

Sensitive voltage interrogation method using electro-optically tunable SPR sensors

Zhiyou Wang,¹ Zheng Zheng,² Kun Wang,³ Yalin Su,² Lei Liu,² Lusheng Song,¹
Yusheng Bian,² Rui Hou,⁴ Shaopeng Li,¹ and Jinsong Zhu^{1,*}

¹National Center for NanoScience and Technology, No.11 Beiyitiao, Zhongguancun, Beijing, 100190, China

²School of Electronic and Information Engineering, Beihang University, 37 Xueyuan Rd., Haidian District, Beijing, 100191, China

³State Key Laboratory of Proteomics, Beijing Proteomics Research Center, Beijing Institute of Radiation Medicine, Beijing, 102206, China

⁴School of Information Engineering, China University of Geosciences, 20 Chengfu Rd., Haidian District, Beijing, 100083, China

*jzhu@nanoctr.cn

Abstract: A novel voltage interrogation method using electro-optically tunable waveguide-coupled surface plasmon resonance sensors is demonstrated. Before measurements, we use a bicell photodetector to detect the reflectance from the sensor and take the differential signal from the photodetector as the resonance condition. For different analytes, by scanning the DC voltage on the waveguide layer of the sensor chip, the resonance condition can be maintained the same. Under this condition, we record the values of this voltage, namely the resonant voltage. Theoretical calculations and experimental results show the resonant voltage has a highly linear and sensitive response to analyte's refractive index. This method is simple in configuration, and complicated signal processing algorithms can be avoided.

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References and links

1. J. Homola, "Surface plasmon resonance sensors for detection of chemical and biological species," *Chem. Rev.* **108**(2), 462–493 (2008).
2. B. Liedberg, I. Lundstrom, and E. Stenberg, "Principles of biosensing with and extended coupling matrix and surface plasmon resonance," *Sens. Actuators B Chem.* **11**(1-3), 63–72 (1993).
3. L. M. Zhang and D. Uttamchandani, "Optical chemical sensing employing surface plasmon resonance," *Electron. Lett.* **24**(23), 1469–1470 (1988).
4. B. Liedberg, C. Nylander, and I. Lunström, "Surface plasmons resonance for gas detection and biosensing," *Sens. Actuators* **4**, 299–304 (1983).
5. K. Wang, Z. Zheng, Y. Su, Z. Wang, L. Song, and J. Zhu, "Hybrid differential interrogation method for sensitive surface plasmon resonance measurement enabled by electro-optically tunable SPR sensors," *Opt. Express* **17**(6), 4468–4478 (2009).
6. N. J. Tao, S. Boussaad, W. L. Huang, R. A. Arechabaleta, and J. D'Agnesi, "High resolution surface plasmon resonance spectroscopy," *Rev. Sci. Instrum.* **70**(12), 4656–4660 (1999).
7. J. J. Chyou, C. S. Chua, Z. H. Shih, C. Y. Lin, K. T. Huang, S. J. Chen, and S. F. Shu, "High efficiency electro-optic polymer light modulator based on waveguide-coupled surface plasmon resonance," *Proc. SPIE* **5211**, 197–206 (2003).
8. J. N. Yih, F. C. Chien, C. Y. Lin, H. F. Yau, and S. J. Chen, "Angular-interrogation attenuated total reflection metrology system for plasmonic sensors," *Appl. Opt.* **44**(29), 6155–6162 (2005).
9. X. Ma, X. Xu, Z. Zheng, K. Wang, Y. Su, J. Fan, R. Zhang, L. Song, Z. Wang, and J. Zhu, "Dynamically modulated intensity interrogation scheme using waveguide coupled surface plasmon resonance sensors," *Sen. Actuators A* **157**(1), 9–14 (2010).
10. C. C. Teng and H. T. Man, "Simple reflection technique for measuring the electro-optic coefficient of poled polymers," *Appl. Phys. Lett.* **56**(18), 1734–1736 (1990).
11. J. Gu, G. Chen, Z. Cao, and Q. Shen, "An intensity measurement refractometer based on a symmetric metal-clad waveguide structure," *J. Phys. D* **41**(18), 185105 (2008).
12. L. N. Aksyutov, "Temperature dependence of the optical constants of tungsten and gold," *J. Appl. Spectrosc.* **26**(5), 656–660 (1977).

13. A. Kausaite, M. van Dijk, J. Castrop, A. Ramanaviciene, J. P. Baltrus, J. Acaite, and A. Ramanavicius, "Surface plasmon resonance label-free monitoring of antibody antigen interactions in real time," *Biochem. Mol. Biol. Educ.* **35**(1), 57–63 (2007).
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1. Introduction

Surface plasmon resonance (SPR) sensors have been widely explored as a label-free, highly sensitive and real time tool in both fundamental and applied biochemistry as well as in other areas [1]. In SPR sensing systems, attenuated total reflection (ATR) is the most common configuration, in which the wave vector of TM-polarized light of a specific wavelength at an incident angle matches that of the surface plasmon wave (SPW) and the reflectance reaches minimum, producing a dip in the spectrum. In this configuration, with a prism as the coupler, angular, wavelength and intensity interrogation schemes are most commonly used in the labs and commercial instruments [2–4].

In the angular or wavelength interrogation, the position corresponding to the minimal reflectance is denoted as the resonant angle or wavelength, to represent the resonance condition. The resonance conditions are very sensitive to the optical properties of the dielectric medium, such as refractive index (RI), high detection resolution has been realized in the two interrogations. However, since bottoms of the dips are similar to be a parabolic function of the incident angle or wavelength of the light, the resonant angle or wavelength is hard to determine very accurately from the spectra. The cost for the high resolutions are complicated apparatuses to get enough amount of data points, such as high-precision rotational stage or spectrometer, and various data processing methods to further post-process the data.

To overcome these disadvantages, Wang etc. have proposed a hybrid differential interrogation method [5]. In the method, during a low-speed angular interrogation, the reflectance was simultaneously modulated by a higher frequency AC electrical signal. The demodulated signal was closely associated with the first derivative of the reflectance power to incident angle. Since the value of the derivative was zero at the resonant angle, simple linear fitting and zero-finding algorithms could be used to determine the angle. This method simplifies the data processing methods used and realizes sensitivity similar to that of angular interrogation is possible.

To further simplify the data processing method and apparatus employed in the SPR sensing, we propose and experimentally demonstrate a novel voltage interrogation method that can get the corresponding resonant voltages in scan of DC voltage applied on a tunable SPR sensor by keeping the resonance conditions the same for different analytes at a fixed wavelength. Since the voltage can be controlled more precisely and rapidly, we can realize accurate voltage scans easily and get the resonant voltages directly, thus no further data processing methods are required. We use a convergent incident light and a bicell photodetector to collect the divergent reflectance and measure the differential signal from the photodetector to represent the resonance conditions [6] instead of the angular or wavelength scanning setups, to reduce the complexity in configurations. The tunable SPR sensor used in our work is an electro-optically (EO) tunable WCSPR sensor [5,7], which promises a high signal-to-noise ratio (SNR) in finding the resonance condition in detection [8]. In the following sections, we will prove the feasibility of this interrogation method and demonstrate it experimentally.

2. Principle of the method

The EO tunable WCSPR sensor chip in our work has three layers, i.e., the upper gold layer U, the dielectric waveguide layer W, and the lower gold layer L. The power reflectance R of the WCSPR sensor can be calculated using the Fresnel equation [5], where the indices 0 to 4 represent the substrate, the upper gold layer, the waveguide layer, the lower gold layer and the analyte, respectively.

Figure 1 shows the distribution of the divergent reflectance from the WCSPR sensor at two cells of the bicell photodetector, where the bottom of the SPR dip is at the center of the

two cells and each cell covers the same range of angles. We divide the SPR dip into three regions according to their angular slope. Region I and III are regions suitable for intensity interrogation where the slopes of R and incident angle are nearly constant, while region II is the bottom of the dip.

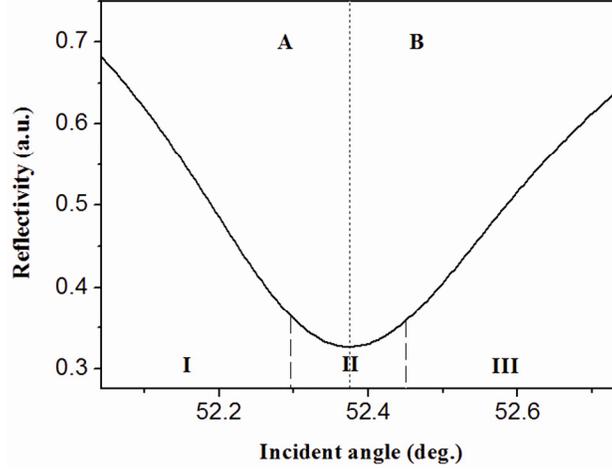


Fig. 1. Distribution of the reflectance from the WCSPR sensor on the bicell photodetector.

We know R can be expressed as a function of incident angle θ , n_2 and n_4 when the structure of the WCSPR sensor is determined [5,9]. Before applying the DC voltage to the waveguide layer of the sensor, the signals collected at A and B cell, S_A and S_B , can be written as:

$$S_A = \int_I R(\theta, n_2, n_4) + \int_{II} R(\theta, n_2, n_4), S_B = \int_{II} R(\theta, n_2, n_4) + \int_{III} R(\theta, n_2, n_4) \quad (1)$$

We notice the symmetry of the dip in region II of Fig. 1, the integrations in S_A and S_B in this region are almost equal. Thus the differential signal from the photodetector I_1 can be expressed as:

$$I_1 = \int_I R(\theta, n_2, n_4) - \int_{III} R(\theta, n_2, n_4) \quad (2)$$

After n_4 changes, we scan the voltage on the waveguide layer until tuning the dip back to the resonance condition. In this case, we denote the DC voltage as the resonant voltage. The signals collected at A and B cells, S'_A and S'_B , can be written as:

$$S'_A = \int_I R(\theta, n_2 + \Delta n_2, n_4 + \Delta n_4) + \int_{II} R(\theta, n_2 + \Delta n_2, n_4 + \Delta n_4) \quad (3a)$$

$$S'_B = \int_{II} R(\theta, n_2 + \Delta n_2, n_4 + \Delta n_4) + \int_{III} R(\theta, n_2 + \Delta n_2, n_4 + \Delta n_4) \quad (3b)$$

From Eqs. (3a) and (3b), the differential signal I_2 can be expressed as:

$$I_2 = \int_I R(\theta, n_2 + \Delta n_2, n_4 + \Delta n_4) - \int_{III} R(\theta, n_2 + \Delta n_2, n_4 + \Delta n_4) \quad (4)$$

According to [9], with higher order terms of Δn_2 and Δn_4 ignored, the Taylor expansion of Eq. (4) can be expressed as:

$$\begin{aligned}
I_2 &= \left[\int_I [R(\theta, n_2, n_4) + \Delta n_2 \left. \frac{\partial R}{\partial n_2} \right|_{n_2, n_4} + \Delta n_4 \left. \frac{\partial R}{\partial n_4} \right|_{n_2, n_4}] \right. \\
&\quad \left. - \int_{III} [R(\theta, n_2, n_4) + \Delta n_2 \left. \frac{\partial R}{\partial n_2} \right|_{n_2, n_4} + \Delta n_4 \left. \frac{\partial R}{\partial n_4} \right|_{n_2, n_4}] \right] \\
&= I_1 + \left(\int_I (\Delta n_2 \left. \frac{\partial R}{\partial n_2} \right|_{n_2, n_4} + \Delta n_4 \left. \frac{\partial R}{\partial n_4} \right|_{n_2, n_4}) \right) \\
&\quad - \left(\int_{III} (\Delta n_2 \left. \frac{\partial R}{\partial n_2} \right|_{n_2, n_4} + \Delta n_4 \left. \frac{\partial R}{\partial n_4} \right|_{n_2, n_4}) \right)
\end{aligned} \tag{5}$$

According to the principle of intensity interrogation [2], we define

$$S_{j, n_k} = \left. \frac{\partial R}{\partial n_k} \right|_{n_2, n_4} \quad (j = I, III, k = 2, 4) \tag{6}$$

where θ_0 is the resonance angle in Fig. 1. Here, we assume that, in region I and III, the sensitivity between the change of R and the shift of the SPR angle is constant.

We already know the relation between the DC voltage and Δn_2 as [9]:

$$\Delta n_2 = -\frac{1}{2} n_2^3 \frac{V_{DC}}{d_2} r_{33} \tag{7}$$

where d_2 is the thickness of the waveguide layer.

When I_1 approaches I_2 , from Eqs. (5)-(8), we get the sensitivity S between the resonant voltage and Δn_4 as:

$$S \sim \frac{2d_2}{r_{33}n_2^3} \frac{\int_I S_{I, n_4} - \int_{III} S_{III, n_4}}{\int_I S_{I, n_2} - \int_{III} S_{III, n_2}} \tag{8}$$

When n_2 and n_4 are in the dynamic range of the traditional intensity interrogation [4,9], S can be treated roughly as a constant. Calculation of S indicates by using the differential signal from the bicell photodetector as the resonance condition, we can keep it the same for different analytes by applying the resonant voltage on the waveguide layer and the voltage has a linear response to RI of the analytes. In our practice, n_2 is around 1.6, r_{33} is at scale of 10pm/V and d_2 is several micrometers. We use these typical parameters in Eq. (8) and estimate the scale of S as 10^4 V/RIU [5].

From the above calculations, when the bottom of the SPR dip has a small deviation from the center of the photodetector, the differential signal in the region II approaches zero while it has a linear response to the deviation in other regions, thus the differential signal from the photodetector will have a linear response to the deviation. This helps us to approximate the position of the bottom to the center of the photodetector.

3. WCSPR sensor fabrication and experimental setup

The WCSPR sensor chip used in our experiments is fabricated on a slide of ZF3 substrate glass and fabrication steps of the chip have been reported in [5]. The RI of the polymer used in our experiment is 1.6044. In our experiment, the thicknesses of the upper gold layer, the waveguide layer and the lower gold layer are 30nm, 2um and 30nm, respectively. We use parallel contact poling method to make the waveguide layer possess the desired electro-optical

characteristics. After the poling step, we measure the EO coefficient r_{33} of the film by the simple reflection method and the EO coefficient r_{33} is 36 pm/V in our experiment [10].

The experiment setup to demonstrate the voltage interrogation method is shown in Fig. 2. The tunable sensor chip is attached to a 45°-45°-90° triangular ZF3 prism with index-matching fluid (refractive index~1.7). The scanning voltage applied on the waveguide layer of the sensor chip is controlled by a DC power source of high output precision (Keithley 6430 sourcemeter), whose output can be controlled and collected by a computer. A micro-fluidic sample channel made of polydimethylsiloxane (PDMS) attached onto the lower gold surface of the sensor chip to hold the analyte. A collimated 10mW semiconductor laser ($\lambda = 980\text{nm}$, Thorlabs) is passed through a p-polarized polarizer and focused by a 50mm focal-length lens through the prism onto the upper gold layer of the sensor chip. The reflectance from the sensor was collected by a bicell photodetector (OSI Optoelectronics, SPOT-2D) mounting on a precision translation stage and the photocurrents are converted to voltages with a homemade circuit and measured by a lock-in amplifier (Stanford Research SR830). The differential signal from the bicell, A-B, is measured by the amplifier and recorded by the computer.

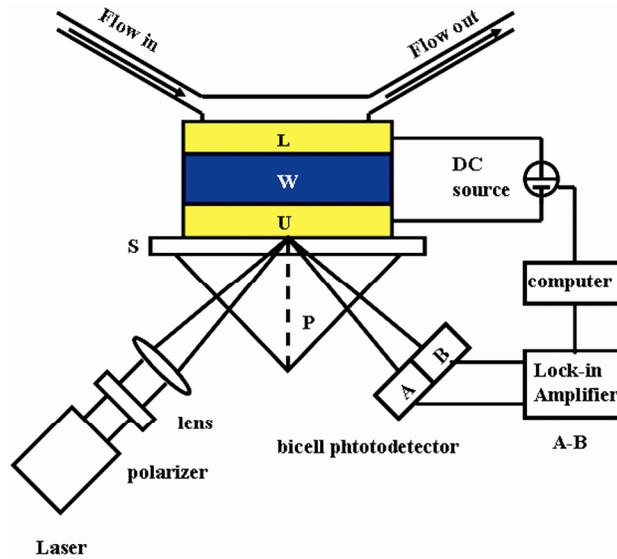


Fig. 2. Experiment setup for differential intensity based tunable detection. P, ZF3 prism; S, ZF3 substrate glass; U, upper gold layer; L, lower gold layer; W, waveguide layer.

The analytes used in our experiment are glucose solution of 0%, which is deionized water, 0.1%, 0.2%, 0.3% and 0.4% by weight, respectively. After using the traditional angular interrogation using a photodiode (API, PDB-C615-2) to check the SPR response to different samples and the electrical tunability of the sensor, the incident light is changed to the convergent light and the photodiode is replaced by the bicell to realize the voltage interrogation. Before detection, the sensor is rotated to SPR angle for one of the samples in detection and the dark line in the reflectance due to the SPR dip should be at the center [6]. Then we rotate the photodetector to make the reflectance fall on it perpendicularly. This step can be finished with little calibration time. During the voltage scan the scanning rate is 3 steps/s, while the light is modulated at 1 kHz.

4. Results and discussion

The reflectivity of WCSPR mode of the sensor is measured by the angular interrogation over a range of incident angles. 0.4 wt% glucose solution is used as the analyte. Figure 3 shows the normalized reflectivity versus the incident angle and the resonance angle of the WCSPR mode is 52.39°.

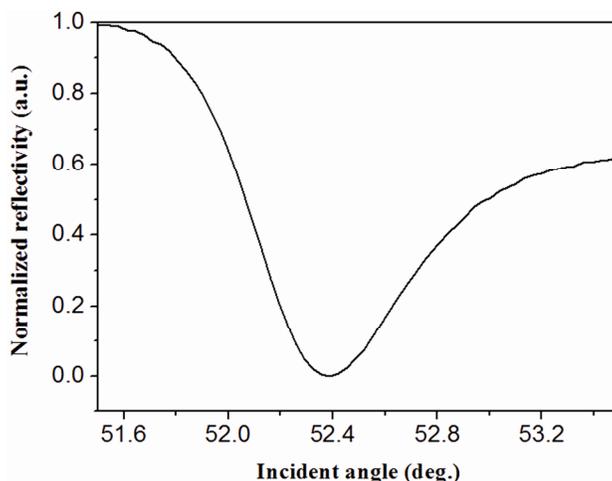


Fig. 3. Angular dependent response of the WCSPR sensor for glucose of 0.4 wt% concentration.

The SPR responses of the sensor to glucose solutions of different concentrations by the angular interrogation are shown in Fig. 4(a). We get the same angular moving trend of the SPR dip as in [5] when the glucose concentration increases. We find the depth increases while the dip shifts. In Fig. 4(b), we check the SPR angular responses of the different DC voltages applied on the waveguide layer with deionized water as the analyte. When the voltage decreases, the SPR angle increases and the depth of the SPR dip increases. In the figures, we find though the depths of the SPR dips change, the shapes of the dips are almost the same during the shifts. Thus variation in the differential signal caused by the depth change of the SPR dip due to change of analyte can be compensated by tuning RI of the waveguide layer. This allows us to reach the resonance condition for different analytes in the voltage interrogation.

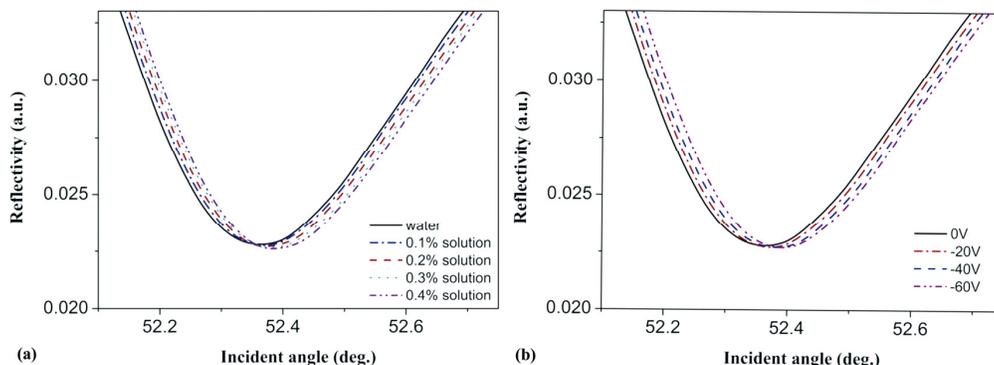


Fig. 4. (a) Angular shift response of the WCSPR sensor chip to glucose solution of different concentration;(b) Angular shift response of the WCSPR to the DC voltage applied with deionized water as the analyte.

In the voltage interrogation, the incident light has a convergent angle of 0.8° . Before detection, we keep the output of the power source as zero and take 0.4 wt% glucose solution as the analyte. We fix the positions of the sensor and the photodetector to record the differential signal as the resonance condition. The resonant voltage for this analyte is zero.

After recording the resonance condition, we change the analyte to the glucose solutions of different concentrations in detection. Since the S calculated is high, small change of RI of the analyte as 10^{-5} RIU will cause a change in the resonant voltage around 0.1 V. To make the scanning procedure less time consuming, for each analyte, we scan the voltage applied on the

waveguide layer in a step as -0.1V from -60V to 0V and measure the differential intensity for each step. We stop the scanning until the differential signal representing the resonance condition is reached. We record the corresponding value of voltage as the resonant voltage. The resonant voltages for the different analytes are shown in Fig. 5. In Fig. 5, the sensitivity between the resonant voltage and RI of the analytes in our experiment is $\sim 7.5 \times 10^4 \text{ V/RIU}$. This sensitivity is of the same scale as the S estimated.

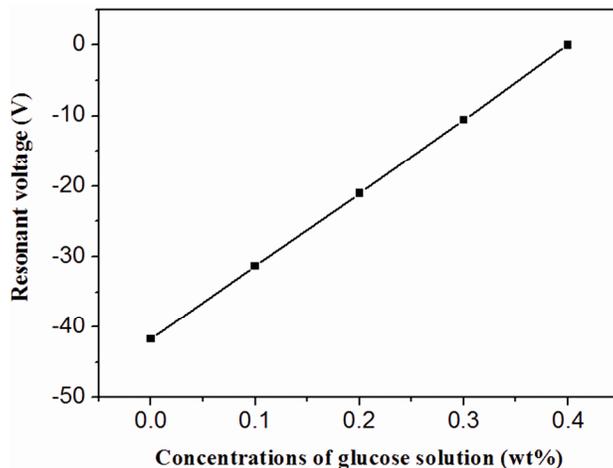


Fig. 5. Resonant voltages for glucose solutions of different concentrations.

We calculate S as $8.6 \times 10^4 \text{ V/RIU}$ by using the structure parameters of the SPR sensor in Fig. 4, which is almost the same with the sensitivity observed in our experiment. The difference between them may be caused by the approximations in Eq. (8).

After calculating the sensitivity of the voltage interrogation in experiment, we check the long term stability with the analyte as the deionized water for 100 minutes and the results are shown in Fig. 6. In our experiment, though calculation of the differential signal can help to suppress the noise associated with fluctuation of light source, the mechanical drift can't be eliminated entirely and results in small vibrations of the signal during the detections, and it needs to be compensated by applied some extra voltages during the interrogation. To achieve the goal, we try to scan the voltage at the available minimal step by the precise power source for the different analytes and get the resonant voltages with the compensating voltage included, which results in a fluctuation in the resonant voltages as shown in Fig. 6. We calculate the standard deviation (SD) of the resonant voltage is around 0.2V , the resolution of the voltage interrogation is at the level of 10^{-6} RIU , then. The reasons for the fluctuation are complicated. The removing of the rotational stage can't suppress the mechanical drift entirely. Our guest-host EO polymer employed as the waveguide layer in our sensors has a very high thermal stability with DC voltage applied since it has been applied in high frequency light modulator [7]. However, variation of room temperature still can't be ignored in the detections. We note that a $0.1 \text{ }^\circ\text{C}$ temperature variation can lead to a RI variation of 0.86×10^{-5} for water samples [11] and 0.86×10^{-5} for gold [12]. In simulation, this results in a resonant voltage fluctuation of around 0.08V , corresponding to a detected RI variation of the analytes of 10^{-6} , which is better than the angular interrogation. By using more stable mechanical parts and more efficient temperature controller in experiment to suppress the fluctuation, a higher resolution can be expected.

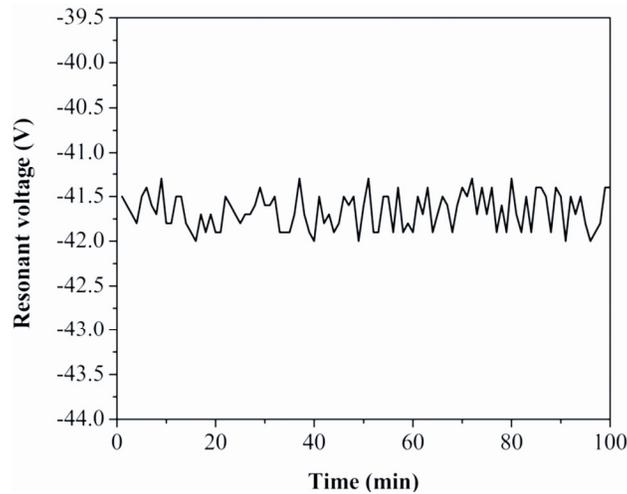


Fig. 6. Long term stability of measured resonant voltage of deionized water.

To further demonstrate the method, we apply it to protein-protein binding kinetic analysis. We prepare surface of the lower gold layer of the sensor chip according to [13] and record the resonance condition with 1x phosphate buffer solution (PBS) as the analyte. Using Protein G as antigen on the surface, we flow Human IgG as antibody of different concentration, 4n mol/ml and 8n mol/ml, at 5ul/min. Considering the need of real-time detection, we change the voltage scanning speed to 10 steps/s and get the resonant voltage measurement of the kinetic curves in Fig. 7. In detection, we can't control the temperature of the flow cell strictly. Thus temperature change lead to measurement errors as the fluctuations of the curves. When the antibody concentration is low, the binding signal is weak. In this case, we can measure the resonant voltage in real time. Under the aid of Scrubber, a kinetic analysis software, we fit the kinetic curve of 4n mol/min antibody and get the interaction constants k_a and k_d of $1.75 \times 10^4/Ms$ and $1.66 \times 10^{-3}/s$, which are of the same order of magnitude with our results from commercial SPR imaging system.

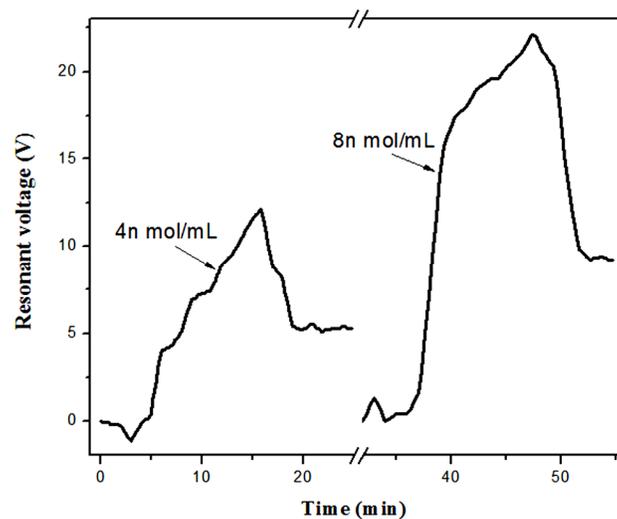


Fig. 7. Real-time resonant voltage measurement of protein-protein binding of different concentrations.

In most of other current interrogation methods using SPR sensors, data processing methods are necessary to remove the noise in detection further and get the resonance information. Different from these methods, we get the resonant voltage directly during the voltage scan and don't need the data processing methods. The resolution in our method is about the same level compared with the traditional angular interrogation. However, the electric devices in our method respond much faster and the scanning time is expected to be reduced.

Another feature of our method is that we can control the detection sensitivity of the method in a range according to Eq. (8). The sensitivity of the resonance angle to RI of the waveguide layer and the analytes in the experiment can't be varied much if we can change structure parameters of the sensor chip [9]. However, we can enhance the sensitivity by fabricating a thicker waveguide layer in the sensor chip or getting a lower r_{33} from the poling process. Considering output range of the power source in measurements and our fabrication conditions, we choose the parameters in the above sections for the demonstration.

5. Conclusion

We present a novel voltage interrogation method using EO tunable SPR sensors. In contrast to most of the previous SPR detection methods using data processing methods to determine the resonance information, we obtain the resonance voltage corresponding to different analytes directly from the fast scan of the voltage applied on the waveguide layer of our tunable WCSPR sensors in a simple configuration. The tunable WCSPR sensors enable a reasonably large dynamic range similar to that of the intensity interrogation method and a high sensitivity within the range. We notice the shapes of the SPR dips produced by our sensor vary for different analytes and different applied voltages on the waveguide layer of our sensor. However, detection results in our method are robust against this variation. Experimentally, we fabricate and test the EO tunable WCSPR sensor chip, and the results are in good agreement with theoretical prediction. We also demonstrate its applicability on protein-protein binding kinetic analysis.

The differential signal collected from the bicell photodetector can help to suppress the fluctuations in light source. Removing of the data processing steps reduces the complexity of our method further. If we suppress the mechanical drift and temperature fluctuation better, the voltage interrogation method can be further used in practice.

Acknowledgments

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