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Cancer Detection Biosensor Design and Risk Analysis using COMSOL Multi-Physics

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Abstract: Cancer is the root cause for a large number of deaths worldwide. Early detection and effective treatments are the two greatest challenges in the fight against cancer. In this paper, our aim is to report a simple, biosensor for early detection and risk analysis of cancer based on meta-materials containing structure utilizing theoretical model. The proposed label-free sensor has the potential to exhibit high sensitivity and selectivity for detecting different cancer cells, such as leukemia, cervical cancer, and breast cancer. According to the simulation results, if the refractive index of a sub-layer is nearer to the refractive index of the samples, the sensor is more sensitive. Also, due to the nanometre size of SRRs, it is easy to detect nanometre-sized specimens. The biosensor has a very high resolution so that the capability of measurement and detection of cancer cells is enhanced. The proposed design also shows sufficiently separated resonant peaks for different levels of risk of cancer cells.

Keywords: Meta-material Biosensor, Biomarkers, Cancerous Cells, Frequency Selective Surface, Split-Ring Resonator, Refractive Index, Incident Angle, Finite Element Method

I. INTRODUCTION

One of the key challenges in health monitoring and disease diagnosis applications is the problem of anomaly detection, e.g., early cancer detection and stage of risk which has received significant attention in medicine and other related fields [6][8].There are various methods for detection such as CT scan, Biopsy, Infrared spectroscopy etc.[5][9][10] Cancer detected exosomes are attractive biomarkers for early detection. Classical blood tests may not be able to detect biomarkers secreted by cancer samples in the early stages of a cancer due to the very low concentration of the biomarkers inside the body. However, closer to the cancer cells, the concentration of the cancer biomarkers is high such that reliable detection is possible if blood in the proximity of the cancer cells is tested.[6] [4]A biosensor is an analytical device used for the identification of an analyte that conglomerates a vital element with a physicochemical indicator. There are numerous type of biosensor namely enzyme-based, tissue based, magnetostrictive and piezoelectric biosensors, etc[4]. Electromagnetic sensors are sensitive to changes in the refractive index, and thus can be detected by changing the refractive index [2] Normal cells, in different parts of every organ of the body, have a specific refractive index. For instance, the refractive index varies from 1.3 to 1.42 in different regions of the human brain. Anyhow, the concentration of protein inside the cell mainly determines the cell's refractive index. A tumour or a cancer cell is considerably more water than a normal cell. This increase in water volume causes cancerous tissues to have a higher dielectric coefficient and higher electrical conductivity and therefore a higher refractive index. Using the variations of the refractive index of the body tissues, and according to the type of tissue cells, a refractive index based sensor can be designed to determine the type of tissues and cells. So in this paper, our primary purpose is the design and simulation of a supersensitive biosensor [16]in the Infrared (IR) wavelength range[12]. Because of the significant mismatch between sample sizes and the wavelength of infrared light, both spatial resolution and sensitivity are limited [1]. One way to overcome this mismatch is to use the light fields that are localized by the use of the meta-materials[3][7][11]. Metamaterials are designed media whose electromagnetic properties are different from the electromagnetic properties of their constituent components. They are often generated by incorporating in a array with various types of artificially fabricated, extrinsic, low dimensional in homogeneities in some background substrate. Metamaterials are proven to exhibit unique electromagnetic characteristics which do not occur in natural materials.

The model that we have chosen for the proposed biosensor is based on the Frequency-Selective Surfaces (FSS) using metamaterial. The FSS[12] be made up of a periodic 2D arrays of Split Ring Resonators (SSRs)[13][15], which are suitable for the detection of chemical or biological thin films because they can be tiny and their frequency response can be tuneable for different applications. Thus a refractive index based cancer detection and risk analysis is proposed with a supersensitive biosensor made of metamaterials.[2][3][7][11].

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Further this paper explains the structure of biosensor in SECTION 1, fundamental data for modeling is provided in the SECTION 2, array structure is shown in SECTION 3, sensitivity of the proposed model is given in SECTION 4, risk analysis method is discussed in SECTION 5, conclusion and further proceedings are given in SECTION 6.

II. PROPOSED SENSOR STRUCTURE

The proposed biosensor is an array of SRRs that are regularly arranged along the x and y directions over a dielectric substrate FIG 1. To avoid the additional simulation volume and increase the simulation speed, we use a single cell to minimize the simulation volume. FIG 2. shows the unit cell for process simulation. In this design, electromagnetic waves are emitted from the source port and measured at the output port. The biosensor is located between these ports, and under tested samples are placed on or proximity the SRR. We have used sub-layers in this work. family of insulators, which is SiO_2 and the other kind of transparent material that is 950 PMMA, TiO_2 resist can also from be used.

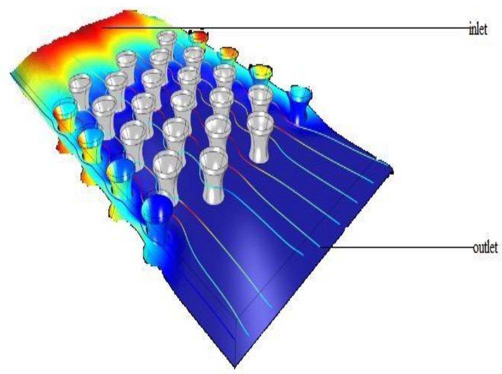

Fig 1: An overview of the periodic

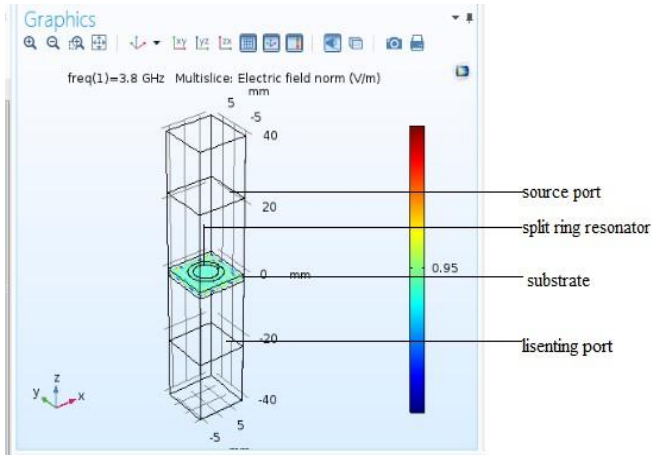

Fig 2: A single cell of the proposed biosensor structure of the biosensor

At IR frequency range, insulator substrates are shown better results. Insulators at this frequency provide much better filtering and a excellent resonance frequency. The general relation for refractive index is $n = n0 + i\kappa$, where n0 is the actual refractive index and represents the phase velocity, and κ the imaginary part of the refractive index, which is known as extinction coefficient, and represents the attenuation when the electromagnetic wave propagates within the material . Here,the effect of energy loss of all layers is considered. We use transmission (T) and reflection (R) coefficients for our work evaluation, which can be obtained from the following equations:

$T = |S21|^2$ (1)
$R = |S11|^2$ (2)

Where S21 is the transmission coefficient and S11 is the reflection coefficient that can be determined as:

$S21 = (1-Z^2)\Gamma/(1-Z^2\Gamma^2)$, $S11 = (1-\Gamma^2)Z/(1-Z2\Gamma2)$
$Z = \exp(-jkn_{eff}L) = \exp(\pm\omega j p_{eff}\, \mu_{eff} L)$

Here, L is the effective length, neff is the effective refractive index, eff and μeff are the effective permittivity and permeability. Also Γ is the coefficient of reflection and Z0 is the relative impedance that are obtained from the following relationships:

$\Gamma = (Z0 - 1)/(Z0 + 1)$ (3)

The technique used here to solve the differential equations is the finite element method (FEM) that has a very high accuracy. We know that the ratio of the refractive index is as follows [83]:

$n = C/\upsilon$ (4)

Where c is the speed of light in vacuum and υ is the speed of light in the environment. However, the rate is related to the frequency and wavelength with:

$\upsilon = \lambda f$ (5)

As a result, we will have:

$n = \lambda 0 f0/\lambda f$ (6)

The light frequency, f, does not change when enters the environment, so f0=f and eventually we will have: $n = \lambda 0/\lambda$ (7)

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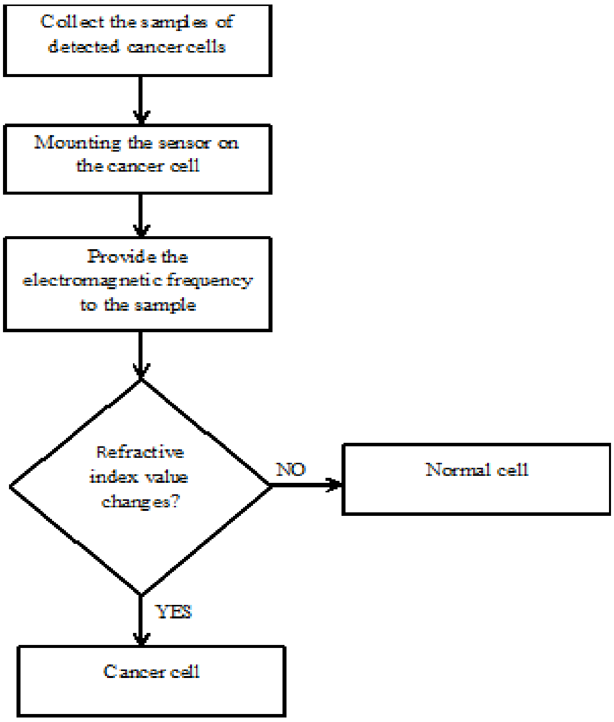
Due to the above relationship, the change in the refractive index of the environment causes a change in the wavelength (λ0 is constant). By keeping the sample on the biosensor, the total refractive index of the entire system changes and thereby displaces the resonance frequency of the system.

IV.METHODOLOGY



V. ARRAY STRUCTURE

To compare the simulation result of the single-cell mode with array mode, we also simulate the biosensor when the substrate of the array structure is SiO2. By selecting 1µm distance between the SRRs, the interference between them will be very low, and the results are the same as the single-cell mode. As we see, only the output amplitude value has changed, that has no effect on the resonant frequency of the system, which is actually our crucial parameter. Therefore, the critical advantage of this work is a reduction of the computational volume and increment of the simulation speed.

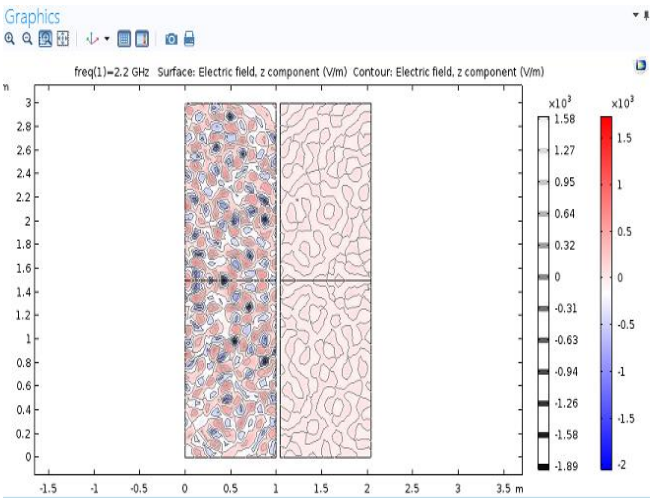


Fig4:Difference between normal cell and cancer cell based on refractive index

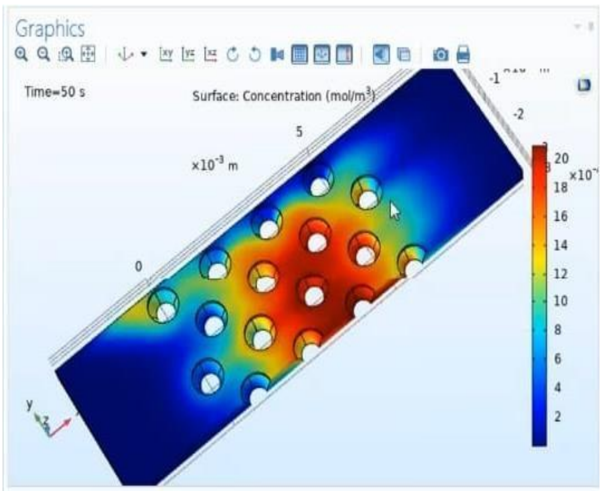


Fig 3: Array structure

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VI. SENSITIVITY

Δn is the difference between the refractive indices of the substrates and under test samples. Given that the refractive index of SiO2 is very close to the refractive index of the samples, they are therefore more sensitive. Hence, the SiO2 has a higher sensitivity which is equal to 658, while for TiO2 and PMMA are 653 and 633, respectively, as shown in TABLE 1. The radiation angle beam of the waves can affect the results, and thus we can achieve the best performance by adjusting the angle of the incidence ,frequency of the system versus the radiation beam angle. As can be seen, by increasing the radiation angle, the resonant frequency of the system shifts to lower wavelengths (higher rates). As a result, we can adjust the system's resonance frequency in the desired range without manipulating the dimensions of the biosensor just by changing the angle of the radiation.

FWHM (nm) FoM SS(nm/RIU) 119.2 258 658 SiO2 5.1 2431 653 TiO2 115.6 225 633 PMMA

Table 1: Maximum Values of Sensitivity

FWHM (nm)	FoM	SS(nm/RIU)	
119.2	258	658	SiO2
5.1	2431	653	TiO2
115.6	225	633	PMMA

VII. RISK ANALYSIS

The cancer cells exhibit their own properties and so we can compare these properties with normal cells such as refractive index of cancer cells, so called lable-free sensors. Various values of refractive index and the concentration of biomarkers are used for this risk analysis part as shown table 2

Table 2: Types of cancer and refractive indices

Cases	Refractive index
Without sample	-
Normal cell	1.353
Jurkat	1.390
HeLa	1.392
PC12	1.395
MDA-MB-231	1.399
MCF - 7	1.401

Table 3: Types of cancer and resonant frequencies

Cases	Resonant Frequency
Without sample	9.43 (GHz)
Normal cell	8.87 (GHz)
Jurkat	8.81 (GHz)
HeLa	8.80 (GHz)
PC12	8.799 (GHz)
MDA-MB-231	8.794 (GHz)
MC7	8.789 (GHz)

VI. CONCLUSION

In summary, a metamaterial biosensor was designed to detect cancerous cells and find the stage of risk which has a specific resonance frequency around 1550 nm. Dimensions of the resonators of the biosensor were designed according to the sub-layer of SiO2 for operation at this frequency. With regard to the refractive index of cancer samples, the resonance frequency of the system varies and can be measured by transmittance variation relative to the absence of any sample on the system, to detect cancerous or normal cells. The sensitivity for SiO2 is 658 which is highest. The FoM for this sub-layers is 258. According to the simulation results, when the refractive index of a sub-layer is closer to the refractive index of the samples, the sensor will be more sensitive and hence the risk analysis can be done.

Further this can be proceeded for next step of effective treatment by designing a nano- sensor based on molecular communication and drug delivery system incorporated with it. The external monitoring and treatment by this development process will have huge impact in the current scenario and helps in decreasing the mortality rate because of cancer

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