Photonic crystal-based biosensor for detection of human red blood cells parasitized by plasmodium falciparum

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Abstract

In this paper, a biosensors based on a two-dimensional photonic crystal (2D PhC) waveguide including a ring resonator is designed and simulated based on refractive index changes of red blood cells. The proposed biosensor structure consists of an elliptical photonic crystal ring resonator and two linear waveguides containing silicon nitride rods in a 2D rectangular lattice with circular rods. The biosensor is utilized to detect the stages of the Plasmodium falciparum cycle in red blood cells and to diagnose malaria disease. The proposed design distinguishes with high sensitivity between normal red blood cells and cells infected with Plasmodium falciparum. This biosensor is very compact, consists of gold rods in the air background and works very well at two input central wavelengths of 0.514 and 1.55 μm. The finite-difference time-domain (FDTD) method is used to simulate and investigate the device. The biosensor is extremely compact which is very suitable for lab-on-chip applications and exhibits higher sensitivity at both input central wavelengths compared with that of previously reported sensors.

Keywords Plasmodium falciparum · Photonic crystal · Ring resonator · Biosensor · Visible wavelength · FDTD · PWE

1 Introduction

Malaria is a dangerous human disease that is one of the leading causes of morbidity and mortality in children as well as adults in endemic countries. About 44% of the world’s population is at risk for the disease (Nureye and Assefa 2020). Its rapid and efficient diagnosis is essential to prevent complications and mortality, as well as to treat and manage the disease (Bilal et al. 2015). The five types of Plasmodium that cause the disease are P.falciparum, P.vivax, P. ovale, P. malariae, and P. knowlesi, of which most malaria deaths are associated with P. falciparum infections. The parasite is generally transmitted to humans by the bite of an infected Anopheles mosquito (Molina-Franky et al. 2020). At
this time, the life cycle of Plasmodium begins and the parasites enter the bloodstream in the form of sporozoites and attack the liver cells. When the hepatocytes are destroyed, the parasites enter the bloodstream as merozoites and attack the red blood cells and finally begin an intraerythrocytic cycle. This cycle causes structural and biochemical changes in red blood cells. The beginning of this cycle is the ring phase, which is caused by merozoites attacking red blood cells, followed by mononuclear trophozoites. Later, trophozoites transform into multinucleated cells called schizonts, which are formed by the breakdown of hemoglobin and the production of hemozoin (Liu et al. 2016). In the intraerythrocytic cycle, infected erythrocytes show a heterogeneous distribution of refractive index throughout the cytoplasm of the cell, while healthy erythrocytes have a homogeneous refractive index distribution (Akpa Marcel et al. 2019). This significant refractive index difference between healthy and infected red blood cells can be used as an essential parameter for the diagnosis of malaria (Bendib and Bendib 2018).

The main method for confirming malaria infection is based on a blood smear examination with a light microscope, which requires an experienced and trained laboratory specialist, and the speed of achieving results is relatively slow (Ragavan et al. 2018). The other two methods used to diagnose malaria include rapid diagnostic testing (RDT) and polymerase chain reaction (PCR). In the former, there are many concerns about their sensitivity and specificity that limit their impact, and the latter are expensive and time consuming and require trained personnel (Krampa et al. 2020). The use of RDT and light microscopy to diagnose malaria in febrile patients is sufficient, however, a more efficient and faster tool is needed to diagnose malaria (Bilal et al. 2015). Sensitivity and specificity of optical techniques to produce high-precision data are essential for improving the tools available in future research on blood diseases (Bendib and Bendib 2018).

Photonic crystal (PhC)-based biosensor is one of these optical techniques that has been considered due to its properties such as light confinement and compression (Sharma and Sharan 2015). The sensing mechanism in photonic crystals is based on the propagating mode effective index change. The propagating mode effective index change is produced by two methods, the first by changing the refractive index of the PhC cover medium or homogeneous sensing and the other method by changing the thickness of an ultra-thin layer of immobilized receptor molecules on the PhC surface or surface sensing (Dell’Olio and Passaro 2007). With changes in refractive index, the resonance wavelength of the PhC has changed, which leads to high sensitivity, which is the basis for detecting label free PhC biosensors (Divya et al. 2018).

Photonic crystals are highly compact and suitable for use in lab on a chip. They are easy to design and can detect small changes in the refractive index with a small sample size (Zhang et al. 2017). Photonic crystal ring resonator (PCRR) has the advantages of very high sensitivity, small size, high quality factor and very good light confinement (Sharma and Sharan 2015). PCRR-based sensors are used to measure temperature (Zegadi et al. 2019; Rajasekar and Robinson 2018), pressure (Rajasekar and Robinson 2018; Krishnan and Robinson 2014), force and strain (Mai et al. 2011), biomolecules such as DNA (Hsiao and Lee 2010). Also, determining various components of blood (Sharma and Sharan 2015; Rajendran et al. 2018) and determining the concentration of glucose in urine (Robinson and Dhanlaksmi 2016) are other applications.

Metallic photonic crystals (MPhC) are ordered synthetic nanostructures composed of units such as nanoholes, nanorods, nanopyramids, and nanospheres which are used in the fabrication of optical sensors, metamaterials, solar energy conversion and molecular detection (Cai et al. 2017).
In this paper, we design and simulate a two-dimensional (2D) PhC biosensor with a rectangular arrangement of gold rods distributed in the air background with both input central wavelengths of 0.514 and 1.55 μm. It should be noted that most sensors have been designed and reported at the wavelength range of near infrared, especially at 1.55 μm. This is because at near infrared wavelengths the ratio of wavelength change to refractive index change is higher than that of the visible wavelengths (Liu et al. 2017). The is also the case for malaria biosensors. The design priority of the biosensor at the input central wavelength is 0.514 μm because at wavelengths of less than one micrometer, water absorption is negligible and causes less damage to biological cells, which is the advantages of the proposed biosensor that is excited by visible light. Also, abundant access to high-performance detectors, low-cost light sources and high performance are other advantages (Subramanian et al. 2015).

2 Proposed 2D PhC-based biosensor design

As it is shown in Fig. 1, the 2D PhC-based biosensor is created with a ring resonator from a rectangular arrangement of gold rods (yellow area) in the air background (white area). The ring resonator in the middle of the structure can be made of rods with different geometry as will be described later on. The gold permittivity can be defined via the Drude model as (Chen et al. 2019; Hassani and Skorobogatiy 2009; Hameed et al. 2015):

$$\varepsilon(\omega) = \varepsilon_\infty - \frac{\omega_p^2}{\omega(\omega + i\omega_c)}$$  \hspace{1cm} (1)

where $\varepsilon_\infty$ is the dielectric permittivity of gold at high frequency and its value is 9.75, $\omega_p = 1.36 \times 10^{16}$ rad/s is the plasma frequency and the value of $\omega_c$ is $1.45 \times 10^{14}$ rad/s. The air refractive index is 1 and the radius of the rods and the lattice constant are 0.2 and 0.45 μm, respectively. The number of rods in the x and z directions is 13 and 21, respectively. The size of this biosensor is $9.82 \times 6 \mu m^2$.

**Fig. 1** The proposed 2D PhC-based biosensor. The yellow area corresponds to gold rods and the white region is related to the air background. Silicon nitride (Si$_3$N$_4$) rods, shown in orange.
It should be noted that the ring resonator shown in Fig. 1 was created by removing and changing the radius of the gold rods. The input and output waveguides is generated by removing six gold rods. Inside the waveguides were placed silicon nitride (Si$_3$N$_4$) rods, shown in orange in Fig. 1.

The refractive index of silicon nitride was obtained according to the following Sellmeier equation (Bååk 1982):

\[ n^2(\lambda) = 1 + \frac{2.8939\lambda^2}{\lambda^2 - (0.13967)^2} \]  

(2)

The chemical, mechanical, and thermal stability of silicon nitride, as well as its range of transparency, from visible to mid-infrared, are important features for biochemical and medical measurement applications. High-accuracy sensors based on light guiding mechanisms have been reported in photonic integrated circuits (PICs) made of silicon nitride. Silicon nitride has two important physical properties: very low propagation loss and nonlinear response. The latter is used to generate specific selective wavelengths. Many wavelengths can be combined together due to very low propagation loss in very complex circuits (Porcel et al. 2019). The proposed biosensor structure was optimized by changing the radius of the gold rods adjacent to the ring resonator and the output and input waveguides, as well as the silicon nitride rods. The goal of optimization is to achieve high sensitivity, high quality factor and high normalized output power simultaneously.

Two important parameters for evaluating any biosensor are quality factor and sensitivity. Quality factor is the ratio of resonant wavelength ($\lambda_{\text{resonant}}$) to full width at half maximum (FWHM) of the output of the waveguide, expressed as:

\[ Q = \frac{\lambda_{\text{resonant}}}{\text{FWHM}} \]  

(3)

Sensitivity of the ratio of resonance wavelength changes to changes the refractive index is expressed as (Mohammed et al. 2019):

\[ S = \frac{\Delta \lambda}{\Delta n} \]  

(4)

Normalized output power indicates the amount of power loss. The higher the normalized output power, the lower the power loss (Sharma and Sharan 2015).

Parameters obtained from the sensor output spectrum, such as Q factor in experimental investigation, are related to the fabrication challenge. Deviation of these parameters in practice from theoretical calculations is related to the fabrication method and the precise fabrication performance. In other words, if there is a precise method and performance in the fabrication, the Q factor and a parameter such as sensitivity will be very close to the theoretical calculations.

Elliptical gold rods with a larger radius of $R_A$ ($\mu$m) and a smaller radius of $r_A$ ($\mu$m), and circular gold rods with a radius of $R_B$ ($\mu$m), form the ring resonator, shown in Fig. 2 with the letters A and B, respectively. Elliptical gold rods, including input and output waveguides with a larger radius of $R_C$ ($\mu$m) and a smaller radius of $r_C$ ($\mu$m), shown in Fig. 2 with the letters C. Also, in the middle of the ring resonator, which is shown with the letter D, an elliptical gold rod with a larger radius of $R_D$ ($\mu$m) and a smaller radius of $r_D$ ($\mu$m) has been used.

In recent years, methods such as lithography, atomic layer deposition, and laser etching have been widely used to achieve two-dimensional MPCs due to their uniformity and high
fabrication capacity (Cai et al. 2017). Also, in 2007, fabrication of elliptical and square gold nanopillars on planar silica substrate has been reported by Focused ion beam (FIB) milling method (Dhawan et al. 2007). Electron beam lithography has been used to fabricate metallic arrays in the form of nanocylinder (Barbillon et al. 2007), nano-grating (Hoa et al. 2008), double split nanoring with two semicircles of different radius (Cleary et al. 2009), nanopyramid (Jin et al. 2010), and nanoblock (Segawa et al. 2010). The same method has been used to fabricate arrays of gold nanostructures in the form of dimer and trimer triangles and to control the distance between these triangles in silicon nitride substrate (Koh et al. 2011). Also, the same method has been used to fabricate 2D hybrid photonic crystals consisted of gold nanodots (Stodolka et al. 2005). Although the proposed biosensor has a fabrication challenge, but there are also fabrication challenges for other sensors such as PCF based on SPR (Rifat et al. 2019). Therefore, the experimental study and practical application of the proposed biosensor according to the mentioned fabrication methods, can be a potential work in the future.

Phosphate-buffered saline (PBS) is used as a reference material with a refractive index of 1.336 (Barroso et al. 2019). When this biosensor is immersed in a sample containing buffer, air gives way to buffer. To use erythrocytes as analytes, they must be isolated from whole blood and diluted in PBS buffer, which is done by the process of sequentially centrifuging the blood and discarding the serum and plasma and adding buffer as reported in the articles (Chopra et al. 2016; Dharmadhikari et al. 2013). To identify normal and infected red blood cells, their solution replaces the PBS buffer, which changes the refractive index and changes the light propagation in the photonic crystal. The refractive indices of normal red blood cells and infected red blood cells diluted in PBS buffer are 1.399, 1.395, 1.383, and 1.373 in the ring stage, trophozoite stage, and schizont stage, respectively (Park et al. 2008). The proposed scheme is simulated by OptiFDTD software using FDTD method, which is a numerical method for solving Maxwell equations for photonic crystal structures (Mohammed et al. 2019). As well as, the band gap of 2D PhC structure without defect is calculated through the FDTD method with the Lumerical software. Especially for PhC-based sensors, when using the FDTD and plane-wave expansion (PWE) simulation methods, an excellent agreement has been observed between the simulation results and the experimental data (Mohammed et al. 2019).
3 Results and discussion

The FDTD method is used to simulate photonic band gaps (PBGs) of 2D PhC structure without defect. FDTD calculations are confirmed by comparing the results with the PWE method for rectangular lattice of silicon (n = 3.46) rods without defect in PBS buffer with the same lattice constant and rod radius. PWE method was performed with optiFDTD software. In Figs. 3 and 4, the solid red lines and the black dots show the bands calculated using PWE and FDTD methods for TM and TE modes, respectively.

As can be seen from Figs. 3 and 4, there is no photonic band gap for TM and TE modes. This study confirms our FDTD approach because the FDTD results are well consistent with the results produced by the PWE method. As shown in Fig. 5 in gray, the proposed 2D MPHe structure without defect has two PBGs in the buffer for transverse electric mode (TE). In metallic photonic crystals, there is a cut-off frequency (Degirmenci and Landais 2013), and the frequency range between the zero and cut-off frequencies forms the first band. Therefore, the first band is between 0 and 0.762665 \( a/\lambda \). The second band gap is between 0.77047 and 0.977396 \( a/\lambda \), which is related to the wavelength range of 460.407 to 584.059 nm. The second PBG was used to design the biosensor at the input central wavelength of 0.514 \( \mu m \).

Also, as shown in Figure 6, this structure has a PBG in the buffer for transverse magnetic (TM) mode. This PBG is between 0.290555 and 0.406783 \( a/\lambda \), which is in the wavelength range of 1106.241 to 1548.760131 nm and is not considered. In Fig. 7, the photonic band gaps of the 2D PhC structure without defect it was shown for transverse electric mode (TE) and refractive indices, normal red blood cell and malaria-infected blood cells.

Table 1 shows, the PBG wavelength range shifts to larger values as the background refractive index increases. However, in the second band gap 0.514 \( \mu m \) wavelength is still in the PBG wavelength range for this range of refractive indices.

![Fig. 3 Band structure of 2D photonic crystal in rectangular lattice of silicon rods without defect for transverse magnetic mode (TM) in PBS buffer](image)
The Proposed 2D PhC-Based Biosensor is also excited by a Gaussian modulated continuous wave from a light source with a central wavelength of 0.514 μm using the Anisotropic Perfectly Matched Layers (APML) boundary conditions.
The spatial step sizes $\Delta x$ and $\Delta z$ of the grid in FDTD simulation were considered to be 10 nm. The time step size $\Delta t$, for the stability of the simulation, must satisfy the following relation:
where $c$ is the speed of light in free space (Zegadi et al. 2019). Simulations were also performed during 100,000 time steps. The optimization of the radii of gold rods and silicon nitride rods, which are $R_{A,C}$, $r_A$, $R_B$, $r_C$, $R_D$, $r_D$ and $R_{Si_3N_4}$ for normal red blood cells ($n = 1.399$), is shown in Table 2.

As can be seen in Fig. 8a, the reason for choosing the 0.22 $\mu$m size for $R_B$ is that at 0.2 and 0.18 $\mu$m the Normalized output power Transmission is low and resonant wavelengths are close to each other and overlap. The output spectrum is also widened at 0.18 $\mu$m. This problem also exists for $R_{A,C} = 0.2$, $r_A = 0.16$, $r_C = 0.1$, and the shape of the output spectrum has become unusual. The value of Normalized output power Transmission for the radii of $R_{A,C}$, $r_A$ and $r_C$ in Fig. 8b, c and d are compared with the values of 0.22, 0.14 and 0.12 $\mu$m, respectively.

As can be seen in Table 2, the values highlighted in green have a good balance between sensitivity, quality factor and normalized output power simultaneously.

### Table 1
The values of PBG width, normalized frequencies, and wavelength range for the first band gap and second band gap, respectively, for the refractive index, PBS, normal red blood cells, and malaria-infected red blood cells

| Refractive Index                | PBG width (first band gap) | Normalized frequencies (first band gap) | PBG width (second band gap) | Wavelength range (nm) (second band gap) |
|---------------------------------|-----------------------------|----------------------------------------|-----------------------------|----------------------------------------|
| Normal red blood cell 1.399     | 0.734832                    | 0.734832                               | 0.21224                     | 472.1995–607.4949                     |
| Ring stage 1.395                | 0.73676                     | 0.73676                                | 0.22591                     | 464.741–606.166                       |
| Trophozoite stage 1.383         | 0.742016                    | 0.742016                               | 0.223454                    | 462.3926–600.2041                     |
| Schizont stage 1.373            | 0.746473                    | 0.746473                               | 0.222436                    | 461.253–597.476                       |
| PBS buffer 1.336                | 0.762665                    | 0.762665                               | 0.206926                    | 460.407–584.059                       |

### Table 2
The optimization of the radii of gold rods and silicon nitride rods

| $R_{SiN_3}$ (µm) | $R_{A,C}$ (µm) | $r_A$ (µm) | $R_B$ (µm) | $r_C$ (µm) | $R_D$ (µm) | $r_D$ (µm) | Sensitivity (nm/RIU) | Quality factor | Normalized output power Transmission |
|------------------|----------------|------------|------------|------------|------------|------------|----------------------|---------------|-------------------------------------|
| 0.08             | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 348.634              | 62.293        | 0.310450357                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 357.317              | 62.293        | 0.310450357                         |
| 0.12             | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 355.782              | 62.293        | 0.201255324                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 352.568              | 62.293        | 0.180112587                         |
| 0.1              | 0.22           | 0.12       | 0.22       | 0.12       | 0.3        | 18          | 361.556              | 62.293        | 0.270049368                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.14       | 0.3        | 18          | 354.613              | 62.293        | 0.248784327                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.28       | 18          | 357.366              | 62.293        | 0.299314109                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.32       | 18          | 356.985              | 62.293        | 0.31457014                          |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 359.184              | 62.293        | 0.292653987                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 354.922              | 62.293        | 0.292653987                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 357.366              | 62.293        | 0.292653987                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 359.184              | 62.293        | 0.292653987                         |
| 0.1              | 0.22           | 0.14       | 0.22       | 0.12       | 0.3        | 18          | 359.184              | 62.293        | 0.292653987                         |

$R_{A,C}$: The values of $R_A$ and $R_C$ are the same

See Figure 8 and text.
The electric field distribution of elliptical ring resonator of designed biosensor at the resonant wavelength 0.52508 μm is shown in Fig. 9. Transmission spectra for PBS and normal and malaria-infected erythrocytes were obtained with optimized values using OptiFDTD software. Shift changes in the resonant wavelength of the normalized output power transmission spectrum were observed due to changes in the refractive index between the buffer as well as healthy and infected red blood cells, the results of which can be seen in Fig. 10.
Figure 10 shows a red shift at the peak resonance wavelength from 0.502576 μm for PBS buffer to 0.52508 μm for normal red blood cells. The reason for the resonance wavelength shift is the change in the Propagation of light in interaction with the analytes (Jindal et al. 2016). After obtaining the transmission spectrum from the analytes, the quality factor, sensitivity and peak value of the normalized output power transmission spectrum were calculated for each of them, the results of which are given in Table 3.

As it can be seen in the Fig. 11, there is a very good linear relationship between the resonance wavelength shift and refractive index changes with regression coefficient of 1. Also, the sensitivity value for this biosensor is in the range of refractive index 1.336 to 1.399 equal to 357.1 nm / RIU. Similar biosensors operate at wavelengths such as 1.55 and 2.09 μm (Bendib and Bendib 2018; Mohammed et al. 2020; Kalyani and Sharma 2017). Biosensors have been reported to detect malaria-infected red blood cells at near-infrared wavelengths, especially at 1.55 μm. Since the analytes refractive index was measured at a wavelength of 0.514 μm, our biosensor design was performed in this wavelength range, but the sensitivity due to this wavelength region and the small size of this biosensor with the reported biosensors is comparable. Even this proposed biosensor

Figure 10 Normalized output power transmission spectrum for PBS, normal red blood cell, and malaria-infected red blood cells at input central wavelength of 0.514 μm

| Refractive Index          | Resonant Wavelength (μm) | Normalized output power Transmission | Sensitivity (nm/RIU) | Quality factor |
|---------------------------|--------------------------|--------------------------------------|----------------------|----------------|
| Normal red blood cell 1.399 | 0.52508                  | 0.311075                             | 357.2168             | 142.2426       |
| Ring stage 1.395          | 0.523634                 | 0.305411                             | 356.9152             | 148.0285       |
| Trophozoite stage 1.383   | 0.519328                 | 0.28697                              | 356.4207             | 142.883        |
| Schizont stage 1.373      | 0.515744                 | 0.269702                             | 355.8953             | 152.513        |
| PBS buffer 1.336          | 0.502576                 | 0.186021                             | Ref                  | 170.7128       |
had a much higher sensitivity in the range of 1.55 μm with the same dimensions than the reported biosensors.

Our proposed biosensor has a very high sensitivity at the input central wavelength of 1.55 μm, which is caused by a slight change in the previous structure and is the same size. The manipulation of the structure is in the form of changes in the sizes of $R_{Si3N4}$ and $r_c$, which are 0.18 and 0.1 μm, respectively. The first PBG was used to design the biosensor at input central wavelength of 1.55 μm. For this simulation, the refractive index of silicon nitride according to the following Sellmeier equation was obtained (Luke et al. 2015):

$$n^2(\lambda) = 1 + \frac{3.0249\lambda^2}{\lambda^2 - (0.1353406)^2} + \frac{40314\lambda^2}{\lambda^2 - (1239.842)^2}$$ (6)

The simulation conditions are like 0.514 μm. The normalized output power transmission spectrum is shown in Fig. 12.

The quality factor, sensitivity and peak value of the normalized output power transmission spectrum are shown in Table 4.

As shown in Fig. 13, there is a very good linear relationship with the regression coefficient of 1. Also, sensitivity value of 893.7 nm / RIU was obtained.

Comparing Tables 3 and 4, it can be seen that the sensitivity, quality factor and normalized output power are higher at the input central wavelength of 1.55 μm. Also, as shown in Table 5, the proposed biosensor at the input central wavelength of 1.55 μm

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Fig. 11 Resonance wavelength as a function of refractive index changes of PBS, normal red blood cell, and malaria-infected red blood cells at input central wavelength of 0.514 μm
with a very compact size has a higher sensitivity than the results reported in the articles shown. However, given the benefits of working at the visible wavelength described at the beginning of this article, and also because of our proposed biosensor, which operates in the wavelength range from 0.514 μm, detects normal and infected red blood cells with high sensitivity in laboratory conditions where their refractive index has been measured. In other words, our proposed biosensor operates in the wavelength range from 0.514 μm, the wavelength at which refractive indices are measured.
In this paper, a 2D PhC-based biosensor with a ring resonator has been designed to detect the Plasmodium falciparum cycle in red blood cells at input central wavelengths of 0.514 and 1.55 μm. This biosensor is compact with dimensions of 9.82 × 6.00 μm² and exhibits high sensitivity working based on the change of the peak resonance wavelength shift due to the change of the refractive index, which is a very linear change. The results show that the sensor has a very good linear response with a regression coefficient of 1. According to the simulation results, the sensitivity of this biosensor for the refractive index range from 1.336 to 1.399 at the central input wavelengths of 0.514 and 1.55 μm is equal to 357.1 RIU / nm and 893.7 nm / RIU, respectively. The design priority of the biosensor at the input central wavelength is 0.514 μm because at wavelengths of less than one micrometer, water absorption is negligible and causes less damage to biological cells. Also, abundant access to high-performance detectors, low-cost light sources and high performance are other advantages. Finally, to the best of our knowledge it is for the first time that such a versatile biosensor is designed in the visible wavelength range where the measured refractive indices are available.

![Fig. 13](image_url) Resonance wavelength as a function of refractive index changes of PBS, normal red blood cell, and malaria-infected red blood cells at input central wavelength of 1.55 μm

### 4 Conclusion

In this paper, a 2D PhC-based biosensor with a ring resonator has been designed to detect the Plasmodium falciparum cycle in red blood cells at input central wavelengths of 0.514 and 1.55 μm. This biosensor is compact with dimensions of 9.82 × 6.00 μm² and exhibits high sensitivity working based on the change of the peak resonance wavelength shift due to the change of the refractive index, which is a very linear change. The results show that the sensor has a very good linear response with a regression coefficient of 1. According to the simulation results, the sensitivity of this biosensor for the refractive index range from 1.336 to 1.399 at the central input wavelengths of 0.514 and 1.55 μm is equal to 357.1 RIU / nm and 893.7 nm / RIU, respectively. The design priority of the biosensor at the input central wavelength is 0.514 μm because at wavelengths of less than one micrometer, water absorption is negligible and causes less damage to biological cells. Also, abundant access to high-performance detectors, low-cost light sources and high performance are other advantages. Finally, to the best of our knowledge it is for the first time that such a versatile biosensor is designed in the visible wavelength range where the measured refractive indices are available.
Table 5  Comparison of articles related to photonic crystals-based biosensors for malaria diagnosis with this biosensor proposed in this article

| Ref                   | Year | Refractive index | Sensitivity (nm/RIU) | Quality factor | Techniques                                      | Input central wavelength (μm) | Size (μm²) |
|-----------------------|------|------------------|----------------------|----------------|-----------------------------------------------|-------------------------------|------------|
| Kalyani and Sharma    | 2017 | Normal red blood cell 1.402 | **                    | **             | Nanocavity Photonic Crystal                  | 1.55                          | 21 × 19   |
|                       |      | Ring stage 1.395 | **                   | **             |                                               |                               |            |
|                       |      | Trophozoite stage 1.383 | **                   | **             |                                               |                               |            |
|                       |      | Schizont stage 1.373 | **                   | **             |                                               |                               |            |
| Bendib and Bendib     | 2018 | Normal red blood cell 1.402 | **                   | **             | Photonic crystal bio-sensor based on ring resonator | 2.09                          | 11 × 11   |
|                       |      | Ring stage 1.395 | **                   | **             |                                               |                               |            |
|                       |      | Trophozoite stage 1.383 | **                   | **             |                                               |                               |            |
|                       |      | Schizont stage 1.373 | **                   | **             |                                               |                               |            |
| Mohammed et al.       | 2020 | First design Normal red blood cell 1.402 | 731.20               | 1535.27        | Cavity photonic crystal                       | 1.55                          | 11.4 × 9.2|
|                       |      | Ring stage 1.395 | 741.30               | 1755.69        |                                               |                               |            |
|                       |      | Trophozoite stage 1.383 | 759.65               | 2430.21        |                                               |                               |            |
|                       |      | Schizont stage 1.373 | 777.61               | 2576.14        |                                               |                               |            |
|                       |      | Second design Normal red blood cell 1.402 | 401.44               | 7187.27        | Nanocavity                                    | 1.55                          | 9.4 × 5.5 |
|                       |      | Ring stage 1.395 | 406.13               | 5978.36        |                                               |                               |            |
|                       |      | Trophozoite stage 1.383 | 416.27               | 5390.00        | Photonic Crystal                              | 1.55                          |            |
|                       |      | Schizont stage 1.373 | 427.18               | 5974.80        |                                               |                               |            |
| Ref       | Year          | Refractive index | Sensitivity (nm/RIU) | Quality factor | Techniques                                                                 | Input central wavelength (μm) | Size (μm²)   |
|-----------|---------------|------------------|---------------------|----------------|----------------------------------------------------------------------------|-------------------------------|--------------|
| First design |              | Normal red blood cell 1.399 | 357.2168            | 142.2426       | 2D Photonic crystal biosensor with a ring resonator                        | 0.514                        | 9.82 × 6.00  |
|           |               | Ring stage 1.395 | 356.9152            | 142.883        |                                                                           |                               |              |
|           |               | Trophozoite stage 1.383 | 356.4207            | 148.0285       |                                                                           |                               |              |
|           |               | Schizont stage 1.373 | 355.8953            | 152.513        |                                                                           |                               |              |
| Second design |              | Normal red blood cell 1.395 | 893.8225            | 164.5777       | 2D Photonic crystal biosensor with a ring resonator                        | 1.55                         | 9.82 × 6.00  |
|           |               | Ring stage 1.395 | 893.8544            | 170.3833       |                                                                           |                               |              |
|           |               | Trophozoite stage 1.383 | 895.8088            | 190.1891       |                                                                           |                               |              |
|           |               | Schizont stage 1.373 | 898.9764            | 212.771        |                                                                           |                               |              |

** Not available
Declarations

**Conflict of interest** The authors declare that they have no conflicts of interest.

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