Results in Engineering 20 (2023) 101506

Contents lists available at ScienceDirect

Results in Engineering

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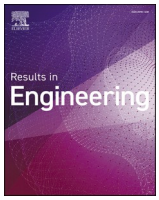

The effect of temperature on permittivity measurements of aqueous solutions of glucose for the development of non-invasive glucose sensors based on electromagnetic waves

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ARTICLE INFO

Keywords:
Permittivity
Dielectric constant
Temperature effect
Non-invasive biosensor
Glucose

ABSTRACT

This article presents for the first time an empirical study that shows the importance of considering temperature when analyzing the permittivity (dielectric constant) of aqueous glucose solutions of various concentrations. The permittivity is a parameter that is investigated by researchers as a biomarker for non-invasive measurement of glucose without drawing blood. The development of this technology will allow personalized healthcare diagnostics to monitor and prevent diabetes. Since human glucose levels in the blood vary in the range of a few milligrams per decilitre, estimating such small variations of glucose will require a highly accurate and repeatable sensing technology. Electromagnetic (EM) waves, specifically in the microwave and terahertz frequency ranges, have shown promise in detecting changes in the electrical properties of blood plasma as they relate to glucose concentration. However, it's important to note that while this technology shows promise, it is still in the research and development phase. It is shown here that the body temperature can affect the accuracy of the blood glucose measurements. Experiments were conducted with different glucose concentration solutions under various temperatures and the complex permittivity of the glucose was studied across a wide frequency range from 400 MHz to 11 GHz. The rise in thermal energy normally causes dipolar liquids like water to vibrate and rotate disrupting the alignment of the dipoles in response to an electric field thereby reducing its permittivity. Empirical results however show that for aqueous solution of glucose the permittivity increases with rise in temperature from 16 °C to 37 °C. This is attributed to the polar nature of the water and glucose molecules that becomes more pronounced with increased thermal energy. Based on the experimental results an accurate analytical expression is derived that considers the temperature of the aqueous glucose solution. The accuracy of the analytical expression is shown experimentally to be above 99%. The findings from the study should enable the design of accurate non-invasive glucose monitoring devices based on electromagnetic sensing techniques.

1. Introduction

According to the World Health Organization there are currently 420 million people globally that are living with diabetes [1]. In fact, deaths related to diabetes have increased by 70 % between 2000 and 2019. This debilitating disease affects about 8.8% of the world's population, and it is estimated to increase to 9.9% by the year 2045, which translates to roughly one person in ten [2]. The consequence of diabetes is that it can severely damage the major organs, including the heart, eyes, kidney, and brain [3]. However, the effects of diabetes can be kept at bay by controlling the blood glucose level. In adults, the glucose concentration in the range of 50–180 mg/dL is considered to be healthy.

Glucose monitoring plays a crucial role in helping people to lead a healthy lifestyle. Even though there are several ways to measure the level of glucose in the body they are all essentially invasive techniques including the continuous glucose monitor (CGM). Traditional techniques of measuring glucose involve drawing blood by pricking the finger [4–6]. A person afflicted with diabetes needs to prick their finger

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https://doi.org/10.1016/j.rineng.2023.101506
Received 13 August 2023; Received in revised form 25 September 2023; Accepted 9 October 2023
Available online 10 October 2023

at least twice daily, and over a year they would have pricked their finger more than 700 times. However, CGM works by inserting a miniature sensor needle under the skin to measure the glucose level in the interstitial fluid. This sensor determines the level of glucose every few minutes and wirelessly transmits the information to a remote monitor. Even though CGM can be used to manage Type 1 or Type 2 diabetes, the sensor needs to be replaced every seven days, which can be expensive. CGM modality of body glucose measurement has several limitations, which are (i) it underestimates glucose excursions, i.e., fluctuations in the blood sugar, (ii) it requires daily calibration for accuracy, and (iii) it can take about five to 25 minutes longer to show rise in glucose readings compared to venous blood glucose.

Wireless wearable healthcare devices are becoming very popular. These small electronic devices can measure multiple body parameters such as temperature, blood pressure, blood oxygen, breathing rate, physical movement, and the electrical activity of the heart. However, there is a need for intelligent wearable non-invasive sensor for real-time monitoring of blood glucose. This sensor must be designed such that it be accommodated into a smart watch-like device. It should be able to determine the level of glucose from biofluids such as perspiration. Reported in Ref. [7] is a distinct correlation between the glucose concentration, permittivity, and microwave signals [7]. This means the permittivity of glucose can be used as a direct biomarker to determine the level of glucose in the blood. It should be noted that microwave signals are non-ionizing radiation and are not harmful to human health at low power levels of exposure. The Federal Communications Commission (FCC) and other regulatory agencies around the world have established guidelines and safety standards to limit human exposure to non-ionizing radiation. The license free frequency bands centered at 915 MHz, 2.45 GHz and 5.8 GHz are classified under the industry, scientific and medical (ISM) bands. The maximum power at ISM bands is restricted to 1 Watt (30 dBm) [8,9].

In the literature published to date on non-invasive measurement of glucose using electromagnetic (EM) waves, no one has considered the effects of temperature on the measurements [5,7,10]. This paper presents the results of a new study showing how the permittivity of aqueous solutions of glucose are affected by temperature variations. The experimental results presented here show that if the temperature of the aqueous glucose solution is not considered in the permittivity measurements there will be error in the prediction of the glucose concentration level. It is shown here that a small error in permittivity can translate into a significant error in the glucose concentration level.

The paper is structured as follows: Section 2 covers materials and methods, Section 3 presents experimental results, Section 4 discusses overall results, and the work is concluded in Section 5.

2. Materials and methods

2.1. Tested solutions

According to the World Health Organization (WHO) normal fasting blood glucose concentration is between 70 mg/dL and 100 mg/dL [11]. It is recommended that the glucose level in blood be maintained in the range between 80 mg/dL and 130 mg/dL prior to eating a meal. Hypoglycemia is a condition when the glucose level falls below 80 mg/dL and immediate medical treatment is required. On the other hand, Hyperglycemia occurs when the glucose level is above 180 mg. Hyperglycemia that lasts can exacerbate and cause serious health problems including a diabetic coma. After eating a meal, glucose in the blood climbs up to 180 mg/dL but this will eventually fall after a couple of hours. Considering these glucose levels, six solutions of different glucose concentrations were accurately prepared as listed in Table 1. The solution medium was prepared using deionized water. These glucose solutions were used in the subsequent experiments to understand how the permittivity of each of these solutions was affected by temperature. A sample of glucose solution with 5000 mg/dL concentration was considered only for research purposes as it is very unlikely for blood glucose levels to reach such high levels.

Table 1
Aqueous glucose solutions used in the study.

Sample	Glucose concentration level (mg/dL)	Clinical condition
1	55	Hypoglycemic
2	80	Normal
3	120	Normal
4	180	Normal after meals
5	300	Hyperglycemic
6	5000	hyperglycemic

2.2. Measurement setup

The permittivity of the aqueous glucose solution samples in Table 1 were measured using a precision dielectric measurement system from SPEAG. The probe used in the study is Dielectric Assessment Kit (DAK) 3.5 mm designed to measure the permittivity from 200 MHz to 20 GHz. The measurement setup is shown in Fig. 1. The probe, which is connected to a Vector Network Analyzer (VNA), was immersed into the glucose sample such that the electromagnetic (EM) fields at the probe end are perturbed by the glucose solution under test and the resulting reflection coefficient (S_{11}) was measured with the VNA. The complex permittivity was then computed from using the following expression [12]:

$$\boldsymbol{\varepsilon}^{*} = \boldsymbol{\varepsilon}^{'} - \boldsymbol{j}\boldsymbol{\varepsilon}^{''} = \boldsymbol{\varepsilon}^{*} + \frac{\boldsymbol{\sigma}^{*}}{\boldsymbol{j}\boldsymbol{\omega}} = \left(\boldsymbol{\varepsilon}^{'} + \frac{\boldsymbol{\sigma}^{''}}{\boldsymbol{\omega}}\right) - \boldsymbol{j}\left(\boldsymbol{\varepsilon}^{'} + \frac{\boldsymbol{\sigma}^{'}}{\boldsymbol{\omega}}\right) \quad (1)$$

where $\boldsymbol{\varepsilon}^{'}$ is the real part of the permittivity and represents the ability of the glucose solution to store the EM energy, and $\boldsymbol{\varepsilon}^{''}$ is the imaginary part of the permittivity and represents the degree of EM energy is lost in the solution. $\boldsymbol{\sigma}^{*} = \boldsymbol{\sigma}^{'} + \boldsymbol{j}\boldsymbol{\sigma}^{''}$ is the complex electric conductivity and $\boldsymbol{\omega}$ is the angular frequency.

The permittivity of the six glucose samples of various concentrations listed in Table 1 were studied over a temperature range (10°C to 37°C) encompassing the human body temperature and across the frequency range between 400 MHz and 11 GHz. The measurement of the dielectric constant was taken at an interval of 100 MHz in the specified frequency range. Prior to conducting the experiment, the DAK probe was calibrated. The calibration was crucial prior to taking measurements for several reasons, i.e., (i) to mitigate any systematic errors in the readings and ensure that the probe provides accurate and reliable measurements, (ii) to negate manufacturing variations and differences between individual probes, (iii) to account for temperature-related variations, (iv) to adjust the probe's response to different frequencies, ensuring that measurements are accurate and consistent across the desired frequency range, and (v) to account for environmental factors, such as humidity and pressure, which can influence dielectric measurements. Three high-quality standards were used in the calibration. The initial standard was 'open', in this case, the probe is exposed to an open environment. In the next stage, the probe was 'shorted' using a Copper (Cu) strip. And finally, the probe was immersed in a defined load. In this case, the load was deionized water at room temperature (23°C).

2.3. Measurement procedure

The steps taken to measure the permittivity were as follows:

1. Preparation: Calibrate the dielectric measuring probe using reference standards with known permittivity values. This step ensures that the instrument is set up correctly and provides accurate measurements.
2. Sample Preparation: Prepare the glucose solutions of specified concentrations. Ensure that the solutions are at the desired temperature.

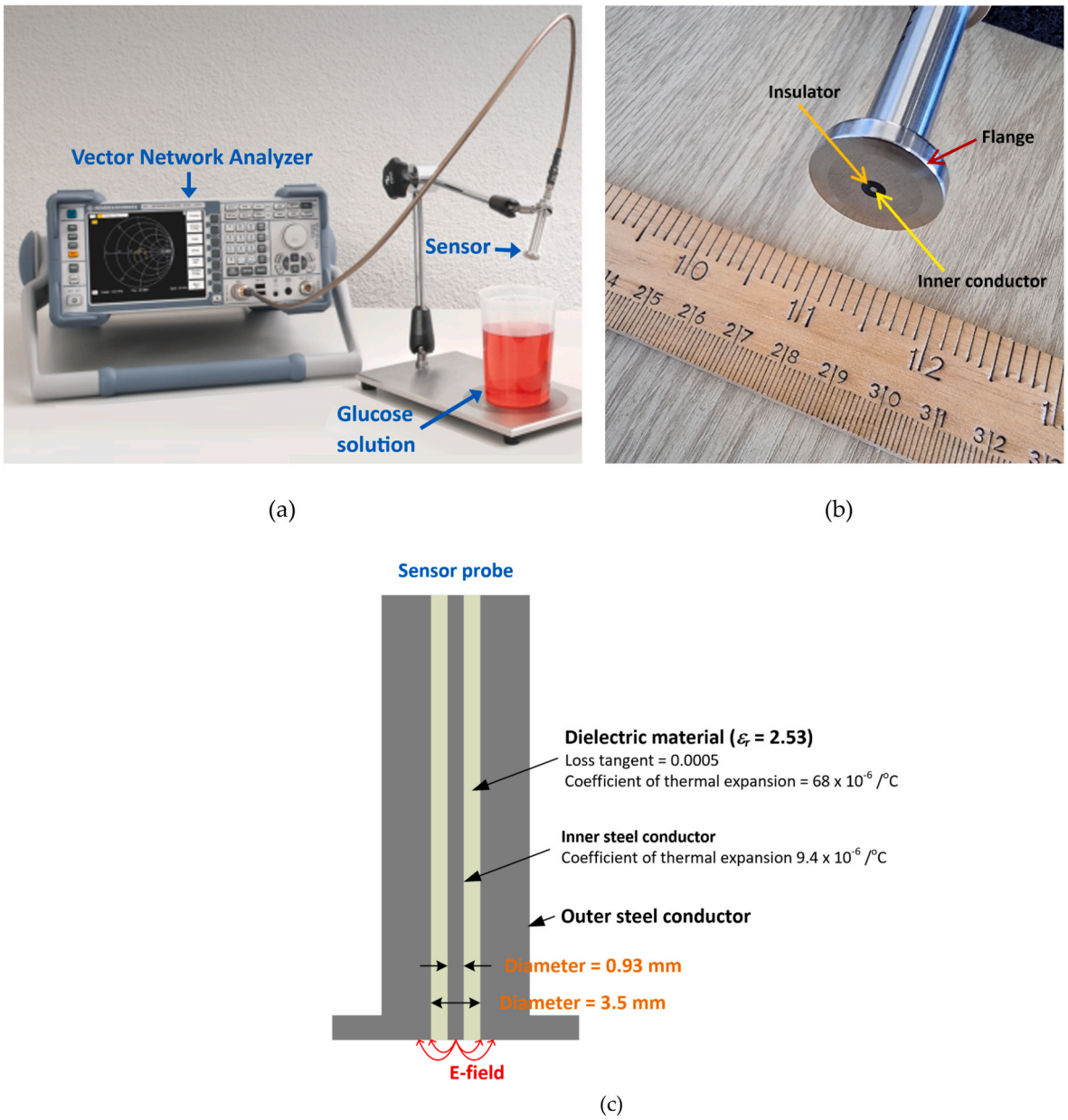

Fig. 1. (a) Measurement setup showing SPEAG's dielectric probe sensor (DAK 3.5 mm) inserted in a glucose solution to measure its permittivity (please note, red dye was added to the glucose solution purely for the purpose of clarity in the picture), (b) close-up view of the probe sensor, and (c) cross-section of the coaxial probe sensor. Note, the coefficient of thermal expansion of water is 210 × 10^{-6}/°C.

3. Measurement Setup: Immerse the probe into the glucose solution. Make sure it is properly positioned.
4. Measurement: (i) Initiate the measurement on the instrument, (ii) Allow the measurement to stabilize over 10 min, and (iii) Record the permittivity value provided by the instrument.
5. Repeat Measurements: Take multiple measurements of the same solution and calculate the average.
6. Cleansing: Clean the probe with deionized water and dry before taking new measurements.

Initially the temperature of each glucose sample was lowered to precisely 10°C. This was done by refrigerating the samples. However, when the samples were exposed to the lab environment for measurement, the temperature of the sample began to increase. It was therefore necessary to stabilize the temperature of the samples. The temperature of the samples was continuously monitored using a digital thermometer. All measurements were conducted in a temperature-controlled environment. The permittivity of each sample at the specified temperatures were measured with the DAK probe across 400 MHz and 11 GHz at intervals of 100 MHz. The permittivity measurements were made after immersing the probe fully in the aqueous glucose solutions for 10 min to negate the effects of the thermal expansion coefficients constituting the probe. To maintain the measurement accuracy and prevent contamination the dielectric probe was cleaned with deionized water each time it was used with a different glucose solution.

3. Experimental results

The permittivity (ε') of the glucose samples of concentration 55 mg/dL to 300 mg/dL were measured with the DAK probe between 400 MHz and 10.9 GHz. The measured results in Fig. 2(a) show the permittivity of glucose to decrease from 78 to 60 with increase in frequency from 400 MHz to 10.8 GHz. At low frequencies, the glucose molecules in the dipole fluid (deioniszed water) have enough time to polarize and align

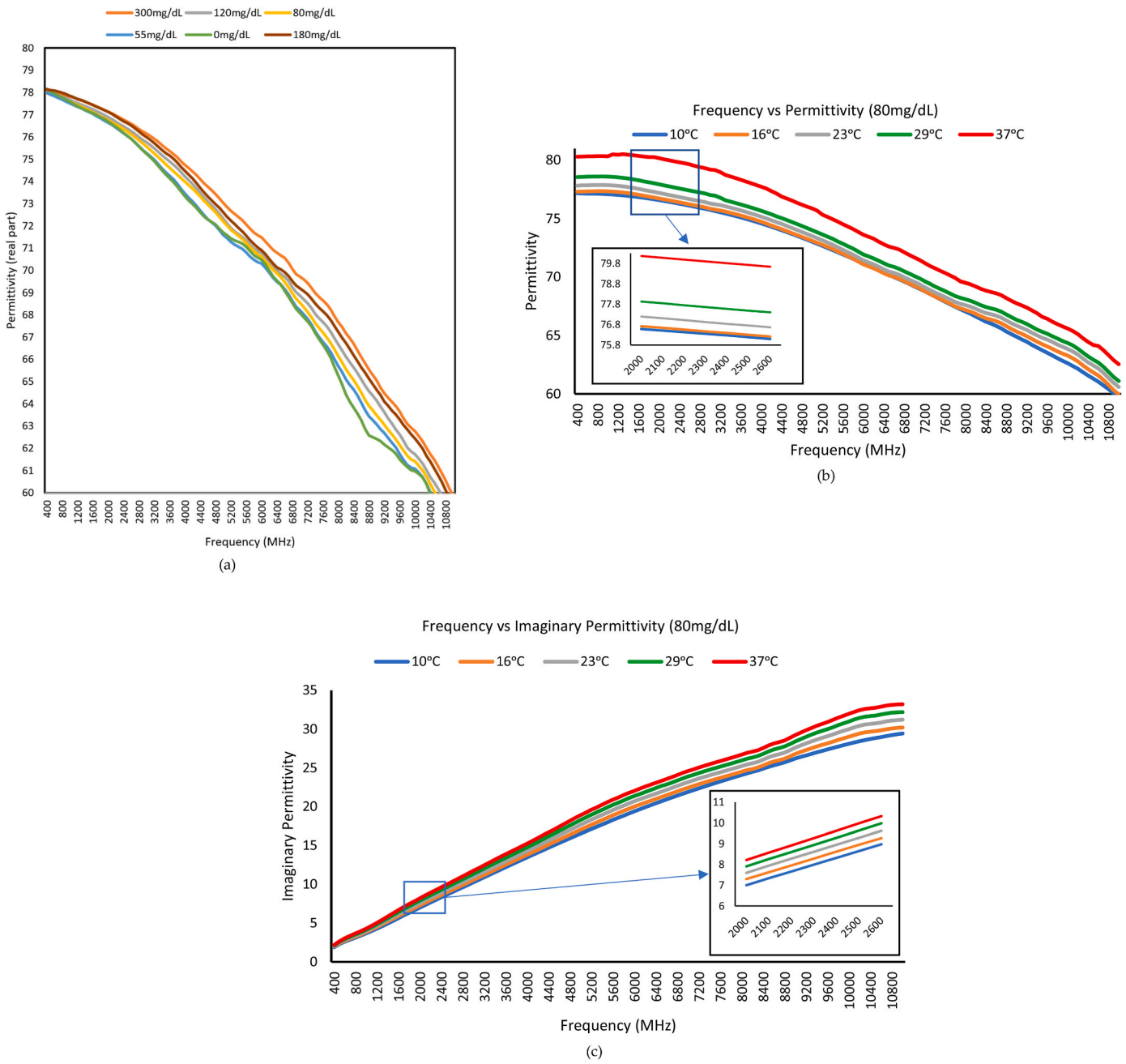

Fig. 2. Measured permittivity of the glucose sample as a function of frequency, (a) real part of glucose concentrations from 55 to 300 mg/dL, (b) real part of 80 mg/dL glucose concentration as a function of temperature, and (c) imaginary part of 80 mg/dL glucose concentration as a function of temperature.

themselves with the alternating electromagnetic field. This alignment contributes to a higher permittivity. However, at higher frequencies, the molecules don't have sufficient time to adjust their orientation fully, resulting in reduced polarization and a lower permittivity. The permittivity of the glucose solutions of different concentration converge at 400 MHz however the differential in the measurements becomes pronounced with increase in frequency. In fact, the permittivity at any given frequency tends to increase with increase in glucose concentration. This is because glucose is a polar molecule which reacts to an applied electric field. As the concentration of glucose in the solution increases, more polar molecules are available to respond to the electric field, thus increasing the overall permittivity of the solution. This graph confirms the use of permittivity as a biomarker for determining the concentration of glucose in body fluids.

Fig. 2(b) and (c) show the real and imaginary parts of the permittivity, respectively, of the 80 mg/dL glucose sample measured at five different spot temperatures, i.e., 10°C, 16°C, 23°C, 29°C, and 37°C, across 400 MHz and 10.8 GHz. Fig. 2(b) shows the real part of the permittivity decreases with increase in frequency, and at any given frequency the permittivity increases with temperature. Both water and glucose are polar molecules and as the temperature is increased, the kinetic energy of molecules in the solution increases. The resulting molecular motion leads to more rapid oscillations of molecules resulting in a greater ability to respond to an applied electric field, which in turn leads to a higher permittivity. A close up view between 2 GHz and 2.6 GHz show the variation in permittivity with freqency to be approximately linear. Also, at any frequency between 2 GHz and 2.6 GHz, the permittivity gap between 10°C and 16°C is much closer. Also, the permittivity gap between 10°C and 23°C is much tighter at frequencies between 5.6 GHz and 7.6 GHz.

The imaginary part of the permittivity of glucose increases with increase in frequency, as shown in Fig. 2(c). As explained earlier at higher electromagnetic frequencies the glucose molecules don't have enough time to fully reorient themselves, leading to incomplete alignment and energy dissipation. This energy dissipation is manifested as an increase in the imaginary part of the permittivity. Across 400 MHz and 10.8 GHz, the imaginary part of the glucose permittivity increases from around 2 to 32. Also, the gap of the imaginary permittivity tends to increase with increase in frequency. A close up view in Fig. 2(c) between 2 GHz and 2.6 GHz shows that the imaginary part of the permittivity having a linear relationship with increase in frequency, and the gap between the imaginary part of the permittivity is approximately the same for the five spot temperatures between 10°C and 37°C.

The mechanism behind the change in permittivity with frequency and temperature can be explained using the equation for complex permittivity is given by Ref. [13]:

$$\varepsilon^* = \varepsilon_\infty + \frac{\varepsilon_o - \varepsilon_\infty}{1 + j\omega\tau} \tag{2}$$

where ε_o is permittivity at low frequency, ε_∞ is permittivity at high frequency, ω is angular frequency, τ and is relaxation time. This relationship of relates permittivity with frequency. According to Ref. [14] the imaginary part of the dielectric constant are given by:

$$\varepsilon' = \varepsilon_\infty + \frac{\varepsilon_o - \varepsilon_\infty}{1 + (\omega\tau)^2} \quad and \quad \varepsilon'' = -\frac{(\varepsilon_o - \varepsilon_\infty)\omega\tau}{1 + (\omega\tau)^2} \tag{3}$$

$$\varepsilon_o - \varepsilon_\infty = \left(\frac{3\varepsilon_o}{2\varepsilon_o + \varepsilon_\infty}\right) \frac{4\pi n g \mu^2}{3kT} \tag{4}$$

where n dielectric constant, μ is dipole moment, g is parameter related to dipole interaction, and T is the temperature. Eqn. (4) shows how the permittivity is related to temperature. Precise mathematical models that predict the permittivity as a function of temperature are presented in Section 3.2.

The above results show different concentration samples of glucose solution exhibit a similar permittivity trajectory as a function of frequency however the differential in the magnitude of the permittivity of the glucose solutions (80 mg/dL and 300 mg/dL) is within a fraction of a percentage at any given frequency. It should be noted that at any given frequency even though the variation in the permittivity of the different concentration samples is relatively small and the change in the permittivity with temperature is small too, however this small variation in the permittivity corresponds to a large variation in the glucose concentration level as evident in Fig. 3. Hence, the measurement of the permittivity as a function of temperature is crucial in accurately measuring the glucose concentration in the body.

The relationship of the real part of permittivity as a function of frequency for aqueous glucose solutions of concentration between 55 mg/dL and 300 mg/dL can be expressed as

$$\varepsilon'(f) = \gamma + 10^{-5} f(\rho - 0.0185f) \tag{5}$$

where γ is the permittivity constant with a value of 77.16, f is the frequency in MHz, and constant ρ is 8.67 for glucose concentration samples of 55 mg/dL to 300 mg/dL. Table 2 shows the real value of permittivity calculated with Eqn. (5). The accuracy of the equation is above 99.9% for the frequency range between 2 GHz and 2.6 GHz. The high accuracy of theoretical model is essential in biosensors where small errors can have significant consequences. Such a model is important to predict the permittivity of the aqueous glucose solutions of various concentration levels (55–300 mg/dL) with great accuracy over a wide frequency range (400 MHz - 10.8 GHz). The accuracy of the model heavily relies on the quality and quantity of the experimental data used for curve fitting. Eqn. (5) was determined from measurements made using a high precision dielectric probe and VNA instrument, both of which are highly costly.

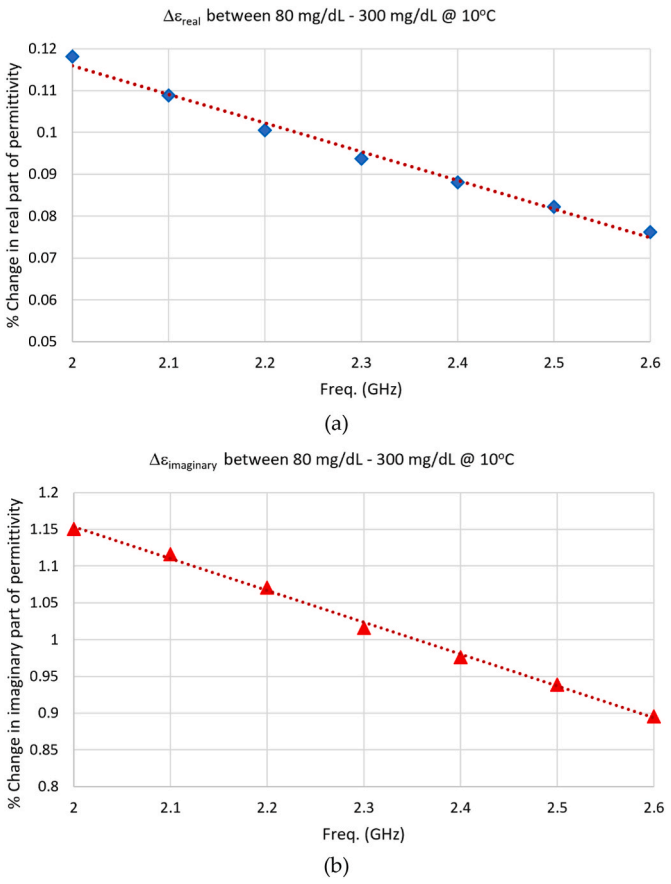

Fig. 3. Difference in the permittivity between the glucose sample of 80 mg/dL and 300 mg/dL at 10 °C, (a) real part, and (b) imaginary part.

Table 2
Accuracy of Eqn. (5) with glucose concentration sample of 80 mg/dL.

Frequency (MHz)	Measured ε'	Calculated ε'	Accuracy (%)
2000	76.5837	76.5934	99.98
2100	76.511	76.52622	99.98
2200	76.4342	76.45534	99.97
2300	76.3537	76.38076	99.96
2400	76.2709	76.30248	99.96
2500	76.1858	76.2205	99.95
2600	76.0978	76.13482	99.95

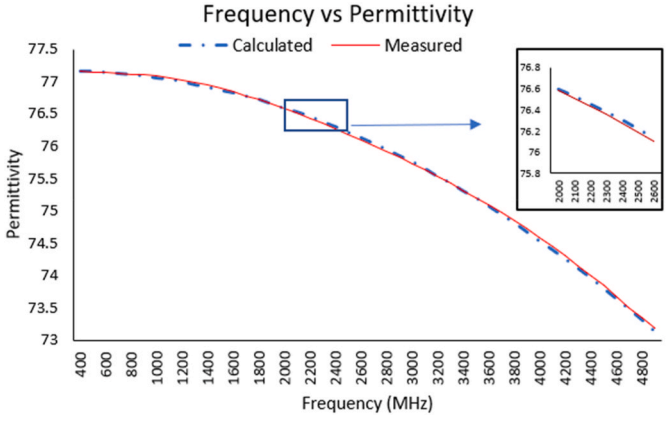

Fig. 4. The real part of permittivity of the glucose sample (80 mg/dL) as a function of frequency when compared with the values calculated using Eqn. (5).

Fig. 4 shows graphically the accuracy of Eqn. (5) in predicting the real part of the permittivity of the specified glucose samples.

Similarly, an expression was obtained to predict the imaginary part of permittivity of the glucose as a function of frequency. It is evident from Fig. 2(c) the imaginary part of permittivity increases linearly from 400 MHz to 5 GHz, thereafter it begins to deviate from the linear trajectory. The expressions to predict the imaginary part of the permittivity are:

$$\varepsilon^{'}(f) = f(x) = \begin{cases} \zeta + 0.0032f, 0 < f\ (MHz) < 4999 \\ \eta + 0.316f^{0.52}, 5000 \leq f\ (MHz) \leq 11000 \end{cases} \quad (6)$$

where f is the frequency in MHz, constant ζ is 0.586, and constant η is −9.79. Table 3 shows Eqn. (6) predicts the imaginary part of permittivity with an accuracy of over 99 % between 2 GHz and 2.6 GHz. For frequencies between 5 GHz and 10 GHz, Tables 3 and 4 show that Eqn. (6) predicts the imaginary permittivity with an accuracy of above 98%. Fig. 5 shows graphically the accuracy of Eqn. (6.).

3.1. Relationship between temperature and real part of permittivity

Measurements of permittivity (real part) were conducted at 2.5 GHz on aqueous solutions of glucose that cover normal fasting blood glucose levels (70–100 mg/dL), hypoglycemia (<70 mg/dL) and hyperglycemia (>180 mg/dL). Purely for experimental purposes the permittivity was also measured at extreme low and extreme high glucose concentrations. Fig. 6 shows the measured permittivity (real part) of the glucose samples and how it changes with increase in temperature from 10°C to 37°C. The permittivity of the different glucose concentration samples follows a similar trend. The measured values of permittivity can be approximated to follow an exponential trajectory. Listed in Table 5 are the measured values of the permittivity (real part) at various temperatures for different glucose concentration samples.

3.2. Mathematical model of the real part of the permittivity as a function of temperature

The relationship between permittivity (real part) as a function of temperature can be modelled by the following expression obtained from curve fitting of the measured data:

$$\boldsymbol{\varepsilon}^{'}(t) = \alpha + \beta e^{0.12T} \quad (7)$$

where the constant α is 76.05 for the samples with glucose concentration of 55 mg/dL to 300 mg/dL, β is a constant of magnitude 0.0433, and T is the temperature in °C. Results in Fig. 6 show the comparison between the calculated and measured values of the real part of the permittivity for various glucose concentration samples. Table 6 shows that Eqn. (7) can predict the real part of the permittivity with an accuracy of above 99.9% for aqueous glucose solutions of concentration between 55 and 300 mg/dL over a temperature range between 10 and 37°C.

The development of non-invasive sensors for glucose monitoring is for human use. Since the temperature of a human is unlikely to be more than 40°C, hence this study only considers the dielectric property of glucose solutions below this temperature. Presented in Table 7 is the measured permittivity (real part) for an 80 mg/dL glucose aqueous solution at various temperatures between 36 and 37.78 °C. The result in the table shows the permittivity to increase with rise in temperature, in particular, the magnitude of the permittivity increases from 79.2 to 80.1 with an increase in temperature from 36°C to 37.78°C. The rise in permittivity is due to the glucose undergoing dissociation and ionization to a small extent when dissolved in water. As temperature rises, the kinetic energy of molecules increases, which can lead to more dissociation or ionization of glucose (solute) molecules. This can result in an increase in the number of charged particles (ions) in the solution, which, in turn, can increase the solution's permittivity.

Table 3
Accuracy of Eqn. (6) with glucose concentration sample of 80 mg/dL for freq. up to 5 GHz.

Frequency (MHz)	Measured ($\varepsilon^{'}$)	Calculated ($\varepsilon^{'}$)	Accuracy (%)
2000	7.00133	6.986	99.7
2100	7.33366	7.306	99.6
2200	7.66303	7.626	99.5
2300	7.99257	7.946	99.4
2400	8.23351	8.266	99.3
2500	8.65035	8.586	99.2
2600	8.97431	8.906	99.2

Table 4
Accuracy of Eqn. (6) with glucose concentration sample of 80 mg/dL for freq. > 5 GHz.

Frequency (MHz)	Measured ($\varepsilon^{'}$)	Calculated ($\varepsilon^{'}$)	Accuracy (%)
5000	16.5355	16.70424	98.9
6000	19.3988	19.33901	99.6
7000	21.9054	21.77008	99.3
8000	24.08	24.03937	99.8
9000	26.1989	26.17609	99.9
10000	28.0875	28.20156	99.5

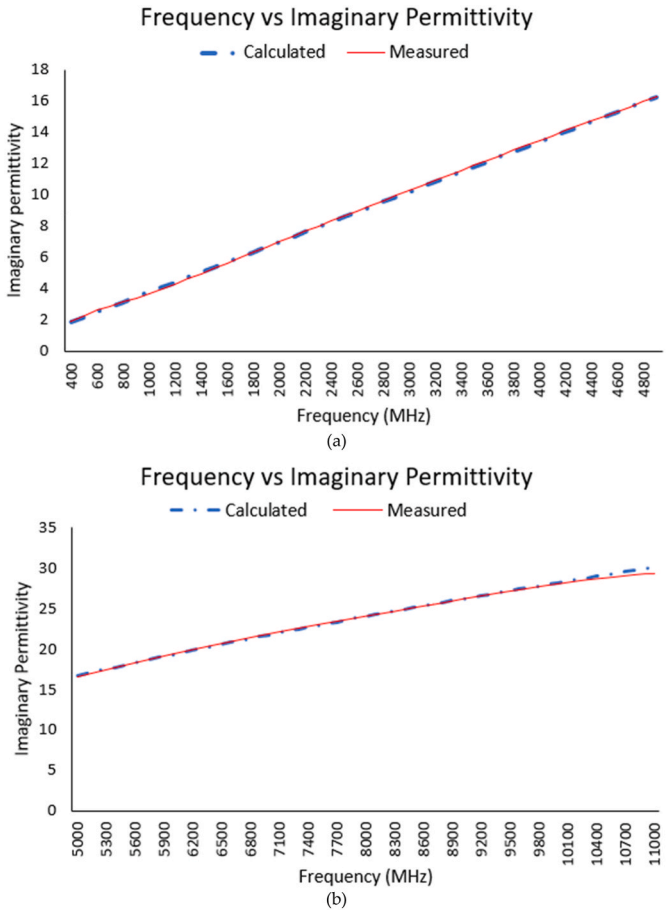

Fig. 5. Calculated using Eqn. (6) and measured imaginary part of the permittivity of the 80 mg/dL aqueous glucose sample as a function of frequency.

3.3. Mathematical model of the imaginary part of the permittivity as a function of temperature

The measured imaginary part of the permittivity of the different aqueous glucose concentration samples at various temperatures are

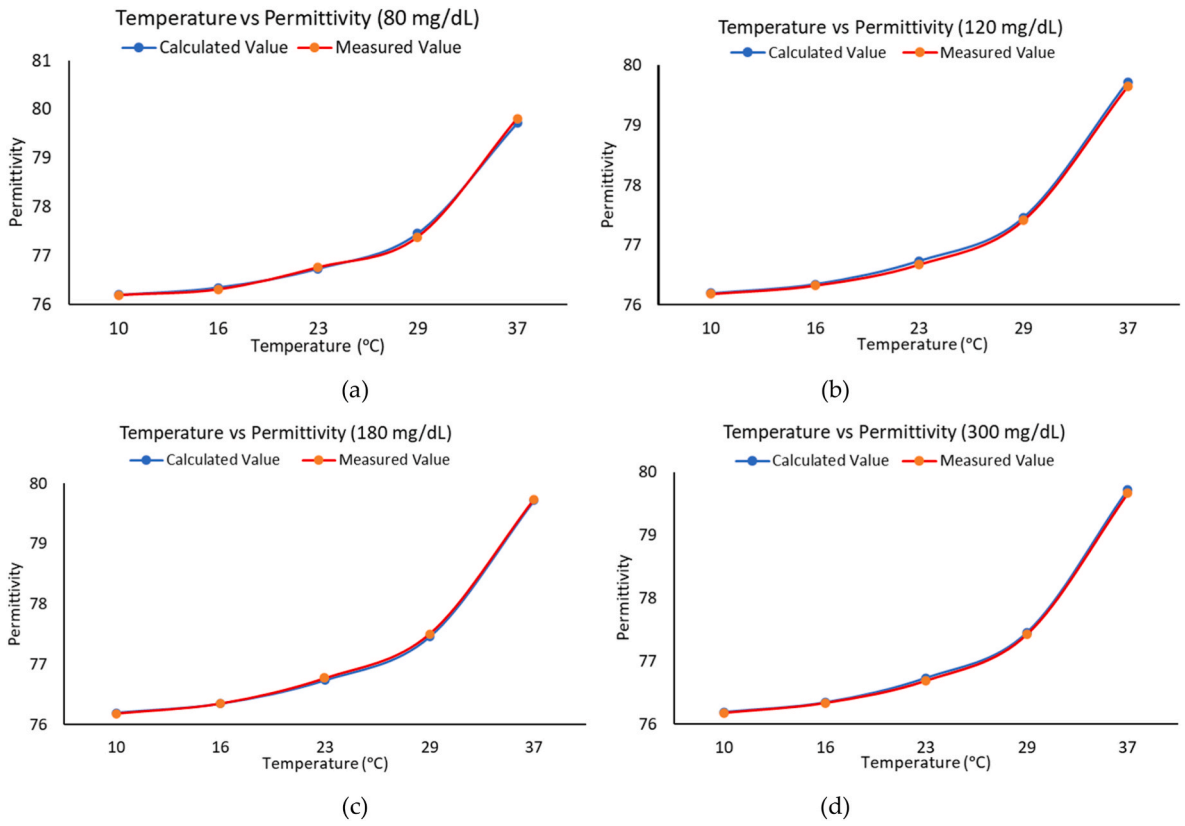

Fig. 6. Real part of permittivity as a function of temperature at 2.5 GHz for glucose concentration samples of (a) 80 mg/dL, (b) 120 mg/dL, (c) 180 mg/dL, and (d) 300 mg/dL.

Table 5
Measured permittivity (real part) at different temperatures.

Glucose concentration (mg/dL)	Permittivity (ε') @ 10°C	Permittivity (ε') @ 16°C	Permittivity (ε') @ 23°C	Permittivity (ε') @ 29°C	Permittivity (ε') @ 37°C
55	76.1750	76.3466	76.6909	77.4260	79.6611
80	76.1858	76.3021	76.7559	77.491	79.7261
120	76.1847	76.3252	76.6772	77.4123	79.6474
180	76.1804	76.3464	76.7681	77.5032	79.7383
300	76.1829	76.3386	76.6928	77.4279	79.6630
5000	76.4070	76.5534	76.8161	77.5512	79.7863

Table 6
Accuracy of Eqn. (7) for different glucose concentration samples.

Glucose Level (mg/dL)	Accuracy (%) @ 10°C	Accuracy (%) @ 16°C	Accuracy (%) @ 23°C	Accuracy (%) @ 29°C	Accuracy (%) @ 37°C
55	99.97	99.99	99.94	99.96	99.92
80	99.99	99.94	99.97	99.9	99.99
120	99.98	99.97	99.92	99.94	99.91
180	99.98	99.99	99.95	99.93	99.97
300	99.98	99.99	99.94	99.96	99.92

Table 7
Permittivity (real part) for 80 mg/dL glucose sample at different temperatures.

Temperature (°C)	ε'
36	79.20
36.5	79.50
37	79.72
37.5	79.95
37.78	80.10

given in Table 8.

The mathematical expression representing the imaginary part of the permittivity as a function of temperature obtained from curve fitting of the measured data is given by:

$$\varepsilon''(t) = \gamma + \delta T \tag{8}$$

where the constant γ is 8.15 for the samples with glucose concentration of 55 mg/dL to 300 mg/dL, δ is a constant equal to 0.05, and T is the temperature in °C. Graphs in Fig. 7 show the comparison between the calculated and measured values of the imaginary part of the permittivity for various glucose concentration samples. Table 9 shows the imaginary part of the permittivity can be predicted using Eqn. (8) with an accuracy of above 98.8%.

4. Discussion

Glucose sensors reported in literature to date are based on split ring resonators [15,16]. The permittivity of the material on which the sensor is fabricated plays a significant role in determining the size of the sensor.

Table 8
Imaginary part of the permittivity at different temperatures.

Glucose sample (mg/dL)	ε'' @ 10°C	ε'' @ 16°C	ε'' @ 23°C	ε'' @ 29°C	ε'' @ 37°C
55	8.61085	8.91849	9.18881	9.45913	9.72945
80	8.65035	8.94333	9.28832	9.63331	9.9783
120	8.66140	8.89844	9.17792	9.4574	9.73688
180	8.66240	8.89723	9.25883	9.62043	9.98203
300	8.66361	8.89546	9.20110	9.50674	9.81238
5000	8.46670	8.70171	8.96492	9.22813	9.49134

These sensors are designed to operate at a specific frequency and measure the permittivity to determine the concentration of the glucose. The sensors reported in literature do not take into consideration the effects of temperature when measuring the permittivity of the glucose.

The measured results presented here reveal that the variation in the permittivity level of the glucose with temperature at any frequency may appear to be very small and this is the reason why the effect of temperature is ignored. In fact, the experimental results presented here show the difference in permittivity for glucose concentrations between 80 mg/dL and 300 mg/dL is less than 1%. However, a small variation in permittivity corresponds to a large variation in glucose concentration levels. Hence, a small error in the measurement of permittivity with temperature will result in a large error in the computation of glucose level. The results presented here demonstrate the importance of considering the body temperature when measuring the permittivity of glucose based on non-invasive sensors using microwave-oriented techniques. Accurate measurement of glucose levels is crucial for managing diabetes effectively and preventing healthcare complications. Diabetes is a chronic condition characterized by elevated blood glucose levels, and maintaining these levels within a target range is essential to prevent both short-term and long-term complications. Accurate glucose measurement will help individuals with diabetes make informed decisions about their diet, medication, and lifestyle choices.

5. Conclusions

Daily blood glucose monitoring is vital for people with diabetes mellitus to manage their disease and prevent complications. Existing tests for glucose monitoring including GGM are invasive and with associated disadvantages. It's important to note that while there has been significant progress in the development of non-invasive glucose monitoring techniques, many of these methods are still in the experimental or early stages of development. Hence, research in the development of non-invasive techniques for glucose monitoring is evident in scientific literature. The scientific studies reported in literature on the development of non-invasive glucose sensors measure the permittivity of glucose using electromagnetic radiation to determine the glucose level. However, these techniques do not consider the effects of temperature on the permittivity measurement. The study presented in this paper demonstrates the importance of considering temperature in permittivity measurements. The experimental results show that the variation in the permittivity level of the glucose with temperature may appear to be relatively small however a small variation in permittivity translates to a large variation in glucose concentration levels thus rendering the reported glucose sensors subject to inaccuracy [17,18]. The temperature of the human body varies based on several factors such as the surrounding environment, the human's health levels etc. Based on the findings of this study, it can be concluded that non-invasive glucose

Table 9
Accuracy of Eqn. (8) for different glucose concentration samples.

Glucose Level (mg/dL)	Accuracy (%) @ 10°C	Accuracy (%) @ 16°C	Accuracy (%) @ 23°C	Accuracy (%) @ 29°C	Accuracy (%) @ 37°C
55	99.53	99.65	98.89	98.53	97.3
80	99.99	99.92	99.90	99.65	99.78
120	99.86	99.50	98.90	98.51	97.36
180	99.85	99.54	99.57	99.78	99.82
300	99.85	99.38	98.93	99.02	98.12

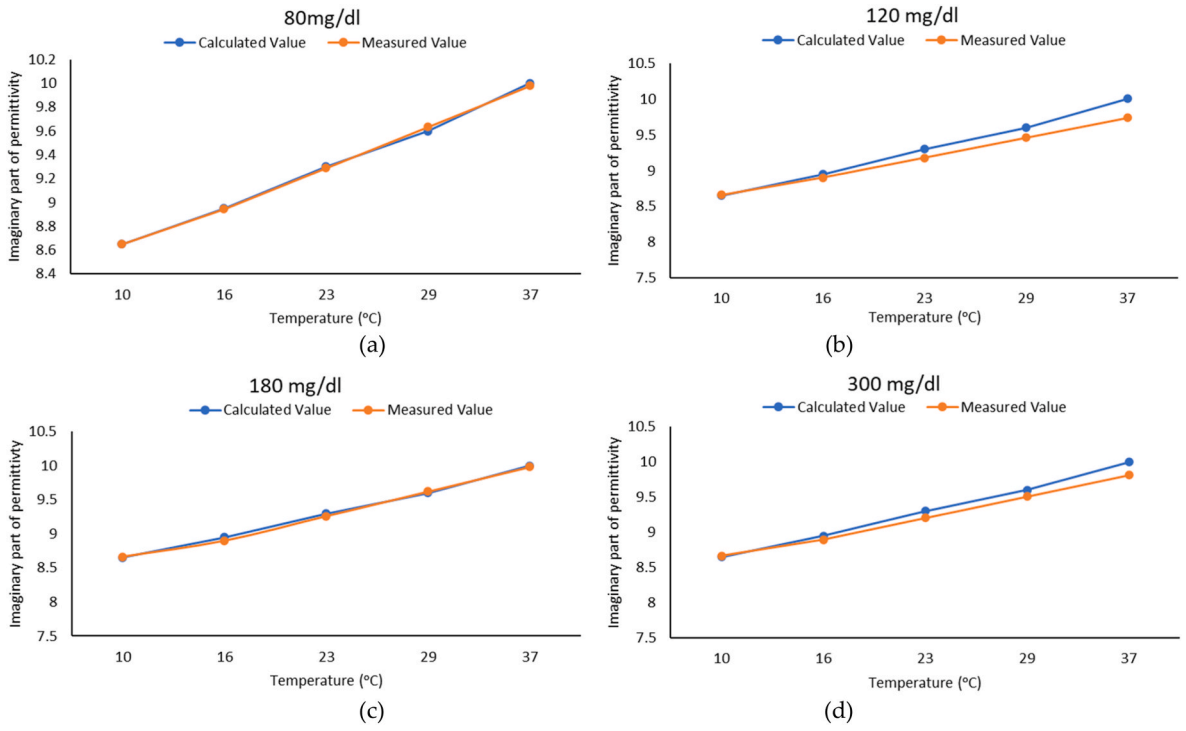

Fig. 7. Imaginary part of permittivity as a function of temperature at 2.5 GHz for glucose concentration samples of (a) 80 mg/dL, (b) 120 mg/dL, (c) 180 mg/dL, and (d) 300 mg/dL.

monitoring devices using electromagnetic sensing techniques should also consider temperature as a biomarker of the individual. Because the change in the permittivity of the glucose fluid with temperature is marginal it is recommended the sensor use an artificial intelligent classification algorithm such as KNN (K-Nearest Neighbor) to significantly improve the accurately of the glucose levels. Accurately characterizing the permittivity of aqueous glucose solutions is an important in the development of non-invasive biosensors. To further improve the methodology for these measurements, several future improvements and developments must be considered. This includes (i) development of a more sensitive measurement technique or instrument to detect even smaller changes in permittivity, (ii) using advanced signal processing and data analysis methods to enhance the precision of measurements, and (iii) develop method for precise temperature control during measurements since temperature can affect permittivity. This work should help in the development of highly precise non-invasive glucose monitoring devices, which are crucial for determining appropriate insulin dosages, managing blood sugar levels, and preventing hyperglycemia or hypoglycemia episodes.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

The research was carried out at the Center for Communications Technology, London Metropolitan University.

References

[1] World Health Organization. https://www.emro.who.int/noncommunicable-diseases/world-diabetes-day/world-diabetes-day-2021.html, 2021.

[2] E. Standl, K. Khunti, T.B. Hansen, O. Schnell, The global epidemics of diabetes in the 21st century: current situation and perspectives, Eur J Prev Cardiol 26 (2_suppl) (2019) 7–14, 10.1177/2047487319881021. PMID: 31766915.

[3] K. Kuziemski, W. Słomiński, E. Jassem, Impact of diabetes mellitus on functional exercise capacity and pulmonary functions in patients with diabetes and healthy persons, BMC Endocr. Disord. 19 (2) (2019), https://doi.org/10.1186/s12902-018-0328-1.

[4] S.K. Vashist, Continuous glucose monitoring systems: a review, Diagnostics 3 (2013) 385–412, https://doi.org/10.3390/diagnostics3040385.

[5] S. Mohanram, S.A. Edward, Measurement of blood glucose using non-invasive methods – a review, J. Phys. Conf. (2021) 1–17, https://doi.org/10.1088/1742-6596/1964/6/062022.

[6] A. Soni, et al., Fifteen-minute consultation: practical use of continuous glucose monitoring, Arch. Dis. Child Educ. Pract. Ed. 107 (2022) 188–193, https://doi.org/10.1136/archdischild-2020-321190.

[7] V. Turgul, I. Kale, Characterization of the complex permittivity of glucose/water solutions for noninvasive RF/Microwave blood glucose sensing, IEEE International Instrumentation and Measurement Technology Conference Proceedings (2016) 1–5, https://doi.org/10.1109/I2MTC.2016.7520546.

[8] The ISM Band – A review of the essentials, http://signalpro.biz/ism1.pdf.

[9] Federal Communications Commission FCC 02-328, file:///C:/Users/bvird/Downloads/FCC-02-328A1%20(1).pdf.

[10] T. Chang, H. Li, N. Zhang, X. Jiang, X. Yu, Q. Yang, Z. Jin, H. Meng, L. Chang, Highly integrated watch for noninvasive continual glucose monitoring, Microsystems & Nanoengineering (2022) 1–9, https://doi.org/10.1038/s41378-022-00355-5.

[11] Global Report on Diabetes, World Health Organization (WHO), 2016. https://www.who.int/publications/i/item/9789241565257.

[12] D. Popovic, C. Beasley, M. Okoniewski, J.H. Booske, Precision open-ended coaxial probes for in-vivo and ex vivo dielectric spectroscopy of biological tissue at microwaves frequencies, IEEE Transaction on microwave theory and methods 53 (5) (2005) 1713–1722.

[13] P. Debye, Polar Molecules" Chemical Catalogue Co NY, 1929.

[14] H. Fröhlich, General theory of the static dielectric constant, Trans. Faraday Soc. 44 (1948) 238–243.

[15] N. Sharafadinzadeh, M. Abdolrazzaghi, M. Daneshmand, Highly sensitive microwave split ring resonator sensor using gap extension for glucose sensing, in: IEEE MTT-S International Microwave Workshop Series on Advanced Materials and Processes for RF and THz Applications, IMWS-AMP), 2017, pp. 1–3, https://doi.org/10.1109/IMWS-AMP.2017.8247400.

[16] G. Saleh, I.S. Ateeq, I. Al-Naib, Glucose level sensing using single asymmetric split ring resonator, Sensors 21 (2021) 2945, https://doi.org/10.3390/s21092945.

[17] A.E. Omer, et al., Low-cost portable microwave sensor for non-invasive monitoring of blood glucose level: novel design utilizing a four-cell CSRR hexagonal configuration, Sci. Rep. 10 (2020) 1–20, 15200.

[18] C.G. Juan, et al., Microwave planar resonant solutions for glucose concentration sensing: a systematic review, Appl. Sci. 11 (2021) 1–24, 7018.