

## Article

# Spiral Shaped Photonic Crystal Fiber-Based Surface Plasmon Resonance Biosensor for Cancer Cell Detection

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**Abstract:** This work presents the design and simulation of an all-optical sensor for detection of cancer cells. The proposed device is based on the surface plasmon resonance effect on a spiral shaped photonic crystal fiber structure. The finite element method (FEM) based simulations are carried out for the different cancer cells, such as HELA, Basal, Jurkat, and MDA-MB-231, MCF7, and PC12 detection. The sensor has shown the maximum sensitivity of  $-289 RIU^{-1}$  for the refractive index of the detection of breast cancer cell with the resolution of  $2.33 \times 10^{-4}$ . The sensor is effective for the refractive index range of 1.36 to 1.401. The structure is based on spiral shaped photonic crystal fiber, and has shown promising linear sensing response to support the practical feasibility of the device. The proposed sensor design is effective in detecting cervical cancer, skin cancer, blood cancer, breast cancer type 1, breast cancer type 2, and adrenal gland cancer.

**Keywords:** PCF; optical sensor; SPR; biosensor; refractive index



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## 1. Introduction

Photonics biosensing platforms combine high sensitivity, selectivity, and durability, due to which they have tremendous advantages in the detection of many diseases, such as cancer, diabetes, malaria, etc. Recent surveys have revealed that more than ten million people lost their lives due to cancer in 2020, accounting for one out of six deaths worldwide [1,2]. Cancer is an epigenetic disorder which leads to unregulated cell growth, causing the formation of tumors in the human body [3]. Various types of cancer categories are Basal cell cancer, lung cancer, breast cancer, leukemia, prostate cancer, blood cancer, cervical cancer etc. [4]. Early detection of cancerous cells increases the chances of survival of patients and better response to treatment. Optical biosensors have the potential for fast and precise detection, reliable imaging of cancer cells, monitoring of onto-genesis of cancer cells, and determination of the effectiveness of anti-cancer chemotherapy agents. Numerous methods, such as Raman Spectroscopy [5–7] and surface-enhanced Raman Spectroscopy [8] have been investigated to detect cancer cells which employ Photonic Crystal Fiber (PCF)-based Surface Plasmon Resonance (SPR) biosensors. New designs, such as Hollow Core

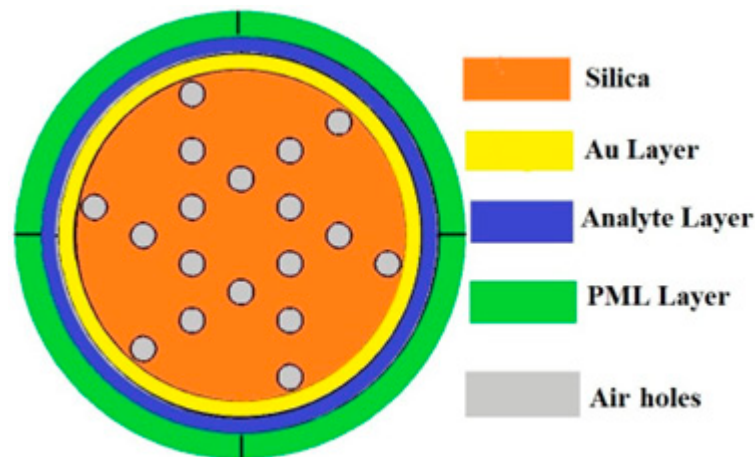
PCF (HC-PCF) [8,9], dual-core [10], and twin core PCF (TC-PCF) [11], have been used for effective biosensing. A dual-parameter SPR-PCF sensor is also designed that can measure both temperature and the magnetic field simultaneously. On either side of the fiber core, there are two elliptical channels in this sensor [12]. Many PCF-based SPR biosensors sense variations in Refractive Index (RI) with various optical parameters, and are classified as refractive-index-based biosensors. Due to flexibility of designing, scalable, and efficient birefringence [13–15] ease of dispersion tailoring, and various nonlinear properties [16–18], PCFs can be easily tailored to acquire the desired responses as sensing elements. Due to this, immense interest has developed in the usage of PCF for SPR-based biosensing [19]. Traditional prism-based SPR sensing difficulties, such as bulky design, accurate incident angle, and a huge number of adjustable mechanical components, which restrict the diverse range of applications, are all remedied by PCF SPR imaging technologies [20]. SPR is an optical phenomenon which is manifested by the collective oscillation of surface plasmons (i.e., free electrons). These electrons are found on the boundary of metal and dielectric surfaces. Any small change in RI due to an unknown analyte causes the shift of peak in the loss spectrum. When the wavelength of the surface electrons matches that of the incoming photons, resonance occurs. Here, at reverberation (resonance) frequency, Surface Plasmon Polariton (SPP) [21] interacts with the permeable center. Thus, the electric field at the core is leaked towards the metal, the dielectric medium and the corresponding mode are called SPP mode. This SPP mode is hyper sensitive in nature to even small changes in the analyte's RI [22]. SPR based PCF sensors have applications in DNA detecting [23], gas sensing [24], monitoring of water sample [25], and early detection of cancer [26]. The SPR technology is used in accordance with various schemes, such as prism emerged [27], Mach Zehnder interferometer [28], but there are optomechanical issues in SPR technology, such as complex and bulky system, oblique incidence required, and limited analysis throughput. These limitations can be overcome with PCF-based biosensors. In PCF-SPR sensors, plasmonic materials perform a vital role in the design and development of sensors. Different types of plasmonic materials, such as silver [29], zinc oxide [30], gold [31,32], titanium dioxide [33], and graphene [34,35], are used for designing and fabrication of SPR biosensors due to their unique properties. In this paper, gold is selected as a plasmonic material for designing PCF-based SPR biosensors as it is immune to oxidation in a wet environment, and it is very widely used in various biosensing applications. It is necessary that metal coating should be consistent. The proposed design is externally metal-coated PCF-SPR sensor which makes it feasible for fabrication. [36]. The refractive index component was used to analyze cancer cells from the cervical (HeLa), adrenal gland (PC12), blood (Jurkat), and breast (MCF-7 and MDA-MB-231) types. The suggested study is innovative because it proposes a model of a highly sensitive PCF-SPR based biosensor for the separation of malignant cells from healthy cells using correct FEM-based computational techniques. The article has been structured as follows: Section 2 comprised the basic principles and mathematical method involved in the sensor design. Section 3 includes all the details regarding the obtained results, and their comparison with the existing literature, followed by a conclusion.

## 2. Biosensor Design and Geometry

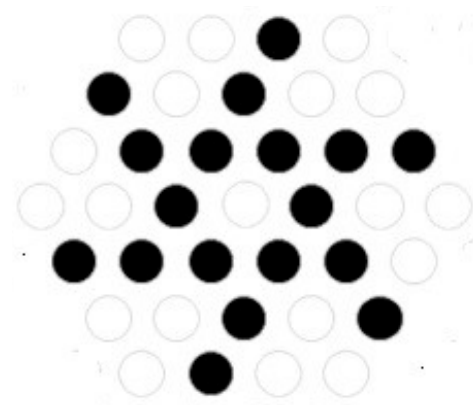
The cross-section schematic of the proposed spiral shaped photonic crystal fiber based surface plasmon resonance biosensor is shown in Figure 1. The sensor design is based on a PCF made up of silica ( $\text{SiO}_2$ ) with circular air holes in spiral shaped cladding. This structure can be realized by stacking the silica capillaries (shown as black circles) and rods (shown as white circles) in a conventional hexagonal lattice, as shown in Figure 2. This stack can then be drawn into a fiber using the stack-and-draw technique. Such a hexagonal lattice-based design of the spiral PCF has been recently fabricated [37]. The distance between any two air holes pitch  $\Lambda$  is  $2.3 \mu\text{m}$ , and the hole diameter  $d$  is  $1 \mu\text{m}$ . To construct a solid core for light confinement, one air hole is removed from the first layer of hexagonal lattice. This configuration is suitable for producing surface plasmons. A 25 nm thick gold film is deposited over the PCF as a plasmonic material for effective sensing.

This can be implemented using the chemical vapor deposition (CVD) process. A 2.6  $\mu\text{m}$  cancer cell identification layer is placed above the plasmonic layer. Finally, to shield the PCF's interior structure from outer air disturbances, a “perfectly matched layer (PML)” of thickness 0.3  $\mu\text{m}$  is placed above the cancer cell detecting layer. The Sellmeier Equation (1) used for calculating RI of silica is as follows [38]:

$$n^2(\lambda) = 1 + \frac{B_1\lambda^2}{\lambda^2 - C_1} - \frac{B_2\lambda^2}{\lambda^2 - C_2} - \frac{B_3\lambda^2}{\lambda^2 - C_3} \quad (1)$$



**Figure 1.** Cross-section schematic of proposed PCF-SPR biosensor.



**Figure 2.** A scheme to make a stack of silica rods and capillaries.

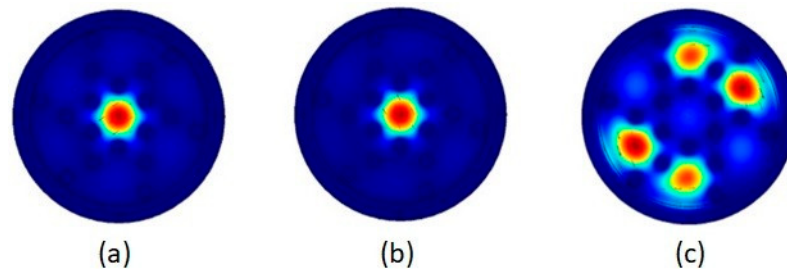
Here,  $n$  represents the refractive index of silica while  $\lambda$  denotes the operating wavelength.

For silica, Sellmeier coefficients  $B_1$ ,  $B_2$ ,  $B_3$ ,  $C_1$ ,  $C_2$ , and  $C_3$  are taken as 0.696166300, 0.407942600, 0.897479400, 0.00467914826, 0.0135120631, and 97.9340025, respectively. The Drude Lorentz Model, which is depicted in (2), is used to calculate the value of Gold's dielectric constant [39].

$$\epsilon_{Au} = \epsilon_{\infty} - \frac{\omega_D^2}{\omega(\omega + jy_D)} - \frac{\Delta\epsilon.\Omega_L^2}{(\omega^2 - \Omega_L^2) + j\Gamma_L\omega} \quad (2)$$

Here,  $\epsilon_{Au}$  is the permittivity of gold,  $\epsilon_{\infty}$  is the permittivity of gold at high frequency,  $\omega = 2\pi c/\lambda$  (angular frequency), where  $c$  is the velocity of light,  $\omega_D = 2113.6 \text{ THz} \times 2\pi$  (plasma frequency),  $y_D = 15.92 \text{ THz} \times 2\pi$  (damping frequency), and  $\Delta\epsilon = 1.09$  (weighting factor).

$\Omega_L = 650.07 \times 2\pi$  THz (Lorentz oscillator strength) and  $\Gamma_L = 104.86 \times 2\pi$  THz (Spectral width). The modal analysis of the proposed PCF design was carried out with COMSOL Multiphysics 5.3 employing the Full-Vectorial Finite Element Method (FV-FEM) with perfectly matched layers (PML). Figure 3a–c shows electric fields in X-polarized, Y-polarized fundamental and SPP modes, respectively.



**Figure 3.** (a) X-polarized core mode (b) Y-polarized core mode (c) SPP mode.

When the effective indices of plasmon and core modes are comparable, confinement losses are computed to attain peak values at the same wavelength. The variations at this peak wavelength are detected using the amplitude interrogation method. As a result, calculating confinement losses is extremely important for these sensor's performance. Here, Equation (3) is utilized to calculate the confinement losses [40].

$$\alpha \left( \frac{db}{cm} \right) = 8.686 \times k_0 \times \text{Im}(n_{\text{eff}}) \times 10^4 \quad (3)$$

$k_0 = 2\pi/\lambda$  is defined as a wave number,  $\lambda$  is the operating wavelength. The sensor's resolution determines the degree of analyte RI detection. The proposed PCF-SPR biosensor's resolution ( $R$ ) was calculated using Equation (4) [41]:

$$R = \Delta n_a \frac{\Delta \lambda_{\min}}{\Delta \lambda_{\text{peak}}} \quad (4)$$

Here,  $\Delta n_a$  is the change in analyte RI,  $\Delta \lambda_{\text{peak}}$  is the difference in resonance peak shift and  $\Delta \lambda_{\min}$  is the instrumental peak wavelength.

In PCF-based SPR sensors, sensitivity is a crucial metric. An amplitude approach can be used instead of the spectral method to detect the analyte refractive index variations. Unlike the spectral approach, this method detects changes by studying only specific wavelengths rather than a broad range of wavelengths. Amplitude Sensitivity can be calculated using Equation (5) [42]:

$$S_A(\lambda) \left[ RIU^{-1} \right] = - \frac{1}{\alpha(\lambda, n_a)} \frac{\partial \alpha(\lambda, n_a)}{\partial n_a} \quad (5)$$

where  $\partial n_a$  is the variation in the analyte's refractive index,  $\partial \alpha(\lambda, n_a)$  is the variation in propagation losses with  $n_a$  at wavelength  $\lambda$ , and  $\alpha(\lambda, n_a)$  is the confinement loss for analyte's refractive index,  $n_a$  at wavelength  $\lambda$ .

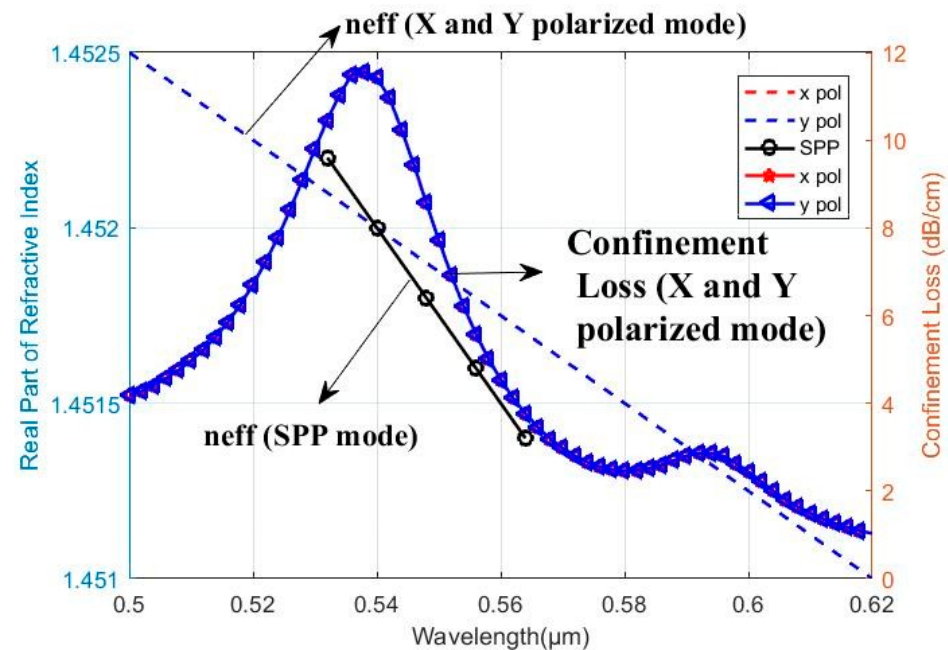
### 3. Results and Discussion

The sensing mechanism of the proposed sensor is based on the difference in wavelength of resonance peak for different analyte refractive index,  $n_a$  corresponding to cancerous cells and healthy cells. The proposed biosensor seeks to identify several cancer kinds, such as cervical cancer, skin cancer, blood cancer, breast cancer-type 1, breast cancer-type 2, and adrenal gland cancer has HELA, Basal, Jurkat, MDA-MB- 231, and MCF7 and PC12 respectively as cancer cells. The changes in the refractive index of normal (healthy) and cancer-affected cells are shown in Table 1.

**Table 1.** The difference in refractive index among normal and cancer affected cells.

| Type of Cancer | Type of Cell | R.I. of Normal Cell | R.I. of Cancer Affected Cell | References |
|----------------|--------------|---------------------|------------------------------|------------|
| Skin           | Basal        | 1.360               | 1.380                        | [43,44]    |
| Breast         | MDA-MB-231   | 1.385               | 1.399                        | [45,46]    |
| Breast         | MCF-7        | 1.387               | 1.401                        | [45,46]    |
| Blood          | Jurkat       | 1.376               | 1.390                        | [47,48]    |
| Adrenal Gland  | PC12         | 1.381               | 1.395                        | [49]       |
| Cervical       | Hela         | 1.368               | 1.392                        | [49]       |

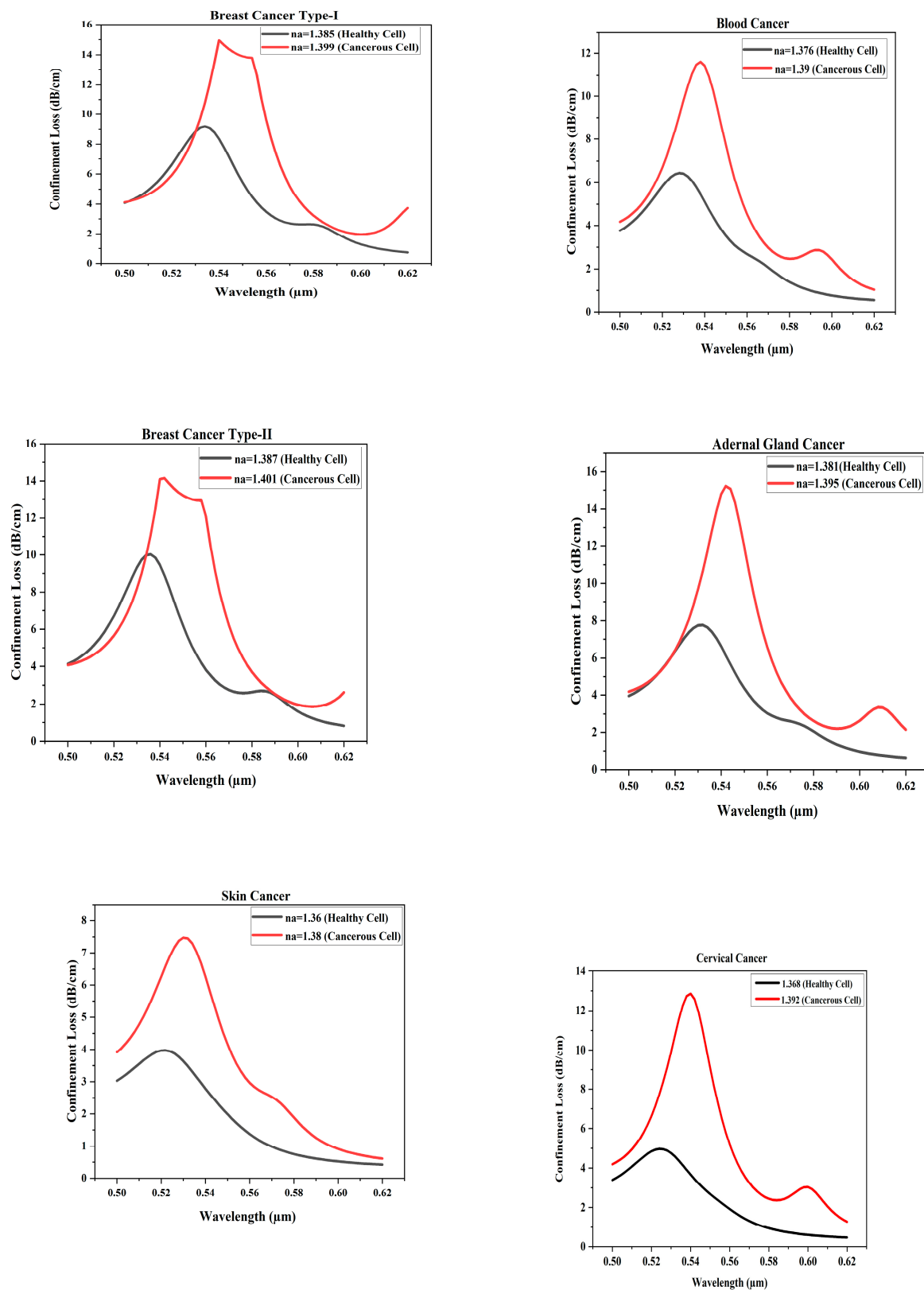
Figure 4 shows the resonance condition for the Jurkat (cancerous) cell. At 540 nm wavelength, the intersections of the efficient indices of the fundamental core mode (blue-dotted) and plasmon mode (black line) can be seen. At that wavelength, the propagation losses are at their peak due to the high-energy transfer from the fundamental core mode to the plasmon mode [50–52]. This is confirmation of the occurrence of a resonance phenomenon. Here, the values for the X-polarized fundamental mode and Y-polarized fundamental modes are the same, so the graph overlaps in both modes.



**Figure 4.** The resonance behavior of proposed PCF-SPR biosensor for Jurkat (cancerous) cell.

The confinement loss vs. wavelength for all cancer types considered in this investigation is shown in Figure 5a–f. The black and red line represents normal (healthy) and cancer-affected cells, respectively. When the normal cell in the analyte channel switched places with malignant cells, the confinement loss increases, and the peak shifted to longer wavelength, and similar behavior was observed for all types of cells. This is due to the strong metal-dielectric interaction, which is affected by the high value of analyte RI. The main basis of the amplitude interrogation approach is shifting in those peaks along the wavelength. The value of amplitude sensitivity and resolution for different cancerous cell is shown in Table 2.

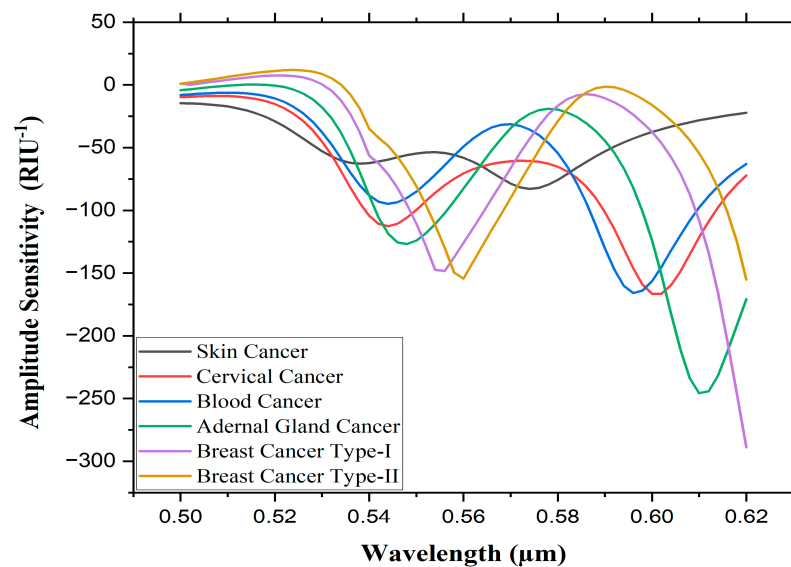
Equations (4) and (5) are employed to calculate the proposed biosensor’s resolution and amplitude sensitivity, respectively. The highest amplitude sensitivity value is obtained as  $-289 \text{ RIU}^{-1}$  for Breast Cancer (Type-1) (MDA-MB-231 cell) with  $2 \times 10^{-5} \text{ RIU}$  resolution value as shown in Figure 6.



**Figure 5.** Confinement loss properties of the proposed PCF-SPR biosensor for different kinds of normal and malignant cells.

**Table 2.** Proposed PCF-SPR biosensor’s sensitivity analysis.

| Type of Cancer | Type of Cell | R.I. Change Cell | Resolution            | Amplitude Sensitivity (RIU <sup>−1</sup> ) |
|----------------|--------------|------------------|-----------------------|--------------------------------------------|
| Skin           | Basal        | 1.360–1.380      | $2 \times 10^{-5}$    | −83                                        |
| Breast         | MCF-7        | 1.387–1.401      | $2.33 \times 10^{-4}$ | −154.5                                     |
| Blood          | Jurkat       | 1.376–1.39       | $1.4 \times 10^{-4}$  | −165.9                                     |
| Cervical       | Hela         | 1.368–1.392      | $1.5 \times 10^{-5}$  | −166.7                                     |
| Adrenal Gland  | PC12         | 1.381–1.395      | $1.4 \times 10^{-4}$  | −245.5                                     |
| Breast         | MDA-MB-231   | 1.385–1.399      | $2.33 \times 10^{-4}$ | −289                                       |



**Figure 6.** The amplitude sensitivity of proposed PCF-SPR biosensor.

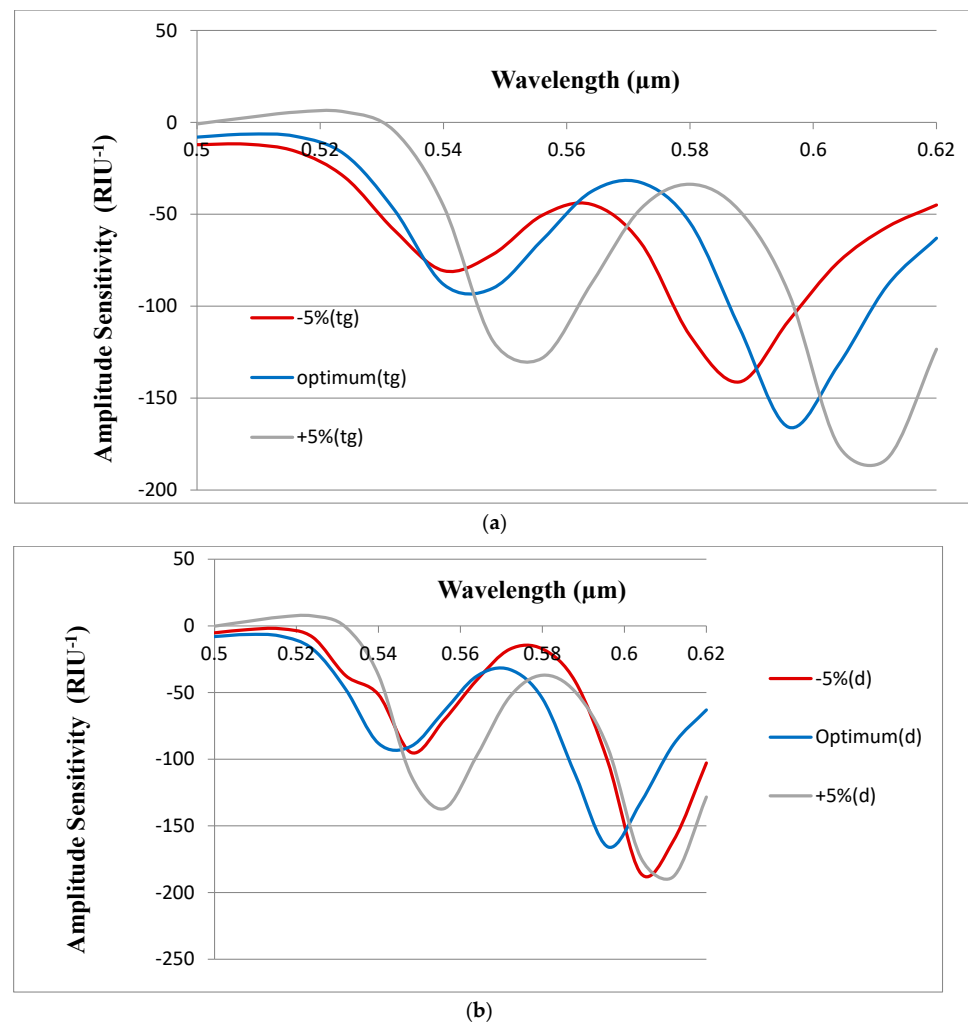
#### *Changes of $\pm 5\%$ in $t_g$ and $d$ for Fabrication Tolerance Assessment*

In order to proof the fabrication feasibility of the proposed design, a tolerance study [53] is made, as shown Figure 7. Figure 7 shows the sensor’s Amplitude sensitivity also varies within a tolerance of  $\pm 5\%$  of the  $t_g$  (gold layer) and  $d$  (air hole diameter) compared to that obtained using the optimized value of  $t_g$  and  $d$ . It may be seen from Figure 7 that within a tolerance of  $\pm 5\%$ , a slight shift occurs in the resonance wavelengths of the optimized parameters.

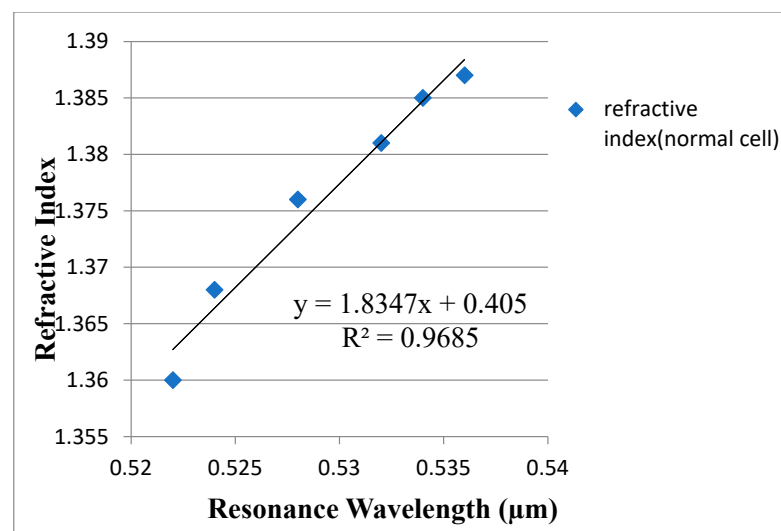
The linearity response is an important aspect of sensor design. For sensor applications, a high linearity response is a desirable metric to evaluate sensor performance. The linear fitting curve for the resonance wavelengths (for healthy cell) and for analyte refractive index ranging from 1.36 to 1.39 is shown in Figure 8. For such a Y-polarized fundamental mode, Equation (6) gives the relevant linear fitting model. The slope of this equation is used to compute the average sensitivity for various refractive index values.  $R^2$  is used to determine the sensor’s linear response. A high  $R^2$  value (0.9685) is estimated for the suggested biosensor, as shown in Figure 8. As a result, the presented biosensor has a satisfactory linear sensing response, indicating that the sensor design has significant potential.

$$y = 1.8347x + 0.405 \quad (6)$$

As a result, compared to the previous approaches, the proposed sensor has shown promising characteristics. Table 3 tabulates the results of previously published designs in comparisons to the proposed work. The comparison is based on the sensor’s sensitivity, detection range, refractive indices, and resolution. Noticeably the presented PCF-based SPR biosensor has shown good results when evaluating sensor performance.



**Figure 7.** Fabrication tolerance analysis of the proposed sensor within a tolerance of  $\pm 5\%$  of the (a) tg, and (b) d.



**Figure 8.** Linear fitting characteristics of proposed PCF-SPR biosensor.

**Table 3.** Comparison between the proposed PCF-SPR biosensor's design, wavelength range, RI range and sensitivity to existing sensors.

| Wavelength Range (nm) | Sensor's Design                                    | R.I. Range | Amplitude Sensitivity | Sensor's Resolution   | Ref.      |
|-----------------------|----------------------------------------------------|------------|-----------------------|-----------------------|-----------|
| 480–650               | D-shape                                            | 1.33–1.37  | 216 RIU <sup>−1</sup> | $4.6 \times 10^{-5}$  | [40]      |
| 1080–1560             | Quasi D-shape<br>Dual core Circular lattice        | 1.42–1.46  | 230 RIU <sup>−1</sup> | NA                    | [53]      |
| 580–720               | Circular lattice PCF sensor<br>hybrid              | 1.33–1.36  | 266 RIU <sup>−1</sup> | $3.75 \times 10^{-5}$ | [54]      |
| 633                   | TiO <sub>2</sub> /Au/graphene<br>layer-based (SPR) | 1.36–1.401 | 292.86 deg/RIU        | NA                    | [55]      |
| 500–620               | Spiral shape                                       | 1.36–1.401 | 289 RIU <sup>−1</sup> | $2.33 \times 10^{-4}$ | This work |

The suggested biosensor has a simple design, an external sensing approach, and a coating with plasmonic material. When compared to existing sensors, the suggested biosensor has produced appropriate sensing parameters. The given biosensor can accurately recognize a variety of malignant and healthy cells, which is advantageous in biomedical applications involving cancer exposure. This spiral shaped biosensor design can be utilized with visible light range (500–620 nm) sources, which proved the practical feasibility of the structure.

#### 4. Conclusions

Spiral shaped PCF-based SPR biosensor for cancer cell detection is proposed in this paper. The numerical analysis of the sensor characteristics is done, and the same has shown promising results with gold coating as a plasmonic material. The device has shown high sensitivity of  $-289 \text{ RIU}^{-1}$  for the refractive index of the detection of breast cancer cells with the resolution of  $2.33 \times 10^{-4}$ , which is more than the previously published work. The Spiral PCF design is based on a hexagonal lattice, so it can be fabricated using a conventional stack and draw process and yields high amplitude sensitivity. The proposed sensor can be used for the detection of different types of cancer cells at an early stage. This spiral shaped biosensor design can be utilized with visible light range (500–620 nm) sources, proving the structure's practical feasibility.

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