An In-Vitro Study of Wireless Passive Inductor Integrated Cavity for Future long-term Implantable resonator-based Glucose Monitoring

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***Abstract*— In this paper, a label-free biosensor is developed for monitoring the glucose level in the solution. A wireless passive inductor integrated cavity (IIC)-based biosensor is studied. The proposed IIC consists of a passive spiral inductor integrated cavity resonator for continuous monitoring of capillary blood glucose. The proposed method is based on the cavity perturbation theory, where the solution with different glucose levels perturbs and interacts with the passive IIC-based biosensor. The variation in the effective permittivity ϵ_{eff} and permeability μ_{eff} of the cavity resonator due to different glucose levels changes the equivalent capacitance and inductance of the proposed IIC. In turn, the corresponding resonance frequency changes. The in-vitro measurements are performed on deionized water glucose solutions of various glucose concentrations within the range of 75 mg/dL to 250 mg/dL. The results demonstrate that the sensor's resonant frequency increases with the increase in glucose level in the solution with a sensitivity of 32 kHz/mgdL^{-1}.**

I. INTRODUCTION

With an unhealthy lifestyle, the number of adults with diabetes has rapidly grown worldwide every year. Diabetes mellitus is one of the chronic diseases affecting over four hundred million. The insulin hormone for a person has diabetes, is either barely inside the body or the body resisting it. Therefore, the concentration of glucose increases in the bloodstream and can hardly get into cells [1], [2]. Thus, diabetes (Type 1 and type 2) always correlates with increasing glucose in the blood. Therefore, many methods have been reported the concentration of glucose in the blood as an indication of the level of diabetes [3]. With the increase of the glucose level in the blood, the glucose inside each cell becomes insufficient which may cause the risk of other chronic diseases, such as stroke, retinal damage, and slow wound healing. Therefore, it is essential to monitor the glucose concentration in blood in order to avoid the risk of high blood sugar and diabetic complications [4], [5].

Among many methods that have been studied the glucose level in the blood, the electrochemical technique is commonly used. The electrochemical technique shows excellent potential for observing the glucose level in the blood, such as finger-pricking or thin lancelet implanted devices. Finger-pricking devices are commonly used for detecting the glucose level in the blood. A diabetic patient can easily check the glucose level, thus this technique is known as self glucose monitoring. However, it is painful for the patient to use in the long-term because the process of this technique is required pricking the finger many times in the day for many years. Further, a thin lancelet implanted device has gained more attention, since it can continuously monitor the glucose in the blood. However, it is also required pricking the body many times for many years. Therefore, other technologies are needed based on non-invasive or long-term implantable devices to avoid finger pricking. However, high sensitivity, selectivity, and accuracy of the measurement is still a challenge with the comparison with finger-pricking devices that interacts directly with blood [6].

Several non-invasive or implantable devices have been recently developed for detecting the glucose level in the fluid, such as optical and microwave technologies. For instance, fluorescence spectroscopy is an optical minimally invasive method [7]. It has a high sensitivity for detecting low glucose concentration, but it is well-known its toxic properties to the tissues, in particular in the long-term use. Further, surface plasmon resonance (SPR) technique is also an optical minimally invasive method [8] with high sensitivity, but it is bulky in size. On the other hand, microwave spectroscopy is one of the promising candidates for observing the glucose level either for non-invasive [9]–[12] or invasive [13]–[15] techniques. The resonator is able to monitor the change in the permittivity of the surrounding medium (glucose solution) when the glucose level changes in the solution. The microwave spectroscopy is label-free and non-ionizing wave. In RF/microwave spectroscopy, different methods, such as free space, transmission line, and cavity resonator have been reported for observing the behavior of different materials. These methods are well studied in [16]. Among these methods, the resonant cavity is commonly used because of its high sensitivity for detecting the permittivity change, because it has narrow-bandwidth.

Therefore, for high sensitivity continuous glucose monitoring, the proposed passive IIC-based biosensor is designed and fabricated. In this work, a full passive resonator-based biosensor is studied for continuous glucose monitoring, where the proposed IIC interacts with different glucose levels in the deionized-water. The change in the frequency of the proposed IIC-based biosensor is tracked due to the changes in the electrical properties of the surrounding medium of the resonator, where the glucose solution interacts with the resonator. The proposed IIC-based biosensor is label-free, real-time, and wirelessly coupled by an external reader. The sensor is small in design to be implanted in the body and interacts with capillary blood glucose. Further, the electrical properties of different glucose concentrations in the solution are studied wirelessly.

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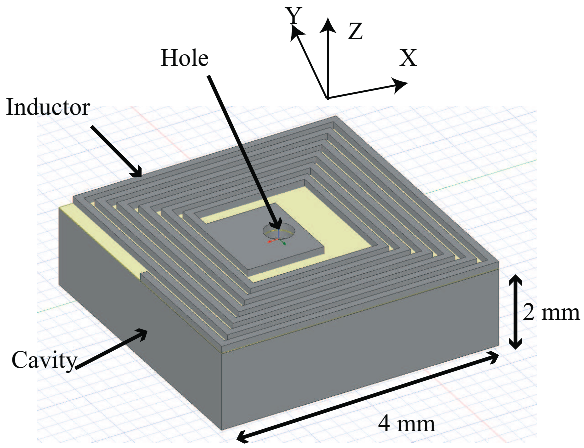

Fig. 1: Structure of the passive sensor.

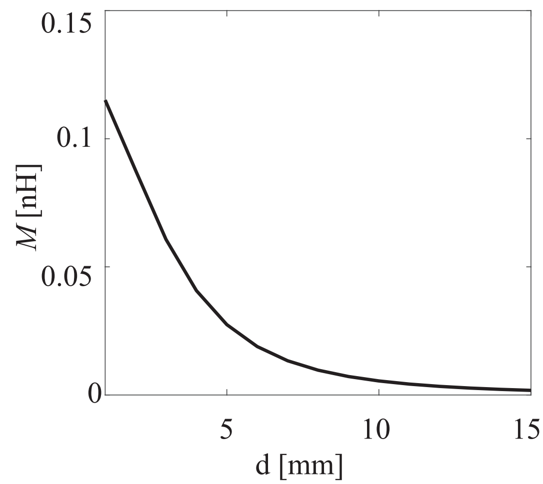

Fig. 2: Mutual inductance between the reader and sensor.

II. Overall System Structure and System Analysis

A spiral inductor is integrated with a metallic cavity, as shown in Fig. 1. The space inside the cavity is filled with FR4 dielectric material with a thickness of 2 mm. At the center of the proposed IIC-based biosensor, there is an empty hole for the fluid flow through it. The area of the proposed IIC-based biosensor is 4 mm×4 mm. Besides, the detailed parameters of the inductor are presented in Table I. The inductance is given as $L_i = 150$ nH, where the inductance of the spiral inductor can be expressed as [17]

$$L = \frac{2\mu_0}{\pi} n^2 d_{avg} (ln(\frac{2.07}{\phi}) + 0.18\phi + 0.13\phi^2) \quad (1)$$

$$\phi = \frac{1-\alpha}{1+\alpha} \quad (2)$$

where d_{avg} and α are the average diameter of the square area, and the ratio of outer diameter to the inner diameter, receptively. Further, The mutual inductance is studied between the The inductor coil of the proposed IIC-based biosensor and inductor of the reader, as given in [18], where the mutual inductance decreases by increasing the distance d, as shown in Fig. 2. Therefore, the signal strength of the passive sensor (dip s_{11}) is increased when M is increased [19].

TABLE I: The inductor parameters for proposed IIC

No. Turns	Thickness	Line space	Hole diameter
6	0.017 mm	0.1 mm	0.3 mm

The circuit model of the proposed IIC is demonstrated in Fig. 3. the inductor L_i is coupled with external reader inductor. The resonance ω_s of the the proposed IIC-based biosensor is derived as

$$\omega_s = \frac{1}{\sqrt{L_s C_s}} \quad (3)$$

where L_s and C_s are the equivalent inductance and capacitance of proposed IIC-based biosensor, respectively. The sensor is inductively powered using an external reader that is a circular spiral inductor. It has self inductance L_r and parasitic capacitance C_r. In addition, the equivalent impedance Z_{in} viewed from the reader side can be derived using KVL (Kirchhoff's Voltage Law) circuit analysis as

$$Z_{in} = \frac{V}{I_1} = j(\omega_0 L_r - \frac{1}{\omega_0 C_r}) + \frac{\omega_0^2 M^2}{j(\omega_0 L_i + \omega_0 L_c - \frac{1}{\omega_0 C_i} - \frac{1}{\omega_0 C_c}) + R_s} \quad (4)$$

where V, I_1, and R_s are the exciting voltage, current across the reader, and the resistance of the sensor, respectively. Therefore, reflection coefficient (S_{11}) is derived as

$$S_{11} = \frac{Z_{in} - Z_0}{Z_{in} + Z_0} \quad (5)$$

where Z_0 is characteristic impedance at the reader side.

The interaction of the proposed IIC-based biosensor with different levels of glucose through the cavity hole causes a change in the effective permittivity ϵ_{eff} and permeability μ_{eff} of the proposed IIC-biosensor. Thus, the electric and magnetic fields of the proposed IIC-based biosensor changes. Figs. 4(a) and 4(b) show the field distribution inside the cavity hole when the proposed sensor is empty and when it

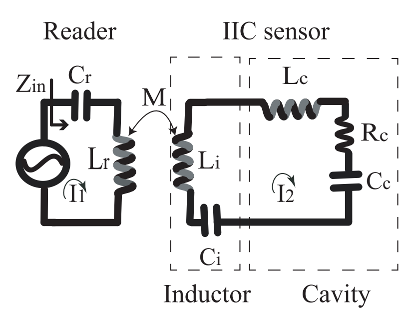

Fig. 3: Equivalent circuit model for the passive resonator, the proposed IIC-based biosensor inductively coupled to the external reader.

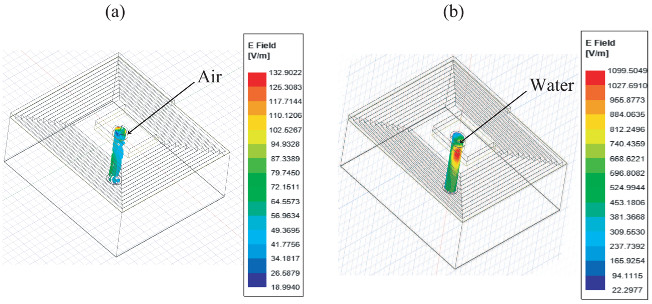

Fig. 4: HFSS-simulated electric field distributions inside the hole of the passive IIC-biosensor. (a) Air inside the hole. (b) Water inside the hole.

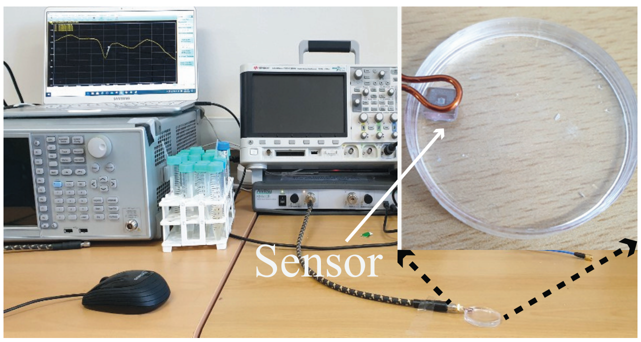

Fig. 5: Experimental setup along with the fabricated sensor. Fabricated passive IIC is completely surrounded and covered in the glucose solution and coupled with the external reader.

is perturbed by a high-loss solution (i.e., water). Introducing different glucose concentration levels to the proposed IIC-based biosensor causes a change in the effective permittivity and permeability. As a result, the corresponding resonance frequency of the proposed IIC-based biosensor changes. An approximate fractional change in the resonance frequency when the solution surrounding the proposed IIC-based biosensor is given as [20]

$$\frac{\omega - \omega_0}{\omega_0} \approx \frac{-\int_{V_0}(\Delta\epsilon_{eff}\,|\mathbf{E}_0|^2 + \Delta\mu_{eff}\,|\mathbf{H}_0|^2)dV}{2\int_{V_0}\epsilon_{eff}\,|\mathbf{E}_0|^2 + \mu_{eff}\,|\mathbf{H}_0|^2\,dV} \tag{6}$$

where V_0 is the volume of the proposed IIC-based biosensor. This means that any change in the effective permittivity and permeability of the proposed sensor by the perturbed solution will change the resonance frequency. Further, the variation in the perturbed solution properties across the cavity hole changes the effective permittivity by $\Delta\epsilon_{eff}$ and permeability by $\Delta\mu_{eff}$, which are corresponding to the change in the proposed IIC-based biosensor resonance.

III. Measurements and Results

For a diabetic patient, the normal range of glucose level in the blood within the range of 75mg/dL to 200 mg/dL. Thus, an aqueous glucose standard solution of 75 mg/dL, 100 mg/dL, 150 mg/dL, and 250 mg/dL were prepared, which is proper for a clinical test of glucose. Firstly, the stock solution of 250 mg/mL was prepared by mixing 2.5 g of D-glucose powder with 10 dL of deionized water. Then, other concentrations were made by mixing the deionized water with the stock solution by different ratios. 4 mL of the glucose solution was added into the petri dish. The proposed IIC-based biosensor was placed in the petri dish, and it was fully immersed in the glucose solution. Then the resonance of the sensor was tracked through the external reader.

Prior to measurements, a vector network analyzer (VNA) was kept in a calibration mode. The calibration was made using three standards, i.e., open, short, and load in order to reduce the effect of undesired losses during the measurements. The external reader was connected with VNA via coaxial cable.

Fig. 7 shows the measurement setup, where the fabricated passive sensor was surrounded by different glucose concentrations. The resonance of the proposed IIC-based biosensor was observed from the reader side at a distance of 5 mm between the reader and sensor. The inductor and cavity are made with copper that has a conductivity of 5×10^7 S/m. The proposed IIC-based sensor was coated with polyethylene terephthalate (PET) except the cavity hole position to allow the glucose solution to perturb the cavity. PET was used as an insulator material to prevent the proposed IIC-based biosensor from shorting, and it is one of the most commonly used synthetic biomaterials. During the experiments, the passive sensor had the same condition when introduced different glucose concentrations, such as the same distance

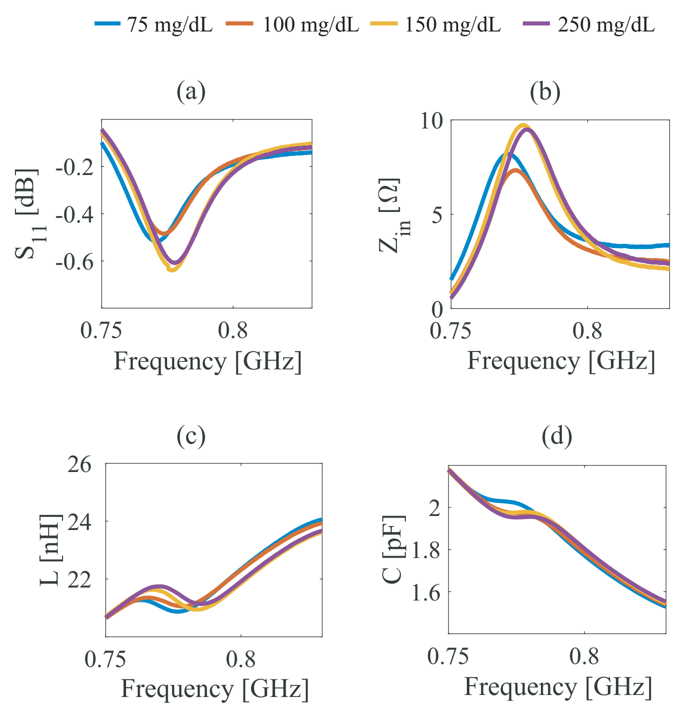

Fig. 6: Measured sensor response wirelessly from the reader side, with 5mm distance between the reader and sensor, with different glucose concentrations: (a) S_{11}. (b) Z_{in}. (c) Inductance. (d) Capacitance.

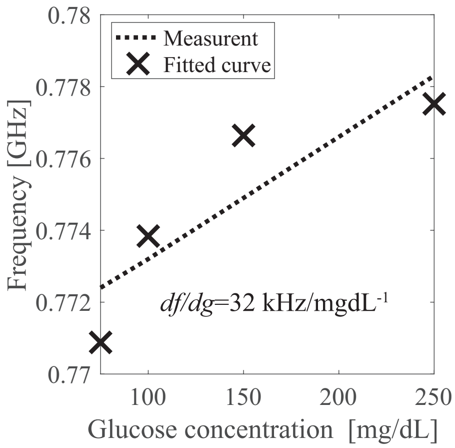

Fig. 7: Experimental setup along with the fabricated sensor. Fabricated passive IIC is completely surrounded and covered in the glucose solution and coupled with the external reader.

between the sensor and the reader, and all the experiments were done at room temperature. The change in the resonance of the proposed IIC-based biosensor was observed when the concentration of the glucose changed. Further, the resonance frequency increased by increasing the concentration of the glucose inside the solution, as demonstrated in Figs. 6(a), 6(b), 6(c), and 6(d). This is caused due to the decrease in the effective permittivity and permeability of the proposed IIC-based biosensor. Fig. 7 demonstrates the measured and fitted resonant frequencies as a function of glucose solution in the range of 75 mg/dL to 250 mg/dL with a sensitivity of 32 kHz/mgdL^{-1}. This implies that recognizing the change of glucose concentration level in the aqueous solution gives the high possibility to observe the glucose concentration in any other liquid, including blood.

IV. CONCLUSIONS

In this work, a millimeter-scale passive sensor has been illustrated, where the sensor can observe the different glucose concentrations in the solution. Different glucose levels in the solution perturb and interact with the electric and magnetic fields of the passive sensor through the cavity hole. Further, the change of sensor frequency is observed due to the change of effective permittivity and permeability of the sensor. The proposed passive IIC-based biosensor is designed to be small which is considered to be a promising candidate for future implanted devices for glucose monitoring.

Future work involves the in-vivo measurement of glucose concentration in animal body fluids. The passive sensor can be much smaller for easily injectable to the body for continuous long-term glucose monitoring. Further, future work will include improving the inductive coupling between the passive sensor and external reader with replacing VNA with the external portable reader [19] for more convenient to use, and to meet patient needs.

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