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Spectral Analysis of Lymphocyte Cell for Early Detection of Leukemia by Using Photonic Crystal Based Biosensor

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***Abstract*—Early stage cancer cell detection is currently the need of the hour .In this paper, a 2-dimensional photonic crystal based sensor with line-defect has been designed for complete spectral analysis of normal Lymphocyte cell and its components for early stage detection of "Leukemia". As dielectric properties of the cancer cells differ from the normal cell, they can be differentiated and detected using integrated photonic approach. In the present work, MEEP (MIT Electromagnetic Equation Propagation) simulation tool which implements Finite Difference Time Domain (FDTD) method has been used for designing and modelling of the sensor. The shifts in the transmitted output power levels and transmission frequencies have been observed for normal Lymphocyte cell and its components .It has been observed from the band structure obtained from MPB (MIT Photonic Bands) simulation tool that for little change in refractive index (RI) of the bio sample taken into consideration there will be a significant shift in the resonant frequency and hence it acts as a sensor. The designed sensor can differentiate between different components of Lymphocyte cell as well as normal and cancerous cell.This indicates that it is highly sensitive even for little change in refractive index.**

***Keywords*— Photonic crystal sensor, Lymphocyte cell, Leukemia, FDTD , MEEP, MPB.**

I. INTRODUCTION

Cancer is the leading cause of death worldwide, responsible for 8.2 million deaths in 2012 [1]. It is expected that annual cancer cases will rise from 14 million in 2012 to 22 million within the next two decades [1].Lymphocytes are one of the types of white blood cell that helps body fight infection. Abnormal Lymphocyte cells are responsible for causing "Chronic Lymphocytic Leukemia" [2],[3]. Blood plasma constitutes cellular elements such as Red Corpuscles (Erythrocytes), platelets (thrombocytes), and five types of White corpuscles (Leukocytes). Lymphocytes are one of the types of Leukocytes which migrate out of post capillary venules into lymphatic tissue or connective tissue and perform their functions both within and outside the blood stream. One third of all circulating Leukocytes consist of Lymphocyte cells which are formed in variety of lymphoid tissues [2]. Depending on their size which varies from (6-30 μm) they are functionally divided into T-cells, B-cells and Natural Killer (NK) cells [3].

Lymphocytes cells are generally round in shape and have large dense nuclei with a transparent thin -rim of cytoplasm. T-Lymphocyte cells which are immune-competent are long-lived and constitute two-thirds of Lymphocytes that are circulating in the blood and lymph systems [3]. For identification and characterization of lymphocyte cells their morphological and functional characteristics are needed to be studied.

The existing methods for differentiation and detection of cancer cells are biopsy, endoscopy, X-ray and magnetic resonance imaging. These methods require large investments and expensive machine setup. In most of the cases, cancer is diagnosed only after it has been metastasized intensively. Early detection of cancer improves chances of survival of the patient and better response to the treatment. Thus fast, efficient and accurate methods for cancer detection and clinical diagnosis are urgently required.

There are different optical techniques which can be employed for the sensing applications, such as photonic band gap method, spectroscopy, optical imaging, fluorescence, and others. Photonic sensing technology has paved way to efficient characterization and evaluation of the bio-materials [5]-[8]. The scalability and selectivity of integrated photonic aids in the development of the sensor design which can assess the minutes of bio-materials, escalating detection of most fatal and common diseases such as hematological disorders and cancer in earlier stages [9],[10]. They can be used to screen the target cell lines or to analyze the changes in the protein contents of cell in cancer research and proteomics [10], [11].

The photonic crystal based sensor is compact, robust, consumes low power, and portable which can give instant analysis of complex bio-materials [12]-[15]. In this paper, a two-dimensional photonic crystal based sensor model is proposed for complete analysis of Lymphocyte cell and its components.

In Section II of this paper an integrated photonics approach has been proposed for developing a photonic crystal based structure for spectral analysis of normal Lymphocyte cell and its components. In Section III of the present work the design of the proposed sensor has been described in detail.

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In Section IV, the transmission and reflection spectrums for normal Lymphocyte cell and its components are shown after the designed optical sensor is simulated by using MEEP (MIT Electromagnetic Equation Propagation) simulation tool which implements FDTD (Finite Difference Time Domain) method. Also band structure of the cell and its components has been shown by using MPB (MIT's Photonic Band) simulation tool. In section V, comparison with various approaches has been done and obtained results have been discussed thoroughly. In Section VI, conclusions have been made about the present work. In future, the designed structure can be fabricated as a lab-on-chip sensor for complete analysis of Lymphocyte cell and its differentiation with cancerous cells as authors have already worked on the GDSII file for the designed sensor structure [5] for different medical application.

II. Theory

Photonic crystal is the refractive index profile of different material arranged periodically in two or three dimensions and in different lattice structures [12],[13]. There are two configurations in which it can be fabricated: rods in air configuration and holes in slab configuration [12]. The peculiar characteristic of photonic crystal is that it can control flow of light by acting as a narrowband wavelength reflectance filter where at the resonant wavelength 100% of incident light will get reflected back while all other wavelengths are transmitted through the sensor structure [12]. The light perturbation can be manipulated by creating defects either line defect or point defect. The propagation of light in photonic crystal is explained by Equation (1) which is obtained by solving Maxwell's electromagnetic equations [24].

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

In the above Equation (1), 'ϵ' is permittivity (dielectric function $\epsilon = \eta^2$, where 'η' is the RI), 'ω' is frequency. The above equation (1) tells that the frequency 'ω' is inversely proportional to the dielectric function 'ϵ'.

In the present work, the modeling and simulation of sensor has been done by using MEEP (MIT Electromagnetic Equation Propagation) tool [16]. MEEP solves the time varying Maxwell's equation and implement Finite Difference Time Domain Method (FDTD)[17],[18]. MEEP computes the transmitted flux at the specified regions, and the frequencies by solving P(t) of the Poynting vector at each time , and then Fourier transform this to find P(ω) [17],[18] in as shown in "(2)," given below.

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

To find the value of P(ω) , MEEP computes the integral P(t) of the Poynting vector at each time, and then Fourier-transform the value obtained. The flux at the specified regions and the frequencies that we want to compute can be computed by MEEP [17].

For solving the Eigen states and Eigen frequencies of the Maxwell's equation MPB (MIT Photonic Bands) simulation tool has been used. The Eigen frequencies and resonant wavelengths are obtained as the output of the simulation results in MPB. The band structure is obtained plotting these Eigen frequencies against 'k- points' [19],[20].

From literature survey [9]-[11] it has been found that the dielectric constant of normal cell varies from 1.8225 to 1.8769, where as for cancer cell it varies from 1.9376 to 1.9628 .In the present work, a detailed study has been done on refractive index profile [14] of a healthy Lymphocyte cell and its components. The database tabulated in Table I is for normal Lymphocyte cell. From Table I, it can be observed that the change in refractive index of different components of Lymphocyte cell is very small. The sensor design proposed in the present work is highly sensitive and able to capture the minute change in the refractive index profile within the Lymphocyte cell.

III. Sensor Design

We propose a two-dimensional (2D) photonic crystal based structure for complete spectral analysis of a healthy Lymphocyte cell and its different components. The sensor designed consists of a hexagonal 2D computational cell of lattice size of 17 x 17.3205 x 0 in x-y direction. The designed sensor has rods in air configuration with "line defect". The air i.e. the background of the sensor is dipped in the blood sample and the sensor device is absorbed with Lymphocyte cells. A Gaussian light source will pass through it through the input port of the sample. The propagation of electromagnetic waves takes place within the sensor device. Dielectric properties of Lymphocyte cell and its components differ from each other. Depending upon the dielectric properties of the Lymphocyte cell and its components the propagation of light will vary and hence its optical properties i.e. transmission and reflection characteristics will get changed.

Design of the sensor device is shown in "Fig. 1" given below:

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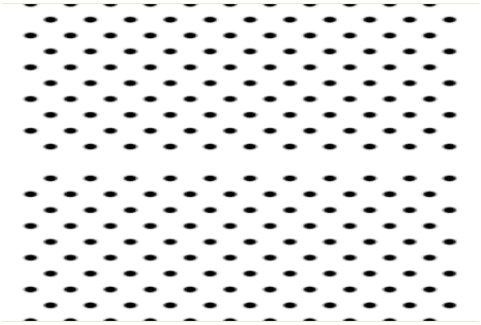

Fig.1. Design of photonic crystal based sensor with rods in air configuration.

Designing and simulation of proposed sensor is done with the help of MEEP tool. Design specifications are given below:

1. Hexagonal lattice structure of matrix 15x20.
2. Rods in air configuration.
3. Thickness of Perfectly matched layer (PML) =1.0 a.
4. The size of computational cell is 17 x 17.3205 x 0.
5. Resolution = 10.
6. Lattice constant 'a'=1μm.
7. Radius of rods 'r'=0.17 μm.
8. Dielectric constant of silicon slab =11.56.
9. Dielectric constant of background of the photonic crystal will change with respect to bio-sample taken into consideration.
10. Number of frequencies at which flux is calculated = 500.
11. Polarization = TM.

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 present in normal Lymphocyte cell. The refractive index (η) of each component of Lymphocyte cell has been taken into consideration. The changed value of refractive index (η) can be compared with existing refractive index (η) values of each constituent maintained in database for further clinical analysis and detection.

In the present work, we have used MPB (MIT Photonic Bands) tool for computing band structure [19]. MPB solves the Eigen states and Eigen frequencies of the Maxwell's equation which is the output of MPB.

Band structure can be obtained by plotting Eigen frequencies versus 'k' points [19][20].For MPB simulation computations have been done for 250 bands with 1.000000e-07 tolerance for TM polarization for the grid size is 170x174x1 having cell volume of 294.449.

IV. Simulation Results

The main components of a Lymphocyte cell are plasma membrane (lipid), cytoplasm (protein and water) and nucleus (protein and water). Each component has a specific refractive index value [11], [15]. For a cell to retain its original state the content of the cell should be optimum .The overall refractive index for normal cell varies from 1.35 to 1.37 [10], [11]. As the content of the cell changes the overall refractive index of the cell also changes and hence the optical properties of the cell changes. Cancer is caused due to change in protein content of the cell [10], [11]. For a cancer cell, the overall refractive index changes from 1.39 to 1.40 [10],[11].

With the help of MEEP simulation tool the transmission spectrum has been obtained for Lymphocyte cell and its different components .MATLAB tool has been used for plotting transmission graphs and band structure. As the refractive index of the bio-sample taken into consideration will change according to different components of the Lymphocyte cell the shifts in the transmitted output power levels and transmission frequencies can be observed from transmission spectrums which act as signatures for the designed sensor structure.

Table I shows input refractive index (RI) (where dielectric constant, $\epsilon = \eta^2$) Lymphocyte cell and its components [2], normalized transmitted output power and normalized transmission frequencies.

TABLE I
Input Refractive Index, Normalized Output Power and Normalized Transmission Frequency for Lymphocyte cell and its components.

Biosample	Refractive index (η)	Normalized Output Power	Normalized Transmission Frequency
Lymphocyte cell	1.37	0.2934411	0.41653306
Cytoplasm	1.35	0.3159622	0.37204408
Nucleus	1.39	0.3120085	0.41232464
Plasma	1.48	0.3339060	0.39428857

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The distinct shifts in transmitted output power levels and output transmission frequencies can be observed from transmission spectrums shown in "Fig. 2", "Fig. 3", "Fig. 4"and "Fig. 5" for normal Lymphocyte cell and its components i.e. cytoplasm, nucleus and plasma .The transmission spectrum for normal Lymphocyte cell is shown in "Fig. 2" given below :

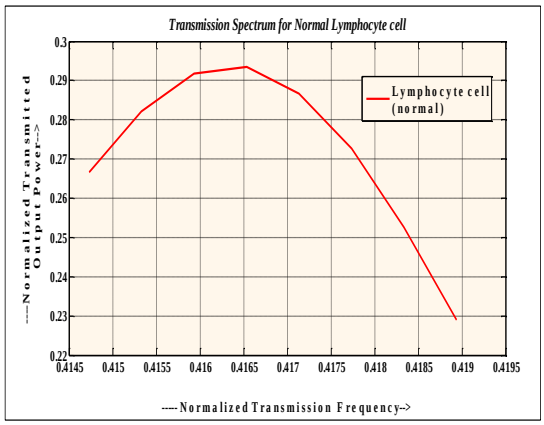

Fig.2.Transmission spectrum for normal Lymphocyte cell

The transmission spectrum for cytoplasm of normal Lymphocyte cell is shown in "Fig. 3" given below:

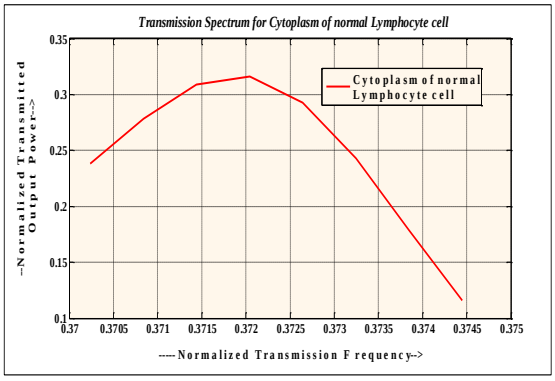

Fig. 3. Transmission spectrum for cytoplasm of normal Lymphocyte cell .

The transmission spectrum for nucleus of normal Lymphocyte cell is shown in "Fig. 4" given below:

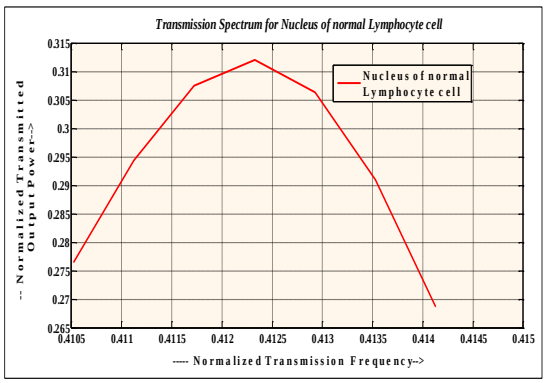

Fig.4. Transmission spectrum for nucleus of normal Lymphocyte cell.

The transmission spectrum for plasma of normal Lymphocyte cell is shown in "Fig. 5" given below:

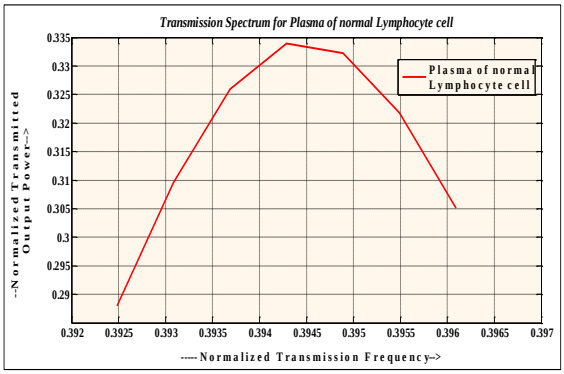

Fig. 5. Transmission spectrum for plasma of normal Lymphocyte cell.

The transmission spectrum for each component of Lymphocyte cell differs as observed from "Fig. 2", "Fig. 3", "Fig. 4"and "Fig. 5". The distinct shifts in transmitted output power levels and output transmission frequencies can be observed from transmission spectrums shown in "Fig. 2", "Fig. 3", "Fig. 4" and "Fig. 5" for normal Lymphocyte cell and its components i.e. cytoplasm, nucleus and plasma and thus each spectrum will act as a signature of the corresponding component of healthy Lymphocyte cell for the designed sensor. Table II given below shows transmission power in decibels (dB) and Quality factor for each component of Lymphocyte cell.

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TABLE II
LYMPHOCYTE CELL AND ITS COMPONENTS, TRANSMITTED OUTPUT POWER AND QUALITY FACTOR

Name of Bio-sample	Transmitted Output Power (in dB)	Quality Factor (Q-Factor)
Lymphocyte cell	-10.6495	8033
Cytoplasm	-10.0072	1133
Nucleus	-10.1176	8688
Plasma	-9.5275	1255

Reflection spectrum has been obtained by using MEEP simulation tool for Lymphocyte cell and its components as shown in "Fig. 6" given below:

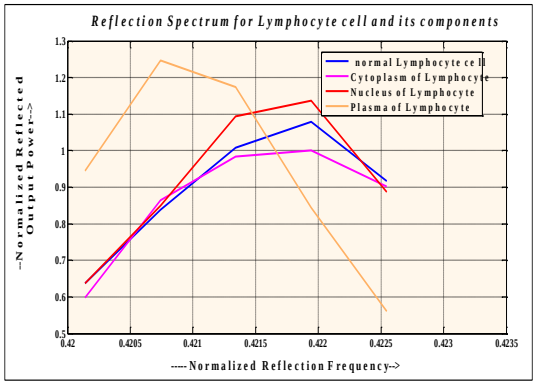

Fig. 6. Reflection spectrum for normal Lymphocyte cell and its components.

The reflection spectrum details are given in Table III given below. The normalized reflection frequency for normal lymphocyte cell and its components is 0.42194.

TABLE III
LYMPHOCYTE CELL AND ITS COMPONENTS, REFRACTIVE INDEX, REFLECTED OUTPUT POWER AND REFLECTED POWER IN DB

Biosample	Refractive index (η)	Normalized Reflected Power	Reflected Power in dB
Lymphocyte cell	1.37	1.0786	0.6572
Cytoplasm	1.35	1.0012	0.0104
Nucleus	1.39	1.1369	1.114
Plasma	1.48	1.2460	1.910

With the help of MPB simulation tool we can obtain the band structure for Lymphocyte cells and its components as shown in "Fig. 7" given below. The change in the resonant frequency with respect to change in the refractive index of components of normal Lymphocyte cell has been observed and is shown in Table IV and "Fig. 7".

TABLE IV
LYMPHOCYTE CELL AND ITS COMPONENTS, REFRACTIVE INDEX, RESONANT FREQUENCY AND WAVELENGTH

Name of Bio-sample	Refractive index (η)	Resonant Frequency(c/a)	Wavelength (in μm)
Lymphocyte cell	1.37	0.34442	1.5253
Cytoplasm	1.35	0.345037	1.5268
Nucleus	1.39	0.343798	1.5239
Plasma	1.48	0.344576	1.5257

The band structure is obtained for various components in the blood using the output from MPB simulation tool and is shown in "Fig. 7". The 'k' wave vector is plotted against resonant frequency.

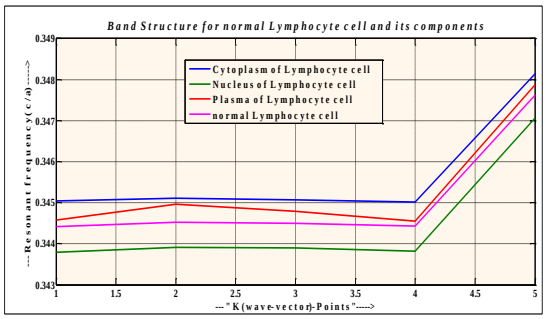

Fig.7. Band structure for Lymphocyte cell and its components.

From the band structure we can observe that even a slightest change in RI alters the resonant frequency. The designed sensor is sensitive even to small change in the refractive index of bio-sample.

From transmission spectrum, reflection spectrum and band structure it is clear that the sensor designed can be used for complete spectral analysis of a healthy Lymphocyte cell. These transmission spectrums act as signature for a normal Lymphocyte cell and any deviations in these values are indicator of diseased cells.

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V. Results And Discussions

In the present work, the optical properties of Lymphocyte cell and its components has been obtained.A comparative study for the present work and the work done by authors in [15] has been done.In [15] the basic stucture is photonic crystal based gratings strucutre with a line defect .The line defect in [15] is due to placement of silicon rods at different lattice constant.This type of structure is difficult to fabricate .In the present work, a two dimensional 15 x 20 photonic crystal structure with rods in air configuration has been designed which is easy to fabricte for analysis of Lymphocyte cell. In [15] the transmission spectrum has been obtained by using MEEP tool and spectral analysis has been done in time-domain only .In [15] the normalized transmission peak obtained for Lymphocyte cell is 0.25508 and normalized transmission frequency obtained is 0.28527. But in the present work the authors have analyzed Lymphocyte cell in frequency domain also and a detailed study has been done on the band structure of Lymphocyte cell by using MPB simulation tool.

Light scattering patterns are sensitive to refractive index, and hence more accurate results can be obtained by considering these parameters. One such method is "Scanning Flow Cytometer (SFC)," [21]. For fast detection of light patterns scattered by single particles which allows a detailed measurement of the entire angular light scattering pattern can be done by using SFC but it requires costly machine setup.

Fluorescence based methods requires labeling of the cells which is again time-consuming and expensive. Also labeling can interfere with the shape and contents of the original cell.

In practical nucleus structure is inhomogeneous. "Cell imaging" method considers simplest model of mononuclear cells as a homogeneous sphere and uses "Confocal microscopy" for measurement [22]. The results obtained are less accurate due to "model errors" that occur due to imperfect alignment of SFC and non-central position of the particle in the flow.

Few characterization methods are based on solving "Direct and inverse light scattering" problems by using optical models of the single particles [23],[24]. In [25],[26] light scattering properties of lymphocytes had been studied and more complicated models such as five-layer spherical model of mononuclear blood cells had been developed where inhomogeneous nucleus has been considered in the wavelength range of 405-543 nm. But these methods require lots of computation time and these complex models are not practically possible.

In the present work the transmission and reflection characteristics of lymphocyte cell have been studied both in time -domain and frequency-domain by using MEEP and MPB simulation tools respectively in the wavelength range of 1530-1565 nm. The graphs obtained are distinct and the method requires very less time for simulation without any need for generating optical model of the cell.

VI. Conclusion

Spectral analysis has been done for normal Lymphocyte cell and its various components. As the dielectric properties of healthy Lymphocyte cell differs from cancerous or unhealthy cell it can be differentiated and detected using the designed photonic crystal based biosensor. It has been observed from the transmission and reflection spectrums that for little change in refractive index (RI) of the biosamples taken into consideration there will be distinct shifts in the transmitted and reflected output power levels, transmission and reflection frequencies and resonant wavelengths and hence the designed sensor can be used for in-depth analysis of Lymphocyte cell and its various components. The transmission and reflection spectrums obtained for the designed sensor acts as signature for a healthy Lymphocyte cell and can be used in medical diagnosis purpose. In future, the designed sensor further can be developed into lab-on-chip device which will make cancer detection easier, efficient and less expensive.

REFERENCES

[1] World Health Organization. Fact sheet N ° 297. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/(Updated February 2014).

[2] http://ect.downstate.edu/courseware/histomanual/

[3] http://en.wikivet.net/ymphocytes.

[4] X. Fan, I. M. White, S. I. Shopova, H. Zhu, J. D. Suter, and Y. Sun, "Sensitive optical biosensors for unlabeled targets: A review," Anal. Chim. Acta 620, 8– 26 (2008).

[5] Poonam Sharma and Preeta Sharan, "Design of Photonic Crystal Based Biosensor for Detection of Glucose Concentration in Urine", IEEE J.Sensors , vol. 15, issue 2, pp. 1035-1042, Feb 2015.

[6] W. C. L. Hopman, P. Pottier, D. Yudistira, J. V. Lith, P. V. Lambeck, R.M. D. L. Rue, and A. Driessen, "Quasi-one-dimensional photonic crystal as a compact building-block for refractometric optical sensors",IEEE J. Sel. Top. Quantum Electron. , vol. 11, no. 1, pp. 11-16,2005.

[7] F. Prieto, B. Sepulveda, A. Calle, A. Llobera, C. Domynguez, A. Abad, A. Montoya, and 1. M. Lechuga, "An integrated optical interferometric nanodevice based on silicon technology for biosensor applications",Nanotechnol. , vol. 14, no. 8, pp. 907-912, 2003.

[8] C. Y. Chao, W. Fung, and 1. 1. Guo, "Polymer microring resonators for biochemical sensing applications", IEEE J. Sel. Top. Quantum Electron. , vol. 12, no. 1, pp. 134-142, 2006.

[9] 'Water Distribution in Cancer and normal Cells', Chien-Chung Tsai, Prof.Sheng-Lung Huang.(Available from : laser.ee.ntu.edu.tw/).

[10] X. J. Liang, X. M. Zhang, A. Q. Liu et al., "An Approach to Cancer Cell Diagnosis Using Integrated Photonic Chip," Proceeding of Asia-Pacific Conference of Transducers and Micro-Nano Technology 2004, pp. 276-80, Sapporo,Japan, Jul. 4-8, 2004.

[11] X..Liang, A.Q.Liu, X.M.Zhang, P.Yap, T.C.Ayi and H.S.Yoon, "Determination of refractive index for single living cell using integrated biochip," Solid-State Sensors, Actuators and Microsystems, 2005. Digest of Technical Papers. TRANSDUCERS '05. The 13th International Conference on (Volume:2). pp. 1712 - 1715 Vol. 2 .,doi: 10.1109/SENSOR.2005.1497421 .

[12] J. D. Joannopoulos, S. G. Johnson, J. N. Winn, and R. D. Meade, Photonic Crystals: Molding the Flow of Light, Princeton University Press, Princeton, NJ, 2008.

[13] R. D. Meade, A. M. Rappe, K. D. Brommer and J. D. Joannopoulos, "Existence of a photonic band gap in two dimensions," Appl. Phys., Lett., vol.61 ,1992, pp.495.

[14] Poonam Sharma, Sandip Kumar Roy, Preeta Sharan , "Design and simulation of photonic crystal based biosensor for detection of different blood components," in Proc. IEEE Region10 Symposium (TENSYMP-14), Kuala Lumpur , Malyasia,April2014,pp.171-176, doi:10.1109/TENCONSpring. 2014.683019.

[15] Poonam Sharma and Dr.Preeta Sharan, "An Optical Sensor for Propagation Analysis of Lymphocyte Cell for Cancer Cell Detection",in Proc. IEEE GHTC-SAS, Trivandrum, Sep 2014, pp.93-98,doi:10.1109/GHTC-SAS.2014.6967565.

[16] A. F. Oskooi, D. Roundy, M. Ibanescu, P. Bermel, J. D. Joannopoulos, and S. G. Johnson, "MEEP: A flexible free-software package for electromagnetic simulations by the FDTD method," Comp. Phys. Commun. ,vol. 181, pp. 687–702,2010.

[17] K.S.Yee, "Numerical solution of initial boundary value problems involving Maxwell's equations in isotropic media," IEEE Trans.Antennas Propagat.,vol. AP-14, pp. 302-307, 1996.

[18] http://ab-initio.mit.edu/MEEP/Tutorial.

[19] http://ab-initio.mit.edu/wiki/index.php/MPB.

[20] http://ab-initio.mit.edu/wiki/index.php/MPB_User_Tutorial.

[21] Maltsev, V.P. and Semyanov, K.A., "Characterisation of Bio-Particles from Light",(2004).

[22] Brock, R.S., Hu, X., Weidner, D.A.,Mourant, J.R., and Lu, J.Q., "Effect of detailed cell structure on light scattering distribution: FDTD study of a B-cell with 3D structure constructed from confocal images," J. Quant. Spectrosc. Radiat.Transfer, 102, 25–36, (2006).

[23] Yang, Y., Zhang, Z., Yang, X., Yeo, J.H.,Jiang, L., and Jiang, D. , "Blood cell counting and classification by nonflowing laser light scattering method," J. Biomed. Opt., 9, 995–1001,(2004).

[24] Semyanov, K.A., Zharinov, A.E., Tarasov, P.A., Yurkin, M.A., Skribunov,I.G., and van Bockstaele, D.R. et al. in Optics of Biological Particles (eds A.G. Hoekstra, V.P. Maltsev, andG. Videen), Springer, Dordrecht, pp. 269–280 ,(2007).

[25] Strokotov, D.I., Yurkin, M.A., Gilev,K.V., van Bockstaele, D.R., Hoekstra,A.G., Rubtsov, N.B., and Maltsev, V.P. Is there a difference between T- and B- lymphocyte morphology? J.Biomed. Opt., 14, 064036–064012, (2009).

[26] Hoekstra, A.G., Grimminck, M.D., and Sloot, P.M.A. Large scale simulation of elastic light scattering by a fast discrete dipole approximation. Int. J. Mod. Phys.C, 9, 87–102,(1998)