Interferometric optical sensor for measuring glucose concentration

Kun-Huang Chen, Cheng-Chih Hsu, and Der-Chin Su

With a specially designed probe, the phase difference between *s* and *p* polarization of light reflected under surface-plasmon resonance is measured by use of a common-path heterodyne interferometer. For specific ratios of phase difference to glucose concentration, the glucose concentration can be estimated as a function of the measured phase data. A prototype was set up to demonstrate the feasibility of this sensor, which was experimentally tested in the range 40–500 mg/dl with a small quantity of solution and had a measurement resolution of 1.41 mg/dl at 25 °C.

OCIS codes: 040.2840, 120.3180, 120.5050, 240.6680.

1. Introduction

Measurements of glucose concentration are often parts of biochemical analyses. Several methods for measuring the concentration of a glucose solution have been proposed[1–4]; the measurement resolution was ~10 mg/dl. In this paper we propose an interferometric optical sensor for measuring glucose concentration that is based on the effect of surface-plasmon resonance[5–9] (SPR) and on heterodyne interferometry.[3,10] In a specially designed probe, the phase difference between *s* and *p* polarization of light reflected under SPR is measured with a common-path heterodyne interferometer. For a specific ratio of phase difference to glucose concentration, the glucose concentration can be estimated from knowledge of the measured phase data. Because the reflected light is measured, only a small quantity of test solution is required. In addition, the probe can easily be operated with high resolution in real time. A prototype has been built to demonstrate its feasibility.

2. Materials and Method

This interferometric optical sensor is shown schematically in Fig. 1. The sensor consists of a heterodyne light source, a light-guiding module, a specially designed probe, an analyzer (AN), a photodetector (D), an electronic signal-processing unit (ESPU), and a seven-segment display. The light-guiding module has two graded-index lenses, L_1 and L_2, and a polarization-maintaining fiber (PMF). The specially designed probe is an isosceles trapezoid prism with base angle 71°; a thin gold film is deposited upon its base surface, which is in contact with the test glucose solution, as shown in Fig. 2. So this probe is a SPR apparatus in a Kretschmann–Raether configuration.[8]

For convenience, the $+z$ axis is chosen to be along the direction of light propagation and the $+x$ axis is along the horizontal plane. The light beam coming from the heterodyne light source has a frequency difference f between *s* and *p* polarization, and its polarization plane lies at angle α to the x axis. This light beam is guided into the polarization-maintaining fiber by lens L_1 and is collimated by lens L_2 attached to one side surface of the probe. Then the light beam penetrates the surface normally and is incident at 71° onto the boundary surface between the prism and the thin gold film. Because the base angle is designed to be 71°, the incident angle is near the resonant angle. Consequently the surface plasmons are excited. The reflected light beam passes through the analyzer with the transmission axis at 45° to the x axis and is detected by the photodetector. The detected intensity is

$$\begin{aligned} I_t &= |E_t|^2 \\ &= \tfrac{1}{4}\,[\cos^2\alpha r_p^{\,2} + \sin^2\alpha r_s^{\,2} \\ &\quad + 2\cos\alpha\,\sin\alpha r_p r_s \cos(2\pi f t + \phi)], \end{aligned} \tag{1}$$

The authors are with the Institute of Electro-Optical Engineering, National Chiao Tung University, 1001 Ta-Hsueh Road, Hsin-Chu 300, Taiwan, China. D.-C. Su's e-mail address is t7503@faculty.nctu.edu.tw.

Received 26 February 2003; revised manuscript received 1 July 2003.

0003-6935/03/285774-03$15.00/0

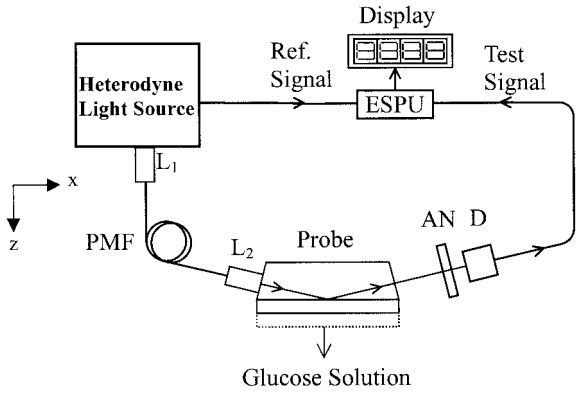

Fig. 1. Schematic diagram of the optical sensor.

where r_p and r_s are the reflection coefficients of p and s polarization, respectively, and ϕ is the phase difference between the p and s polarization coming from the reflection at the boundary surface under the conditions of SPR[5,8]:

$$r_q = \frac{r_{12}^{\,q} + r_{23}^{\,q} \exp(i2k_{z2}d)}{1 + r_{12}^{\,q} r_{23}^{\,q} \exp(i2k_{z2}d)}, \qquad q = p, s, \quad (2)$$

$$\phi = \arg(r_p) - \arg(r_s), \quad (3)$$

where k_{z2} is the wave vector in the thin gold film, d is the thickness of the thin gold film, $r_{ij}^{\,q}$ is the Fresnel reflection coefficient between the ith and the jth media, and subscripts i and j are any of 1 (glass prism), 2 (thin gold film), or 3 (glucose solution), whose refractive indices are n_1, $n_2 = n + ik$, and n_3, respectively.

The electrical modulation signal of the heterodyne light source is filtered and becomes the reference signal. It has the same form and can be expressed as[10]

$$I_r = \tfrac{1}{2}[1 + \cos(2\pi ft)]. \quad (4)$$

Both of these two sinusoidal signals are sent to the electronic signal-processing unit, and ϕ can be obtained. From Eqs. (2) and (3) it is obvious that ϕ is strongly dependent on n_3. In general, n_3 is nearly proportional to its associated concentration c. By substituting the data of ϕ into a specific ratio of ϕ versus c, we can estimate the associated concentration c.

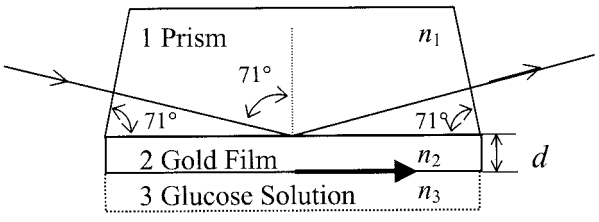

Fig. 2. Reflection at the boundary surface between a prism and a thin gold film under SPR.

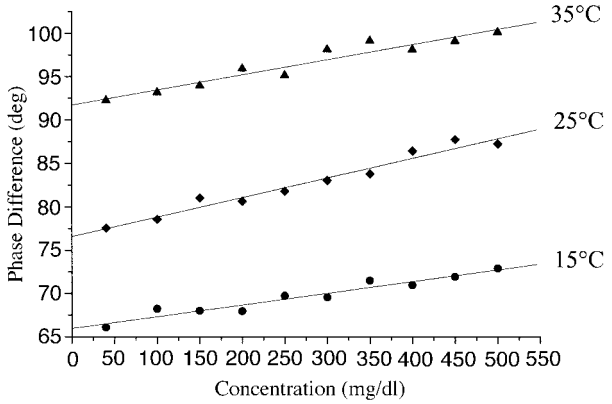

Fig. 3. Measurement results and associated fitting curves of phase difference versus glucose concentration at 15, 25, and 35 °C.

3. Experiments and Results

To demonstrate the feasibility of the proposed instrument we set up a prototype of this interferometric optical sensor to test glucose solutions of different concentrations at three temperatures. The heterodyne light source[11] consisted of a He–Ne laser with wavelength 632.8 nm, a half-wave plate, and an electro-optic modulator driven by a function generator. The conditions $f = 1$ kHz and $\alpha = 5°$ were used. The specially designed probe was a BK7 isosceles trapezoid prism with base angle 71° and a thin gold film of 40-nm thickness deposited onto its back surface. The refractive indices of the prism and the thin gold film were measured in advance with an ellipsometer (Model Eta; Stag, Inc.) and were 1.5151 and $0.2108 + 3.5963i$, respectively, at a wavelength of 632.8 nm. Test solutions were prepared according to the definition of concentration in weight percent. Chiral parameter g of each solution was measured with the optical heterodyne polarimeter proposed by Lin and Su.[12] Then the concentration of each solution could be calibrated by comparison of the measured g and the data from Ref. 13. For convenience, the light-guiding module was omitted from our experiments, and we let the light beam be incident normally onto the side surface of the probe.

The experimental results and their associated fitting curves appear in Fig. 3, where the measurement results at 15, 25, and 35 °C are shown. It is clear that with this optical sensor and the associated ratio of ϕ to c at a nominal temperature, the concentration of glucose solution can be obtained from the measured data of ϕ.

4. Discussion

In our experiment there were two extreme conditions, 40 mg/dl at 35 °C and 500 mg/dl at 15 °C. The associated plasmon resonant angles were 71.06° and 70.95°, respectively. Although the plasmon resonant angle varied with the concentration, the shift in resonant angle in our experiments was small. For convenience, the incident angle in the probe was fixed to 71°, which is the resonant angle associated with a concentration of 40 mg/dl at 25 °C. Consequently,

reflection coefficient r_p was small. So the condition $\alpha = 5°$ was used in our experiments to enhance the contrast of the test signal.

Considering the angular resolution of the electronic signal-processing unit, the polarization-mixing errors, and the second-harmonic error, the total phase difference errors $|\Delta\phi|$ could be decreased to 0.03° in our experiments.[14] Slopes s of the three fitting curves for 15, 25, and 35 °C in Fig. 3 were 0.0134, 0.0213, and 0.0167 deg(dl/mg), respectively. Then, substituting these data into the following equation:

$$\Delta c = |\Delta\phi|/s, \tag{5}$$

we obtained the associated resolutions Δc of the measurement. They were 2.24, 1.41, and 1.8 mg/dl, respectively, and were better than those obtained with the previous methods.[2,3] The main reason for the better resolution is that this sensor operates under conditions of SPR; hence a small variation in the concentration can introduce an abrupt variation in optical phase. This phase variation can be measured accurately by the optical heterodyne interferometric technique. As a result, this method provides better resolution. In addition, the incident angle is equivalent to the resonant angle at 25 °C, so the measurement resolution at 25 °C is the best in our experiments.

Although the measurement resolution is enhanced as the thin gold film becomes thicker, both the intensity and the contrast of the test signal decrease rapidly. To compensate for these conditions, we chose $d = 40$ nm for our experiments. In addition, if a light-guiding module is added, the probe can be moved conveniently to the test solution, and this sensor can be operated easily.

5. Conclusions

In this paper we have proposed an interferometric optical sensor for measuring glucose concentration that is based on the effect of surface plasmon resonance and on heterodyne interferometry. Because of the introduction of a light-guiding module, its own common-path interferometric configuration, and the presence of an electronic signal-processing unit, this sensor has such merits such as a simple structure, easier operation in real time, rapid measurement, and high stability. A prototype was set up to demonstrate its feasibility, which was experimentally tested in the range 40–500 mg/dl and had a measurement resolution of 1.41 mg/dl at 25 °C.

This study was supported in part by the National Science Council, Taiwan, under contract NSC 91-2215-E-009-020.

References

1. Y. Liu, P. Hering, and M. O. Scully, "An integrated optical sensor for measuring glucose concentration," Appl. Phys. B **54,** 18–23 (1992).
2. C. Chou, Y. C. Huang, C. M. Feng, and M. Chang, "Amplitude sensitive optical heterodyne and phase lock-in technique for small optical rotation angle detection of chiral liquid," Jpn. J. Appl. Phys. **36,** 356–359 (1997).
3. C. M. Feng, Y. C. Huang, J. G. Chang, M. Chang, and C. Chou, "A true sensitive optical heterodyne polarimeter for glucose concentration measurement," Opt. Commun. **141,** 314–321 (1997).
4. R. J. Mcnichols and G. L. Cote, "Optical glucose sensing in biological fluids: an overview," J. Biomed. Opt. **5,** 5–16 (2000).
5. Y. C. Cheng, W. K. Su, and J. H. Liou, "Application of a liquid sensor based on surface plasma wave excitation to distinguish methyl alcohol from ethyl alcohol," Opt. Eng. **39,** 311–314 (2000).
6. C. H. Liao, C. M. Lee, L. B. Chang, and J. H. Tsai, "Effects of a metal film and prism dielectric properties of surface plasmon resonance in a multilayer," Jpn. J. Appl. Phy. **36,** 1105–1111 (1997).
7. Y. C. Cheng, W. K. Su, C. M. Lee, L. B. Chang, J. H. Liou, J. M. Shen, and T. H. Scoong, "Design and measurement of a dielectric sensor based on surface plasma excitation," Appl. Surf. Sci. **136,** 260–267 (1998).
8. A. A. Kolomenskii, P. D. Gershon, and H. A. Schuessler, "Sensitivity and detection limit of concentration and absorption measurements by laser-induced surface-plasmon resonance," Appl. Opt. **36,** 6539–6547 (1997).
9. K. J. Kasunic, "Comparison of Kretschmann–Raether angular regimes for measuring changes in bulk refractive index," Appl. Opt. **39,** 61–64 (2000).
10. M. H. Chiu, J. Y. Lee, and D. C. Su, "Refractive index measurement based on the effects of total internal reflection and the use of heterodyne interferometry," Appl. Opt. **36,** 2936–2939 (1997).
11. D. C. Su, M. H. Chiu, and C. D. Chen, "Simple two-frequency laser," Precis. Eng. **18,** 161–163 (1996).
12. J. Y. Lin and D. C. Su, "A new type of optical heterodyne polarimeter," Meas. Sci. Technol. **14,** 55–58 (2003).
13. T. W. King, G. L. Cote, R. McNichols, and M. J. Goetz, Jr., "Multispectral polarimetric glucose detection using a single Pockels cell," Opt. Eng. **33,** 2746–2753 (1994).
14. M. H. Chiu, J. Y. Lee, and D. C. Su, "Complex refractive-index measurement based on Fresnel's equation and the uses of heterodyne interferometry," Appl. Opt. **38,** 4047–4052 (1999).