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RESEARCH ARTICLE

DESIGN AND ANALYSIS OF BLOOD COMPONENTS BY USING OPTICAL SENSORS

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ABSTRACT

Optical biosensors are powerful detection and analysis devices that have vast applications in biomedical research, healthcare, and pharmaceuticals. This paper includes design of a 2-dimensional photonic crystal based biosensor with line defect which can detect different components of blood. Analysis has been done for blood serum albumin, blood plasma, glucose, white blood cells and red blood cells. Analytical work has been done using Finite Difference Time Domain (FDTD) method. Modeling and designing of photonic crystal is done with the help of simulation tools MEEP and MPB. Simulation results shows different blood components like blood serum albumin, blood plasma, glucose, white blood cells, and red blood cells and their peak has been observed. It has been observed from the band structure that for little change in refractive index there will be a moderate shift in the frequency and hence it acts as a sensor.

INTRODUCTION

A biosensor is a self-contained device, which is capable of providing specific quantitative or semi-quantitative analytical information using biological recognition element. Optical biosensors have ability to detect biological analytes such as proteins, cells and DNA. The basic idea lies in the concept that biological molecules have distinct permittivity greater than that of air and water. As a result, these materials can reduce the propagation velocity of electromagnetic waves that pass through them. This change in the propagation speed of light is translated into a quantifiable signal which is proportional to the amount of biological material present on the sensor surface. There are a number of detection methods: refractive index (RI) method for detection of bio-analytes, fluorescence for DNA sequencing, optical absorption for detection of analytes in a solution, Surface Plasmon Resonance and Raman spectroscopic for HIV detection and DNA sequencing. Fabrication of photonic crystal based biosensors as a lab-on-a-chip with nano-scale reliability leads to simplification of optical system that consist of optical components, such as light sources, detectors and sensors, on one single chip. Photonic integrated circuits based on bandgap structures provide high sensitive device since the light routing and processing can be accomplished by a waveguide circuit. Blood is a bodily fluid in human beings and animals that delivers oxygen and nutrients such as fatty acids, glucose and amino acids to the cells and transports metabolic waste products such as carbon dioxide, urea and lactic acids away from these cells. Blood plasma constitutes 55% of blood fluid and contains proteins such as albumin, glucose, minerals, hormones, carbon dioxide and blood cells (RBCs or erythrocytes which contain hemoglobin) and white blood cells (including leukocytes and platelets).Other important components of blood plasma are serum albumin, various proteins, and various electrolytes such as sodium and chloride. Hematological disorders can cause many fatal diseases and early detection of these diseases can save many lives. Some of the existing detection methods are complicated, time consuming and tedious. One such method is based on Mie theory which explores the light scattering and absorption properties of human blood for medical diagnostic purposes [1]. To obtain optical behavior of blood under various conditions such as osmolarity [2][6], oxygen saturation[2] or shear rate[3][5] is very difficult because of the highly concentrated hemoglobin content of the cell and interfering waves from neighboring cells. Another method is Double integrating sphere technique combined with inverse Monte Carlo Simulation (IMCS)[2][7] is again problematic because measurements are taken for undiluted blood in the wavelength range of 400 to 570nm.In this method, the high concentration of scattering cells combined with high absorption complicates the detection of ballistic photons even when highly intense light sources are used. In conventional methods samples of blood are collected, preserved and transported to the laboratories for analysis. The time taken with conventional methods is 2-3 days or at least 24-36 hours. The process takes more time for analysis and adds to the cost of analysis. This implies that there is a need for sensors which can analyze these bioanalytes in a shorter period of time. The advantages of these sensor technologies are the low cost, low energy, contact-free and provide direct measurements and analyses of substances.

A report by the World Economic Forum and the Harvard School of Public Health (September-2011) shows that 63% of all deaths worldwide currently stem from Non-Communicable Diseases (NCDs) such as cardiovascular diseases, cancers, diabetes and respiratory diseases (example asthma due to allergies)[8]. Several people die each year due to fatal diseases such as leukemia, hemophilia, Hepatitis B and C, anemia, and diabetes. The root cause of most of these diseases is hematological disorders which can be cured if detected early and on timely.

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The ultimate goal of this paper is to design a sensor, which can be fabricated as a lab-on-a-chip sensor, to detect blood components. Development of photonic crystal based biosensors will reduce the response time, size and cost of the sensor system and allows a very large bandwidth.

THEORY

Photonic Crystal

Photonic crystal is an artificial dielectric structure in which refractive index is periodically modulated with the period of the order of a wavelength. The important feature of a photonic crystal is that it prohibits the transmission of the electromagnetic wave in certain range of frequencies called photonic band gaps [9]. The light beam propagates through the photonic crystal without scattering for most of the wavelengths, but for some wavelengths, no light propagates through the photonic crystal: this property of the photonic crystal is called a photonic band gap property[10][11] .The photonic crystal can be one-dimension, two-dimensional and three-dimensional. The two-dimensional photonic crystal is considered in this paper for the sensor design since three-dimensional photonic crystal needs complex topology. The band structure for the photonic crystal is obtained by plotting the resonant frequency against the 'k', wave vector. The photonic band gap can be referred as 'optical insulator'[9]. For sensing application, this photonic band gap property can be explored. The band gap property can be altered with the help of defect created in the photonic crystal[15][16]. The defect engineering allows the controlled flow of the light inside the photonic crystal. The types of defects are: point defect and line defect. Light can be trapped in photonic crystal with the use of point defect, while the use of line defect is to create waveguide in the photonic crystal[16].

The propagation of light in photonic crystal is explained by the master equation (Equation 1). The master equation is obtained by solving Maxwell's electromagnetic equations [9].

$$\nabla \times \left(\frac{1}{\epsilon}\nabla \times H\right) = \left(\frac{\omega}{c}\right)^2 H \text{.....(1)}$$

In the above Equation (1), ϵ is permittivity (dielectric function $\epsilon=n^2$ where 'n' is the refractive index), ω is frequency. The above Equation (1) tells that the frequency 'ω' is inversely proportional to the dielectric function ϵ. Finite Difference Time Domain (FDTD) Method: FDTD is a direct solution of Maxwell's time-dependent curl equations. It employs no potentials. Instead, it applies simple, second-order accurate central -difference approximations for the space and time derivatives of the electric and magnetic fields directly to the respective differential operators of the curl equations[13]. With this approach continuous electromagnetic field in a finite volume of space is sampled at discrete points in a space lattice and at discrete points in time[13]. In order to discretize the equations with second-order accuracy, FDTD methods store different field components at different grid locations. This discretization is known as Yee lattice. MEEP tool implements the finite difference time domain method[17][18].

The simulation tool MEEP helps for the application of FDTD method for computation of transmission spectrum. The transmitted flux can be computed at each frequency ω. For fields at a given frequency ω, this is the integral of the Poynting vector, over a plane on the far side of the photonic crystal structure[18]:

$$P(\omega)=\text{Re } \hat{n}. \int E_\omega (x)^* \times H_\omega (x)\, d^2 x \text{……(2)}$$

MEEP computes the integral P(t) of the Poynting vector at each time, and then Fourier-transform this to find P(ω). MEEP computes the flux at the specified regions, and the frequencies that you want to compute [18].

SENSOR DESIGN

We propose a design of a photonic crystal based sensor which will detect the components of blood like blood plasma, glucose, RBC, WBC, blood serum albumin. The design of sensor consists of a 2 dimensional photonic crystal with line defect. The sensor which is designed consists of 2-dimensional, hexagonal lattice photonic crystal with line defect. The rods in air configuration are used. When the sensor device is dipped in blood sample, the air is replaced by the sample. The light is passed through the photonic crystal from one end and detected from another end. The light will interact with the components in the blood, when the sensor is dipped in the blood sample. Depending on the dielectric constant the propagation of the light will vary in the photonic crystal. Design of the sensor device is shown in Figure 1.

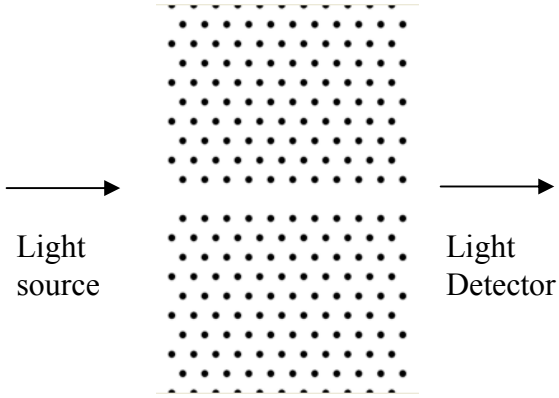

Figure 1. Design of the sensor using photonic crystal with rods in air configuration with defect

Designing and simulation is done with the help of MPB and MEEP tools. Design Specifications are:

1) Rods in air configuration
2) Hexagonal lattice structure
3) Lattice constant 'a'=1μm
4) Radius of rods 'r'=0.19μm
5) Dielectric constant of rods 12
6) Background dielectric constant is changed with respect to sample taken
7) Height of rods infinity
8) Light source: Gaussian Pulse with center frequency at 0.4 and width of the pulse is 0.3
9) Wavelength of light 1550nm.

Designing and simulation is done with the help of MPB and MEEP tools. The MPB algorithm is explained in following steps:

a.Give specifications to define geometry of the cell.
b.Give specifications for dielectric constant of the components.
c.Observe and plot the changes in frequency in band structure and transmission.

The MPB, MIT Photonic Bands, solves the Eigen states and Eigen frequencies of the Maxwell's equation. The Eigen frequencies are obtained as the output of the simulation in MPB. The band structure is obtained plotting these Eigen frequencies against 'k' points [9][10].
MEEP implements the FDTD method for computational electromagnetism. MEEP simulates Maxwell's equations, which describe the interactions of electric (E) and magnetic (H) fields with one another and with matter and sources [11]. The MEEP algorithm is explained in following steps:

a.Define the geometry of the photonic crystal.
b.Define the region to compute flux.
c.Specify the number of frequency required.

MEEP uses "dimensionless" units, where the values of ϵ_0, μ_0 and 'c' constants are unity. The transmission spectrum is obtained for different components of blood. The change in the frequency can be observed as the dielectric constant in the background of the photonic

crystal is changed according to the blood components like blood plasma, glucose, RBC, WBC, blood serum albumin. The refractive index of these blood components are taken into consideration. The database of refractive index of each component is maintained.

RESULTS

The transmission spectrum is obtained for various components in the blood using the output from MEEP simulation tool. The shift in the frequency is observed as the dielectric constant is changed corresponding to the different components in blood. The transmission spectrums are shown in Figure 2, 3 and 4 for different components in blood.

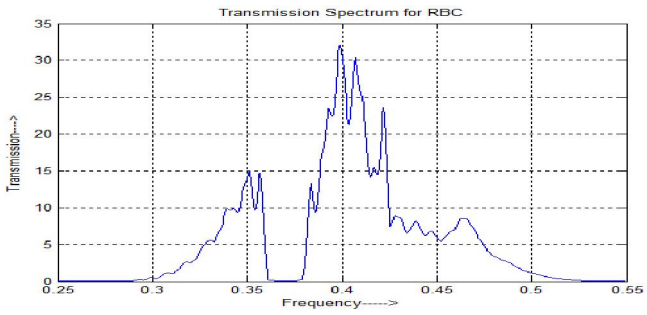

Figure 2. Transmission spectrum for the RBC components in blood.

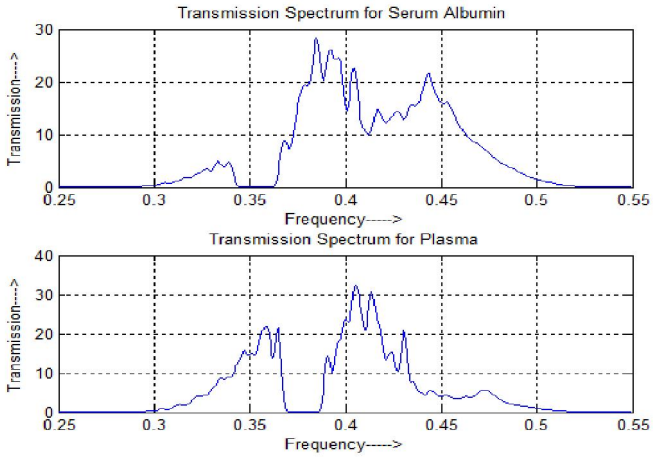

Figure 3. Transmission spectrum for the Serum Albumin and Plasma components in blood

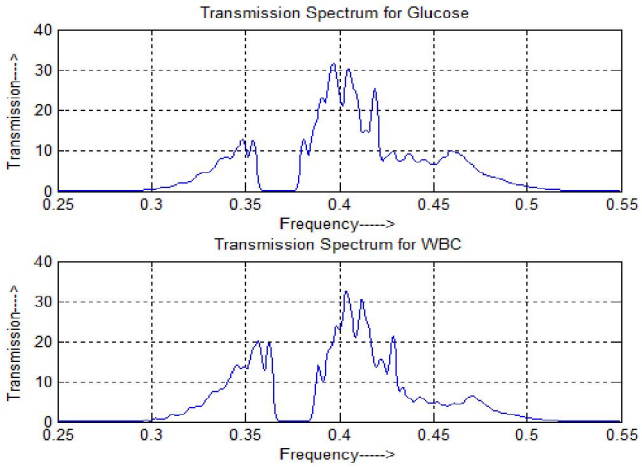

Figure 4. Transmission spectrum for the Glucose and WBC components in blood

The band structures are obtained for various components in the blood using the output from MPB simulation tool. The 'k' wave vector is plotted against resonant frequency. The shift in the frequency is observed as the dielectric constant is changed corresponding to the different components in blood.

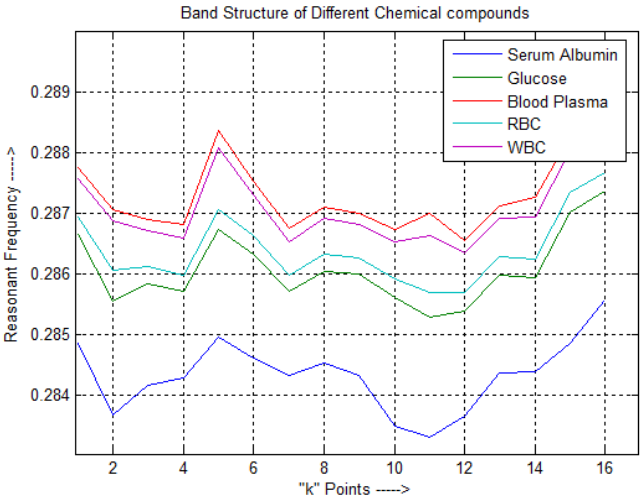

Figure 5. Band structure for the different components in blood.

The refractive index against resonant frequency graph is obtained in Figure 6. From the graph we can observe that even a slightest change in refractive index alter the frequency. Also, from the graph, it has been observed that as the refractive index is increasing the frequency obtained is decreasing. Hence it proves that the results obtained have satisfied equation (1). The designed sensor is sensitive even to small change in the blood sample.

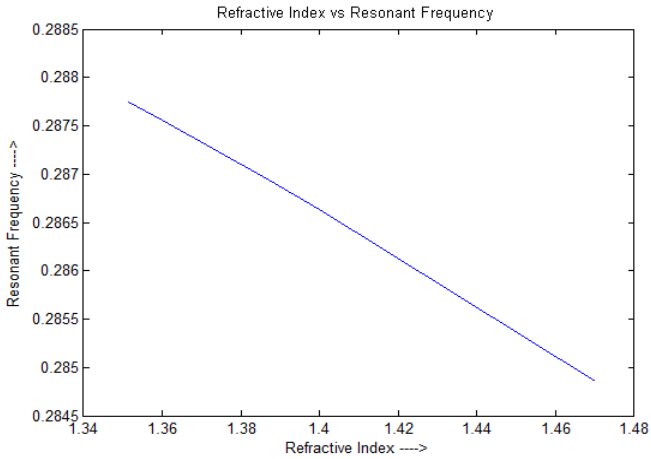

Figure 6. Refractive Index vs. Resonant Frequency

Conclusion

The photonic crystal based sensor is designed and simulated for the detection of blood components. Distinct transmission spectrums are obtained for component in blood. The sensor device is able to detect blood plasma, serum albumin, RBC, WBC and glucose present in water. The sensor design can be fabricated as a Lab-On-A-Chip sensor providing a miniaturized, cost effective, low energy sensor system.

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