Mechanical modulation method for ultra-sensitive phase measurements in photonics biosensing

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Abstract: A novel polarimetry methodology for phase-sensitive measurements in single reflection geometry is proposed for applications in optical transduction-based biological sensing. The methodology uses altering step-like chopper-based mechanical phase modulation for orthogonal s- and p- polarizations of light reflected from the sensing interface and the extraction of phase information at different harmonics of the modulation. We show that even under a relatively simple experimental arrangement, the methodology provides the resolution of phase measurements as low as 0.007 deg. We also examine the proposed approach using Total Internal Reflection (TIR) and Surface Plasmon Resonance (SPR) geometries. For TIR geometry, the response appears to be strongly dependent on the prism material with the best values for high refractive index Si. The detection limit for Si-based TIR is estimated as $10^{-5}$ in terms Refractive Index Units (RIU) change. SPR geometry offers much stronger phase response due to a much sharper phase characteristics. With the detection limit of $3.2 \times 10^{-7}$ RIU, the proposed methodology provides one of best sensitivities for phase-sensitive SPR devices. Advantages of the proposed method include high sensitivity, simplicity of experimental setup and noise immunity as a result of a high stability modulation.

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References and links

1. Introduction

Phase characteristics of light reflected or transmitted from (through) a solid/air or solid/liquid interface can provide important information on properties of the interface, as well as to serve as an extremely sensitive parameter in gas- or biological sensing [1,2]. In particular, employing phase characteristics of light under Surface Plasmon Resonance (SPR) and examining them by interferometry or polarimetry methods, one can achieve 1-2 order of magnitude gain in sensitivity of biosensors compared to conventional amplitude-sensitive devices [1-13]. Surprisingly, phase characteristics can provide a highly sensitive response even in simplest Total Internal Reflection (TIR) configuration, provided the refractive index of the prism is high enough [14]. Since in single reflection geometry the whole range of phase variations is limited, the optimization of instrumental phase sensitivity becomes one of key issues in designing phase-sensitive biosensor devices. In particular, very promising results have been achieved in polarimetry or interferometry schemes using a liquid crystal [15], an acousto-optic [12] or piezoelectric modulators [6]. However, the implementation of these schemes often increases the cost and complexity of measurement methodology, which is not always consistent with potential applications of SPR technology.

In this paper, we introduce a simple methodology on the basis of temporal mechanical modulation of orthogonal polarization components reflected from the sensing interface to extract phase response caused by a bioreaction-related refractive index change. The efficiency of the methodology is demonstrated in both TIR and SPR geometries to provide almost 100 times gain in sensitivity compared to conventional amplitude sensitive methods. The system could be used for testing the polarization of sensitive optical materials as well as for the development of SPR and TIR phase sensitive sensors.

2. Experimental setup and instrumental methodology

A schematic of the proposed configuration is shown in Fig. 1. A 5mW stabilized He-Ne laser operating at a wavelength of 632.8 nm is used as a light source. The light beam is passed through a polarizer 1 to obtain a 90 deg. linearly polarized beam. The beam is then passed through a beam splitter and directed through a Wollaston prism. The angle between the prism optic axis and the incident light polarization is 45°. Having orthogonal linear polarization, output light beams diverge from the prism with the angle of divergence of 20°. Each beam is then modulated by an optical chopper system (SR540) with the frequency of $\nu = 3$ kHz. After the back reflection of the light from the two mirrors, the beams are returned to the Wollaston prism to converge and form a light with a temporally-modulated state of polarization. A fine calibration of the angle between the polarizer (1) and the optical axis of the Wollaston prism provides identical intensities for the two beam components with 180° phase retardation for p-polarization (Fig 1). After passing a half and a quarter wave plates, which serve to optimize the phase retardation, phase modulated light is directed to a sensing block, including a prism of different materials (BK7 glass or SF11 glass or Si). In this work we used two sensing configurations: Total Internal Reflection (TIR) and Surface Plasmon Resonance (SPR). In the TIR geometry, light is directed through the prism and reflected from its inner edge connected to the sensing interface. SPR geometry uses the Kretschmann-Raether prism arrangement. A thing (~ 50 nm) film is deposited on the prism or on the glass slide, which is then brought into an immersion contact with the prism. Light is directed through the prism and reflected from
the gold film. In both cases, the reflected light is directed through a polarizer (analyzer) and then examined by a photodetector. The analyzer is placed just after the sensing block and oriented at +45° with respect to the detector, providing a 3 kHz square waveform intensity modulated light. All angular interrogations are performed using a variable angle goniometer (Thorlabs nanorotator), which provides a high precision and a good resolution for angle variations (0.001 deg). Information on phase-polarization state of light reflected under TIR or SPR is extracted by the examination of the odd harmonics of modulated signal with a help of a lock in amplifier or AC voltmeter. A reference detector is installed into the set-up (Fig. 1) in order to eliminate noises and instabilities related to light source and temperature drifts. The SPR coupling block and optical parts were covered by a specially designed thermoisolation box to minimize thermal and inertial drifts.

![Fig. 1. Schematics of the experimental arrangement (see text for explanation)](image)

Changes of light polarization state in the proposed scheme can be calculated by using the Jones transformation matrix method. The Jones vector for polarized light is defined by $E_{in} = \begin{pmatrix} E_x \\ E_y \end{pmatrix}$, where $E_x = A_x \exp(i\phi_x)$ and $E_y = A_y \exp(i\phi_y)$ are the x and y components of the light wave electric field with initial phase components $\phi_x$ and $\phi_y$, respectively. The modulation of the x-component (p-polarization) with frequency $\nu$ will lead to a relative phase retardation of this component $\psi = A_x f(\nu)$ and a resulting periodic polarization of light. This can be described by the following Jones transformation matrix:

$$J_{Mod} = \begin{bmatrix} \exp(i\psi) & 0 \\ 0 & 1 \end{bmatrix}$$

Corresponding Jones matrix for the tested optical element or sensor will be:

$$J_{Sensor} = \begin{bmatrix} r_p \exp(-i\phi_p) & 0 \\ 0 & r_s \exp(-i\phi_s) \end{bmatrix}$$

where $\phi_p$ and $\phi_s$ are the phase retardation for s and p components respectively and $r_p, r_s$ are their corresponding reflectivities. Then, the light passing through a polarizer with the rotation angle of $\theta$ will give rise to the following matrix:
The final intensity after passing through these elements will be:

$$I = E \cdot E \text{ where } E = J_p J_{\text{Sensor}} J_{\text{Mod}} E_{\text{in}} $$

Here, we simplify the expression taking into account that $A_x = A_y = 1$ and for the polarizer axis of 45 deg.: $\cos(\theta) = \frac{\sqrt{2}}{2}$ and $\sin(\theta) = \frac{\sqrt{2}}{2}$. Therefore, the resulting intensity is given by:

$$I = \frac{1}{2} (r_p^2 + r_s^2 + 2 r_p r_s \cos(\psi + \phi_p - \phi_s))$$

In this paper, we propose to fix the phase modulation amplitude of that could be expressed as retardation $\psi = A_{\psi} f(\nu)$, where $A_{\psi} = \pi$ and $f(\nu)$ is a square function with frequency $\nu$. Indeed, we can decompose the system detector response in two states with the intensity:

$$I_1 = \frac{1}{2} (r_p^2 + r_s^2 + 2 r_p r_s \cos(\pi + \phi_p - \phi_s)) = \frac{1}{2} (r_p^2 + r_s^2 - 2 r_p r_s \cos(\phi_p - \phi_s))$$

$$I_2 = \frac{1}{2} (r_p^2 + r_s^2 + 2 r_p r_s \cos(0 + \phi_p - \phi_s)) = \frac{1}{2} (r_p^2 + r_s^2 + 2 r_p r_s \cos(\phi_p - \phi_s))$$

The resultant detector output can be divided into two components representing the alternating AC and continuous DC components giving by:

$$AC = I_1 - I_2 = 2 r_p r_s \cos(\phi_p - \phi_s), \quad DC = (I_1 - I_2) / 2 = r_p^2 + r_s^2$$

One can find in the literature various polarimetry-based methods to measure the light polarization state. These methods normally involve temporal phase modulation with a help of various modulators [8,10,15]. Phase information is then extracted by Fourier analysis of the odd and even harmonics of the output signal, which, in turn, demonstrate different phase dependences. In this paper, we propose a polarimetry scheme, which enables to test the intensity of the s- and p- light components (DC from the Eq. (5)) as well as the light phase characteristics (AC from Eq. (5)). Indeed, due to the square waveform phase modulation we have only the odd harmonics of the signal that exhibit similar phase dependences. To measure the output signal in the system we can use not only a lock-in amplifier but also the AC/DC digital multimeter, which enables to simultaneously obtain the continuous and oscillating parts of the signal (Eq. (5)).

We performed numerical simulations of sensor characteristics in the TIR and SPR geometries using a SF11 coupling prism. Figure 2 presents angular dependences for the phase and the AC and DC components of the output signal. As shown in the Fig. 2, phase has a sharp jump at the critical angle of TIR and SPR, which appears to be about 37 deg. in both cases. The presence of the phase jump causes the appearance of distinct features in the dependence for DC and AC harmonics. Above the angle of the total reflection, the AC component for the TIR sensor exhibits purely phase dependence due to the angle-independent DC signal. SPR (Fig. 2(b)) geometry with SF11 coupling prism covered by a 50nm gold layer provides much larger phase changes at the surface plasmon coupling angle. Similar to TIR, at larger angles, the AC signal is mainly determined by phase characteristics (Eq. (5)). Both configurations could be used for the development phase-sensitive sensor designs. Here, the
TIR-based configuration proposes very simple sensor geometry, while the SPR-based one provides a much higher sensitivity.

Fig. 2. Responses of AC, DC and phase in the TIR (a) and SPR (b) geometry using a SF11 coupling prism

The angular dependences of the AC signal component in the TIR geometry with Si, BK7, and SF11 prism as well as in the SPR geometry with a SF11 prism are presented on Fig. 3. It is implied that SF11 and BK7 prisms operate in the visible, while Si prism operates in the near infrared where Si is transparent. One can see that the replacement of air by water leads to significant shifts of the phase jump position. The shift of TIR position is stronger for SF11 and BK7 prisms operating in the visible compared to Si. However, in the case of Si the lower shift response is compensated by much a sharper phase feature in the TIR region, which in fact determines a much higher sensitivity of Si-based TIR biosensor compared to the glass-based ones [14]. For SPR sensor, both the sharpness of the phase feature under the resonance and the shift of the resonant angle are substantial, conditioning a much higher net sensitivity of the method compared to TIR.
One of the advantages of the proposed scheme consists in its simplicity. Indeed, all phase information can be obtained through simple wide range multimeter measurements. The application of a lock-in amplifier can further improve the electrical signal-to-noise ratio and eliminate slow electrical noises in the system. In this case, the final periodic signal in the system can be decomposed into harmonics. It is known from Fourier analysis that for an idealized square waveform phase modulation, the signal can be presented by an infinite series of odd integer harmonics:

$$I(t) = A_0 + 4A \sum_{k=1}^{\infty} \frac{\sin((2k-1)2\pi vt)}{2k-1}; A_0 = DC; A = AC/2;$$  \hspace{1cm} (6)

In a more general case, signal harmonics depend on phase retardation introduced by the sensor. Figure 4 shows the calculated signals from the 1st, 2nd, and 3rd harmonics as a function of phase retardation. As shown in the Fig. 4, the signal intensity decreases when the harmonics number increases and the strongest intensity is achieved for the first harmonics. Another advantage of the first harmonics consists in the possibility of an easier external noises filtering. It is clear that the proposed set-up makes possible additional response optimizations for the first harmonics through the introduction of an initial phase retardation into the optical scheme (Fig. 1). As a result, characteristics of the first harmonics can be adjusted for the maximization of the instrumental phase sensitivity (dotted line on Fig. 4).
Using Fresnel’s formulas for a multi-layer system, we can compare the response of the first harmonics of the proposed scheme with intensity and phase characteristics of light reflected under SPR. Figure 5 presents angular dependences of intensity and phase in the Kretschmann-Raether arrangement using a SF11 coupling prism and 35nm gold thin film. As shown in the Fig. 5, the SPR phenomenon is accompanied by a drastic intensity decrease of the p-polarized component and a sharp jump of its phase, changing the total polarization state of light. It is also clearly visible that the intensity of the first harmonic follows the phase dependence and, as a result, the slope of the first harmonics intensity is much sharper compared to the slope of total intensity. In other words, it means that by considering the phase in the first component signal, its sensitivity can be higher compared to the conventional intensity interrogation. It should be noted that the slope of the phase curve has no relevance to the slopes of intensity characteristics, since phase and intensity curves correspond to different axes. To examine conditions of a higher sensitivity of the first component, we recalculated all dependences for different thicknesses of the SPR-supporting metal. Results of such analysis are shown in Fig. 5(b). One can see that for three chosen gold film thicknesses, the first harmonics still exhibits much sharper angular slope, suggesting a more sensitive response to the refractive index change.

Figure 6 demonstrates responses of the reflected intensity and the intensity of the first component as a function of the refractive index of the medium contacting gold. As shown in the Fig. 6, the first harmonics indeed has a much more sensitive response compared to a signal in conventional intensity interrogation as a result of the involvement of sharp phase characteristics in the resulting signal. It is interesting that due to the involvement of intensity characteristics the first harmonics signal exhibit a wider dynamic range compared to pure phase-sensitive schemes [16]. Thus, the first harmonics approach combines the high sensitivity of the phase interrogation with the wide dynamic range of the intensity interrogation.
3. Results

To confirm our theoretical calculation and to test the proposed experimental set-up, we have performed a series of polarization state measurements of the light reflected from the sensing interface. First, we measured phase resolution in the proposed experimental methodology. A standard phase retarder consisting of two birefringent plates ($\lambda/4$ and $\lambda/2$) was placed just before the sensing block (Fig. 1) to finely vary the pumping light phase. Measuring the signal to noise ratio of the exit signal from the photodetector at a fixed retarder-programmed change of phase, we determined that the resolution of phase measurements is extremely low reaching approximately 0.007° Deg. The tests were then carried out in TIR and SPR geometries.

In the TIR geometry, we measured AC and DC responses for two prism materials: BK7 and SF11. As it was predicted by our theoretical modeling, the DC signal amplitude was constant while the AC output sharply rose immediately after the angle of total internal reflection (Fig. 7(a)). Initial curve slope, as well as the phase sensitivity, depended on the relation of prism and tested medium refractive indexes. As shown in the Fig. 7(a), these parameters were much more promising for high refractive index SF11. Further sensitivity improvement can be achieved through the use of Si with its refractive index exceeding 3.4 in the near infrared [14], but the experimental setup used was not designed for IR measurements. As one can see from Fig. 3, showing simulated results for a Si prism with 3.4 RI at 1200nm wavelength, much sharper and larger phase changes must inevitably provide much higher phase sensitivity. It is important that the TIR sensor sensitivity can be further improved by the introduction of an additional phase retardation into the modulated light. For example, it can be done by rotating the $\lambda/2$ waveplate of the phase retarder, placed just before the sensing block (Fig. 1). As follows from Eq. (3), the measured AC response depends on cosines of the phase difference between s- and p-signal components. As shown in Fig. 7(b), the initial 90° retardation provides the sharpest sensor response to phase variations, maximizing the sensor sensitivity.
To estimate the sensitivity of the TIR system, we examined the temporal response of the AC signal at a fixed angular position when liquids with different refractive indices were brought into contact with the prism surface. Using a peristaltic pump, we introduced solutions of water with different concentrations of ethanol. Figure 7(a) shows that a tiny change of the refractive index by $5 \times 10^{-4}$ RIU, caused by the addition of ethanol to water, led to a shift of phase curves (the final positions of the curves are given by dots). Figure 8 shows AC responses for BK7 and SF11 prisms when ethanol was progressively added to water. Knowing the difference of refractive indices of Ethanol and water and taking into account the level of noises in the system, we can determine that the detection limit of our system was about $10^{-5}$ RI, which is almost comparable with the sensitivity of conventional SPR sensors with intensity interrogation. We expect a further improvement of sensing sensitivity through the use of Si-based TIR platform, probably up to one order of magnitude.

For experiments performed with the surface plasmon resonance sensor geometry, an SF11 prism was used in immersion contact with the thin SF11 glass slide, covered with 35 nm of gold. Initially, measurements were performed in air and the first harmonic was used to control the signal. As shown in Fig. 9(a), here again optimization of the initial phase retardation could provide better sensor sensitivity. In our case, a 70° dephasing results in the sharpest phase response. For sensitivity tests, the incident angle was fixed at 30.5 deg. at the point of the
maximum of the first harmonic first derivative. To determine the detection limit of our experimental setup in SPR configuration, we examined responses of the first harmonic under very small changes of the refractive index. In this test, high purity nitrogen (N₂) and argon (Ar) was added one after the other to the gas flow cell. The difference of refractive indices of these gases is about 2*10⁻⁵ [1]. One can see from Fig. 9(b) that SPR system was able to easily differentiate the gases. Knowing the signal change under the replacement of the gases and comparing it with the base noise, that was measured with lock-in integration time 3min, we can determine the detection limit of our system. This limit is estimated to be equal to 3.2*10⁻⁷ in terms of refractive index units (RIU), which corresponds to best values obtained with phase-sensitive SPR devices.

4. Conclusions

We introduced a novel phase-sensitive polarimetric scheme, which uses a temporal phase modulation of the mixed-polarized beam by a mechanical modulator and subsequent analysis of the output signal from AC and first harmonics of modulated frequency. We showed that the proposed configuration can be used in TIR and SPR sensing geometries, providing extremely low detection limits to refractive index changes (10⁻⁵ and 3.2*10⁻⁷ RIU, respectively). The proposed methodology makes possible ultrasensitive phase measurements under a relatively simple experimental arrangement and can be applied for biological and chemical sensing.

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