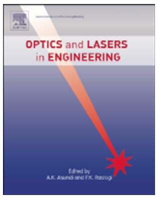
Optics and Lasers in Engineering 46 (2008) 666–670

Contents lists available at ScienceDirect

Optics and Lasers in Engineering

journal homepage: www.elsevier.com/locate/optlaseng



Real-time measurement of glucose concentration and average refractive index using a laser interferometer

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ARTICLE INFO

Article history:
Received 29 October 2007
Received in revised form
29 March 2008
Accepted 7 April 2008
Available online 5 June 2008

Keywords:
Glucose
Laser interferometer
Refractive index
Optical path

ABSTRACT

This study presents a non-destructive, highly precise optical metrology system for measuring the average refractive index of a liquid solution such that its glucose concentration can be derived. The metrology system is employed to measure the average refractive indices of samples with known glucose concentrations ranging from 0 to 200 g/l. By applying a regressional analysis technique to the experimental results, an analytical expression is derived to describe the relationship between the refractive index and the glucose concentration. An excellent agreement is observed between the experimentally determined values of the glucose concentration and the analytically derived results. For an assumed laser interferometer resolution of 1 nm, the measurement resolution of the proposed metrology system is found to be at least $F = 0.05$ g/l, which is significantly better than that of $F = 2$ g/l obtained using the polarimetric glucose sensor presented by Lo and Yu [A polarimetric glucose sensor using a liquid-crystal polarization modulator driven by a sinusoidal signal. Opt Commun, 2006; 259: 40–8].

1. Introduction

Glucose is an optically active (i.e. chiral) substance and thus when a linearly polarized light beam passes through it, the left-circularly polarized and right-circularly polarized components experience a different refractive index and a different propagation speed. As a result, the linearly polarized light undergoes an angular rotation as it is transmitted through the glucose medium. The optical rotation properties of chiral media are generally evaluated by passing a linearly polarized light beam through the sample of interest and measuring the change in the output intensity of the beam using a polarized phase detection technique. In 1992, Cote et al. [1] presented a technique for measuring glucose concentrations using a non-invasive true phase optical polarimetry sensing system. Similarly, in 1997, Feng et al. [2] performed glucose concentration measurements using an optically polarized heterodyne polarimeter and a phase lock-in technique. In 2004, Lin et al. [3] proposed a phase-based approach for measuring small optical rotation angles of chiral media using an optical metrology system comprising a waveplate, two analyzers and a lock-in amplifier. To reduce the scattering effect, Chou et al. [4] determined the phase-sensitive optical rotation angle of a chiral medium using a circularly polarized optical heterodyne interferometer based on a Zeeman laser. Lo and Yu [5] presented a high-resolution polarimetric glucose sensor in which a liquid-crystal-based rotator was used to modulate the azimuth of the linearly polarized light with a sinusoidal signal. Although all of the methods described above are capable of extracting the glucose concentration from the measured optical activity of the sample, they require the use of waveplates, analyzers, lock-in amplifiers, or liquid crystal modulators, and therefore have a complex and expensive experimental setup.

Various researchers have demonstrated the feasibility of using laser interferometers to measure the optical properties of chiral media. For example, Lin [6] used common-path interferometry and heterodyne interferometry techniques to determine the average refractive index of glucose. From Lin [6], it can be known that the stable average refractive index at the corresponding glucose concentration exits. The chiral parameter of glucose is much less than the unity. The refractive indices of the left- and right-circularly polarized lights in glucose are very close to the average refractive index. In order to understand the glucose concentration, the average refractive index can be used. Yeh et al. [7] presented a high-precision optical metrology system based on a laser interferometer for determining the thickness and refractive indices of birefringent optical waveplates. It was shown that the measurement resolution of the proposed system was higher than that of the interferometer hardware itself. In general, the results presented in [6,7] demonstrate that laser interferometry techniques provide an accurate and relatively straightforward means of assessing the optical properties of chiral or birefringent media.

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doi:10.1016/j.optlaseng.2008.04.008

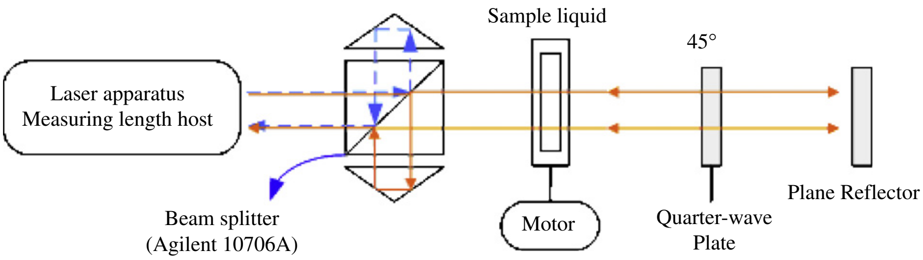

Fig. 1. High-precision optical metrology system for determining refractive index of liquid glucose solution.

The literature contains various studies in which the glucose concentration of liquid samples is measured using a surface-plasmon resonance (SPR) technique. For example, Chen et al. [9] showed that the glucose concentration can be estimated as a function of the measured phase data for specific ratios of the phase difference to the glucose concentration. Their results indicated that the SPR technique enables a measurement resolution of around 0.0141 g/l for glucose concentrations ranging from 0.4 to 5 g/l. From [10] it can be known that the Plasmon resonant angle varied with concentration. Kolomenskii also demonstrates that minute changes in the refractive index of the medium close to the surface of a metal film can be detected owing to a shift in the resonance angle. From the above result, it can be known the SPR method can determine the concentration of the glucose with a small concentration range. In general, the SPR method can determine the small resolution of the glucose concentration. If the range of concentration for the glucose sample is great, it is difficult to measure the phase difference of the glucose sample.

Accordingly, the present study develops a simple yet highly accurate optical technique for determining large glucose concentrations in real time by measuring the average refractive index of the sample. The proposed approach eliminates the requirement for a complex heterodyne lock-in technique and therefore has the advantages of a reduced cost and a straightforward experimental procedure. The validity of the proposed method is demonstrated experimentally using samples with known glucose concentrations ranging from 0 to 200 g/l.

2. Measurement system

Glucose is an optically active substance and therefore has two different refractive indices for left- and right-circularly polarized light, i.e. n_+ and n_-, respectively. For chiral media, these two refractive indices are related via the expression $n_\pm = n \pm g$, where n is the average refractive index and g is the chiral parameter. The value of g for glucose is very small, i.e. around 10^{-7} [6], and thus it can be inferred that $n_+ \cong n_- \cong n$.

2.1. Structural design and experimental procedure

Fig. 1 presents a schematic illustration of the optical metrology system used in the present study to measure the average refractive index of glucose samples. As shown, the system comprises a measuring length host, a beam splitter (Agilent 10706A), two corner cube retro-reflectors, a stepping motor, a quarter-waveplate, a plane reflector and a rectangular cell containing the glucose sample. The light beam emitted from the laser system enters the beam splitter and is split into two linearly polarized light rays with different frequencies and directions of vibration. The first beam, designated as the reference beam (indicated by the broken line), is reflected from the beam splitter into the upper corner cube retro-reflector, which reverses its direction of travel such that it re-enters the beam splitter and is reflected back to the measuring length host. The second beam, designated as the measurement beam (indicated by the continuous line), exits the beam splitter, passes through the sample cell and enters a quarter waveplate, which changes its state of polarization from a linear direction to a circular direction. The circularly polarized light beam is then reflected by the plane reflector such that it passes back through the quarter waveplate, where its state of polarization reverts to a linear direction, and then re-enters the sample cell. (Note that the difference in the vibrational direction of the linearly polarized light beam as its passes through the sample cell in its forward and reverse paths, respectively, is approximately 90°.) When the measurement beam emerges from the sample cell, it re-enters the beam splitter and is split into two beams. One beam passes directly to the measuring length host, while the other is reflected into the lower corner cube retro-reflector, where its direction is reversed such that it re-enters the beam splitter. This beam is then reflected back along its original path through the sample cell before finally arriving back at the measuring length host. From the discussions above, it can be seen that the measurement light beam passes through the sample on four separate occasions, i.e. twice in the forward direction and twice in the reverse direction. As a result, the measurement resolution of the optical setup is significantly improved.

The objective of the optical system shown in Fig. 1 is to measure the refractive index of a liquid solution such that its glucose concentration can be derived. The measurement procedure involves the following basic steps:

(1) The orientation of the beam splitter is adjusted such that the incident light polarized in the vertical direction is transmitted toward the sample liquid cell, while the light polarized in the horizontal direction is reflected toward the corner cube retro-reflector.
(2) The position of the quarter-waveplate is adjusted such that its fast axis is orientated at an angle of 45° to the horizontal axis.
(3) The quarter waveplate is placed in the middle position between the sample and plane refractor such that the measurement light beam enters the sample cell vertically in its first pass in the forward direction and horizontally following its reflection from the plane reflector. Having been reflected from the beam splitter, the light beam re-enters the sample cell horizontally and then passes back through the sample vertically following its reflection from the plane reflector. The light beam is then incident in the measuring length host, causing the interferometer counter to be reset to zero.
(4) Once the interferometer has been reset to zero, the sample cell is rotated through a known angle θ by the stepping motor and the corresponding change in the interferometer readout is recorded.

2.2. Mathematical analysis

Rotating the sample cell changes the length of the optical path in the interferometer system. Assuming that the cell has a