Design and analysis of a metamaterial based biosensor to determine blood glucose concentration

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Article Info ABSTRACT Article history: In this paper, a biosensor utilizing metamaterials is designed and simulated

Received Feb 6, 2024 Revised Mar 10, 2024 Accepted Mar 15, 2024

Keywords:

Antenna sensor Complementary split ring resonator Metamaterial Microwave sensor Non-invasive glucose detection to detect blood glucose concentration. The proposed sensor comprised of a microstrip patch antenna designed on a Rogers RT5880 substrate. A circular-shaped complementary split ring resonator (CSRR) cell is integrated onto the patch of the antenna which acts as the sensing region. The sensor is analyzed in order to ascertain the blood glucose concentration ranging from 50-300 mg/dL in a human finger model. The sensing parameter is amplitude of reflection coefficient, which exhibits variation in response to alterations in the dielectric characteristics of the sample being tested. The Cole-Cole relaxation model is employed to predict the dielectric properties of different finger tissues. An analysis of the characteristics of the CSRR was conducted to illustrate its significance in the realm of glucose detection. The glucose level is determined through the utilization of a linear regression model that describes the relationship between the reflection coefficient of the sensor and glucose level. The sensor demonstrates an impressive sensitivity of 1.792 dB per (mgdL⁻¹) and has the ability of determining glucose levels with a good accuracy, as verified by the application of Clarke error grid. This sensor exhibits enhanced performance compared to some other recent glucose sensors.

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1. INTRODUCTION

The growing rate and potential severity of diabetes, a chronic metabolic condition, has emerged as a significant worldwide health issue. This physiological state occurs when the body's capacity to maintain equilibrium of blood glucose levels (BGL) is compromised, resulting in enhanced concentrations of glucose in the blood circulatory system. The successful management and control of diabetes include the maintenance of a well-balanced diet, regular engagement in physical exercise, diligent monitoring of blood sugar levels and adherence to prescribed medications.

The predominant approach for monitoring glucose levels is an invasive method wherein a lancet is inserted into the skin, allowing for direct measurement of BGL using a glucometer. Although this procedure demonstrates an acceptable degree of precision, it is not without its drawbacks. Some patients may experience pain and discomfort, as well as an increased chance of infection. Additionally, these devices do not facilitate reusability, hence imposing financial burdens on consumers who require regular usage. Hence, there is a growing demand for non-invasive techniques to assess glucose levels.

Several techniques have already been implemented to determine glucose concentration through noninvasive approaches. For instance, optical methods have been proposed such as Raman spectroscopy [1], optical polarimetry [2], near infrared (NIR) and mid infrared (MIR) spectroscopy [3]. But these methods have some limitations like limited sensitivity and accuracy, poor robustness and reproducibility and vulnerability to background noise. Various non-invasive enzyme-based electrochemical techniques have been suggested to detect glucose levels in bio fluids like sweat [4], tears [5], and saliva [6]. Yet it is important to acknowledge that these methods also include some disadvantages, including the presence of interfering contaminants, limited sensitivity, hysteresis, and reduced accuracy.

Radio frequency/microwave (RF/microwave) based glucose biosensors have been extensively integrated due to their numerous advantages. RF/microwave technology possesses the capability to penetrate human tissue to significant depths without inducing any adverse effects. For example, a proposed method for measuring blood glucose concentration involves the use of a microwave cavity-based sensor that features a cylindrical cylinder with a centrally positioned capillary tube [7]. A novel electric LC (ELC) resonator is introduced, which consists of a glass capillary filled with a solution containing both aqueous and blood glucose components [8]. A recent study introduces a circular substrate integrated waveguide (SIW) sensor that incorporates a glass capillary in order to examine the dielectric characteristics of water glucose solutions [9]. Another sensor utilizing an antenna is constructed to emit an endfire beam to conduct in-vitro and in-vivo glucose level measurement [10]. A microwave planar resonant sensor comprising of two identical complementary split ring resonators (CSRRs) is introduced. In this research, one CSRR is employed for the glucose detection application, while another CSRR is used as a reference for monitoring environmental parameters such as temperature and humidity [11].

Nevertheless, a significant drawback of the preceding sensors is their limited sensitivity, resulting in low accuracy when detecting glucose levels. One further obstacle faced by microwave sensors is the issue of inadequate selectivity, which refers to their limited capacity to measure glucose level in a solution amongst the presence of other elements. This study presents a sensor adopting a microstrip patch antenna that incorporates a metamaterial element which is CSRR. The objective of this sensor is to determine the blood glucose concentration within 50 and 300 mg/dL. The sensitivity of this sensor is remarkable, determining at 1.792 dB/(mg/mL). The sensor under consideration also demonstrates a significant correlation between the computed glucose concentrations and the corresponding actual values.

2. METHOD

2.1. Dielectric properties estimation

In this investigation, a simulation is conducted using a multi-layer human finger model in order to ascertain the BGL. Several recent research have presented various models for the structure of the human finger, which consist of multiple tissues [12], [13]. However, these studies have not provided a clear explanation for the selection of specific thicknesses for each layer. The human finger model proposed by Cebedio *et al.* [14] has been considered in this study. They estimated the layer thickness using ultrasound technology on the small finger of an actual human volunteer. The model encompasses six distinct biological tissues, including dry and wet skin, blood, fat, muscle, bone. Additionally, a nail has been incorporated at the top of the skin layer. Each layer is in a square shape with a side length of 3.3 mm, except for the nail layer, which has a width that is half of the other layers. Previous studies suggested the concept of blood as a single thick layer. However, the present model adopts a more realistic approach by defining blood as comprising three distinct and thin layers. Figure 1 displays the layout of the human finger model.

The operating frequency of the sensor is a crucial factor that affects the penetration depth through the finger. The depth of penetration can be described by (1) [15].

$$Dp = \frac{\lambda_0}{2\pi\sqrt{2\varepsilon_{r'}}} \times \frac{1}{\sqrt{1 + (\varepsilon_{r''}/\varepsilon_{r'})^2 - 1}}$$
(1)

Here, λ_0 is denoted free space wavelength which decreases when the frequency increases ($\lambda = c/f$). To analyze the behavior of blood circulating in the finger, mainly penetration through skin and fat layer is required, while penetration via muscle and bone is of less importance. Moreover, research has demonstrated that the sensitivity of biosensors to variations in glucose concentrations is enhanced at higher frequencies. This makes it possible for blood and microwaves to interact more strongly [16]. Hence our choice of higher operating frequency (>10 GHz) is justified.

The dielectric properties of the layers in the human finger model are evaluated utilizing the Cole-Cole relaxation model. The first order Cole-Cole relaxation model is mathematically described by (2) [17].

$$\varepsilon_r(\omega) = \varepsilon_{\infty} + \frac{\Delta\varepsilon}{1 + (j\omega\tau)^{(1-\alpha)}} + \frac{\sigma_s}{j\omega\varepsilon_0}$$
(2)

The work of Gabriel *et al.* [18] provides the parameters included in the Cole-Cole model, that is employed to estimate the dielectric characteristics of various finger tissues. An overview of the dielectric characteristics and thickness of different biological tissues is shown in Table 1. The parameters of the Cole-Cole equation exhibit a dependency on the glucose level in blood, as established by the research conducted by Karacolak *et al.* [19]. Table 2 presents the calculated dielectric properties of different blood glucose concentrations at the sensor's resonant frequency that is 10.54 GHz.



Figure 1. Different layers of the human finger model

Table 1. Overview of finger tissues			
Tissue	Thickness	Permittivity	Loss tangent
Dry Skin	0.6	30.03	0.4150
Wet Skin	1.04	32.44	0.4473
Blood	0.25	Variable	Variable
Fat	2.3	4.56	0.2170
Muscle	2	41.87	0.4261
Bone	4	7.90	0.4582
Nail [20]	0.3	3	-
U. Blood	0.1	Variable	Variable

Table 2. Dielectric	properties	of BGL
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BGL (mg/dL)	Permittivity	Loss tangent	BGL (mg/dL)	Permittivity	Loss tangent
50	52.08	0.5253	200	51.97	0.5269
100	52.04	0.5259	250	51.94	0.5274
150	52.01	0.5264	300	51.90	0.5280

2.2. Sensor design and analysis

An antenna has the capability to function as a sensing device while concurrently serving as a signal transmitter. This type of device is commonly known as an antenna sensor. In this study, a novel antenna sensor is designed utilizing a microstrip patch antenna for the purpose of non-invasive glucose level detection.

2.2.1. Antenna design

The antenna-based biosensor comprises a pair of circular CSRR rings which serves as the sensing region. The sensor design process involves utilizing a Rogers RT5880 substrate which has a thickness of 1 mm. At the center of the substrate, a rectangular patch having dimensions of 17.3×21 mm is positioned.

The thickness of the metals used in the patch, microstrip line and ground of the antenna has been set at 0.05 mm. An inset-cut microstrip line feed technique is employed, whose width is calculated to be 3.1 mm in order to obtain an input impedance of 50 ohm. The inset-cut length is chosen at 5.8 mm, approximately one-third of the patch's length. All dimensions of the rings, including width, spacing, and split gaps, are equal at 0.3 mm. The layout of the sensor and the CSRR element is illustrated in Figure 2. The sensor with CSRR is presented in Figure 2(a). The enlarged representation of the CSRR is shown in Figure 2(b).



Figure 2. The geometry of the sensor: (a) simplified diagram of the sensor with CSRR and (b) layout of the CSRR

2.2.2. CSRR design

The radius of the CSRR rings is a crucial factor in the design aspect of the glucose sensor. The widths of both rings in a CSRR and the distance between them are equal. Consequently, when a particular radius for the outer ring is selected, the radius of inner ring is adjusted accordingly. The variation in properties of the sensor for the alteration of different CSRR parameters is shown in Figure 3. An investigation was conducted using different radii of rings of the CSRRs, as depicted in Figure 3(a). The observation reveals that the most minimal reflection coefficient is obtained for the CSRR, characterized by a radius of 2.4 mm for the inner ring and 3 mm for the outer ring. Hence, the CSRR with this particular configuration has been chosen for the purpose of glucose detecting operation.

The location of the CSRR cell is another significant design aspect. Various placements of the CSRR cell along the length of the patch have been taken into consideration. The impact of different placements of the CSRR can be observed in Figure 3(b). The findings suggest that the sensor exhibits a minimal reflection coefficient when the distance from the center (DC) of the patch is 0.8 mm. Therefore, the optimal placement of the CSRR within the sensor is determined to be 0.8 mm above the center of the patch.



Figure 3. Comparison of S₁₁ (dB) at various (a) CSRR ring radii and (b) CSRR location

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2.2.3. Determination of the sensing region

The analysis of the distribution of electric field and surface current density of the sensor is represented in Figure 4 to identify the area with the maximum sensitivity. Figure 4(a) depicts the electric field distribution and Figure 4(b) shows the surface current density of the sensor. The area surrounding CSRR is associated with the localization of the most significant levels of intense electric field and surface current density. The propagation of an intense electric field will induce an interaction with the glucose sample, resulting in a modification of its relative permittivity and loss tangent. The alteration in these properties will lead to a shift in the S-parameter values of the sensor. Therefore, this particular location that is selected as the designated area wherein the sample under test (SUT) will be positioned.



Figure 4. Determination of the sensing region of the sensor from (a) Electric field distribution, (b) Surface current density

2.2.4. Analysis on metamaterial properties

Metamaterials refer to systematically developed materials, typically organized in periodic arrangements, which exhibit a range of distinctive properties that are not commonly observed in natural materials. Materials that possess the unique property of exhibiting double negative properties, specifically negative permittivity and negative permeability, are commonly referred to as double negative (DNG) materials or left-hand materials (LHM). According to Maxwell's equations, the refractive index of an object is expected to be negative due to its double negative properties. The presence of a negative refractive index in LHM material leads to the accumulation of incident electromagnetic waves [21].

The extracted metamaterial characteristics are illustrated in Figure 5. The real permittivity, real permeability and refractive index of the metamaterial unit cell are depicted in Figure 5(a), 5(b) and 5(c) respectively. The investigation reveals that the metamaterial unit cell, that is CSRR in this study, demonstrates negative values for both permittivity and permeability while operating at the resonant frequency. The refractive index is also negative as it was assumed. Hence, the metamaterial has the potential ability to accumulate strong electric field, a critical factor in facilitating the sensing process.



Figure 5. The metamaterial unit cell: (a) real permittivity, (b) real permeability, and (c) refractive index

3. RESULTS AND DISCUSSION

The multi-layer finger model has been integrated into the sensor as depicted in Figure 6. The electromagnetic waves emitted by the sensor will thereafter penetrate the layers of the finger and engage with the layers of blood. The sensor will identify and evaluate any change in blood permittivity. Figure 7 shows that a rise in blood permittivity results in a corresponding increase in the amplitude of S_{11} (dB).

The sensitivity of the sensor is calculated as the ratio of the variation in the magnitude of S_{11} associated with alterations in glucose concentration. The sensitivity is found to be 1.792 dB per (mg/mL) which indicates that the antenna exhibits a strong response even in the presence of small variations in blood glucose concentrations. Subsequently the value of sensitivity is computed as (3):

$$Sensitivity = \frac{\sum_{i=1}^{n-1} (s_{i+1} - s_i)}{\sum_{i=1}^{n-1} (g_{i+1} - g_i)}$$
(3)

Here, $s_i = i^{th}$ value of reflection coefficient and $g_i = i^{th}$ value of glucose concentration. The simple linear regression technique has been used to predict the BGL based on the acquired values of S₁₁ in dB from Figure 7. The obtained sensing model can be expressed as (4):

$$y = -48 - 0.018x \tag{4}$$

Here, x denotes BGL and y denotes obtained reflection coefficient from the plot. The correlation coefficient (R²) of the sensor has been calculated to be 0.97, indicating a good approximation of BGL from the regression model. The BGL can be computed by employing the mathematical regression model. Table 3 presents an overview of the reference BGL and the resultant BGL values derived from the model, along with the corresponding error.

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Figure 6. Perspective view of the sensor with finger model placed on it

Figure 7. Increase in the magnitude of the S_{11} of the sensor with an increase in BGL

0.37

Table 3. An overview of actual and estimated BGL			
Reference BGL (mg/dL)	Estimated BGL (mg/dL)	Error (%)	
50	52.22	4.44	
100	85	15	
150	162.78	8.52	
200	202.22	1.11	
250	246.11	1.56	

301.11

300

The clinical accuracy of the proposed sensor was verified using the Clarke error grid analysis as depicted in Figure 8. The grid is comprised of five distinct zones, with each zone denoting a distinct level of risk associated with the variation between estimated and reference glucose values. Zone A is commonly known as the clinically accurate zone which has a prediction error rate below 20% [22]. It is obvious from the plot that all of the estimated BGL obtained from our study consistently remain within zone A, indicating a high level of performance for the sensor being presented.



Figure 8. Verification of the sensor using Clarke error grid analysis

Table 4 presents a comparative analysis based on the sensitivity of the proposed sensor with other recently developed sensors. Based on the analysis conducted, it is apparent that the proposed sensor provides greater sensitivity in comparison to other sensors. The enhanced sensitivity enables accurate detection of glucose levels and differentiation between small variations in glucose concentrations. This sensor demonstrates a high level of sensitivity and highly accurate detection capability for glucose levels. These characteristics affirm the superior performance of the sensor.

Table 4. Comparison with other sensors based on sensitivity			
Reference	Sensor structure	Sensing parameter	Sensitivity (dB per mg/mL)
[23]	Four circular SRR sensor	S ₁₁	0.042
[11]	Double CSRR	S_{21}	0.008
[24]	Coplanar single SRR	S ₁₁	0.023
[25]	Chipless SRR sensor	S_{21}	0.083
[26]	Dielectric disk resonator	S ₂₁	0.8 - 1
Proposed sensor	Single CSRR sensor	S ₁₁	1.79

4. CONCLUSION

A biomedical sensor dedicated for determination of glucose concentration was designed and analyzed in this research paper. A DNG metamaterial structure, namely CSRR was integrated on the device in order to exploit its unique characteristics for improved sensing capabilities. The response of the sensor was analyzed to determine glucose level in a human finger model. The Cole-Cole relaxation model was utilized to ascertain the dielectric characteristics of different finger tissues. The return loss of the sensor has been observed to vary in conjunction with changes in glucose concentrations. A regression equation has been developed which establishes a correlation between glucose level with return loss. The sensor shows superior sensitivity of 1.792 dB/(mg/mL) and can determine glucose level within the medically optimal range, as verified from Clarke error grid analysis. However, the possible impact on environmental factors, such as temperature and humidity, was not taken into account; but these elements might influence the result of the sensor. Despite its limitations, the proposed sensor exhibits potential in the non-invasive determination of glucose levels. Further investigation can be conducted on this sensor to enhance its performance and subsequently fabricate it for real-time application.

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