



Photonic Crystals based Biosensors in Various Biomolecules Applications: In Review

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Article Info

Article history:
Submitted 7 April 2023
Revised 18 July 2023
Accepted 20 July 2023

Keywords:
biomolecules, biosensors,
detection, photonic crystal,
sensitivity

Abstract

Over the past decades, photonic crystals have emerged as an interesting photonic structure. It plays a vital role in many fields of optical communication, biomedical sensing, and other applications due to its compactness, high sensitivity, high selectivity, fast responsiveness, etc. Strong light confinement in photonic crystals and adjustment of its geometrical parameters have led to the emergence of photonic crystal biosensors. Biosensors are extensively employed for diagnosing a broad array of diseases and disorders in clinical settings worldwide. Photonics crystal-based biosensor is one of the solutions to detect various diseases. By using literature review method, this paper aims to explore applications of photonic crystal-based biosensors to encounter the sensitivity of various biomolecules. The results show that PhC-based sensors have played a crucial role in the field of optical sensors especially in detecting the sensitivity of various biomolecules in cancer, malaria, and blood component detection, and will produce significant industrial values.

INTRODUCTION

Over the last few decades, change and control over material properties have made significant progress. Revolution in semiconductor technology provides researchers with more opportunities to better understand the properties of materials, one of them is electrical properties. This progress is the first step of a revolution in microelectronic devices, especially devices related to transistors and integrated circuits. This expansion of microelectronics led to the development of optics and photonics (Chiappini et al., 2020). Among other optical devices, optical sensors based on photonic crystals have attracted a lot of attention because of their small size and high sensitivity (Suh et al., 2003). Photonic crystal (PhC) is a nanostructured dielectric material that has sensing properties and can be applied in various fields of optoelectronics (Parandin et al., 2021). Crystal is a periodic arrangement of atoms or molecules, and repeating pattern of atoms or molecules in space is called a crystal lattice. Crystals present a periodic potential for electrons traveling through them, and their conduction properties are determined by element and lattice geometry. Layer in the crystal consists of atoms, however, at PhC the atoms are replaced by a macroscopic medium with a different dielectric constant, while the periodic potential is replaced by a periodic dielectric function (equivalent to the periodic index of refraction). Optical band gaps in PhC allow for manipulation of light propagation and control over the interaction of light with materials. Light in the PhC can be guided without attenuation, so that the spontaneous emission can be eliminated (Joannopoulos et al., 2007).

Various PhC-based sensing devices have been presented in some literatures, and PhC-based sensors have been presented in various sensors and biosensors. Photonic crystal fiber (PCF) is one of the PhC devices that have been demonstrated for biosensing measurements (Skivesen et al., 2007). Optical techniques are revolutionizing the way in which biological questions can be addressed directly in living cells. Its sensitivity, specificity and non-intrusion properties make optical techniques indispensable in generating high-fidelity data, and significantly increase the availability of tools for future research on diseases present in blood cells. One of the optical techniques that can play a role in this field is PhC-based biosensors (Mauritz et al., 2010). Biosensors are primarily used as tools for detecting biological targets and facilitating disease diagnosis and prognosis (Inan et al., 2017). PhC-based biosensors are presented as an early diagnostic tool providing superior sensitivity, reliability, stability, rapid response, and in vivo and in vitro diagnostics (Sharma & Kalyani, 2017). This paper is aimed to explore the potential of PhC-based biosensors on various biomolecules in the detection

of malaria, blood components, and their applications in cancer (Adoghe et al., 2020; Arunkumar et al., 2019; Sara & Bendib, 2018).

METHODS

In this study, a systematic literature review was used, which is a research and development methodology carried out by collecting and evaluating related research on the topic to be studied. This method is usually based on a theoretical foundation that helps in solving the questions contained in the research (Lusiana & Suryani, 2014). In writing articles using a literature review, it is recommended to use a seven-step-research or it can be said that the seven-step model of the Comprises Literature Review (CLR). In the first step, we will determine the topic in this paper, namely to analyze some applications of PhC based biosensors in various biomolecules. Given that the research and development of PhC based biosensors in various biomolecules is being intensified around the world.

After determining the topic, the second step is to examine articles, papers, and literature based on previous research, then stored and organized them using the Mendeley Software. For the next step, the relevant information has been reread and organized and then stored in a folder in the Mendeley Library. After that, the search with MODES (Media, Observations, Documents, Expert, Secondary Data) is expanded to support the validity of the paper. When the components related to the topic for this paper are already complete, information from the various sources is analyzed and synthesized to answer the aims of this paper and present the CLR Report. These seven steps are multidimensional, interactive, emergent, iterative, dynamic, holistic, and synergistic (Williams, 2018).

The advantage of a literature review is that it can help provide an overview of areas with different and interdisciplinary searches. Moreover, literature is the best way to synthesize research findings to demonstrate at the meta-level and uncover areas where more research is needed, which is an important component of creating theoretical frameworks and building conceptual models. Therefore, this research method was the most effective method used in this paper (Snyder, 2019).

RESULTS AND DISCUSSION

1. PhC for Malaria Detection

Malaria is a hazardous disease that can kill more than one million people per year. Early treatment through more effective detection was crucial to be conducted in order to reduce mortality from this disease. Malaria is caused by a protozoan parasite that is transmitted by mosquitoes, and the disease attacks liver cells and red blood cells. The

result of malaria infection was that red blood cells degenerated and their structural characteristics changed. There are three stages of changes in the structure of red blood cells: first, the ring stage takes place within 24 hours with a refractive index of 1.395, then the trophozoite stage within 24-36 hours with a refractive index of 1.383, and finally the schizont stage within 35-48 hours with a refractive index 1373 (Agnero, 2019; Hadjira et al., 2021) A ring resonator has been chosen on a study because of its sensitivity that came from the long lifetime of

the photons in the cavity so that it would provide high field localization, which would increase the sensitivity as well as the interaction between light and matter (Sara & Bendib, 2018). Defects or cavities and changes in the size of each rod cause a defect which would then act as a resonator. Optical resonators could also be designed by localizing light and creating some defects in the structure that impaired the periodicity of the structure (Upadhyay & Kalyani, 2017).

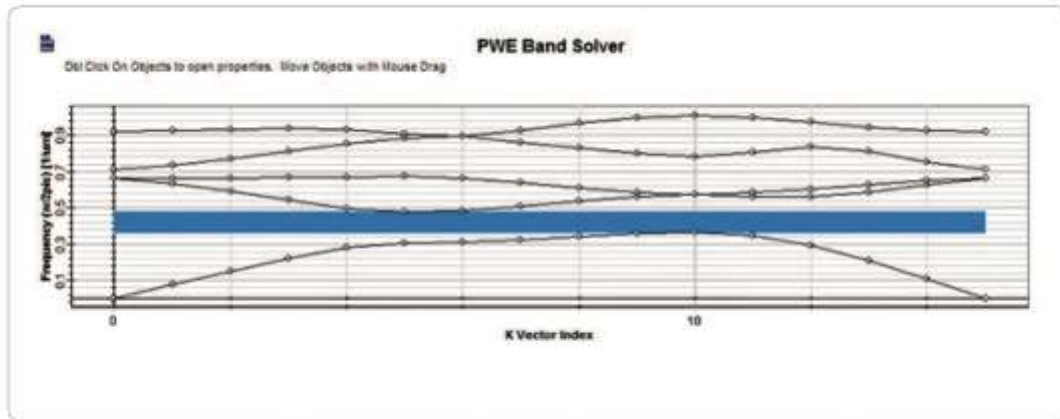


Figure 1. Band Gap (Bendib, 2018).

Using the plane wave expansion method in which the complete structure had a single slit with a wavelength range from 2,099 to 2,756 m, the band gap for the transverse electrical mode of this biosensor was designed and presented in Figure 1 and the transmission spectra for normal red blood cells and red blood cells infected at the ring stage, trophozoite stage, schizont stage which corresponded to its refractive index were obtained. Refractive index of normal red blood cells and red blood cells infected at the ring stage, trophozoite stage, and schizont stage with normalized transmission spectra and band gaps achieved from different infiltrates are presented in Table 1. It can be observed in Figure 2 that the transmittance increases, while the refractive index decreases. The

displacement of the power transmission according to refractive index represent the sensing principal of the ring resonator sensor.

By using values from Table 1, a curve representing the change in band gap according to the variation of the refractive index is depicted. It can be seen that the variation is linear; a slight change in the resulting coordinates, which is a straight line. The absolute value of the slope of the straight line represents the sensitivity that has reached 151%. A very high level of sensitivity can be seen through the relationship between the band gap and the refractive index of red blood cells. This design can detect within a few minutes and can increase very high sensitivity (Benmerkhi et al., 2016).

Table 1. Analysis Of Transmission And Band Gap According To Refractive Indeks (Bendib, 2018).

Refractive Index		Normalized Power Transmission (%)	Band Gap
1.402	Normal red blood cell	46.1	0.113627
1.395	Infected cell ring stage	60.1	0.11469
1.383	Infected cell trophozoites stage	83.7	0.116512
1.373	Infected cell schizont stage	94.4	0.118028

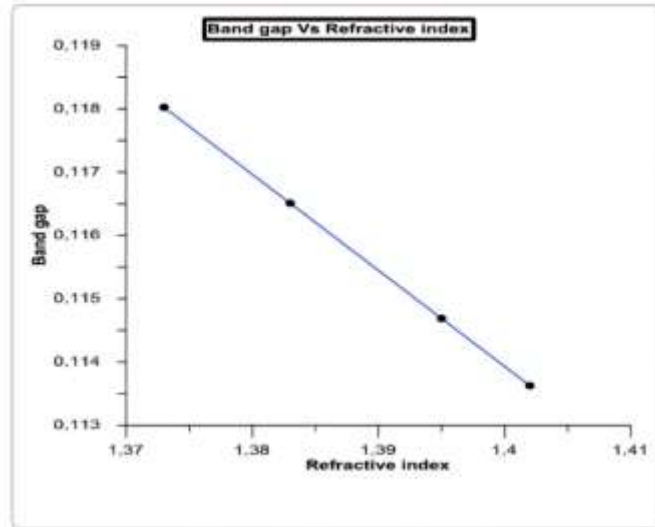


Figure 2. Band Gap vs Refractive Index (Sara & Bendib, 2018)

2. Blood Components Detection

Photonic sensing technology using Photonic Crystal PhC) enables new measurements for the analysis of blood constituents. The greater permittivity of biological molecules than air and water causes the propagation of electromagnetic waves as they pass through the structure to be more variable, and because of this process, the analytes are easier to identify and detect, which can then be used in medical applications Rakemdran (2019), in their research made a PhC-based biosensor design which was designed by arranging a circular rod cubic and then placed in an air background as shown in Figure 3 (Arunkumar et al., 2019). The sensor has an elliptical shape of resonator which is placed in the middle of the structure and it contains input and output ports, which are used to propagate and analyze the optical signal with different wavelengths. Plane wave expansion method was used in this structure, the propagation mode of the Photonic Band Gap (PBG) is shown in Figure 4,

while the band diagram of an elliptical ring resonator after being given deformed lines and points is shown in Figure 5. The guided mode indicates that there is a propagation mode within the PBG region due to the incorporation of the ring elliptical shape of the resonator in the periodic structure. Sensor was designed through line and point defects. Sensor-normalized output spectra for different blood components are shown in Figure 6, and transmission spectra were obtained for various biological constituents present in blood using the outputs of the Finite Difference Time Domain (FDTD) method (Radhouene et al., 2017). Changes in normalized transmission output power levels and equivalent resonant wavelengths for each blood component have been demonstrated experimentally, and thus each spectrum would act as a signal of the appropriate blood constituent for the designed sensor (Lindberg & Öberg, 1993).

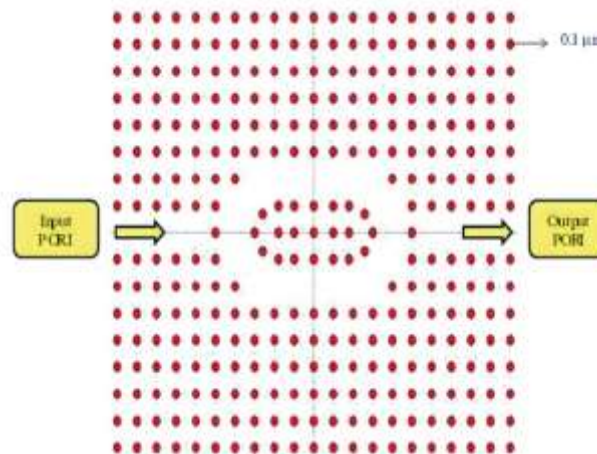


Figure 3. Proposed Biosensor Using Elliptical Ring Resonator (Arunkumar et al., 2019).

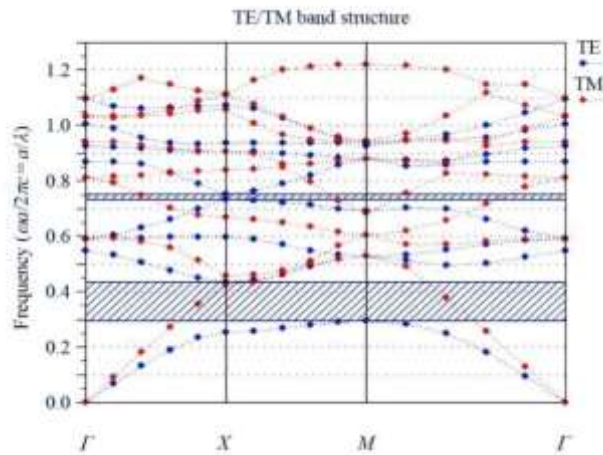


Figure 4. Band Diagram For Circular Rods In 21 x 17 Square Lattice Without Any Defects (Arunkumar et al., 2019).

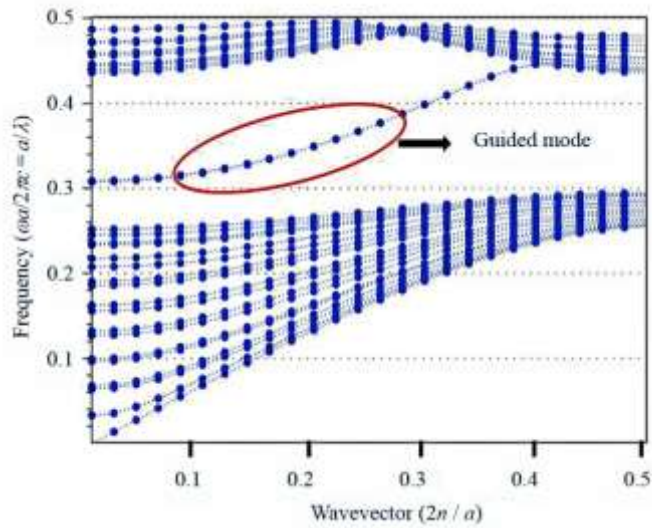


Figure 5. Band Diagram For Circular Rods In 21 x 17 Square Lattice With Line And Point Defects (Arunkumar et al., 2019).

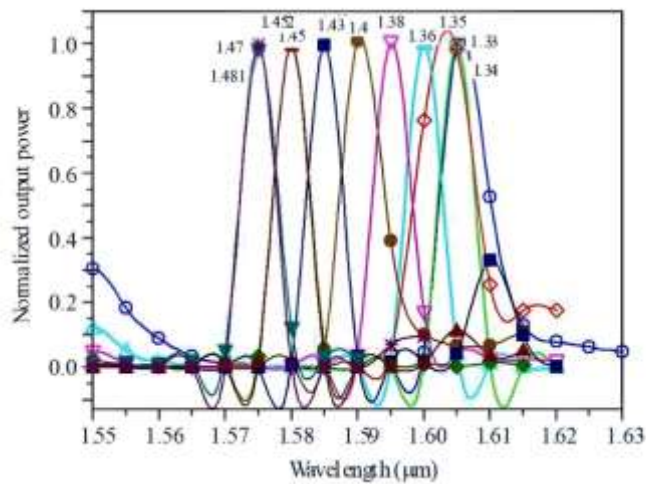


Figure 6. Normalized Output Transmission Spectra For Normal Range Of Blood Components In Blood (Arunkumar et al., 2019).

The blood components with the appropriate refractive index, measured resonance wavelength, Q factor, and output efficiency are presented in Table 2. A change in the normalized transmission output power level and an equivalent resonant wavelength for each blood component has been demonstrated. Thus, each spectrum would act as a signal of the blood constituents according to the sensor design. The accuracy of the proposed model through simulation was about 97% with a fabrication tolerance of 5% (DellOlio et al., 2013).

Examination through blood tests would be carried out by taking a minimum number of samples and then evaluating functional characteristics which would then be compared with the data listed in Table 2 to identify diseases with a shorter time. The resonant wavelength was shifted to a higher wavelength region when the refractive index of the constituents of the blood was also high. With an increase in refractive index, the effective dielectric

strength of the sensor increased which clearly shifted the resonant wavelength to a higher wavelength region (Arunkumar et al., 2019). Functional parameters of the proposed sensor and the comparison of various PhC-based structures are listed in Table 3.

It can be seen that this structure can be used for sensors on physical, chemical, and biological parameters. A high transmission efficiency of 100% was achieved by the circular ring resonator, however, the quality factor and sensitivity of the refractive index were very low. The rhombus ring resonator could provide a solution because this sensor had a high refraction sensitivity of 1000nm/RIU and a transmission efficiency of 100%. From the previous data, it is found that PhC-based biosensors for detecting blood components will meet the demand in today's medical applications.

Table 2. Input Refractive Index, Resonant Wavelength, Quality Factor, And Output Efficiency For Different Blood Components In Blood (DellOlio et al., 2013)

Name of blood components	Refractive index	Resonant wavelength (nm)	Q factor	Output efficiency (%)
Urethane Dimethacrylate	1.481	1575	262	98
Bovine Serum Albumin	1.470	1576	262	99
Polyacrylamide	1.452	1580	263	99
Biotin-Streptavidin	1.450	1580	263	99
Sylgard184	1.430	1585	264	99
Glucose (40 gm/100 ml)	1.400	1590	227	100
Hemoglobin	1.380	1595	265	100
Ethanol	1.360	1600	266	99
Blood Plasma	1.350	1604	160	105
Cypton	1.340	1605	267	98
Water	1.330	1607	178	99

Table 3. Comparison Of Quality Factor, Sensitivity, Detection Limit And Sensing Parameters Of The Proposed Sensor With Reported Sensors (DellOlio et al., 2013).

Reference	Quality factor	Sensitivity (nm/RIU)	Detection limit (RIU ⁻¹)	Sensing parameters/RI range
(Radhouene et al., 2017)	1727	***	***	Temperature
(Mallika et al., 2015)	***	***	***	Temperature
(Hsiao & Lee, 2010)	5522	***	***	Force
(Mai et al., 2010)	1737	***	***	Force and pressure
(Sreenivasulu et al., 2018)	16000	***	***	Force
(Olyae & Bahabady, 2014)	1750	4125	***	133-1.51
(Huang et al., 2014)	35517	330	1.24×10^{-5}	Deuterium water and glycerol solution
(Olyae & Bahabady, 2015)	2700	***	***	1.33-1.48
(Harhouz & Hocini, 2015)	***	260	0.001	Refractive index
(Hocini & Harhouz, 2016)	***	84pm/C	0.001	Temperature
(Arafa et al., 2017)	1.15×10^{-5}	462	3.03×10^{-6}	Glucose concentration
(Arunkumar et al., 2019)	262	***	0.002	Blood components

3. Applications in Cancer

Cancer is the second leading cause of death in the world, accounting for almost 1 in every 6 deaths. This hazardous disease is caused by metastatic, which refers to the rapid, abnormal, and uncontrolled growth and reproduction of the body's cells. Detection of cancer is difficult because the symptoms begin to appear in the late stages (Khani & Hayati, 2022). However, the reduction in mortality from cancer can be done if cancer cells can be detected early. PhC-based biosensors can be used in early detection and prevention of cancer cells because these sensors work on the principle of resonant wavelengths (Baba et al., 1999). Based on this sensing principle, any mechanical deformation caused from within or without the sensor, the resonant wavelength or intensity of the sensor output will vary, thereby indicating sensitivity to internally or externally triggered effects. Anthony et al (2020), in their research designed the PhC-based biosensor shown in Figure 7, by including a linear waveguide with nano-cavities and it was shown that each cell had a different refractive index. This difference in refractive index shifted the intensity of

the resonant wavelength of the sensor (Adoghe et al., 2020).

There were two holes in the center of the structure, and cells were placed into these holes for sensing which then the output of the simulation would be compared. The light that passed through the photonic crystal from one end would interact with the cells in the hole and compare the output to detect which cells were cancerous, because cancer cells or malignant cells have a much higher refractive index when compared to normal cells (Sharma & Kalyani, 2017). The sensor could sense changes in molecules with varying refractive index. The refractive index of the material or blood sample as well as the corresponding increase in light transmission through the sensor are presented in Table 4. The propagation of light waves of different colors through photonic crystal and how they resonated with cavities in a 2D magnetic distribution are shown in Figure 8 and Figure 9. The initial intensity of light entering the sensor was not the same as the output at the point of observation. There was a reduction in light intensity caused by operation in the sensor cavity.

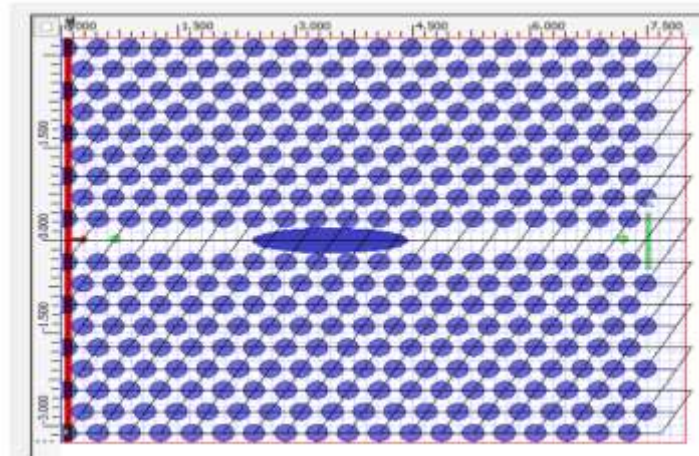


Figure 7. 2D photonic crystal layout (Adoghe et al., 2020).

Table 4. Measured Parameters of Different Cells using the Photonic Crystal Based Biosensor (Baba et al., 1999).

Name of Cell	Effective Refractive Index	Resonant Wavelength (nm)	Transmission Power (%)
Normal Cell	1.350	1.54966	51.9
Jurket Cell	1.390	1.54966	55.1
PhC-12 Cell	1.395	1.54966	55.6
MDA MB 232 Cell	1.399	1.54966	56.0

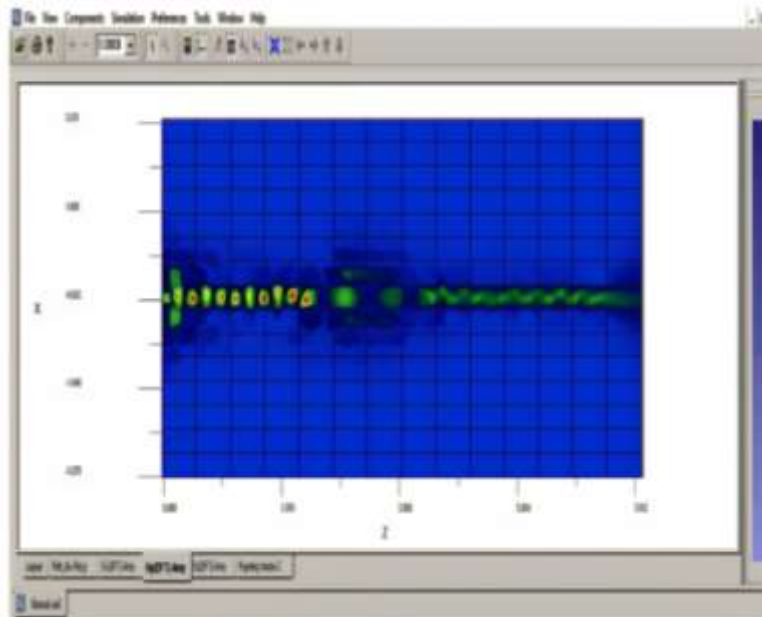


Figure 8. Normal Blood Cell Magnetic Field Distribution In 2D (Adoghe et al., 2020).

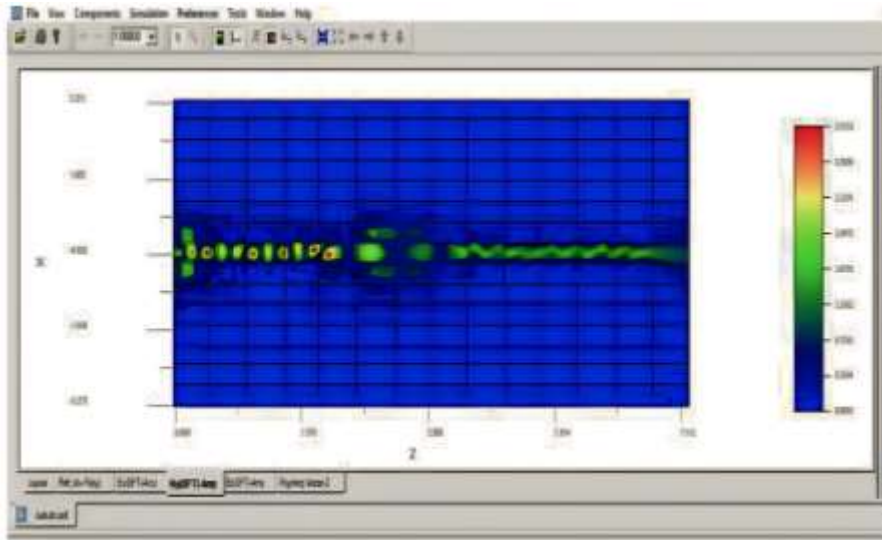


Figure 9. MC7 Cell Magnetic Field Distribution In 2D (Adoghe et al., 2020).

The diffused light would resonate with the blood sample and give an output based on the different refractive index that each blood sample had. This PhC-based biosensor can be used in early detection before more advanced medical symptoms occur. Light-based technology which is generally non-contact to the patient with fewer side effects can be applied easily, and visualization of complex structures and high-level cell diagnosis can be applied via PhC-based biosensors.

CONCLUSION

Based on the above discussion, we can say that PhC-based sensor technology is a very promising branch of modern optics and has many possibilities in the future. If PhC-based sensors succeed to compete with today's commercially available techniques, such sensors have to develop a fabrication technology, improve real-time and industrial applications. It is now clear that many PhC-based sensors possess advanced sensitivities demonstrating their potential in a wide range of sensing applications with their very small size, endurance, flexibility, invulnerability to harsh environments, and more. A review of the reported studies with their related results show that PhC-based sensors have played a crucial role in the field of optical sensors especially in detecting the sensitivity of various biomolecules in cancer, malaria, and blood component detection, and will produce significant industrial values. At that point, readers interested in this field do not only see the unique properties and flexibility in PhC structural designs, but also expand their thinking and come up with several new solutions to further explore the potential of photonic crystal in various sensors.

ACKNOWLEDGEMENT

We gratefully acknowledge the Development of Design and Fabrication of Silicon-based Photonic Crystals to be applied as Biosensors with Fundamental Grant Research scheme (HF-UNS Research) B under contract number 254/UN.27.22/PT.01.03/2022.

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