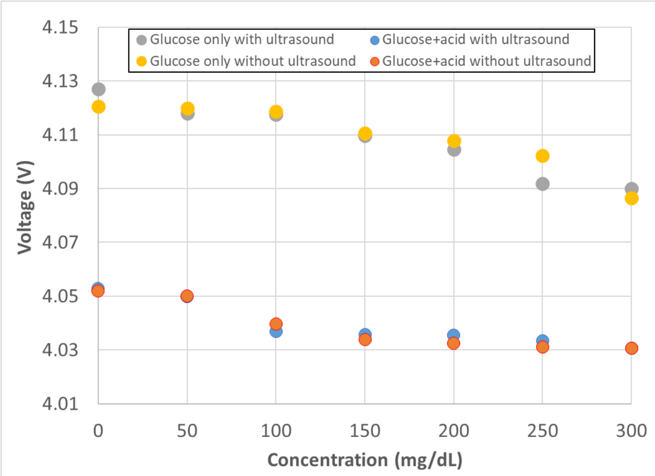

Figure 5. Voltage measured for glucose and glucose+acid with and without ultrasound.

Across all tested concentrations (0–300 mg/dL), the measured voltages for glucose-only solutions were consistently higher than those for glucose + ascorbic acid, under both ultrasound and non-ultrasound conditions, as shown in Figure 5. The reduction in glucose + ascorbic acid responses is more likely due to scattering and solution effects, combined with the strong reducing properties of ascorbic acid, rather than to direct absorbance at 940 nm. The results are consistent with previous electrochemical and optical studies, in which the interference of vitamin C is caused by its redox activity rather than by any specific NIR absorption peak [9, 15, 21].

Despite some interference, the system consistently distinguished between glucose solution alone and glucose with ascorbic acid. This indicates good selectivity capability. The use of ultrasound further enhances the ability to distinguish between glucose solution alone and glucose solution with ascorbic acid, improving detection robustness. Previous studies have also reported that ascorbic acid can interfere with glucose readings in electrochemical systems [9]. This result reinforces its role as a relevant interferent in assessing selectivity.

3.3. Sensitivity Analysis

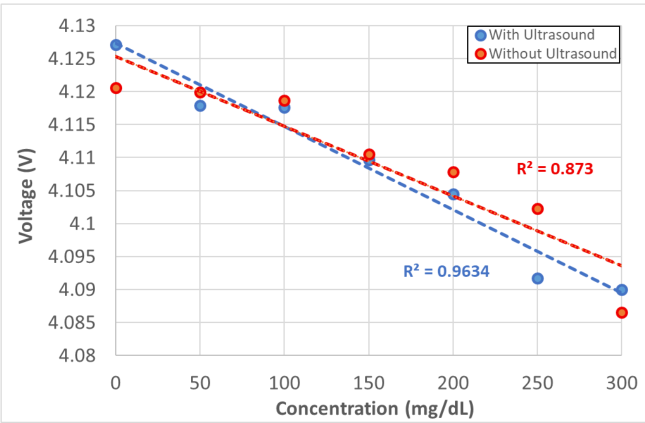

Figure 6. Correlation between glucose (only) concentration and NIR voltage measured.

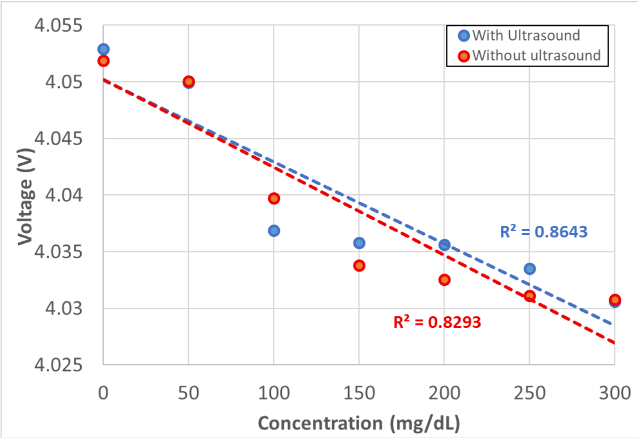

Figure 7. Correlation between glucose + ascorbic acid concentration and NIR voltage measured.

The sensitivity of the NIR prototype was tested with glucose solutions ranging from 0 to 300 mg/dL. A solution of 0 mg/dL was used as a reference point. To assess how other ingredients affected the solution, tests were also conducted on a glucose solution containing 30 mg/dL of ascorbic acid. Figures 6 and 7 show that the voltage reading decreases as the sugar concentration increases. This means the NIR signal weakens as the glucose concentration increases. This is because, when a solution has more molecules, the NIR light reaching the photodiode decreases. This results in a weaker signal as the glucose concentration increases. The results of this study are in good agreement with findings from other studies and with the Beer-Lambert principle [20, 15].

Table 1 summarizes the sensitivity and linearity results of the NIR sensor under different conditions. In terms of sensitivity, the results show an increase from 113 $\mu V/(mg \cdot dL^{-1})$ without ultrasound to 124 $\mu V/(mg \cdot dL^{-1})$ with ultrasound in the glucose solution alone. This increased the sensitivity by 7.37%. The same trend was observed in the glucose solution with ascorbic acid, where the sensitivity increased from 71 $\mu V/(mg \cdot dL^{-1})$ to 74 $\mu V/(mg \cdot dL^{-1})$, corresponding to a 19.60% increase.

Table 1 Sensitivity and Linearity of NIR Sensor under Different Condition

Condition	Sensitivity ($\mu V/mg \cdot dL^{-1}$)	Sensitivity Increase (%)	R^2 Value	RMSE
Glucose (without ultrasound)	113	-	0.8730	0.004035
Glucose (with ultrasound)	124	+7.37	0.9634	0.002461
Glucose + Acid (without ultrasound)	71	-	0.8293	0.003074
Glucose + Acid (with ultrasound)	74	+19.60	0.8643	0.003277

Even though the increase in sensitivity (~11 μV) appears small, the significance of these results lies in the simultaneous increase in linearity (R^2 from 0.8730 to 0.9634) and reduction in RMSE. The increase in linearity indicates that the presence of ultrasound can improve the stability and reproducibility of glucose measurements. This is important for reliable non-invasive monitoring. Although the change in μV levels is small relative to physiological glucose variations in human blood (70–180 mg/dL), it demonstrates the potential of the acoustic-optical combination to enhance signal robustness and reduce interference in glucose measurements [12].

These findings show that ultrasound can improve signal responsiveness across different sample types. This is likely because it increases light-matter interactions and reduces signal variability. Previous studies, like [14], have found that 40 kHz ultrasound can significantly improve glucose measurement accuracy by reducing the Mean Absolute Error (MAE), narrowing the agreement, and increasing the correlation between Perfusion Index (PI) and glucose levels. Other studies, such as [11], have reported that ultrasound bursts can increase the depth of signal modulation by 2.5-fold, allowing their system to clearly distinguish glucose levels, which is something that conventional optical measurements cannot achieve. Additionally, research [5] has shown that ultrasound can enhance the glucose signature by promoting molecular aggregation, further supporting the beneficial role of acoustic waves in optical glucose detection.

Additionally, the use of ultrasound increased linearity, with the R^2 value rising from 0.8730 to 0.9634 in glucose samples alone and from 0.8293 to 0.8643 in glucose samples with ascorbic acid. The RMSE also decreased under both ultrasound conditions, indicating reduced measurement error. Overall, these results confirm that integrating ultrasound improves the efficiency and consistency of NIR-based glucose detection.

3.4. Selectivity Analysis

The selectivity of the NIR sensor was measured by comparing voltage responses to glucose-only and glucose with ascorbic acid solutions across concentrations from 0 to 300 mg/dL. This was done under both ultrasound and non-ultrasound conditions. Table 2 shows that the point-based selectivity values remained high, between 98.08% and 98.63% without ultrasound and between 98.04% and 98.58% with ultrasound. This means voltage deviations were less than 2%. The presence of 30 mg/dL ascorbic acid caused minimal interference in the NIR signal response. These findings show the prototype had strong selectivity. It reliably distinguished glucose concentrations, even in the presence of a reducing substance. Slope-based selectivity analysis also supports this result. This calculated selectivity was 59.67% without ultrasound and 62.83% with ultrasound. Although the slope decreased with ascorbic acid, the improvement observed under ultrasound suggests greater stability in mixed environments.

Ascorbic acid slightly reduced linearity. R^2 values went from 0.8730 to 0.8293 without ultrasound, and from 0.9634 to 0.8643 with ultrasound. However, voltage deviations between glucose-only and glucose + acid remained below 2% across all concentrations, as shown in Table 2. This means ascorbic acid causes minimal interference. The improved slope-based selectivity under ultrasound, from 59.67% to 62.83%, further shows the NIR prototype's robustness, especially with ultrasound. These results are consistent with previous studies on optical glucose sensing [22, 23], which show strong correlation and selectivity, across different detection methods.

Table 2 Point-Based and Slope-Based Selectivity at Each Glucose Concentration Between Glucose Solution Alone Vs. Glucose Solution with Ascorbic Acid with and Without Ultrasound

Glucose Concentration (mg/dL)	Selectivity (%)	
	Without ultrasound	**With ultrasound**
0	98.33	98.20
50	98.30	98.35
100	98.08	98.04
150	98.13	98.20
200	98.17	98.32
250	98.26	98.58
300	98.63	98.55
Slope-based Selectivity		
Slope	59.67%	62.83%

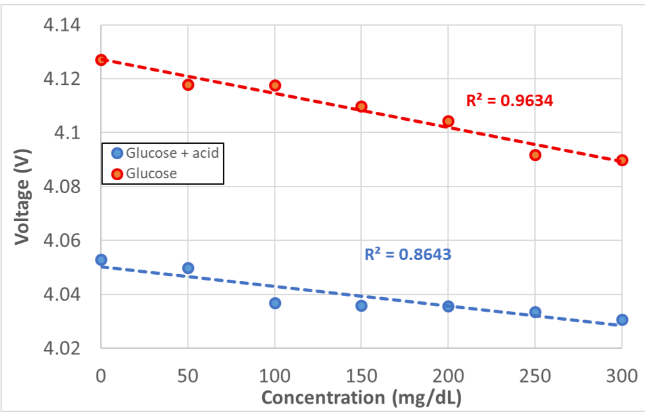

Figure 8. Correlation Between Glucose Solution Composition and NIR Voltage with Ultrasound.

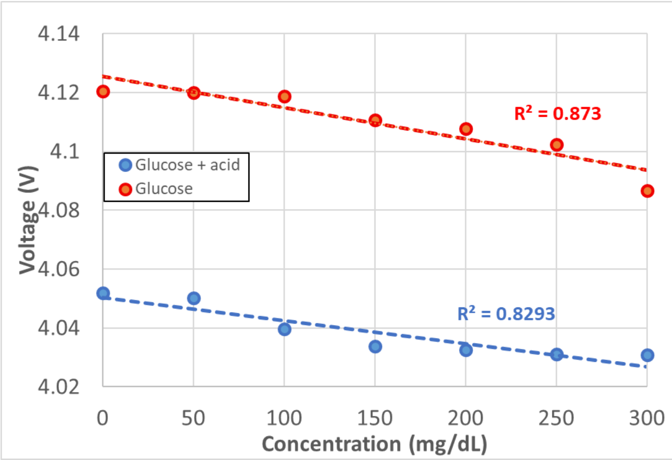

Figure 9. Correlation Between Glucose Solution Composition and NIR Voltage without Ultrasound.

Although the prototype showed improvements in sensitivity and selectivity, its sensitivity values (113 μV/(mg·dL^{-1}) to 124 μV/(mg·dL^{-1})) remain lower than those of commercial glucometers, which typically detect around 10 mg/dL [15]. Compared with other NIR optical systems, such as Attia et al. [20], which reported a rate of 26.25 μV/(mg·dL^{-1}), our system required ultrasound assistance to achieve better linearity (R^2 up to 0.9634) and a reduced rate (RMSE = 0.002461) [15]. This comparison indicates that, although this device has not yet reached clinical standards, combining acoustic and optical mechanisms can improve robustness and shows potential for further development. Overall, the system demonstrated reliable selectivity and resistance to signal distortion by common interfering agents, such as ascorbic acid, thereby reinforcing the effectiveness of ultrasound-assisted NIR detection for glucose detection.

4. CONCLUSION

This study presents the development of a 940 nm NIR detection prototype integrated with 1 MHz ultrasound for glucose detection in aqueous solutions. The system exhibits a consistent inverse voltage response as glucose concentration increases. The incorporation of ultrasound improves measurement performance, as evidenced by increased sensitivity (from 113 μV/(mg·dL^{-1}) to 124 μV/(mg·dL^{-1})), improved linearity (R^2 improved from 0.8293 to 0.8643), and low error (RMSE 0.0 out of 03).

The prototype also exhibits good selectivity under the tested conditions, with voltage deviation remaining below 2% even in the presence of an interfering agent of 30 mg/dL ascorbic acid. These findings also indicate that NIR detection combined with ultrasound can improve signal quality and measurement consistency in a controlled solution-based environment. However, the current results are limited to aqueous glucose solutions and do not account for optical scattering, absorption, or the biochemical complexity of real blood or biological tissues. In addition, the system uses a single NIR wavelength, a single interferent, and a fixed ultrasound frequency of 1 MHz, which limits its spectral, biochemical, and acoustic representations. Future work will focus on validation using tissue-mimicking phantoms, inclusion of additional blood related interferents such as hemoglobin and urea and investigation of different ultrasound frequencies or power levels. These steps are necessary to further evaluate the feasibility of translating the proposed approach towards non-invasive glucose monitoring applications.

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