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Glucose Aqueous Solution Sensing by Modified Hilbert Shaped Microwave Sensor

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Abstract: We present a microwave sensor based on the modified first order Hilbert curve designed for detecting glucose concentration in aqueous solutions by using a real-time microwave near-field electromagnetic interaction technique. We observed S_{11} reflection parameters of the sensor at resonant frequencies depend on the glucose concentration. We could determine the glucose concentration in the 0-250 mg/dl concentration range at an operating frequency near 2.6 GHz. The measured minimum detectable signal was 0.018 dB/(mg/dl) and the measured minimum detectable concentration was 1.68 mg/dl. The simulation result for the minimum detectable signal and the minimum detectable concentration was 0.023 dB/(mg/dl) and 1.3 mg/dl, respectively. Our proposed system has excellent potential to serve as a human bloodless glucometer.

Keywords: Non-invasive; Modified Hilbert; Microwave sensor; Glucose concentration

1. Introduction

Glucose is the main calorimetric energy source for the human body, and it performs critical work in cellular metabolism [1]. However, a high concentration of glucose can be the cause of arteriosclerosis or diabetic retinopathy. In a healthy person, the pre-prandial blood glucose level is under $100mg/dl(0.1wt.\%)$, and the post-prandial blood glucose level is $140mg/dl(0.14wt.\%)$. When a person has diabetes, the post-prandial blood glucose level is greater than $200mg/dl(0.2wt.\%)$ and the pre-prandial blood glucose level is also high. In 2014, 8.5% of adults age 18 years and older had diabetes. In 2015, diabetes was the direct cause of 1.6 million deaths and in 2012 high blood glucose was the cause of another 2.2 million deaths [2]. Knowing the blood glucose concentration for patients with diabetes mellitus is crucial for maintaining it within physiological limits. Blood glucose concentration often needs to be measured several times a day [3].

Presently, the glucose sensors based on an invasive measurement technique are widely used, for example, the finger-prick glucometers which have a low price and provide high accuracy.

However, the invasive glucose sensors have a number of obvious problems such as pain, the risk of infection, tissue damage where blood is taken, etc. It is evident that a non-invasive glucometer would be of great help to achieve a better control of insulin and glucose levels. Therefore, developing the blood glucose sensors based on a non-invasive measurement technique is important for improving and facilitating patient health care [4,5]. Currently there are several types of blood glucose biosensors based on a microwave dielectric waveguide probe [6], an artificial transmission line [7], a band-stop filter [8], a microwave spiral resonator [9], a near-field microwave microprobe [10]. However, the existing devices are limited to sensing samples and trends and require further resolution improvement.

In this paper, we propose a microwave sensor based on the modified Hilbert curve of first order for determination of the D-glucose $(C_6H_{12}O_6)$ concentration. The measurements are done on an aqueous solution by measuring the microwave reflection coefficient S_{11} at resonant frequencies of about $2.6GHz$. The change in reflection coefficient S_{11} is directly related to the change in the glucose concentration due to an electromagnetic interaction between the microwave sensor and the samples. We chose the concentration of glucose from $50mg/dl$ to $250mg/dl$, since this range corresponds to the concentration of glucose in human blood for both normal and diabetic patients. As a background we chose deionized (DI) water.

We also modeled the Hilbert curve sensor by using COMSOL Multiphysics software which accurately predicts response of the microwave signal. The simulated results for S parameters of the sensor in both cases, without and with material under test (MUT) were in good agreement with the obtained experimental data.

2. Design and fabrication

Figure 1 (a) and (b) shows the structural image of the sensor without and with the quartz flask, respectively. A ceramic with dielectric permittivity of about 9.2 and sizes of $20.4mm \times 40.4mm \times 1mm$ was chosen as the substrate. The both sides of ceramic substrate were coated by a thin layer (about $50\mu m$) of silver paste. The sensor was prepared by drying, laser patterning and annealing techniques. The sensor finally was soldered to the conductors.

One side of the sensor which was patterned has a shape as a modified Hilbert-shaped closed curve. The geometry of the modified Hilbert-shaped sensor is shown in Fig. 1 (c). Here $h, s,$ and w are the width of the stripline, length of the Hilbert-shaped curve unit of the first order, and the width of the curve, respectively. The designed parameters of the sensor are $h = 1mm, w = 0.1mm$ and $s = 2.6mm$.

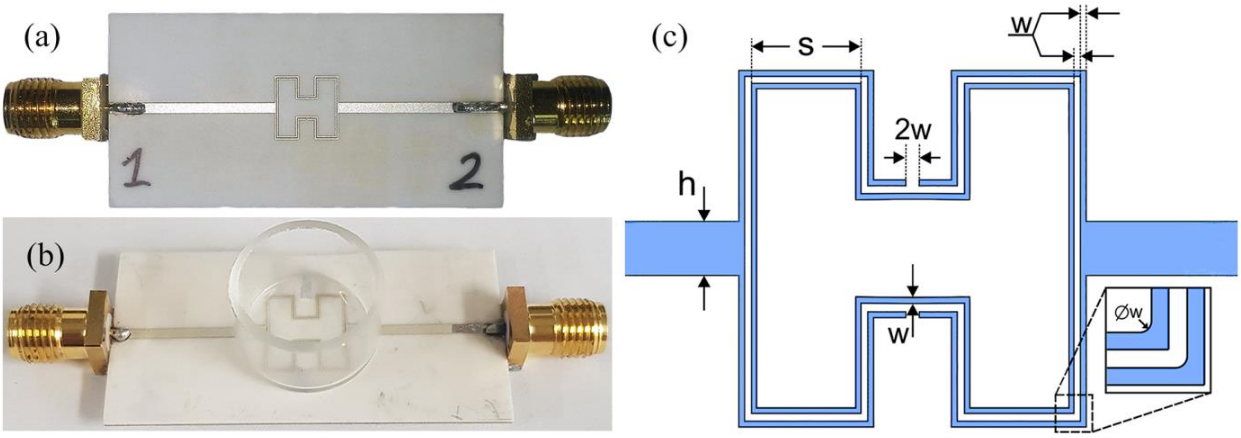

Fig. 1. The modified 1st order Hilbert-shaped fractal sensor (a) without and (b) with quartz vial. (c) The structural geometry of sensor pattern.

In experiment, we placed a quartz flask with aqueous solutions with various concentrations of D-glucose on the sensor and the response was detected by a vector network analyzer (VNA: Agilent E5071B). The dielectric constant of the quartz flask was 3.8, height was $8mm$ and thickness was $1mm$. Outer and inner radius were $7mm$ and $6mm$, respectively. The volume of aqueous solution was kept at $500\mu l$ during all experiments and in the simulation as well. High sensitivity can be achieved when the quartz flask is placed on the symmetric center of the Hilbert curve. The resonator was calibrated with DI water giving an S_{11} minimum of $-26.84dB$. The data acquisition time for glucose real-time monitoring was $0.5s$ and experiments were conducted at a temperature of 25^0C. The microwave Hilbert-shaped sensor for detecting glucose concentration was modeled by using COMSOL simulation software. Changes of the resonant frequency f_0 and reflection coefficient S_{11} of the sensor are caused by the replacement of the MUT as a load. The geometry of the simulated model in COMSOL simulation software and near-field electromagnetic field distribution are represented in Fig. 2. The electromagnetic field intensity is concentrated around the sensing Hilbert-shaped pattern for both the electric field and the magnetic field distribution as shown in Fig. 2 (b), (c).

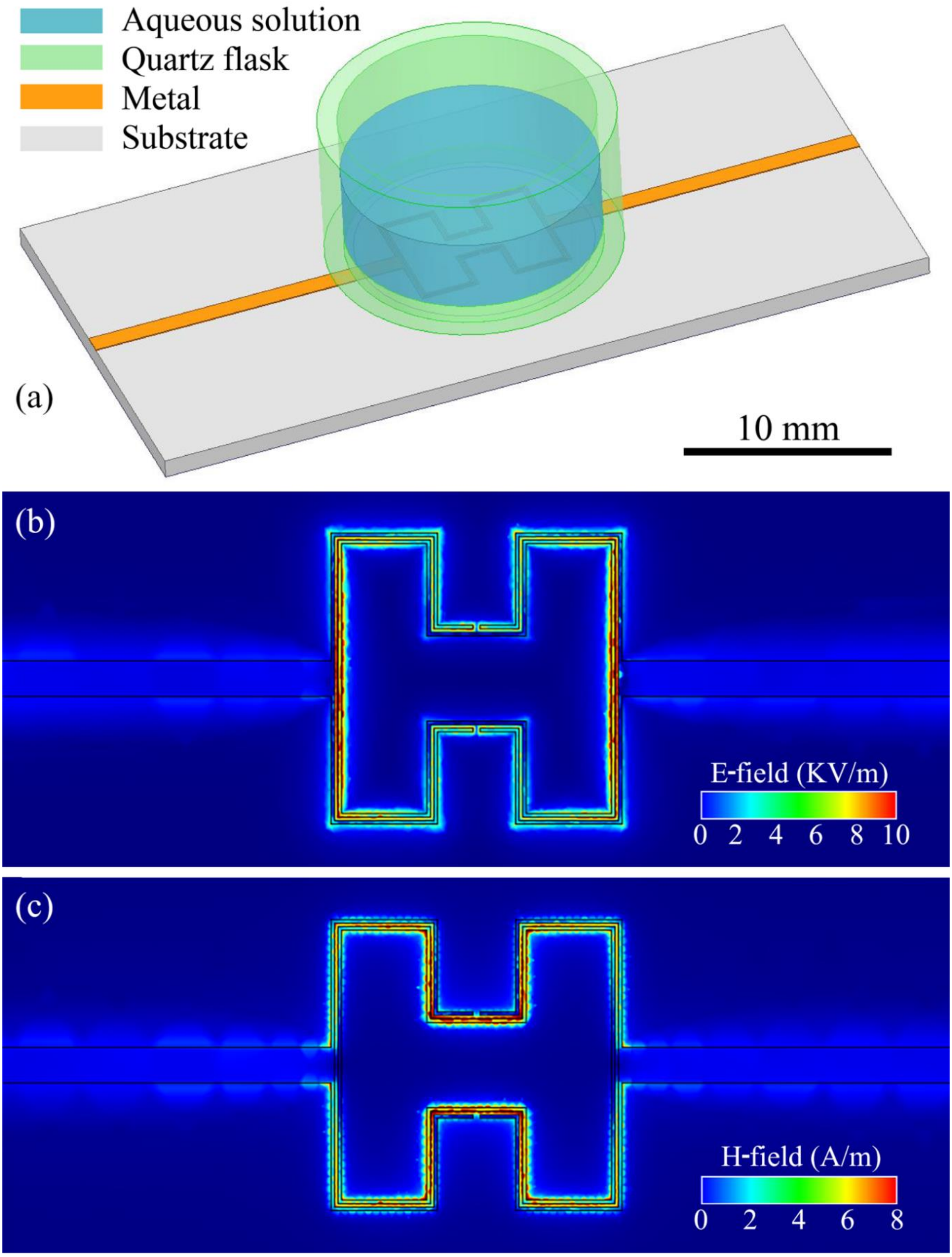

Fig. 2. (a) The geometry of the sensor simulation model in COMSOL. Simulated (b) electric and (c) magnetic near-field distribution at 3.3 GHz.

3. Theoretical background

The operational principle of sensor/MUT system is based on the shift in the microwave reflection coefficient S_{11} due to changes of the electromagnetic characteristics of the MUT, such as the dielectric permittivity and the magnetic permeability. Most biological materials have magnetic permeability close to that of free space that is not changing, thus the changes in magnetic permeability were neglected during our test [11]. The dielectric constant is a parameter that can be experimentally measured. By measuring dielectric properties of a given material, we can indirectly measure other properties of that material related to their molecular structures such as a concentration. The relative permittivity of material has complex form with $\varepsilon = \varepsilon' - j\varepsilon''$, where ε' is the real part of complex permittivity and causes electric energy storage in the material. The imaginary part of the complex permittivity ε'' caused by the conductivity characterizes the energy loss with $\tan\delta = \varepsilon''/\varepsilon'$ when an EM signal passes through the material. The dependence of dielectric permittivity on solute glucose concentration is expressed with the molar increment δ and given by $\varepsilon_g(\omega) = [\varepsilon_0'(\omega) + c\delta'] - j[\varepsilon_0''(\omega) + c\delta'']$ where $\varepsilon_0(\omega)$ is the complex permittivity of DI water ($\varepsilon_0'(\omega) = 78.25$ and $\varepsilon_0''(\omega) = 13.3$ at $3.3GHz, 25^0C$, c is the concentration of glucose, $\delta = \delta' - j\delta''$ is the increase in permittivity when the glucose concentration is raised by 1 unit ($\delta' = 0.00577(mg/dl)^{-1}, \delta'' = 0.00015(mg/dl)^{-1}$) and ω is the field frequency [9,12]. The dependence of dielectric permittivity on concentration and field frequency can be understood with the Debye relaxation model. By increasing the operation frequency the real part of permittivity shows decreasing behavior and the imaginary part shows increasing behavior, whereas by increasing the glucose concentration in the solution the real part of permittivity of the solution decreases and the imaginary part increases [13].

4. Results and discussion

The (a) measured and (b) simulated reflection parameters for the designed unloaded sensor are presented in Fig 3. The resonant frequency is nearly at $3.3GHz$ for both simulated $(3.38GHz)$ and measured $(3.33GHz)$ data. The shift between measured and simulated resonant frequency of about $57MHz$ and about $4.7dB$ can be caused by port mismatching and cable losses, etc. In general, the behaviors of measured and simulated reflection parameters are in good agreement and described the testing process well. Putting the quartz vial with aqueous solution on the sensor (loaded sensor) causes the change of scattering parameters (resonant frequency, amplitude) due change of the total impedance of the system. As was expected, *S*-parameters depended on the variation of the glucose concentration in the aqueous solution. Figure 4 (a) shows simulated and experimental results of microwave reflection coefficient S_{11} profiles for DI water and for D-glucose aqueous solution with glucose concentration range from $50 mg/dl$ to $250 mg/dl$. Both the simulated and experimental curves have the resonant minimum value of S_{11} at the frequency of about $2.6 GHz (2.67 GHz$ vs. $2.53 GHz)$.

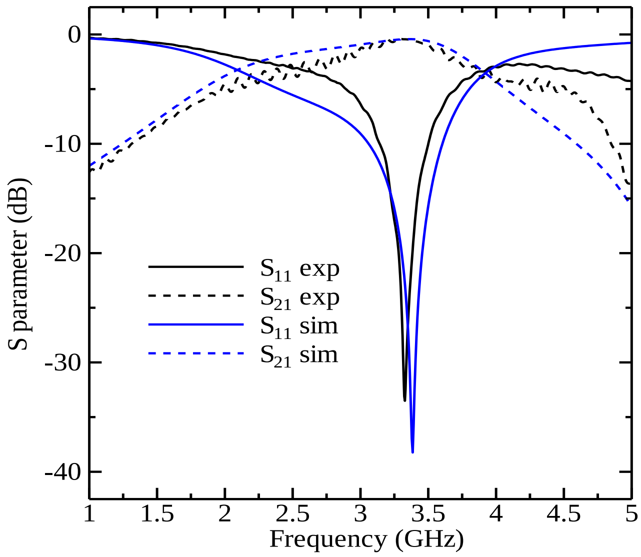

Fig. 3. The experimental and simulated reflection/transmission coefficients of the sensor.

S_{11} increased as the glucose concentration decreased as shown in Fig. 4 (b) for both simulation and experiment. The maximum difference of S_{11} parameter for sensor loaded by DI water and solution with $250 mg/dl$ glucose concentration was about $5.5 dB$ at $2.67 GHz$ in simulation and about $4.6 dB$ at $2.53 GHz$ in experiment. In other cases, the difference monotonously decreases by decreasing the glucose concentration. The relationship between S_{11} and glucose concentration is linear and the S_{11} trend varies with slope of $0.023 dB/(mg/dl)$ in simulation and $0.018 dB/(mg/dl)$ in measurement. Stable linear relationships are important for detection and analyzing glucose concentrations in solution. The minimum detectable concentration $c_{\min}$ of designed sensor defined as

$$c_{\min} = \frac{S_{11}^R}{\Delta S_{11}/\Delta c} \tag{1}$$

where Δc is the concentration variation, ΔS_{11} is the change in S_{11} corresponding to Δc, and $S_{11}^{R} = 0.03dB$ is the resolution of the experimental system. The minimum detectable concentration was found to be $1.3 mg/dl$ and $1.68 mg/dl$ for simulation and experiment, respectively (data are summarized in Table 1).

Table 1. The main operating parameters of the designed sensor.

Sensor parameter	Simulation	Measurement
Dynamic range for S_{11}	5.5 dB	4.6 dB
Resonant frequency	2.67 GHz	2.53 GHz
Sensitivity for S_{11}	0.023 dB/(mg/dl)	0.018 dB/(mg/dl)
Minimum detectable concentration	1.3 mg/dl	1.68 mg/dl

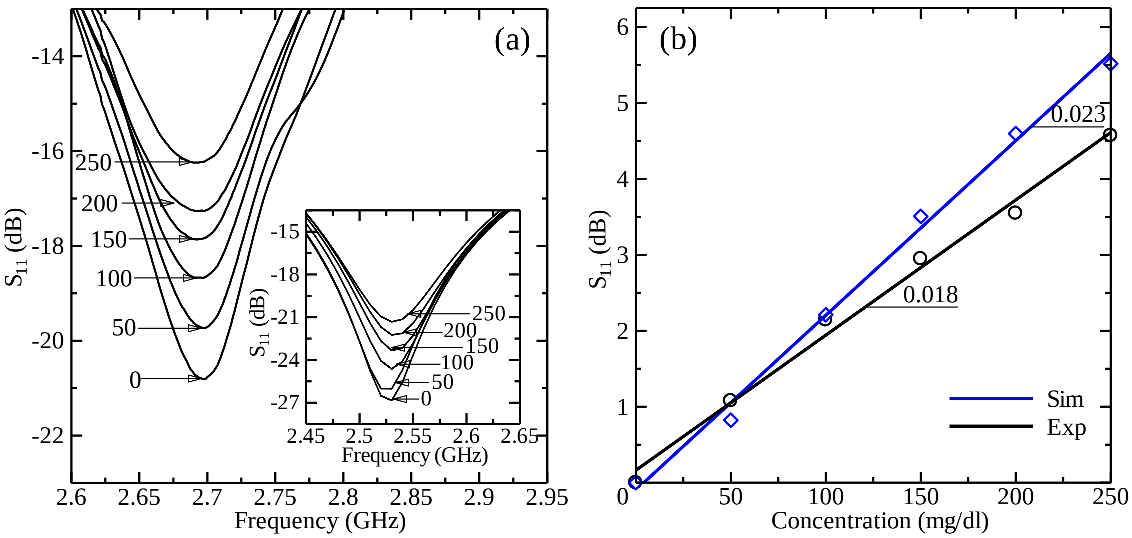

Fig. 4. (a) Simulated and measured (inset) results of microwave reflection coefficient S_{11} profile for DI water and for glucose aqueous solution with different concentrations 50-250 mg/dl for 500 µl volume. (b) The simulated and measured microwave response dependence on D-glucose concentration at the resonant frequency of about 2.67 GHz and 2.53 GHz, respectively.

We also simulated the electromagnetic field interaction between the sensor and the glucose solution, to visualize the electromagnetic field distribution during measurement. Figure 5 shows the simulated subtraction images of $250 mg/dl$ and $0 mg/dl$ (DI water) glucose concentrations for (a), (c) electric field and the (b), (d) magnetic field at (a), (b) sensor/MUT interface (i.e. on boundary of sensor/glucose solution) and at (c), (d) $1mm$ high from sensor/MUT interface (i.e.

inside of the glucose solution), respectively. When the glucose concentration increased, both electric and magnetic fields strengths increased too. Changes in electromagnetic field distribution were due to the increase in complex dielectric permittivity of glucose solution, when the concentration of glucose in solution was increased.

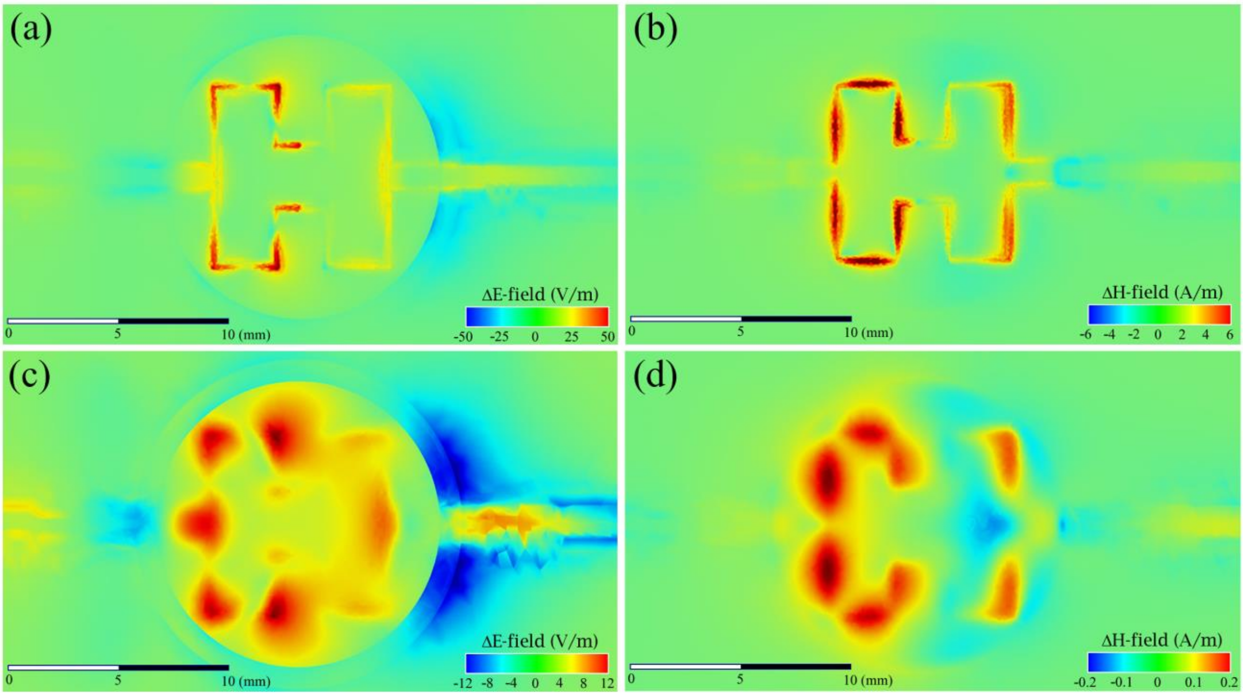

Fig. 5. The simulated subtraction image of 250 mg/dB and 0 mg/dl (DI water) MUTs for (a), (c) electric field and the (b), (d) magnetic field at (a), (b) sensor/MUT interface (i.e. on boundary of sensor/glucose solution) and (c), (d) at 1 mm distance from sensor/MUT interface (i.e. inside of the glucose solution), respectively at an operating frequency 2.67 GHz.

5. Conclusion

The microwave sensor based on modified Hilbert-shaped closed curve was designed and prepared as a non-invasive glucometer for monitoring of glucose concentrations in glucose aqueous solution. The sensor can detect the variation of glucose concentrations in aqueous solution with a non-destructive method.

The linear relationship between measured reflection coefficient S_{11} response and D-glucose concentrations at about $2.6 GHz$ was found to be $0.018 dB/(mg/dl)$. The minimum detectable resolution for glucose concentration was about $1.68 mg/ml$ for $500 \mu l$ MUT volume.

The results show the sensitivity and utility of sensor for glucose monitoring. Finally, it has great potential to offer a good platform for non-invasive and nondestructive measurement of human glycemia.

Acknowledgments

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