

Improvements in DNA Biosensors Using Joint Split Ring Resonators Coupled with Thin Film Microstrip Line

Mohammad Abdolrazzahi^{1*}, Ali Abdolali², and Soheil Hashemy²

¹Electrical and Computer Engineering Department
University of Alberta, Edmonton, Alberta, T6G 2V4, Canada

²Department of Electrical Engineering
Iran University of Science and Technology (IUST), Tehran, 1684613114, Iran

Abstract — Detecting the presence of materials in biomedical science using THz sensors, especially thin DNA strands, needs considerably sensitive sensors. Connection of unit cells in new frequency selective surface (FSS) structure, coupled with transmission line is introduced so that not only helps to miniaturize in sensing applications through THz frequency range, but also has steeper flanks in transitions, thus leads us to have higher sensitivities. All of the results are taken out from resonant frequencies related to reflection (s_{11}), a new property used instead of transmission loss (s_{21}), which is measurable using THz spectrometers. The effect of analyte thickness and dielectric properties of load on frequency response is explained. This approach is a new way in recognizing very small amounts of material even with rather low dielectric constants.

Index Terms — DNA detection, metamaterials, sensitivity improvement, THz biosensors.

I. INTRODUCTION

Pendry et al. [1], in 1999, following Veselago's idea of metamaterials [2], suggested split ring resonators (SRRs) theoretically as being feasible devices that show magnetic response from nonmagnetic conducting materials in microwave region. Smith et al. in 2001 demonstrated the possibility of SRRs using periodic lattice of long metallic wires and double split ring resonators (DSRR) [3]. Excitation of DSRRs with electric fields outside, can bring about LC-resonances, identified by Linden et al. [4] for TE and electric (plasmon) resonances for TM radiation [2], [4], [5].

High quality factor of such structures, lately persuaded researchers to utilize SRRs as sensing devices. The change in resonant frequencies of SRRs after being loaded with biological materials of different dielectric constants, is the main idea; as the rapid transition of frequency response paves the way for identification of small amounts of tissues. Therefore,

recently, thin-film sensing using frequency selective structures (FSS) are widespread.

Feasibility of SRRs as being bio sensing devices has been confirmed in the previous works [5], [6], [7]. In these thin-film sensors frequency of resonance and sensitivity are two important factors to consider both in simulation and in practice. Main problem of the proposed structures, are higher resonant frequencies and lower sensitivities [8]. We introduce a new back-to-back structure that meet both needs, and is useful in identifying minute amounts of biological tissues namely DNA strands, with promising results. All results of the simulations are obtained using CST Microwave Studio with perfectly matched layer (PML) boundary condition. Besides, the evolution process of the structure is explained. Knowing that thickness is another important factor in recognizing the type of material, the effect of load thickness on resonant frequency is illustrated and frequency response of the sensor after being loaded with dielectrics of diverse thicknesses are presented. Fitting with a Gaussian function presented at the end of the article helps to find intermediate corresponding f_r according to desired thickness.

II. METHODS

Interaction of the applied field with metal molecules makes induced currents that result in resonances [2]. In this paper, we used TE illumination, which makes a path for electrons to flow as current along a loop. The fields produced from the induced currents will have constructive or destructive effect on each other as the wave passes through or reflects from the FSS, and finally makes a resonance in reflection at frequency:

$$f_r = \frac{1}{2\pi\sqrt{LC}}, \quad (1)$$

where L stands for inductance of the metal, and C is the capacitance between edges of metals whether in free space or inside substrate. It is clear that the frequency is

inversely proportional to the size (dimension) of the SRR [9].

Dimensions of the structure are derived from observing several demands such as working in THz region as biosensor, small size and simplicity of the structure. Input impedance of thin film microstrip depends on the strip width and substrate height, which is determined uncontrollably due to the resonant frequency and the quality factor of the sensor. According to loading effects of SRRs on microstrip, the input impedance of the sensor is obtained as 220Ω at resonant frequency, using CST simulations. In order to match such device, we need a transmission line (TML) with characteristic impedance $Z_0 = \sqrt{Z_{in}Z_{out}}$, where Z_{in} equals the standard input impedance for measurement, and Z_{out} is the input impedance of loaded thin film microstrip line. Another way of matching the TML is to use interdigital capacitor [10]. As a result, we came up with what is shown in Fig. 1.

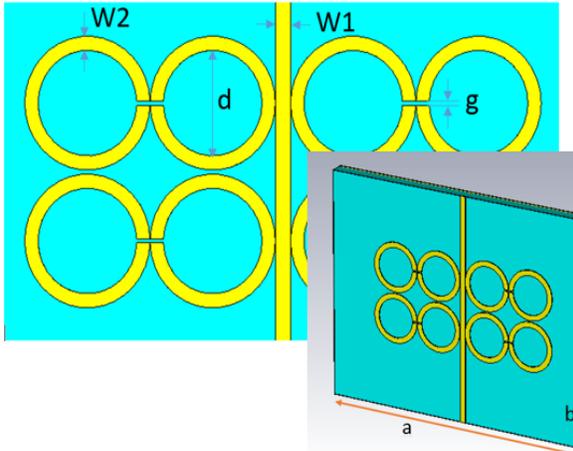


Fig. 1. Dimensions of the structure, $a = 400 \mu\text{m}$, $b = 300 \mu\text{m}$, $w1 = 8 \mu\text{m}$, $w2 = 7 \mu\text{m}$, $d = 52 \mu\text{m}$, $g = 2 \mu\text{m}$ and the aluminum metal of thickness $1 \mu\text{m}$ is over and under $18 \mu\text{m}$ thick silicon (loss free) substrate of $\epsilon_r = 11.9$.

Surface current of the structure after being illuminated through waveguide port at resonant frequency is shown in Fig. 2. It is clear that the density of current is more in the middle of transmission line due to the greatest amount of its interaction with the surrounding media.

In this work, single-stranded deoxyribonucleic acid (ss-DNA) and complementary deoxyribonucleic acid (c-DNA) are the biological elements to be detected and the single SRR for the transducer which converts chemical change into electrical signal. The principle of such biosensor lies in shifting of resonant frequencies due to changes of L or C. Changing the capacitance between the FSS edges, is an easy task as it needs to

introduce other materials to the sensor. We implemented the design using the proposed idea by adding generally biological tissues that impose appreciable change on sensor's effective dielectric constant, as well as resonances occur at different frequencies according to the Equation (1). After such simulations, we will have a rich database of f_r and corresponding external situation. In order to distinguish the surrounding environment using the sensor, we need to use the database in reverse manner by ANN, SVM machines, Fuzzy Logic or etc.

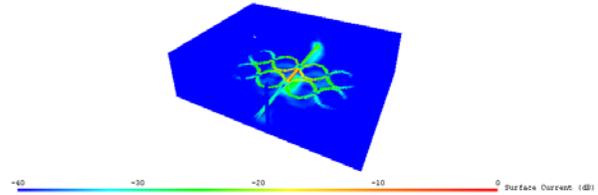


Fig. 2. The surface current of the structure in exposure to the external field at resonant frequency.

III. RESULTS AND DISCUSSION

Selection of the substrate and the FSS metal was due to their THz properties. As Silicon does not show appreciable loss in terahertz, especially lower frequencies, we chose it as loss-free to neglect its effect in our simulations [11]. Gold as the metal that has great capabilities in reacting to biological tissues, more importantly DNA, was suitable for our later diagnosis procedures.

Figure 3 shows the frequency response of the sensor during its configuration process. First of all, having just one SRR gives a deep resonance at 443 GHz; although it is a good one, but for minimization and technical reasons we need to lower the resonant frequency. Therefore, we proceeded in adding extra SRRs to see the differences. Second graph shows a back-to-back structure on one side of the transmission line, the resonances are not satisfactory; whereas, duplicating the latter on the other side makes third frequency response, and having another row yields the final deep and much lower resonant frequency, almost 55% lower than first one. It shows how more resonators can couple with each other as well as possible to have a strong resonance.

Reduction factors finally gave a resonance at 194.6 GHz with reasonably depth of -21.11 dB reflection. In observation of the structures for its Q factor, we noticed that the higher the input impedance, the better the quality factor, that's why we chose the sensor's input impedance to be 220 ohms. After all, the final design has a quality factor of almost $Q = \frac{f_r}{\Delta f} = 121$ that is quite suitable for sensing applications. Some prohibiting probabilities should be avoided, as mentioned below. An important factor is that keeping

the resonators just 2 μm away from the transmission line, totally worsens the response, as shown in Fig. 3. It shows that connecting the rings to each other and to the transmission line, makes higher possibility of coupling and an increase in L , so besides other reported structures, here “connection” works. On the other hand, connecting two rows of SRRs degrades the result as nothing has been gained from the scratch. The coupling effect through a higher electric field concentration between the SRR rows (in close distance), helps us to reduce the resonances in great amounts. Whilst, their connection interfere with the induced opposite currents on face-to-face edges of SRRs so that current flows cancel each at the intersection. As mentioned above several considerations should be taken into account in reaching desired function as a good sample of the prospective biosensors.

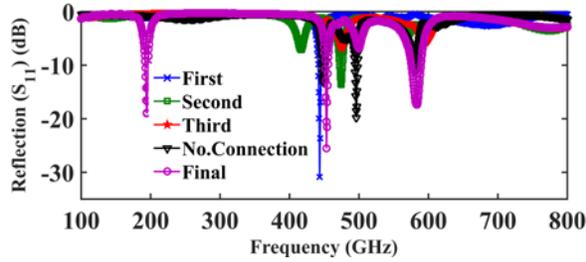


Fig. 3. The frequency response of the structure during different stages of evolution.

We show that the thickness of the analyte inside the gaps of the structure, affects the resonant frequency as well. Suppose that sides of each unit cell (dotted region in inset of Fig. 4) make a capacitance when considered in front of each other, as shown in Fig. 4, as very small sizes of the elements makes it possible to assume semi-TEM fields in the region, the following analysis becomes accurate. The analyte (shown in green color) of thickness t_x fills the gap ($0 < t_x < t$). If we take the edges as parallelization of infinite simple plates of such capacitor, we can calculate the total capacitance after introduction of analytes. As the gap is so small and is quasi-static condition, we have following relationships for capacitance of regions filled with dielectric (Equation (2)), and free space (Equation (3)) regions:

$$C_1 = \epsilon_0 \epsilon_r \frac{t_x b}{d}, \quad (2)$$

$$C_2 = \epsilon_0 \frac{(t - t_x) b}{d}, \quad (3)$$

$$C_{total} = C_1 + C_2 = \epsilon_0 \frac{b}{d} (t + (\epsilon_r - 1)t_x). \quad (4)$$

From Equation (4), it is evident that for a specified dielectric constant, the more thick the analyte, the more capacitance we get. Therefore, frequency of LC-resonance

is lower according to the following relationship:

$$\frac{df_r}{f_r} = -\frac{1}{2} \frac{dC}{C} = -\frac{1}{2} \frac{(\epsilon_r - 1) dt_x}{t + (\epsilon_r - 1)t_x} \quad (5)$$

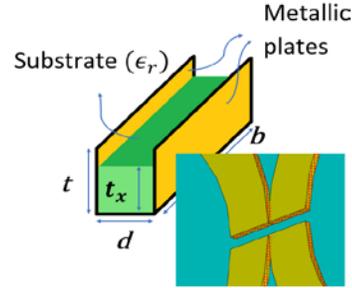


Fig. 4. Filled capacitor, schematic of dotted area in inset.

Infinite number of such capacitances hand in hand to make the total C , required for resonance. Thus in Fig. 6, frequency response of the structure is represented for fixed thickness of 1 μm (filling the free space over substrate) and different dielectric permittivity ranging from 5 to 35. It is clear that increasing the dielectric constant itself, lowers the resonant frequency because of change in C , as is represented in Equation (1). Table 1, which shows sensitivity of the sensor can be understood using the change in resonant frequency with respect to change of the dielectric constant through a wide range of No Load (no analyte mounted) to Full Load (with 1 μm thick biomaterial with distinctive permittivity) status.

High shift of almost average 2.1% (4.1 GHz) per ϵ_r especially in lower dielectric constants represents its high sensitivity and this property guarantees a reliable tool in sensing.

In Fig. 5, the same feature is examined after changing the thickness of the analyte incrementally. It shows that the design is capable of distinguishing the differences among medium with $\epsilon_r = 10$, and various thicknesses. After fitting the data shown in Fig. 5 with a Gaussian function, according to the following equation:

$$f_r(t) = 1.45e16e^{-\left(\frac{t+254.3}{44.03}\right)^2} + 130.4e^{-\left(\frac{t+32.17}{191.8}\right)^2}. \quad (6)$$

We can determine resonant frequency of the structure in intermediate thickness range, as shown in Fig. 7. The diagram shows that the biosensor is able to work with thicker materials up to 23 μm before saturation.

Finally, to check the sensitivity of the biosensor in identification of very small amounts of analytes such as DNA in biology, we examine the sensor with 0.01 and 0.2 μm of DNA strands ($\epsilon_r = 3.2$). Table 2 shows the results, frequency shifts of 1.42 GHz and 2.16 GHz for $t = 0.01 \mu\text{m}$ and $t = 0.1 \mu\text{m}$ respectively, brings about

totally measurable 4.84 dB and 10.7 dB changes in S_{11} depth respectively, for reflection at resonant frequency of unloaded microstrip.

Table 1: The sensitivity of the design according to the load

Dielectric Constant	Change of f_r for Change of ϵ_r (GHz)	Percentage of Change of f_r for Change of ϵ_r (%)
No Load-5	20.5	10.5
No Load-10	37.2	19.1
No Load-15	49.5	25.35
No Load-20	59.2	30.4
No Load-25	66.25	34
No Load-30	74.7	38.4
No Load-35	75.95	38.85

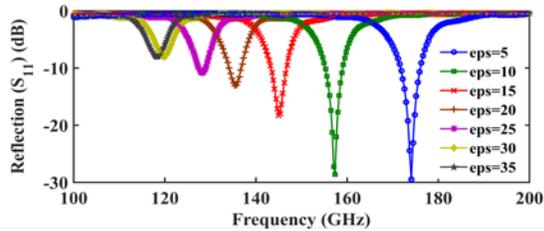


Fig. 5. Resonant frequency shifting according to different dielectric constants of the load with analyte thickness of 1 μm .

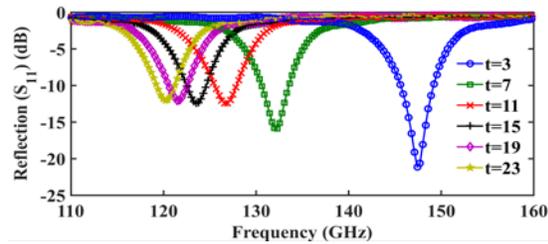


Fig. 6. Frequency response of the structure loaded with homogeneous materials of dielectric constant of 10 and various thicknesses (μm).

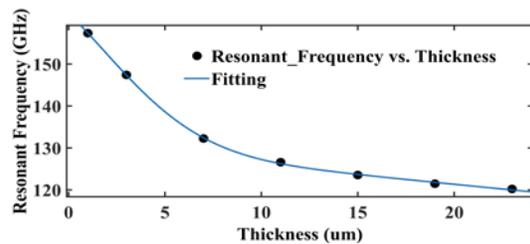


Fig. 7. Fitting of the resonant frequencies according to changes in thickness.

Table 2: Resonant frequencies of loaded microstrip and relevant S_{11}

Thickness of DNA (μm)	Resonant frequency (GHz)	Return Loss at unloaded f_r (dB)
No Load	194.65	-21.11
$t = 0.1$	193.23	-16.27
$t = 0.2$	192.49	-11.04

IV. PRACTICAL NOTES IN DNA STABILIZATION AND MEASUREMENT

We need to immobilize the DNA strands on the silicon substrate in order to measure the resonant frequencies. At first, it is needed to cover the silicon substrate with thin film of carbon to prevent its oxidation in contact with air (formation of amorphous silica layer); otherwise, DNA coupling will be impossible. Therefore, a special pretreatment is needed for subsequent reaction with organic particles, which could be achieved by a reaction of the prepared Si(111) surface with unsaturated ω -functionalized alkenes in the presence of UV irradiation. Figure 8 shows complete procedure for DNA coupling into Si [13], [14], [15].

The process will start with bonding just one strand of DNA on the silicon between the gold slots according to the method aforementioned. Then the sample with DNA strands will be introduced to the structure. The single strands will find their complementary parts in the liquid, and form helix DNA strands or hybridized [12]. Addition of extra strands, enable us to detect new resonant frequency. The change will inform us about the quality and quantity of the present DNA in the liquid. The effect of the added immobilizer to the sensor is not included in the simulations while it will have negligible constant effect on all the conclusions [13], [14].

One of specific usages of the FSS biosensor is diagnosing Leukemia (cancer of blood characterized by mutations in DNA) in its first stages, when the disease has not progressed so much. In the critical period, usual procedures are not able to detect the existence of the cancer simply because of the amount of abnormal tissues in the body are not enough to be distinguished, while it can be halted during the evolution, if detection would be available. The accuracy of the sensory structure, as its diagnosis is related to the interactions of single DNA strands with their complementary ones (DNA hybridization) and the strands will connect only to their pairs and nothing irrelevant, is totally reliable.

This paper introduced the mechanism of such biosensor referring to simulations with CST Microwave Studio, while optoelectronic measurements are capable of verifying the results and the type of measurement setup connection is illustrated in [16] as the structure abovementioned is a thin film microstrip line (TFMSL).

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Muhammad Abdorrazzahi was born in Marand, Iran, in February, 1991. He has received his bachelor's degree at Electrical Engineering Department of Iran University of Science and Technology (IUST). His research interest includes: metamaterial, biosensors, THz, bioelectromagnetics, wave propagation in inhomogeneous medium, scattering and inverse scattering, metamaterial inspired sensors. He is currently pursuing his Ph.D. at University of Alberta, Canada.



Ali Abdolali was born in Tehran, Iran, on May 3, 1974. He received the B.Sc. degree from University of Tehran, and the M.Sc. degree from University of Tarbiat Modares, Tehran, and the Ph.D. degree from the Iran University of Science and Technology (IUST), Tehran, all in Electrical Engineering, in 1998, 2000, and 2010,

respectively. In 2010, he joined the Department of Electrical Engineering, Iran University of Science and Technology, Tehran, Iran, where he is an Assistant Professor of Electromagnetic Engineering. His research interests include electromagnetic wave scattering, radar cross section (RCS) & RCSR, radar absorbing materials (RAM), cloaking, metamaterials, wave propagation in complex media (anisotropic, inhomogeneous, dispersive media), frequency selective surfaces (FSS), bioelectromagnetics (BEM). He has authored or co-authored over 60 papers in international journals & conferences.



Soheil Hashemi was born in Tehran, Iran, on May 13, 1987. He received the B.Sc. and M.Sc. degrees from the University of Tehran in Electrical engineering, in 2010 and 2012 respectively. He is studying the Ph.D. degree at the Iran University of Science and Technology (IUST), Tehran in Electrical Engineering, Fields and Waves. His research interests include bioelectromagnetics (BEM), electromagnetic wave scattering, cloaking, metamaterials, wave propagation in complex media, frequency selective surfaces (FSS) and antennas.