Research Article

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Theoretical Design of Highly Sensitive Ag-Ni-Thiol-based Hybrid SPR Biosensor for Viral Detection

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ABSTRACT

In this work, a biosensor under Kretschmann configuration with enhanced sensitivity utilizing thiol on the bimetallic layers of magnetic material nickel (Ni) over silver (Ag) is proposed and analyzed numerically using the Fresnel equation and the Transfer Matrix Method (TMM). Results have shown that such a hybrid configuration with a well-optimized thickness of a bimetallic layer of Ni over Ag and the proper utilization of thiol with fixed thickness can increase the sensitivity substantially higher than the conventional sensor. The minimum reflectivity, FWHM of the Surface Plasmon Resonance (SPR) curve and sensitivity were examined in order to optimize the thickness of metal layers for the fixed thickness of the thiol. It is observed that sensitivity as high as 321°/RIU is obtained for the configuration consisting of 15 nm of Ni over 40 nm thickness of Ag added with a 4 nm thickness of thiol. Such high-sensitivity sensors can be used for protein-protein interaction and virus detection in the field of biosensing applications.

Keywords: Surface Plasmon Resonance; Biosensor; Sensitivity; Thiol and Bimetal.

1. INTRODUCTION

Surface Plasmon Resonance (SPR) is one of the powerful techniques for the study of biomolecular interactions and the detection of analytes and it is currently being researched as a rapid diagnostic platform for a variety of viral diseases (Karki *et al.* 2022). Recently, SPR techniques finds more applications such as detection of cancerous basal cells (Daher *et al.* 2022), blood plasma (Almawgani *et al.* 2022 a), infected red blood cells with plasmodium falciparum (Daher *et al.* 2023), detection of fat concentration in milk (Almawgani *et al.* 2022b), detection of severe acute respiratory syndrome corona virus-2 (SARs CoV-2) (Uddin and Kabir, 2021; Moznuzzaman and Khan, 2021; Srivastava and Das, 2011) and detection of formalin (Moznuzzaman and Khan, 2021). Silver performs better than Gold (Au) in the SPR because the Ag metal film has a narrower resonance peak, which increases the SPR sensor's accuracy and sensitivity (Maharana and Jha, 2012; Verma and Jha, 2011). In the proposed design, oxidation and corrosion were the problems due to the direct use of Ag layer, as a plasmonic metal was inhibited through attributing bimetallic approach in which Ni layer is used as a protection layer to prevent the deterioration of Ag in ambient conditions. Recently, several approaches on utilizing bimetallic layers for protecting plasmonic metals from oxidization and corrosion with improved performances have been reported (Jha and Sharma, 2009; Yuan *et al.* 2006). Recent interest in plasmonic metals has been focused on ferromagnetic metals such as nickel (Ni) and cobalt (Co) because of their exceptional magneto-optical properties (Maharana and Jha, 2013; Ordal *et al.* 1985). Hence in the proposed design of Ni is considered as a protective layer over Ag. Shah *et al.* suggested that using magnetic materials reduces the cost as well as improves the sensitivity of SPR sensors to a higher extent (Shah and Sharma, 2018). Thiols (RSH) could be found in low molecular weight compounds like protein cysteine residues as well as glutathione. Thiols and their derivatives play important roles in catalysis, regulation, protein folding and triggering due to their high chemical versatility. Thiol-dependent redox systems are common in living organisms and are involved in a variety of living systems (Alvarez and Salinas, 2022). Thiol-tethered DNA can be used as receptors for sensing immobilized receptor molecules (Uddin and Kabir, 2021; Malmqvist, 1999). Sandstrom *et al.* reported the thiol-specific and non-specific binding of single and double-stranded DNA to colloidal gold nanoparticles. The geometry of the bound strands depends on the type of immobilization, with thiol-attached oligonucleotides most likely being more extended from the surface than the nonspecifically bound molecules (Sandstrom and

Akerman, 2003). Uddin *et al.* reported that the thiol-attached DNA is used as a ligand layer for the screening medium because it exhibits excellent SARS COV-2 binding characteristics (Uddin and Kabir, 2021). In this paper, we theoretically proposed a highly sensitive SPR sensor configuration with enhanced sensitivity comprising of bimetallic layers of magnetic material Ni over Ag and thiol layer to tethered specific DNA to be used as a ligand layer for viral detection. Results have shown that such a hybrid configuration with a well-optimized thickness of a bimetallic layer of Ag-Ni with thiol over a BK7 prism can enhance the sensitivity much higher than the conventional sensor.

2. THEORY AND DESIGN CONSIDERATIONS

Fig. 1 depicts a schematic illustration of the suggested SPR sensor configuration.

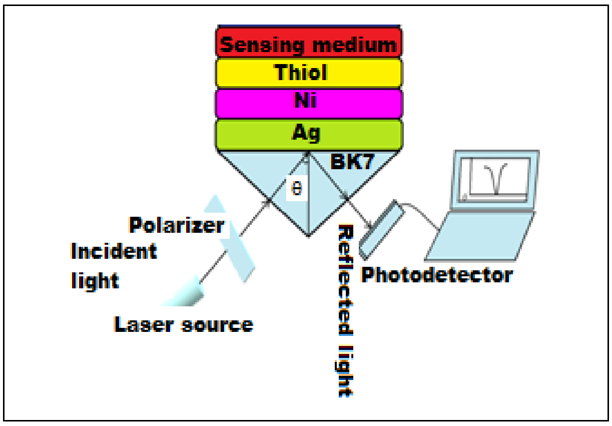

Fig. 1: Schematic diagram of the proposed structure

The proposed structure has five layers and an operating wavelength of 633 nm. The first layer is BK7 prism, which has a refractive index (RI) of 1.515 (Han *et al.* 2019). The second and third layers are Ag and Ni and their RI values were calculated using the Lorentz Drude's formula (Maheswari *et al.* 2021). The fourth layer is thiol whose optimized thickness and refractive index values are 4 nm and 1.4 respectively (Uddin and Kabir, 2021). The last layer of our design is the sensing medium and its RI value from 1.33 to 1.34 ($\Delta n_s = 0.01$) (Uddin and Kabir, 2021). The reflection coefficient is given by, $R_p = |r_p|^2$.

The performance parameters of the SPR sensor - Sensitivity (S), Detection Accuracy (DA) and Quality factor (Q) are calculated using the below equations (Maheswari *et al.* 2021; Maharana and Jha, 2012),

$$S = \frac{\Delta\theta_{res}}{\Delta n_s}(\deg/RIU) \tag{1}$$

$$DA = \frac{1}{FWHM}(\deg^{-1}) \tag{2}$$

$$Q = \frac{S}{\Delta\theta_{0.5}}(\mathrm{RIU}^{-1}) \tag{3}$$

where, Δn_s represents the difference between the RI of the sensing medium. Here, the range of change in RI is considered as 1.33-1.34, which is usually an acceptable change in RI occurring due to the attachment of targeted protein on the specific protein tethered on the thiol layer for viral detection. $\Delta\theta_{res}$ denotes resonance angle changes and $\Delta\theta_{0.5}$ represents full width at half maximum (FWHM) of the reflectance curve.

3. RESULTS AND DISCUSSION

The performance of the SPR biosensor is investigated using the transfer matrix method (TMM) at the wavelength of 633 nm. Here, R_{min} is an important parameter, matching the maximum energy of incident light with a surface plasmon wave (SPW); when the condition occurs, the R_{min} goes to zero (Maheswari *et al.* 2021). Fig. 2 (a & b) shows the variation of R_{min} corresponding to the increasing thickness of Ag from 30 to 55 nm for the fixed thickness of Ni such as 0, 3, 5, 7, 10,12 and 15 nm, respectively. From Fig. 2 (a and b) it is evident that initially high R_{min} values were obtained for all the thickness of Ni layers considered when the thickness of Ag is as low as 35 nm. However, it was found to approach zero respectively at 50, 50, 50, 45, 45 and 40 nm of Ag for 3, 5, 7, 10, 12 and 15 nm thickness of Ni, respectively; found to increase with further increase in the thickness of Ag.

Table 1: Minimum reflectance and sensitivity values for selected thickness of Ag and Ni, without and with thiol

Ag d_2 (nm)	Ni d_3 (nm)	Without thiol		With thiol	
		R_{min}	Sensitivity (deg/RIU)	R_{min}	Sensitivity (deg/RIU)
40	15	0.0005	298	0.0066	321
45	12	0.0014	229	0.0006	235
45	10	0.0032	194	0.0058	194
50	7	0.0077	166	0.0089	166
50	5	0.0013	149	0.0013	143
50	3	0.0003	131	0.0008	131

Table 1 shows R_{min} and sensitivity values for the cases with and without thiol of the proposed bimetal configuration. It is observed that R_{min} and maximum sensitivity values are 0.0005 and 298 deg/RIU corresponding to 40 nm thickness of Ag with the fixed thickness of Ni as 15 nm for the case without thiol and 0.0066 and 321deg/RIU for the case with thiol, for the same thickness of Ag and Ni. The entire configuration is considered with least possible R_{min} values.

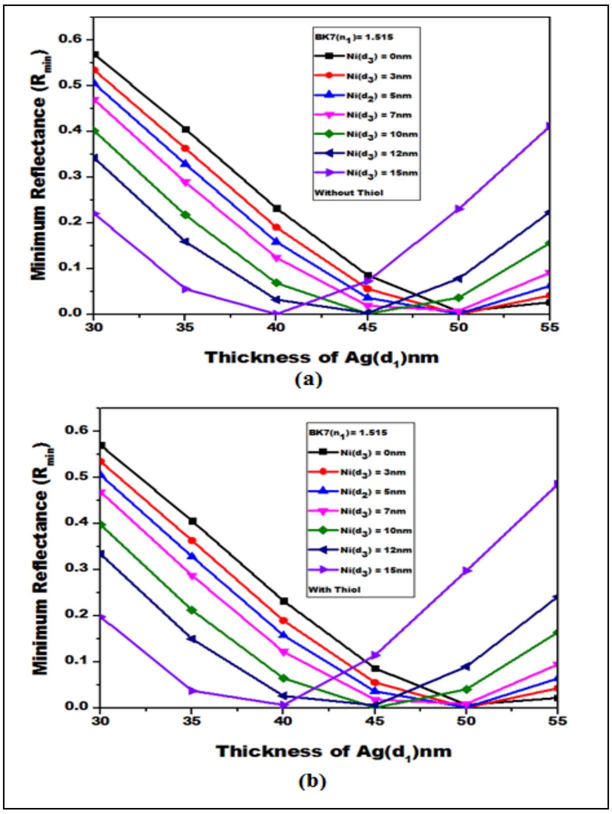

Fig. 2 (a & b): R_{min} plot for the bimetallic (Ag-Ni), without and with thiol configuration

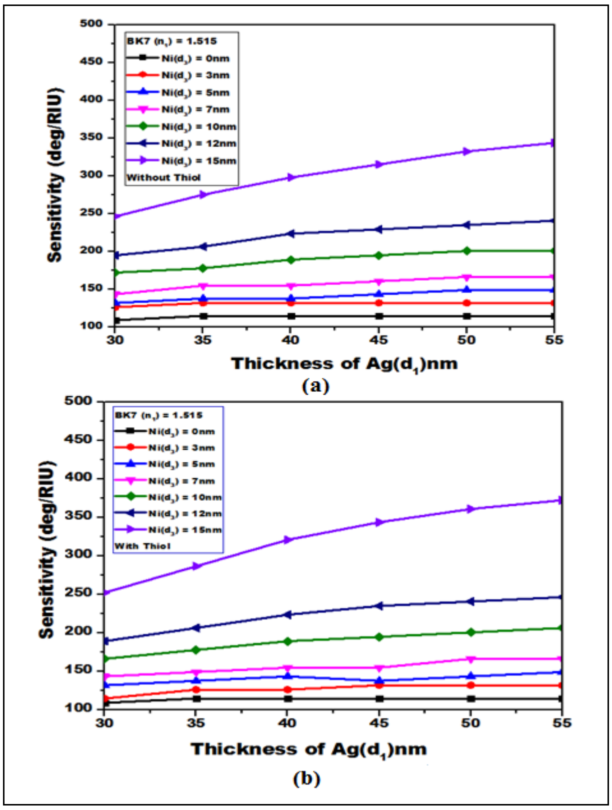

Fig. 3 (a & b): Sensitivity plot for the bimetallic (Ag-Ni), without and with thiol configuration

In order to further investigate the sensitivity of the sensor without and with the influence of thiol layer, the variation of sensitivity corresponding to the varying thickness of Ag with fixed Ni layer thickness was analyzed and are presented in Table 2 and Fig. 3 (a & b) respectively. The maximum sensitivity around 298 deg/RIU with FWHM around 4.66° was obtained for the case without thiol corresponding to thickness of Ag of 40 nm and Ni of 15 nm. However, for the case with thiol (4 nm), maximum sensitivity around 321 deg/RIU with FWHM around 5.03° was also obtained for 40 nm thickness of Ag and 15 nm of Ni. The following phase analyzes the reflectance plot obtained for both cases.

Table 2: Sensitivity and FWHM values for selected thickness of Ag and Ni, without and with thiol

Ag d_2 (nm)	Ni d_3 (nm)	Without thiol		With thiol	
		Sensitivity (deg/RIU)	FWHM (deg)	Sensitivity (deg/RIU)	FWHM (deg)
40	15	298	4.67	321	5.03
45	12	229	3.24	235	3.44
45	10	194	2.87	194	3.01

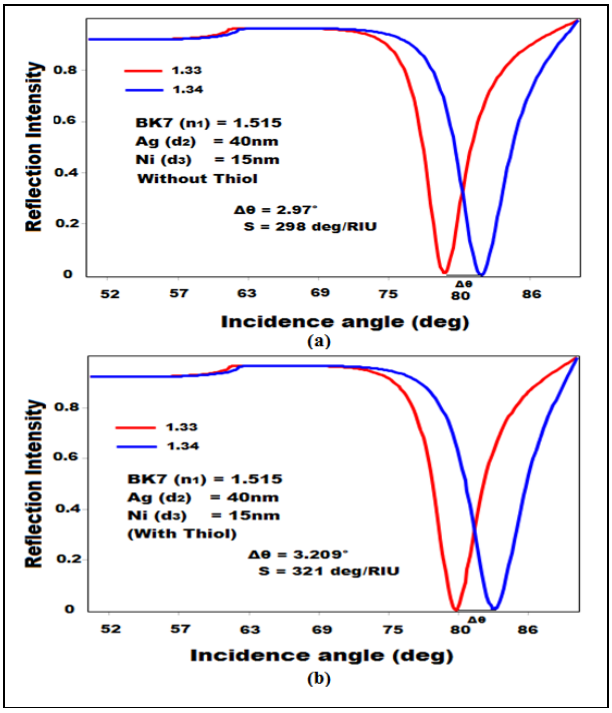

Fig. 4 (a & b): Reflectance plot for 40 nm & 15 nm thickness of Ag-Ni bimetal, without and with thiol

Fig. 4 depicts the reflectance plot obtained for the optimized structure of 40 nm and 15 nm thickness of Ag and Ni for without and with thiol layers cases, respectively. From Fig. 4, it was noted that the well optimized thickness of the Ni layer shifts the reflection dip to a larger incident angle side and hence enhances the sensitivity. It was also noted that the reflectance plot becomes sharper and R_{min} goes lower value for the optimized condition. Moreover, sensitivity, FWHM, DA and quality factor were also analyzed for the optimized case considering the change in refractive index of sensing medium from 1.33 to 1.34 and are tabulated in Table 3. From all the above discussions, the structure was optimized with Ag = 40 nm and Ni = 15 nm, without and with thiol (4 nm); it gives maximum sensitivity, FWHM and the corresponding DA and QF values are listed in Table 3. The comparison table (Table 4) reports the superiority of the present structure with the previously reported similar structures. Hence it was noted the proposed sensor structure is most suitable for viral detection as the structure is well optimized with thiol layer and hence thiol-tethered DNA can be used as a screening medium for excellent binding of different types of viruses.

Table 3: Sensitivity, FWHM, DA and QF values for Ag = 40 nm and Ni = 15 nm, without and with thiol

Configuration	S (deg/RIU)	FWHM (deg)	DA (deg^{-1})	QF (RIU^{-1})
Ag-Ni-Sensing medium	298	4.67	0.2141	63.94
Ag-Ni-Thiol-Sensing medium	321	5.03	0.1988	63.81

Table 4: Comparison of the proposed structure with previous works

References	Structure	Sensitivity (deg/RIU)
Kumar et al	Prism/Ag/Si/BP/Mxene	264
Wu et al	Prism/Ag/BP/WSe_2	279
Proposed	**Prism/Ag/Ni/Thiol**	**321**

4. CONCLUSION

An SPR biosensor was proposed with a novel structure consisting of Ag-Ni bimetallic layer with thiol-tethered DNA serving as the ligand that makes it simple to detect viruses in real time. This numerical analysis based on transfer matrix theory has been carried out to assess the sensor response on parameters such as sensitivity, minimum reflectance and FWHM. The proposed biosensor attains an enhanced sensitivity as high as 321deg/RIU for the inclusion of thiol layer on well-optimized bimetallic layer of 40 nm Ag and 15 nm Ni. This work has provided encouraging results for the use of the suggested sensor configuration for viable viral detection.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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