Non-Invasive Blood Glucose Detection using Metamaterial Based Bio Sensor

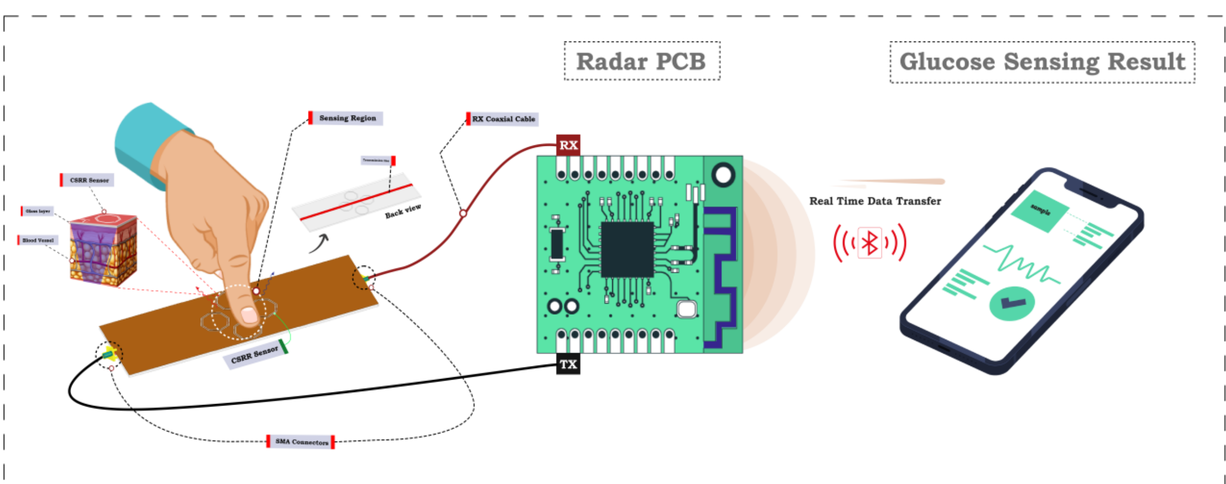
Abstract:

Diabetes presents a significant health challenge worldwide, necessitating accurate and non-invasive methods for monitoring blood glucose levels. While invasive techniques like glucometers have long been used, they pose discomfort and inconvenience to patients. Minimally invasive continuous glucose monitoring devices offer some relief but still come with limitations. As a result, non-invasive glucose monitoring has garnered attention, with microwave-based techniques showing promise in characterizing biological tissues and measuring glucose levels. This study proposes a novel approach using an RF-based biosensor comprising Four Complementary Split Ring Resonators on a Rogers RO4003C substrate, operating at the 2.4GHz ISM band. The study aims to place a finger on the sensing elements and observe S-Parameter magnitude concentration, correlating it with blood glucose levels typical of type 2 diabetes (ranging from 0 to 300mg/dl), as per the Cole-Cole model. This research represents a significant step toward developing a non-invasive, accurate, and accessible method for monitoring blood glucose concentration, potentially improving the management of diabetes and enhancing the quality of life for affected individuals.

Keywords: Non-invasive, Bio-sensor, Metamaterial, CSRR, Blood Glucose

1. INTRODUCTION:

Non-invasive blood glucose monitoring performs through in vitro and in vivo analysis of Differential Continuous Wave Photo Acoustic Spectroscopy (DCW-PAS). The DCW-PAS approach uses amplitude modulation with dual wavelengths of light to identify glucose concentration level. The analysis compares DCW-PAS evaluations including results from invasive blood glucose sensor evaluations of healthy people's Oral Glucose Tolerance Tests (OGTTs). The blood glucose level estimation from photo-acoustic signal and invasive sensors have good correlation [1]. The blood glucose level measure with plasmonic sensor made of barium flint glass, gold film and silicon nitride (Si3N4) substrate. The plasmonic sensor rejects infrared wavelength on normal incidence because of coupling between plasmonic wave and incident plane wave. The impact of glucose concentration or ambient refraction analyze for plasmonic structure sensitivity to blood glucose [2]. A Spoof Surface Plasmon Polariton (SSPP) end fire sensor monitors aqueous glucose solutions and measures on-body glucose. The SSPP end fire sensor radiates and end fire beam into a glucose water solution with minimal effective aperture. At the sensor's CPW port, a set of triangular ground planes suppresses the side-lobes and limit glucose sensing. The SSPP end fire sensor's slow wave nature provides the way for measuring glucose concentrations with enhanced sensitivity [3]. The design of a microwave sensor for non-invasive monitoring of blood glucose concentration is presented. Three distinct microwave resonator structures analyze as suitable candidates. The microwave resonator has an open structure to place patient's finger. The finger's shape and size should fit in the resonator. The variation in blood glucose concentration alters the tissue's dielectric properties and changes the structure's resonant frequency [4]. A combined millimeter-wave radar system detects various glucose concentration levels of duplicate blood samples made in the laboratory. The mmwave radar non-invasively monitors blood glucose of patients with diabetes. The mm-wave radar signal with Discrete Time Fourier Transform finds various glucose concentrations in hemoglobin samples. [5]. The near infrared spectroscopy non-invasively measures glucose concentration in blood. The infrared light pass through finger and blood glucose concentration evaluate by calculating absorbance through Beer-Lambert law. The infrared absorbance is equivalent to blood glucose concentration and finger thickness. [6]. An implanted sensor with telemetry system monitors subcutaneous tissue glucose for long term in diabetic patients. The implantable sensor consists of immobilized glucose oxidase membrane, polydimethylsiloxane membrane, catalase connected to electrochemical oxygen detection and telemetry system for wireless data transmission. [7]. The blood glucose monitor with RF/microwave technology. The RF sensor measure blood glucose level by detecting dielectric changes of blood. The dielectric variation due to glucose causes the sensor frequency to shift below 8Mhz. The frequency shifts also occur due to blood layer, skin, fat, pressure and position of finger [8]. A wearable, minimum invasive autonomous and pseudo-continuous blood glucose monitoring. This wearable micro system design obtains a whole blood sample from a little lanced skin wound utilizing a new micro-actuator based on a shape memory alloy (SMA) and straightly measures the blood glucose level from the blood sample [9].



2. RESONANT METHOD:

Various methods have been developed to study the interaction between microwaves and matter, which can be divided into three categories: free-space, transmission line, and resonant techniques. Among these approaches, the resonant method stands out due to its high precision. This technique relies on the changes in the resonant sensor characteristics, including resonant frequency, bandwidth, and quality factor, resulting from the interaction between a dielectric material and the electromagnetic field. The interaction between the biological tissue and the electromagnetic field can be described by the complex relative permittivity, denoted as

$$\varepsilon r = \varepsilon' r - j\varepsilon'' r \qquad (1)$$

where ε'r represents the tissue's ability to store electrical energy, and ε"r is associated with the losses resulting from the dissipation of electromagnetic energy in the tissues.

3. DESIGN OF BIO SENSOR

To create a miniaturized sensor, we focused on using CSRRs (complementary split-ring resonators) which have a band-stop filter behavior similar to SRRs (split-ring resonators), but with the difference that CSRRs are etched onto a metal layer. Instead of choosing a conventional shape, we utilized a single cell that can be arranged efficiently into a honeycomb structure. This honeycomb CSRR structure was chosen for its ability to achieve better sensitivity. In-vitro measurements were conducted on aqueous glucose solutions mimicking blood glucose concentrations relevant to Type 2 diabetes (0-300 mg/dl). The CSRR design was optimized on a standard substrate using numerical simulations to operate at a specific frequency with high sensitivity to variations in glucose dielectric properties. The aforementioned reference investigated the impact 10 of these design parameters on the detection performance of the CSRRs.

The sensor utilized in this study comprised of four identical resonators arranged in a honeycomb structure. Two individual CSRRs were placed horizontally along the transmission feed line, with a center-to-center distance of C = 12.6 mm, while the other two cells were positioned vertically with the same distance. The sensor was fabricated on a Rogers RO4003C substrate with a dielectric constant of εr = 3.55, a loss tangent of tanδ = 0.0027, and a thickness of HS = 0.8 mm and the substrate's overall dimensions were LS = 66 mm and WS = 20 mm was shown in Figure 1.

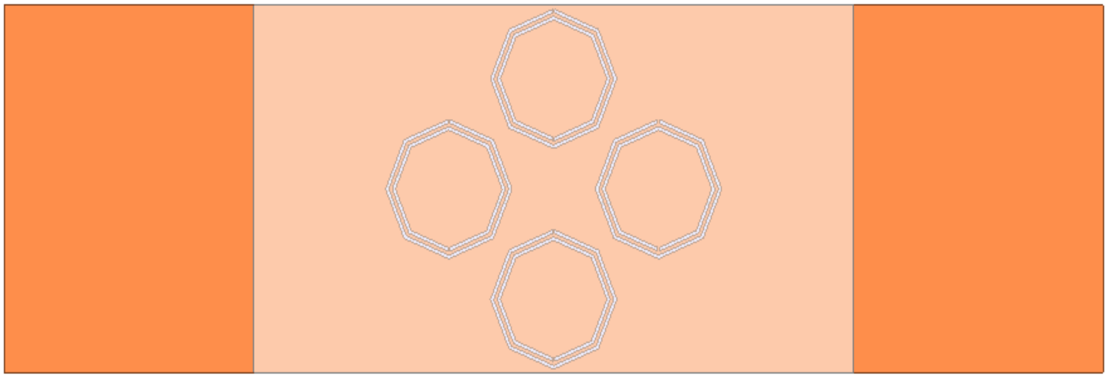


Figure 1. Complimentary Split Ring Resonator bio sensor

The unit-cell included two concentric split-rings that were etched in the copper ground plane. The outer ring of the unit-cell was designed with a diagonal length of R = 7.6 mm, a thickness of outer and inner ring of O1 and O2 is 0.2 mm respectively, also Gap between two rings of t = 0.2mm and a split gap of G = 0.3 mm was shown in Figure 2. The feed-line of the structure is a 50Ω microstrip line whose width was optimized to W = 1.5 mm. This copper line was realized on the upper face of the dielectric substrate with a length of L = 66 mm was shown in Figure 2.

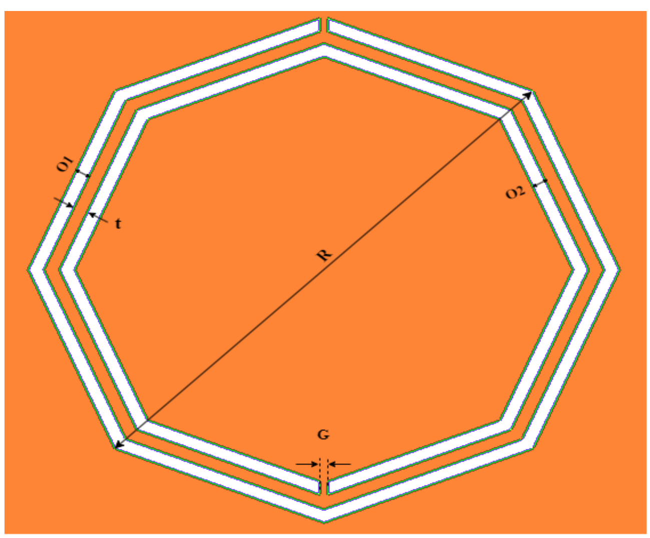


Figure 2. Single Element of CSRR

4. DESIGN ANALYSIS OF COMPLEMENTARY SPLIT RING RESONATOR BIO SENSOR

In the proposed biosensor design analysis, the complementary split-ring resonator (CSRR) was studied for various analyses. The CSRR gap was varied between 0.1mm to 0.3mm, while the stripline thickness was varied between 1.1mm to 1.5mm was shown in Figure 3 and 4. These variations were considered to investigate the performance of the biosensor design. The results obtained from the analysis indicated that the biosensor design's performance was greatly influenced by the variations in CSRR gap and stripline thickness. Therefore, the proposed biosensor design could be optimized by carefully selecting the CSRR gap and stripline thickness values to enhance its overall performance.

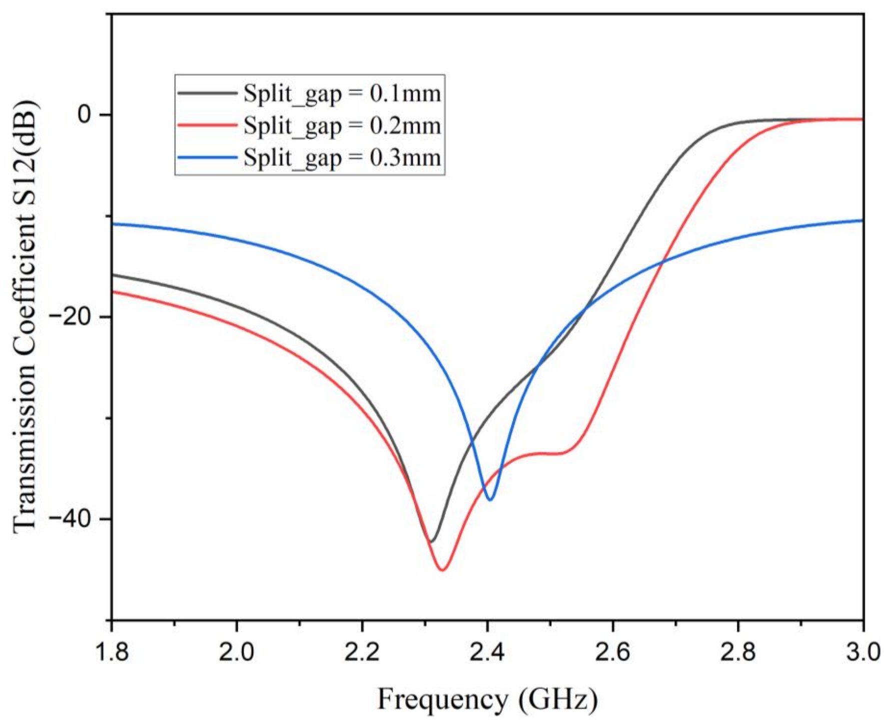


Figure 3. Response of Transmission Coefficient S12 for gap from 0.1-0.3mm

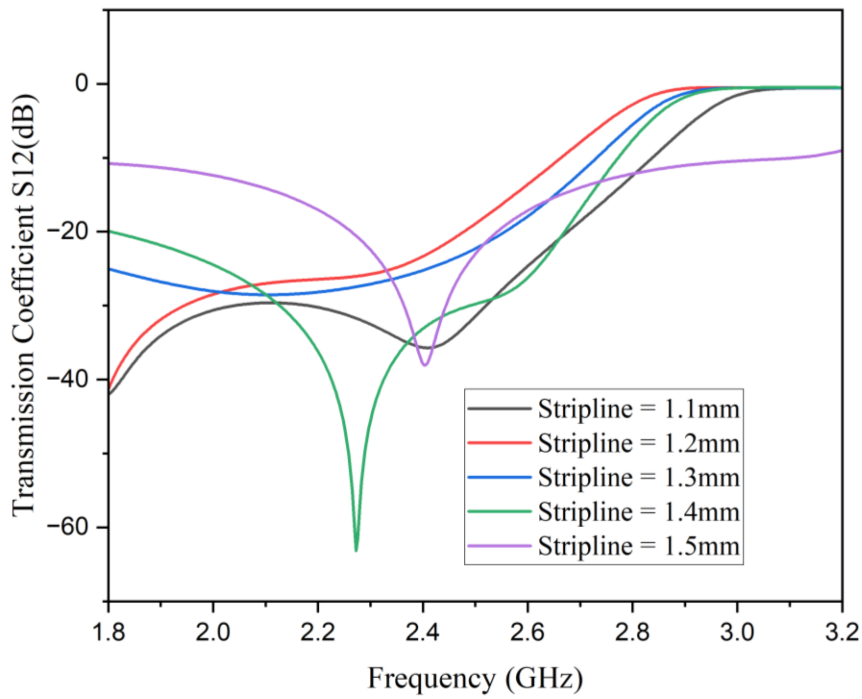


Figure 4. Response of Transmission Coefficient S12 for stripline thickness from 1.1 - 1.5mm.

This result suggests that the 3mm ring radius and 1.5mm strip line width configuration can maintain resonance characteristics comparable to the earlier identified optimal design, while achieving the expected output level. The output graph, presented in Figure 5, consistently demonstrates a resonance peak at 2.4060 GHz within the Transmission Coefficient (S21) parameter. This resonance peak corresponds to a signal strength of approximately -38.0068 dB. The achieved results signify the effectiveness of the optimized configuration in producing a resonant response at the specified frequency, thus validating the success of the design and optimization process for the microwave.

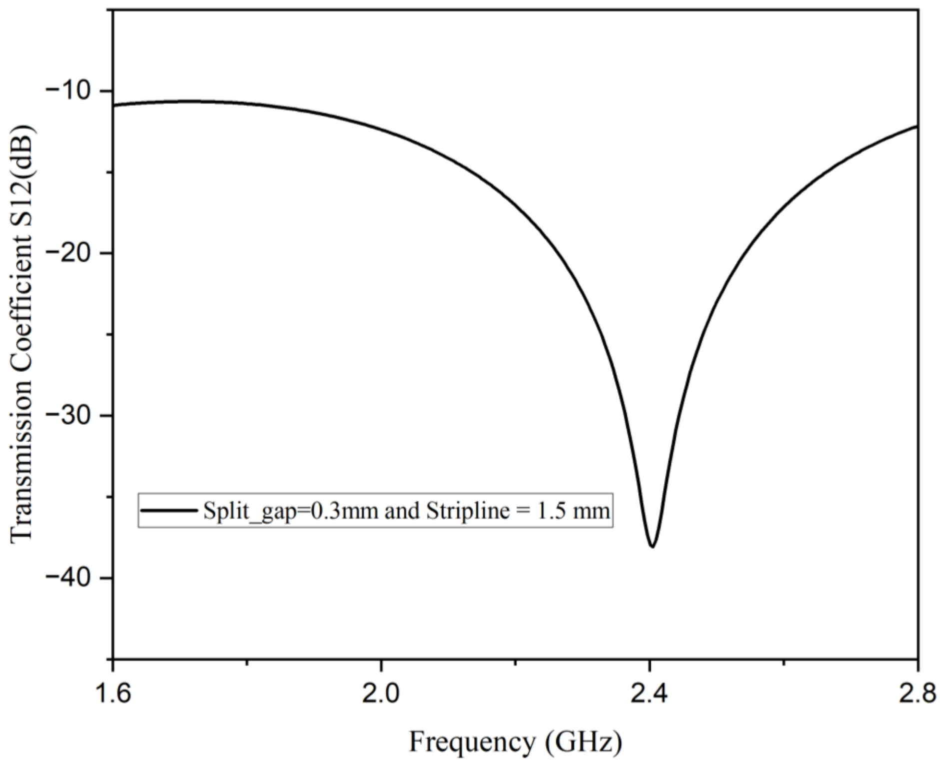


Figure 5. Response of Transmission Coefficient S12 after optimization to 2.4GHz

5. RESULT AND DISCUSSION

Testing blood glucose levels by utilizing a soda lime glass substrate to prevent direct contact between the sensor and the human hand requires thorough analysis of the substrate's influence on sensor performance. The substrate, characterized by dimensions of 36mm length, 20mm width, and 0.15mm thickness, possesses a dielectric constant (εr) of 7.75 was shown in Figure 6. Placing the glass above the sensor initiates changes in the S21 parameter and frequency characteristics, crucial for accurate glucose level determination. The dielectric constant and loss tangent significantly affect electromagnetic wave propagation through the glass, potentially resulting in variations in the S21 parameter as the glass interacts with the sensor. Furthermore, alterations in the glass's dielectric properties may induce frequency shifting, impacting the sensor's resonance characteristics. Understanding these effects is pivotal for optimizing blood glucose testing procedures and ensuring precise measurements.

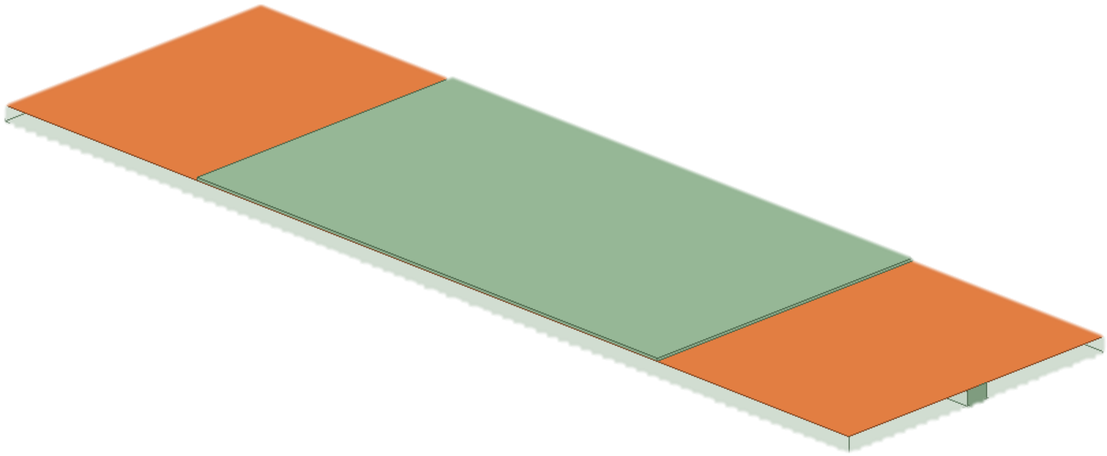


Figure 6. CSRR with testing glass

After positioning the soda lime test glass above the sensor, notable shifts occurred in the sensor's response to electromagnetic waves. The frequency transitioned from its initial value of 2.4060 GHz to a new frequency of 2.0940 GHz, signifying alterations in the sensor's resonant behavior prompted by the electric properties of the glass. Concurrently, the transmission coefficient, represented by S21, underwent a transformation from its original value of 38.0068 dB to a new measurement of 62.8959 dB, as depicted in Figure 7. These variations in frequency and S21 elucidate how the electric properties of the borosilicate glass influenced the sensor's interaction with electromagnetic waves, underscoring the significance of substrate material in sensor performance.

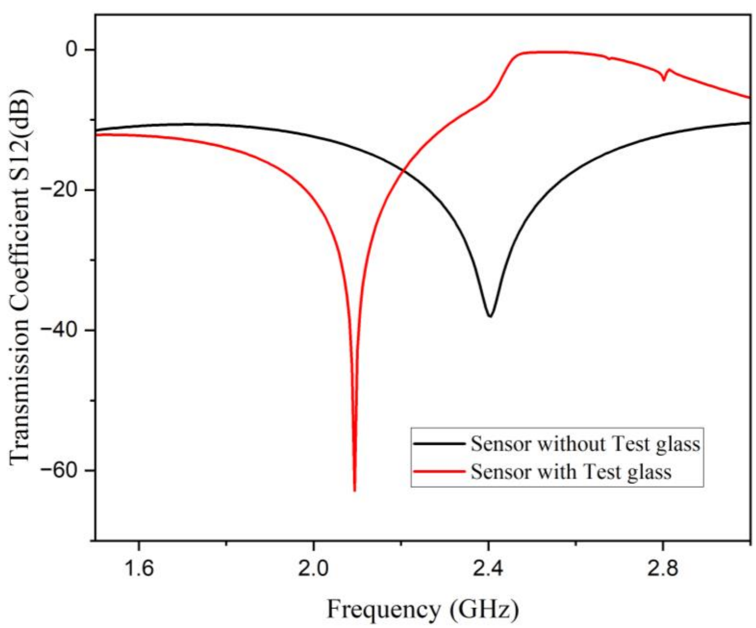


Figure 7. Response of Frequency shifting and Transmission Coefficient S21 of Bio - sensor without Test glass and with Test glass

In order to simulate the interaction of microwaves with a human index finger, a simplified model was created using ANSYS HFSS. This model was developed by taking into consideration the average thickness and relative permittivity of the different layers of the finger was shown in Table 1. Typically, the skin of a finger is made up of three layers: the epidermis, dermis, and hypodermis. The dermis layer contains connective tissues, hair follicles, and sweat glands, while the hypodermis is usually filled with subcutaneous fat. Beneath the hypodermis, one can find the subungual arterial arcades, dorsal digital veins, and the distal phalanx, which is a flat bone that supports the finger pulp. Based on this anatomical information, a simplified model was developed that includes four layers of biological tissues.

Table. 1 Dielectric parameters of different layers

Tissue	Thickness(mm)	Dielectric constant
Skin	1	35
Fat	1	5.5
Blood(0mg/dl)	5	59.70
Bone	6	20

In this model, the finger is represented by a layer of skin followed by a layer of fat, blood, and finally, a rectangular bone. According to the HFSS simulation, the finger length (h) is estimated to be around 10 mm. The dimensions of the finger used in the simulation were carefully selected to ensure that it covers the entire sensitive area of the sensor, representing the central part of the CSRR. Specifically, the dimensions of 13 mm x 13 mm were chosen to match the average size of an adult female index finger, which is commonly used in blood glucose monitoring was shown in Figure 8.

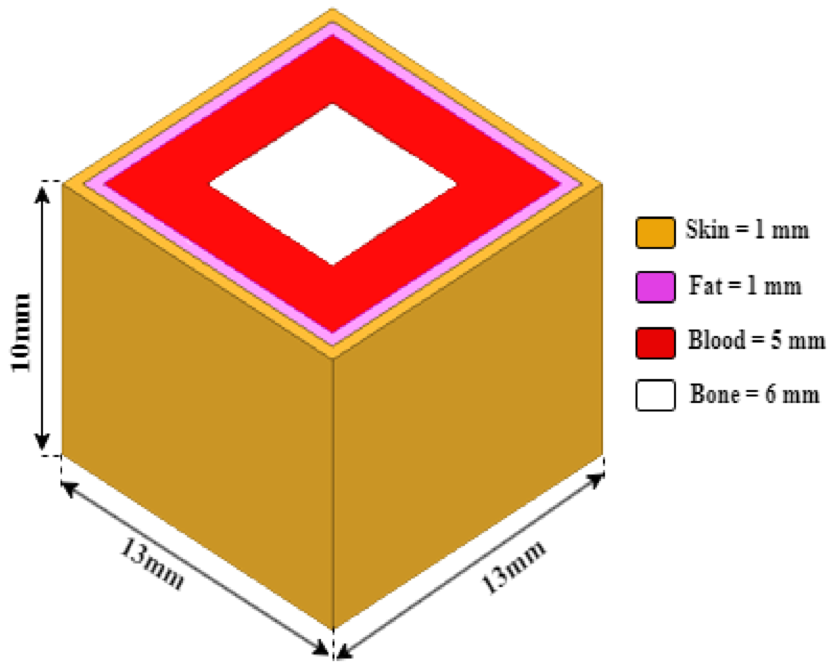


Figure 8. 3D finger model with thickness of layers

Various glucose concentrations from 0 to 300 mg/dl were simulated. Results of the transmission coefficients for CSRR. The simulation was done by assigning dielectric constant or relative permittivity εr and tangent loss tanδ of blood layer from 0 - 300mg/dl was shown in Table 2.

Table 2. Dielectric constant and tangent loss of blood layer from 0 to 300mg/dl

Blood Glucose Concentrations mg/dl	Dielectric constant or relative permittivity (ε_r)	Tangent loss (tanδ)
0	59.70	1.143
50	57.81	0.867
100	59.03	0.619
150	58.67	0.556
200	58.84	0.532
250	58.86	0.516
300	58.80	0.507

glucose concentration increases, the resonant frequency of the sensor tends to shift to higher frequencies, leading to increased sensitivity of the transmission coefficient. Additionally, the amplitude values of the transmission coefficient also increase with rising glucose levels. Altering the glucose concentration from 0 to 300 mg/dl causes a shift in the transmission coefficient of the proposed sensor from 23.02 to 40.86 dB was shown in Figure 9 and observed frequency shift and Transmission Coefficient S12 was shown in Table 3.

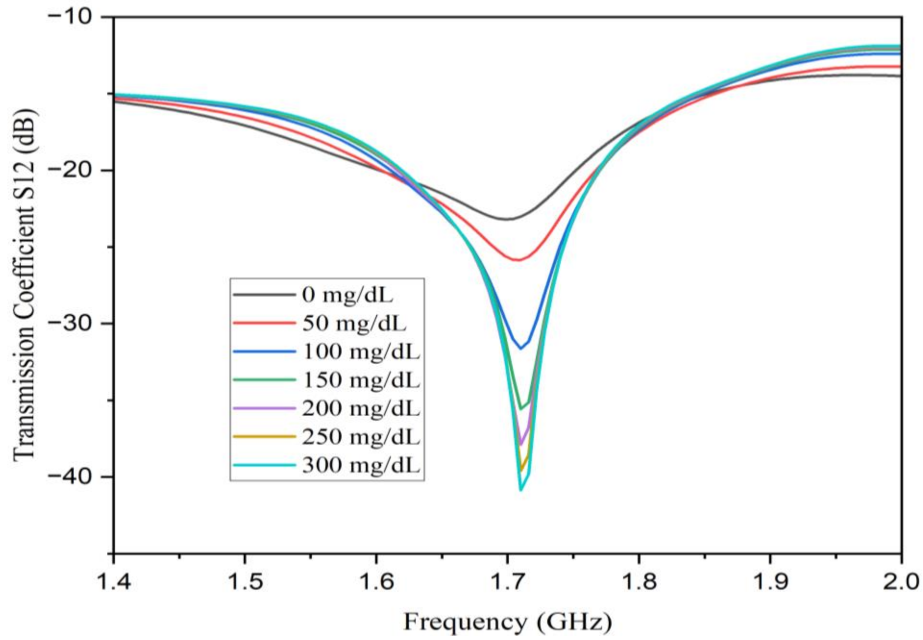


Figure 9. Response of Transmission Coefficient S12 for glucose level 0 – 300 mg/dl

Table 3. Blood Glucose Concentration vs Transmission Coefficient S21

Blood Glucose Concentration (mg/dl)	Resonant Frequency (GHz)	Transmission Coefficient S12 (dB)
0	1.7165	-23.02
50	1.7165	-25.85
100	1.7165	-31.63
150	1.7165	-35.57
200	1.7165	-37.90
250	1.7165	-39.59
300	1.7165	-40.86

CONCLUSION:

In conclusion, the simulation results of the Rf based bio sensor developed for non-invasive detection of glucose level changes in diabetic patients are promising. The sensor design comprises of four CSRRs, and the electromagnetic simulations were carried out using a finger model with the main tissue layers developed with HFSS. The results obtained from the simulation study demonstrate a clear correlation between the glucose concentrations in blood. As the glucose level increases, magnitude of resonant frequency shift towards negative. This shift is attributed to the changes in the dielectric properties of the tissue layers in the finger model caused by variations in the glucose concentration. These findings suggest that the bio-sensor has the potential to provide accurate and reliable measurements of glucose levels in diabetic patients. The non-invasive nature of the sensor could significantly improve patient comfort and reduce the risk of infection associated with traditional invasive methods of glucose monitoring. However, further studies are necessary to validate these results and to optimize the sensor's design for practical applications.

REFERENCES:

[1] Yujiro Tanaka, Takuro Tajima, Michiko Seyama, Kayo Waki. Differential Continuous Wave Photoacoustic Spectroscopy for Non-Invasive Glucose Monitoring. IEEE Sensors Journal 2020;20(8): 4453-4458.

[2] Sandeep Kumar Chamoli, Subhash Chandra Singh, Chunlei Guo. Design of Extremely Sensitive Refractive Index Sensors in Infrared for Blood Glucose Detection. IEEE Sensors Journal 2020; 20(9): 4628-4634.

[3] Abhishek Kandwal, Zedong Nie, Tobore Igbe, Jingzhen Li, Yuhang Liu, Louis WY Liu, Yang Hao. Surface Plasmonic Feature Microwave Sensor with Highly Confined fields for Aqueous - Glucose and Blood-Glucose Measurements. IEEE Transactions on Instrumentation and Measurement 2020; 9456(c): 1-9.

[4] Maria Celeste Cebedio, Lucas Andres Rabioglio, Ivan Exequiel Gelosi, Ramiro Avalos Ribas, Alejandro Jose Uriz, Jorge Castineira Moreira. Analysis and Design of a Microwave Coplanar Sensor for Non-Invasive Blood Glucose Measurements. IEEE Sensors Journal 2020; 20(18): 10572-10581.

[5] la Eldin Omer, George Shaker, Safieddin Safavi-Naeini, Kevin Murray, Richard Hughson. Glucose Levels Detection Using mm - Wave Radar. IEEE Sensors Letters 2017; 2(3): 1-4.

[6] Shyqyri Haxha, Jaspreet Jhoja. Optical Based Noninvasive Glucose Monitoring Sensor Prototype. IEEE Photonics Journal 2016; 8(6):1-11.

[7] Joseph Y Lucisano, Timothy L Routh, Joe T Lin, David A Gough. Glucose Monitoring in Individuals with Diabetes Using a Long-Term Implanted Sensor/Telemetry System and Model. IEEE Trans Biomed Eng 2017; 64(9): 1982–1993.

[8] Volkan Turgul, Izzet Kale. Simulating the Effects of Skin Thickness and Fingerprints to Highlight Problems with Non-Invasive RF Blood Glucose Sensing from Fingertips. IEEE Sensors Journal 2017; 17(22): 7553-7560.

[9] Gang Wang, Michael D Poscente, Simon S Park, Christopher N Andrews, Orly Yadid-Pecht, Martin P Mintchev. Wearable Microsystem for Minimally Invasive, Pseudo-Continuous Blood Glucose Monitoring: The e-Mosquito. IEEE Transactions on Biomedical Circuits and Systems 2017; 11(5): 979-987.