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Research paper

Spectromectric Analysis of Lymphocyte Cell for the Premature Detection of Leukemia by Surface Plasmonic Technique in Nanoplatform

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Abstract

Detection of cancer at early stages has become a top priority in the field of medical science. The existing detection methods require lot of routine tests to confirm that the sample is positive with cancer as there are chances of test results being pseudo- positive. This early stage detection of cancer will proved to be a godsend for those who are the victims of monstrous disease cancer. In this paper, we put forward a new approach for the detection of cancer at early stages by designing a 2-dimensional SPR based sensor for detailed spectral analysis of "Leukaemia" without using any biomarkers. As dielectric properties for cancer cells deviate from the normal cell, they can be identified and detected by implementing photonic approach. In the present work, design & simulations are done using FDTD. The shifts in the output waveforms and wavelengths have been recorded for a normal blood cell and cancerous cell respectively. It is observed from simulation that even for minute change in the RI of the bio analyte of interest and from which it is observed that there is a remarkable shift in the resonant wavelengths thus witnessing the ultra sensitivity of the design. Simulations are done using R-Soft CAD tool. The peak values and wavelength shift differences for normal cells and forleukaemia, the different cell components lymphocyte , nucleus, cytoplasm and the intensity shifts are recorded in order to find the relative sensitivity of the device. The design variation were made by varying sensing layer thickness and extinction coefficient Finally comparison was made between that of normal and abnormal cells to show the wavelength shift differences so that the signature graphs for each cell were obtained in order to determine the intensity of the disease and it depends on the shift in the wavelength. The wavelength shift of early stage leukaemia for cytoplasm, nucleus and lymphocyte are ranging from 2000-250nm. Sensitivity and the quality factor of the sensor have been calculated for the proposed design, the sensitivity achieved is 343nm/RIU and the quality factor is 1800.

Key words: Optical Waveguide; Biosensors; Surface Plasmon Resonance; Refractive Index; Sensitivity, Quality factor;

1. Introduction

1.1. Cancer

'Neoplasia', an un-restrainable Mitotic cell division being an effect of an unconstrained genetic mutation which is being transferred to its descendants thus resulting in the birth of cancer. The genetic mutation and its occurring rate will have the impact on the refractive index of the sample.
Leukaemia a kind of cancer, where the leukocytes are affected or the blood cells in bone marrow undergo unusual variation in its DNA. There are various screening procedures are there to confirm leukaemia .where a patient might undergo routinal and frequent blood examinations which are highly time consuming and are relatively expensive. There is a need for cost effective, accurate and rapid method to detect leukaemia. The surface plasmonic channel biosensor can be the best suitable solution for the above. The refractive indices of each and every component in blood varies and are unique, by exploiting this property it is easy to recognise the abnormalities in an immediate fashion as no biomarkers are required for the recognition.

1.2. Surface Plasmonic Biosensors

SPR is a remarkable optical development in the field of optics, which promises a non-invasive, label-free means of recognition and the characterization of the molecular interactions between an anticipated sample and an immobilized bio molecule in real time. The SPR sensing is achieved by coating a thin layer of a metal onto the glass prism or on an optical (Shalabney ,andAbdulhalim, 2011). The light is incident on the interface of metal and dielectric layer in such a way that there should be persistence of total internal reflection. This is achieved by maintaining the incident angle not less than critical angle(Gosh,and Ray, 2014) . At metal and optical substrate interface, the free electrons present in the metal layer absorbs the energy and there will be generation of localized electromagnetic wave on the metal surface whose wavelength is of ¼ th of the incident light wavelength.
Surface Plasmon poloritons are the native free density oscillations of electrons at the metal dielectric interface Stimulated by incident

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photons (Wijaya ,Lenaerts , Maricot , Hastanin , Habraken ,and Vilcot, 2011). Plasmons have the influence over the refractive index of the sample thus becoming responsible for the uniqueness in the spectral behaviour of the sample

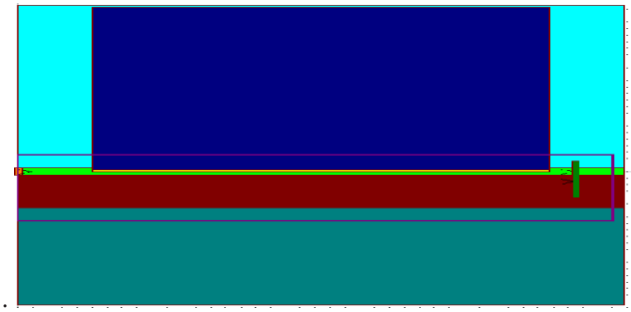

Figure 1: Layout design of SPR based biosensor

1.3 Em Wave Propagation and Dispersion Relation

Maxwells equations provide solutions for problems on EM related dispersion equations and provide melling for optial devices

$$\nabla \cdot D = \rho \quad (1)$$

$$\nabla \cdot B = 0 \quad (2)$$

Where D, B, E and H are displacement, flux density, electric field and magnetic field.
where $\rho = 0$ and $j = 0$. the relations between (E, D) and (H, B) is given by
$D = \epsilon_0 \epsilon E$
$B = \mu_0 \mu H$
ε =relative permittivity (or dielectric constant) =1,
μ=1for a nonmagnetic medium is the relative permeability of the medium.

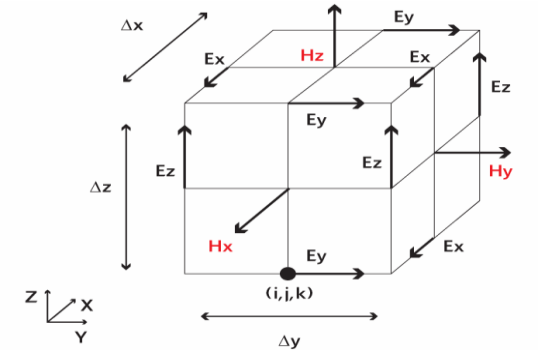

Figure2: An yee cell in 3 dimensional plane corresponding to magnetic field computation.

2. Geometry of SPR Biosensor

We propose a two-dimensional(2D) SPR based structure for spectral examination of a normal blood cell and other constitutes. The designed structure has a metal dielectric combination as an integral part. A Gaussian light used for illumination of interface in order to stimulate the generation of surface plasmons. The propagation of electromagnetic waves takes place within the sensor device. Dielectric properties of the normal cells differ from each other from internal composition point of view. The sensitivity can be determined by finding the difference between the wavelength shifts and the differences in their respective RI (Aaron, and Ho-Pui Ho,2010) values. Design of the plasmonic device is given in figure 2 given below.

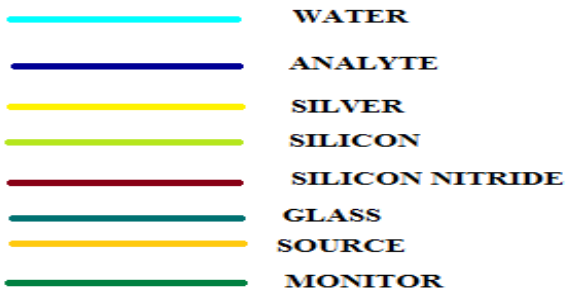

Figure 3: Representation of colour code

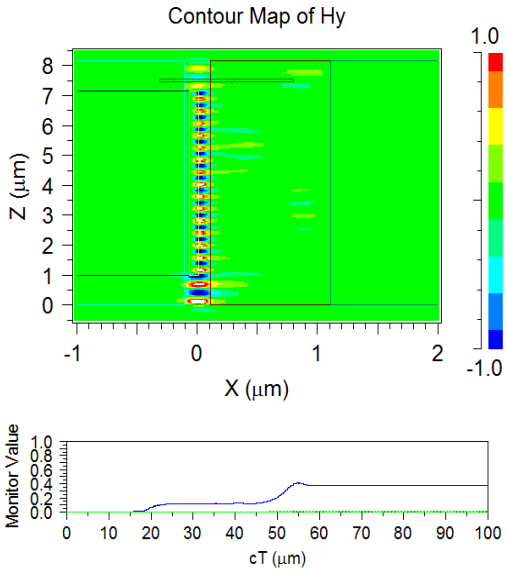

Figure 4: Representation of counter map

Excitation along the interface is depicted in the figure 4 , with x axis as length and the z axis as breadth and the colour-bar towards right side represents the instantaneous values of power. Along with this the monitor power values along the sensing layer of the device is shown just below the contour map.

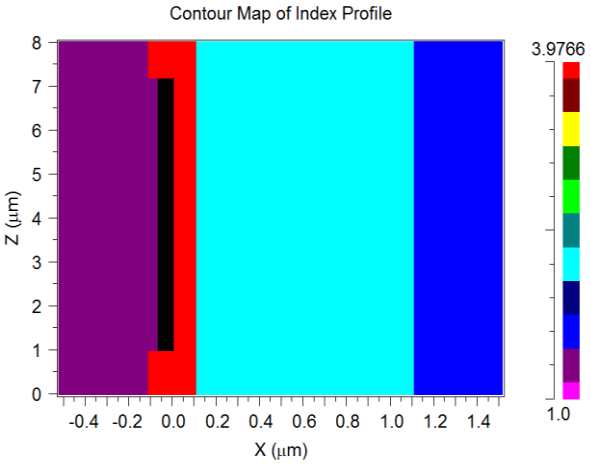

Figure 5: Contour map of index profile

The Figure 5 shows index profile of the design, where each and every colour in the extreme right side of the picture represents the range of the refractive indices by referring which the correctness of the design can be verified. When the incident light on the metal plate is made to propagate along silicon waveguide (Frazier, Kevin, Martyn, Roberts and Richard, 2012).where the light which is propagating will be coupled into two modes, these modes propagates on either sides of the metal layer.

Since the contacts of metal layer are of different indices, will have different propagation constants which results in the phase difference. The variation in the phase will have the impact at the output port. The phase variations reflected intensity of obtained spectrum. When the phase difference is 180^0, depression is observed in the output spectrum.

3. 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 (Ramanavièius, Herberg, Hutschenreiter, Zimmermann ,Lapënaitë, Kaušaitë, Finkelšteinas, 2005).a specific refractive index value. For a cell to retain in its normal state the constituents of the cell should be optimum. The overall refractive index for normal cell varies from 1.35 to 1.37. As the content of the cell changes the overall refractive index of the cell (Shalabney and Abdulhalim,2010).also changes and hence the optical properties of the cell changes. Cancer is caused by the change in protein content of the cell. For a cancer cell, the overall refractive index changes from 1.39 to 1.40. With the help of RSOFT simulation the output simulation spectrum were obtained. 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 (Gupta and Sharma,2005). Design specifications are given below.

Table1: required Design Parameter

Waveguide	Refractive index	Thickness(nm)
Water	1.3	5nm
Silver	0.051585	0.074nm
Si	3.9766	0.22nm
Silicon nitride	2.05	1nm
Glass	1.47	3nm

The above specifications are given for normal lymphocyte cell. RSOFT works in nanoplatform where the values of μ0 and 'c' constants are in unity. The refractive index (η) of each component of Lymphocyte cell has been taken into consideration. The changed value of refractive index (η) is compared with existing refractive index (η) values which can be used for future analysis.

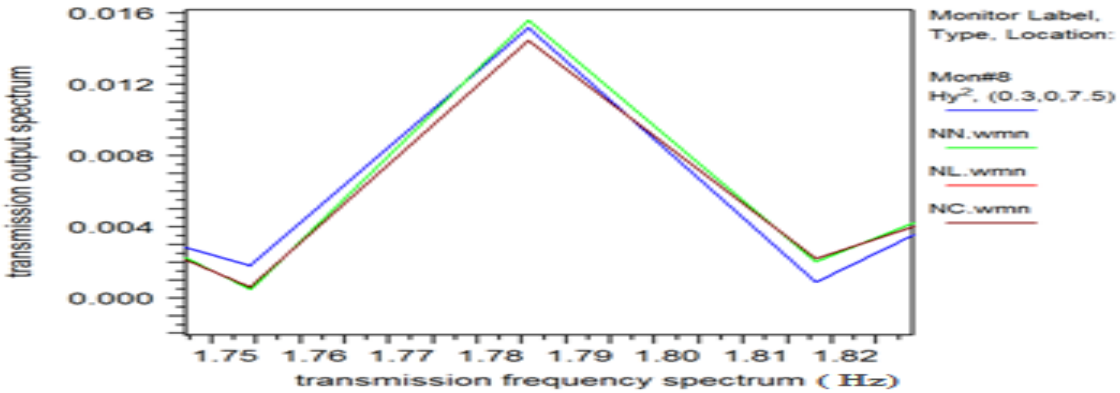

Figure 6: Represents the transmission frequency spectrum for the normal cell values ranging from 1.35-1.37.

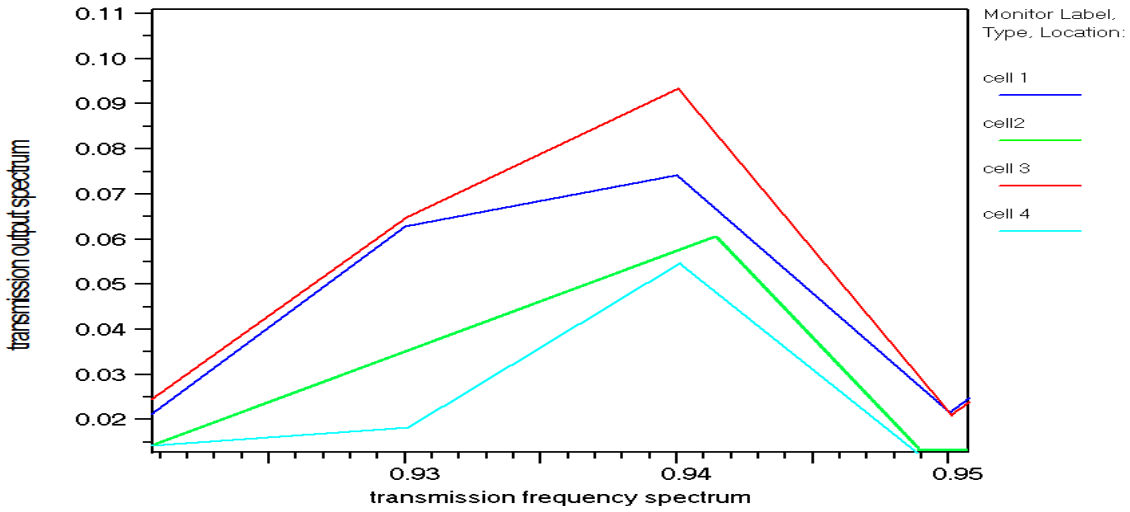

Figure 7: Represents the transmission frequency spectrum for the normal cell values ranging from 1.35-1.37 at resonance.

Table 2: Tabulation Of Normal Cells Withrespect To Frequency

Intensity variation of normal cells at frequency range 1.75-1.82	Intensity variation of normal cells at resonance	
Maximum intensity(normalized)	Maximum intensity (normalized)	frequency
0.055	0.097	0.9405
0.015	0.078	0.938
0.01275	0.059	0.941
0.014	0.057	0.94

The above table provides the details about the behaviour of normal cell at resonance behaviour for frequency range from 1.75 to 1.82 respectively as represented in the figure 7. From the table it is observed that the intensity of the normal cells will have concurrent peaks i.e at frequency 1.585 the peaks for all normal cells are observed. But at resonance the occurrence of peaks are at different frequencies as showed in the figure 8. Demonstrating the signature behaviour i.e. uniqueness of the cells at resonance.

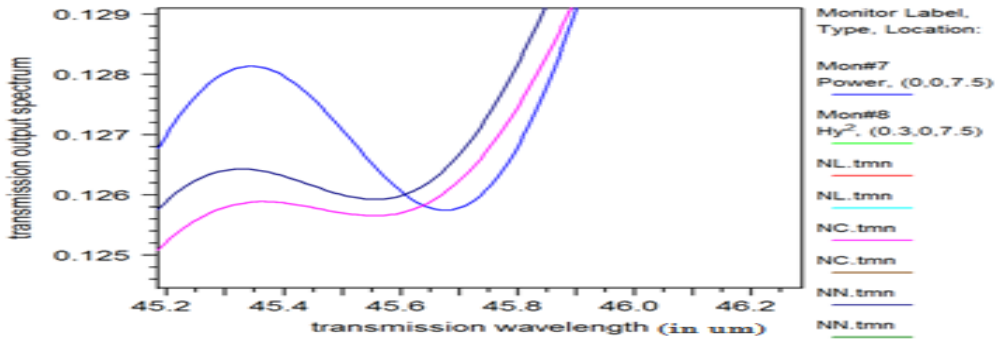

Figure 8: Graphical representation of relative wavelength shift versus output power for normal cell.

The above figure 8 represents the transmission wavelength shift spectrum of normal cells. Where, it is observed that, the resonance behaviour varies from cell to cell.

Table 3: Tabulation of Normal Cells With Respect To Wavelength

INTENSITY SHIFT	0.1254-0.1259
WAVELENGTH SHIFT	200nm

It is easy to discriminate the wavelength shifts of normal and abnormal cells. The change in the wavelength shifts are due to the dissimilarity in the dielectric properties of each cell. The comparison between a normal and abnormal nucleus is done and also comparison between a normal and abnormal *(Khai . Le.B, and Peter (2011*). The table 3 corresponds to the overall wavelength shifts and intensity shifts for normal cells. In this paper the different components of the cells such as lymphocyte , nucleus and cytoplasm have been tested and respective shifts in their frequencies and intensity are recorded.

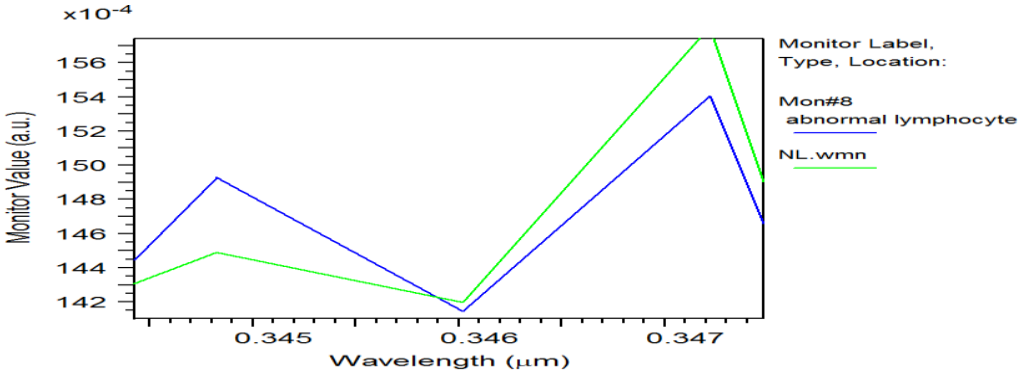

Figure 9: Represents the transmission wavelength shift for the normalised cell and abnormal cells (Lymphocyte).

The figure 9 represents the transmission wavelength shift spectrum of normal and abnormal cells of lymphocyte. We can observe that the wavelength shifts of both the cells occur in a very significant manner. There is also occurrence of in the intensity variation which has been dipicted in the table below.

The table 4 repersentsthe variation intensity from normal lymphocyte to abnormal lymphocyte is 0.0002. The relative wavelength shift is 200nm

Table 4: Tabulation Of Intensity Shifts Of Lymphocyte

INTENSITY SHIFT	0.1445-0.1442
WAVELENGTH SHIFT	200nm

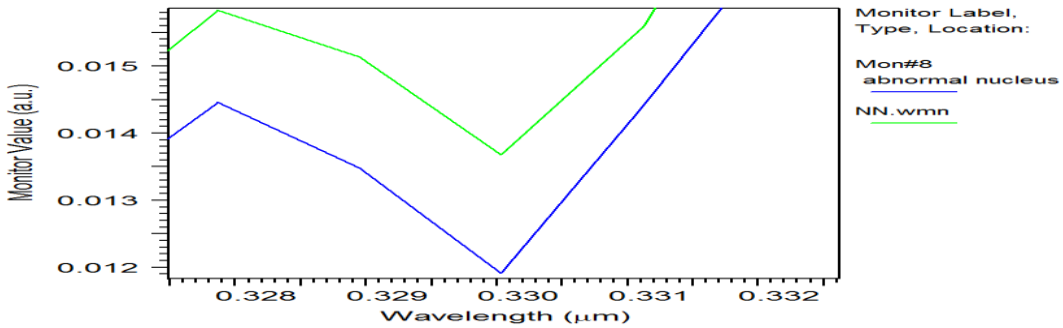

Figure 10: Represents the transmission wavelength shift for the normalised cell and abnormal cells (Nucleus)

The graph 10 represents the transmission wavelength shift spectrum of normal and abnormal cell nuclei. In the previous case we case it is observed that the shifts in the wavelength due the differences between the dielectric properties of the normal and abnormal cell varies by 2000 nm/RIU.

Table 5: Tabulation of Intensity Shifts of Nucleus

INTENSITY SHIFT	0.00245
WAVELENGTH	100 nm

The Intensity and the wavelength shifts are 0.00245 and 100 nm respectively

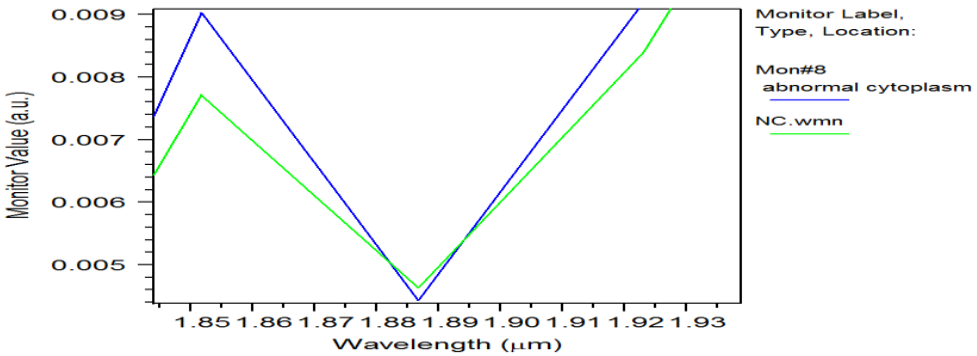

Figure 11: Represents the transmission wavelength shift for the normalised cell and abnormal cell (Cytoplasm).

The graph 11 shows the transmission wavelength shift spectrum of normal and abnormal cell cytoplasm. The shifts in the wavelength due the variation in the refractive indices due adsorption of analyte on to the surface of the sensing layer and the corresponding variation in sensitivity is 6666 nm/RIU. The table 6 refers to the Intensity and Wavelength shifts of normal and abnormal Cytoplasm.

Table 6: Tabulation Of Intensity Shifts Of Cytoplasm

INTENSITY SHIFT	0.0056
WAVELENGTH SHIFT	250nm

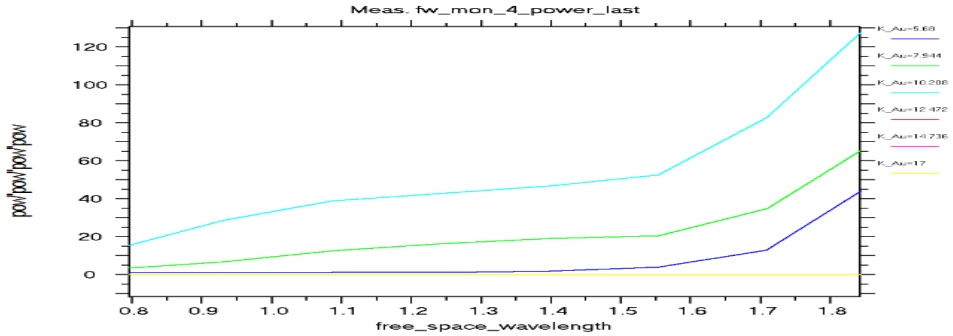

Fig 12: Represents the transmission wavelength spectrum with respect to extinction coefficient of gold metal

The figure 12 portrays the extinction coefficient response with respect to source wavelength of sensing layer with. The graph shows that as the extinction coefficient of the gold is increased the absorption of light also increases simultaneously up to some extend of applied extinction coefficient *(Anker, Hall, Lyandres, Shah, , Zhao,andDuyne,2010).*The absorptivity decreases with the increment in the extinction coefficient by thus witnessing the sensitivity towards the RI variation in the sample. Hence it can be concluded that the extinction coefficient of 10.208 and its corresponding wavelength will yield better performance. The value of K_{au} at 17 the adsorption of light remains 0 throughout the wavelength spectrum.

The table 7 describes the performance of extinction co efficient values for gold layer with respect to maximum intensity, by observing the values, when K_{au}=14 at 1550 nm wavelength ,the performance of device is optimum, which helps in deciding one of the design parameter i.e. source wavelength.

Table 7: Tabulation of Intensity of Extinction Coefficient Factors

Extinction coefficient of Au(K_{au})	Maximum intensity at resonance wavelength (1.5675µm)
5.68	0.25
7.944	0.05
10.208	0.45
12.472	0.15
14.736	0.65
17	0

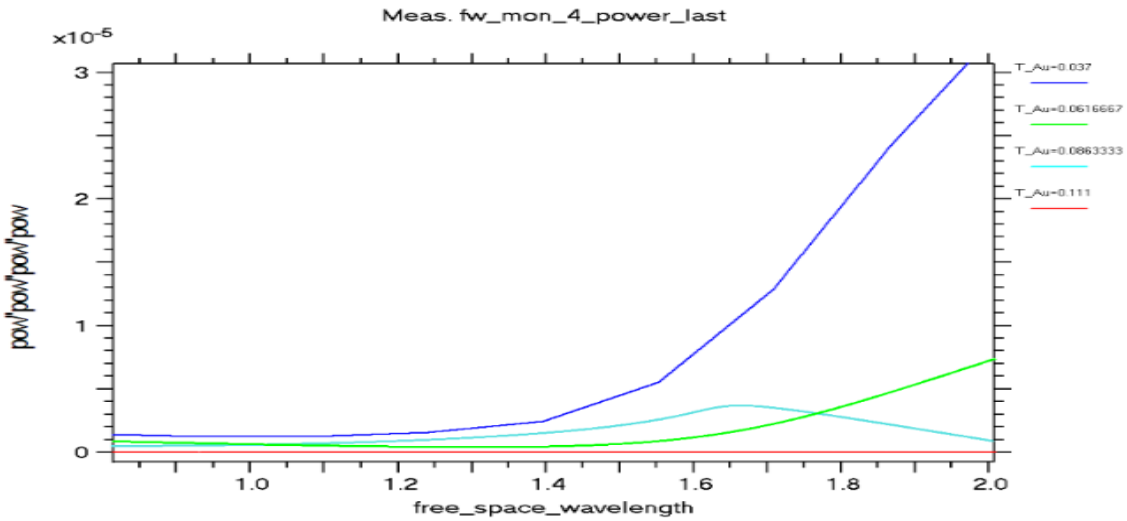

Figure 13: wavelength response for variation in the thickness of gold layer

Figure 13 depicts the wavelength behaviour at the output port for different gold thickness, the adsorption of the analyte molecules decreases with the increase in the thickness of gold layer as it contributes to the smoothness of the surface.The performance of the device is better with the gold layer of thickness 0.037µm. the intensity values for different layer thickness is given in table 8.

Table 8: Tabulation Of Intensity To Thickness Of Gold Layer

Au thickness in µm	Normalized power
0.0036	3
0.06667	1.5
0.08633	06
0.11	0.9

4. Conclusion

The Simulation was done using Rsoft CAD tool. The peak values and wavelength shift differences for normal cells and forleukaemia, the different cell components lymphocyte , nucleus, cytoplasm and the intensity shifts are recorded in order to find the relative sensitivity of the device. The design variation were made by varying sensing layer thickness and extinction coefficient Finally, comparison was made between that of normal and abnormal cells to show the wavelength shift differences so that the signature graphs for each cell were obtained in order to determine the intensity of the disease and it depends on the shift in the wavelength. The wavelength shift of early stage leukaemia for cytoplasm, nucleus and lymphocyte are ranging from 2000-250nm. Sensitivity and the quality factor of the sensor have been calculated for the proposed design, the sensitivity achieved is 343nm/RIU and the quality factor is 1800.

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