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Laser Interference Measurement of Glucose in Liquids

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ABSTRACT. In this study, we are developing a new method, which has been invented by one of our investigators, for measnring the glucose concentration in liquids. The method is called the laser sheet method. The proposed method allows ns to perform an accurate measurement of refractive index of liquid samples. We used this technique to measure glucose eoncentration in distilled water (ranging from 10 to 50%). We obtained a good correlation between the glucose concentration and the refractive index. This method will be further developed to measure glucose concentration in plasma and iu anti-coagulated blood from human volunteers. If the technique is successful, it has the potential of becoming the principle of a new blood diagnostic machine based on laser interference.

Introduction

There are reportedly more than 150 million diabetic people in the world at the moment, and this figure is expeeted to double within the next ten years. Diabetes mellitus is a serious disease that not only affects the patient's internal organs, circulation system and eyesight, but also his/her entire life. It is a medical condition in whieh the body does not adequately produce the quantity or quality of insulin needed to maintain normal circulating blood glucose. In diabetic patients, the synthesis and metabolism of glucose is abnormal that leads to abnormal blood glucose levels in the body tissues. Diabetic patients suffer from many aeute and chronic symptoms and diseases. They are at high risk of heart disease, blindness, reduced blood circulation in extremities often leading to ulcers, gangrenes and limb imputations. It is vital for diabetic patients to monitor blood glucose levels and take medication to control rhe glueose level in their body. Many types of glucose meters are commercially available. Glucose meters are a 3 billion dollar business worldwide. In this study we are investigating a new technique for measuring the glucose level in liquids using laser refraction technique.

In laboratory, the most traditional methods in measuring the glucose concentration are classified as: 1) Enzymatic (for example glucose oxidase and hexokinasse) 2) Colorimetric (for example O-tolidine). In the glucose oxidase method, the enzyme glucose oxidase catalyses the oxidation of glucose to gluconic acid and hydrogen peroxide. Consequently, addition of the enzyme peroxidase and a chromogenic oxygen acceptor, such as o-di-anisidine, results in formation of color that can be measured. It is characterized by high sensitivity, accuracy and reliability. Other traditional methods, such as potentiometery or amperemetry can be used to determine the glucose content during the glucose oxidation reaction. These methods are summarized in reference [1].

Optical techniques have been used extensively at the end of the last century to measure the glucose concentration. Good overviews over non-invasive optical techniques are provided by references [2-4]. In 1975, the first precision optical polarimeter using the Faraday effect was introduced by Gillham [5]. Now, there are many other optical, non-invasive and promising technologies used in a blood glucose monitoring system, which are: 1) near-infrared light (transmission and reflection) (NIR), 2) far-infrared (FIR) radiation spectroscopy, 3) radio wave impedance, 4) optical rotation of polarized light and 5) fluid extraction from skin 6) Spatially-resolved diffuse reflectance 7) frequency-domain reflectance 8) optical coherence tomography 9) Raman spectroscopy 10) pulsed photoacoustic.

The objective of this study is to measure the refractive index of a clear liquid with accuracy better than 10^{-4} and relate it to its glucose concentration. The method was recently developed to examine crude oils and optical fibers [6-9], and has been modified in this work to include capillary tubes filled with glucose solution. In this method, a laser beam impinges on the capillary tubes in a form of a sheet that covers the whole width of the capillary tubes. Consequently, transverse interference fringes will be formed in a vertical arrangement with locations directly related to the angles of refractions and, hence, to the refractive index of the liquid inside the capillary tube. The refractive index changes due to changes in glucose concentration.

Experimental Setup

A schematic diagram of the experimental setup is shown in Fig. 1. Capillary tubes (inner and outer diameters 0.5mm and 1mm, respectively) filled with glucose solution were placed on a fixed holder, one at a time, and were illuminated by a laser sheet from a 50-mW HeNe laser in the z-direction. The sheet was formed by passing the laser beam through a microscope-objective lens, a collimating lens, and a cylindrical lens whose axis was parallel to the axis of the capillary tube (along the x-direction). The formed sheet had a length of approximately 5cm, and a thickness wide enough to illuminate the whole width of the capillary tube. The resulting interference pattern was formed at the capillary tube itself and also in the region behind it where it was projected onto a fixed screen whose plane was kept perpendicular to the z-axis. A digital image of the projected interference pattern was then taken using a CCD camera, stored in a computer and later retrieved for carrying out the analysis.

The thin capillary tubes made it possible for the interference patterns from the glucose solution to be visible in transmission, while the design of the capillary-tube holder made it possible to record the interference patterns immediately after securing the glucose solution sample in place. The measurements were carried out independently from each other. Therefore, the analysis of the resulting interference image of each sample was made on all the interference fringes to search for the correct interference order. All samples were treated under the same exact experimental conditions of room temperature (26°C) and duration of exposure.

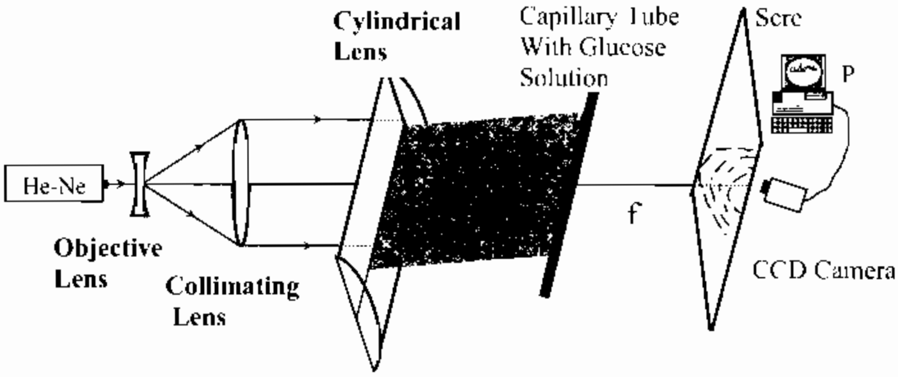
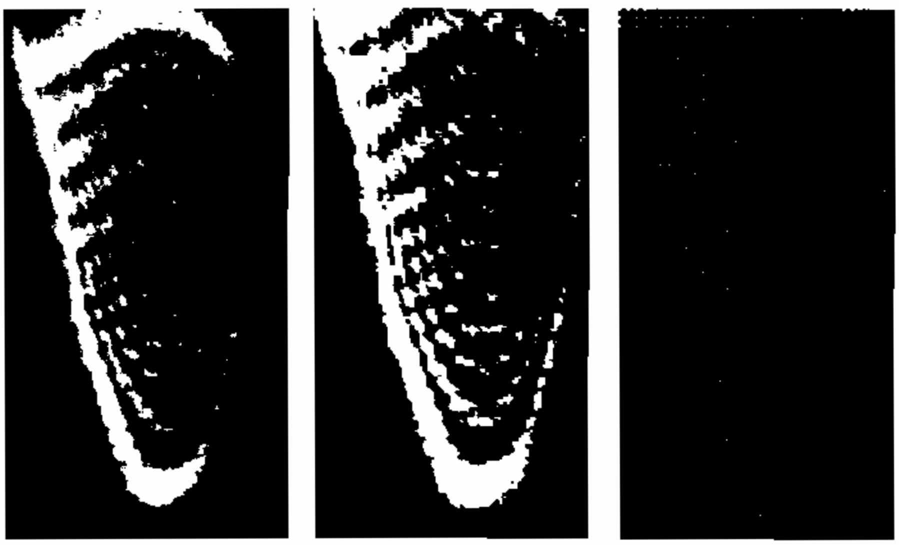


Fig. 1. Schematic diagram of the experimental setup.

Results and Discussion

Image of the resulting transverse interference patterns for one of the samples is shown in Fig. 2.a. The interference patterns shown in Fig. 2.a corresponds to the upper half of the capillary tube only; those corresponding to the bottom half are symmetrically inverted in shape and are not shown in the figure. The patterns comprise only a few number of interference fringes, which were found to be typical for homogeneous liquids and could be explained in terms of two-beam type interferenee between pairs of laser rays passing through different optical media. Figure 3 shows the ray-traeing diagrams of a few of the possible combinations that can produce interference fringes. A fringe can be formed as a result of interference between R3, which passes entirely through the wall of the capillary tube, and R6, which passes perpendicularly through the middle of the capillary tube. Another fringe can be formed by the interference between a laser ray that enters the liquid medium at an angle, i.e. R5, and one of the non-refracted rays that passes through the air on top of the capillary tube, i.e., R2, and a different fringe can also be formed due to interference between R4, a ray that suffers total internal reflection at the glass/liquid interface, and another ray from the group that passes on top of the capillary tube, i.e., R1.



(a) (b) (c)

Fig. 2. (a) Example of a raw image of the transverse interference pattern obtained from one experiment; (b) and (c) Digitally processed images of the raw image in (a).

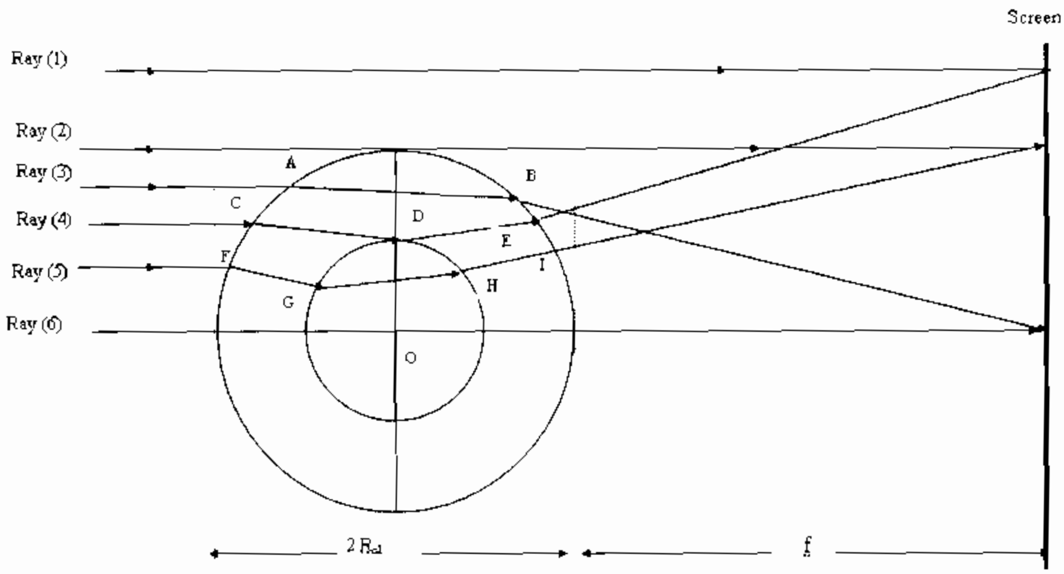


Fig. 3. Ray tracing of selected rays impinging on the upper hemisphere of the capillary tube. The locations of three possible fringes are shown on the screen at the right.

The reason that the interference fringes are bell-shaped has to do with two combined factors. The first is the curved surface area of the capillary tube and the second is the fact that the combination of the lenses in the setup creates a thin laser sheet whose rays are parallel along the y-axis only but not along the x-axis. Therefore, along the x-axis, the axis of the capillary tube itself, the laser sheet acts as a one-dimensional extended source whose rays travel through the media in a tilted, but symmetric, manner. This leads to the formation of tip, corresponding to the ray that is exactly perpendicular to the x-axis, and two symmetric wings, corresponding to pairs of rays having the same angle at each side of the perpendicular ray (in the x-z plane).

The optical paths of these six rays between the tangential lines l_1 and l_2 defined on Fig. 3 can be expressed in terms of the refractive indices of the air (n_{ai}), glass (n_{gl}), and liquid (n_{li}), without taking into consideration the phase change occurring at the media interfaces, as follows:

$$OPL_1 = 2\, n_{ai}\, R_{ou}\,, \qquad (1)$$

$$OPL_2 = 2\, n_{ai}\, R_{ou}\,, \qquad (2)$$

$$OPL_3 = 2n_{ai}R_{ou}(1-\cos\theta_A) + n_{gl}\,\overline{AB}\,, \qquad (3)$$

$$OPL_4 = 2n_{ai}R_{ou}(1-\cos\theta_C) + 2\, n_{gl}\,\overline{CD}\,, \qquad (4)$$

$$OPL_5 = 2n_{ai}R_{ou}(1-\cos\theta_F) + 2\, n_{gl}\,\overline{FG} + n_{li}\,\overline{GH}\,, \qquad (5)$$

$$OPL_6 = 2\, n_{gl}\,(R_{ou} - R_{in}) + 2\, n_{li}\, R_{in}\,, \qquad (6)$$

where R_{in} and R_{ou} are the inner and outer radii of the capillary tube, respectively, θ_A, θ_C, and θ_F are the incident angles at points A, C, and F, respectively. (Explicit equations for these optical path differences in terms of the angles of incidence can be found in Ref. 8).

Before an accurate analysis can be made the images in Fig. 2.a had to be digitally processed. This was done by using MATLAB-based software that was developed to conduct a search for the maximum and minimum brightness of the fringes and to report them as functions of position (x and y). This allowed highly contrasted constructive and destructive interference fringes to be exactly defined. Figure 2.b and c show the outcome of this digital processing on the transverse interference patterns of crude oils D and F.

The refractive indices of glucose solutions were determined for glucose concentrations of 10, 20, 30, 40 and 50% by weight. Figure 4 shows a plot of the refractive index as a function of the glucose concentration. The plot demonstrates an increase in refractive index with the increasing glucose concentration. The accuracy of these data points is based on the parameters that define the locations of the fringes which in turn correspond to displacements that are proportional to ½ λ, and is estimated to be 5×10^{-6}.

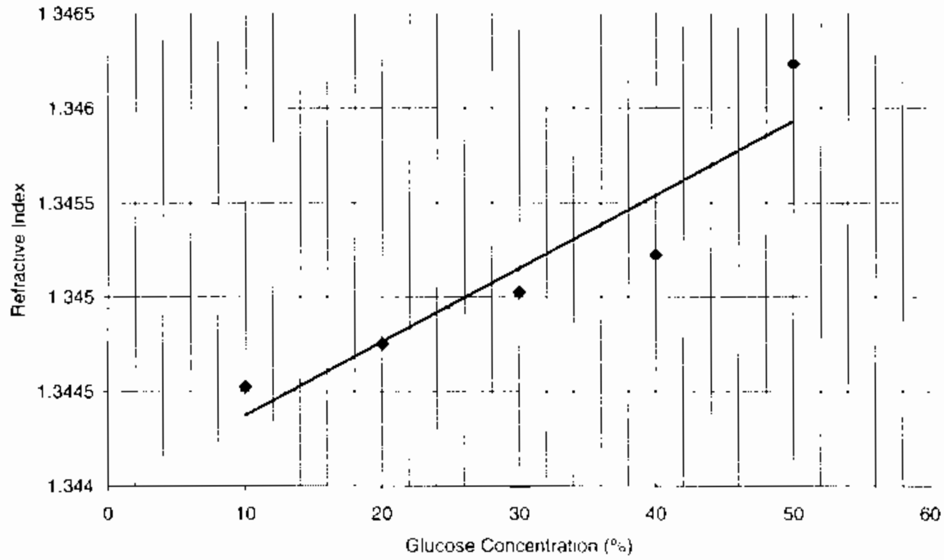


Fig. 4. A plot of the glucose solution refractive index as a function of the glucose concentration.

Conclusiou

In conclusion, our work represents an attempt to measure the glucose concentration in liquids in terms of its refractive index using a capillary tube interferometer. The test tubes filled with glucose solutions were illuminated by a thick He-Ne laser sheet and the resulting transverse interference patterns were projected on a screen whose plane was perpendicular to that of the laser sheet. The patterns showed a few numbers of bell-shaped fringes. The patterns are analyzed using a modified software package and the refractive indices of the glucose samples were determined with accuracy of 5×10^{-6} by measuring the deflection angles of the fringes and then by using Abbe's transformation. We obtained a good correlation between the refractive index and the glucose concentration in water. The high accuracy obtained makes this technique a valuable one for measuring the concentration in our samples. It may also prove useful as a tool for many other applications such as testing the glucose concentration and variation in blood.

Acknowledgment

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قياس تركيز السكر في السوائل بطريقة شريحة الليزر

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المستخلص. في هذة الدراسة، تم تطوير طريقة جديدة، بواسطة أحد المشاركين في البحث، لقياس تركيز السكر في السوائل و تدعى طريقة شريحة الليزر. هذة الطريقة المقترحة تقيس معامل الانكسار لسائل بدرجة عالية من الدقة. وقد استخدمناها لقياس تركيز السكر في الماء المقطر (من ١٠ إلى ٥٠%). وقد تم الحصول على ارتباط جيد بين معامل الانكسار و تركيز السكر. وسوف نستعرض تطوير الطريقة لتصبح جاهزة لقياس تركيز السكر في البلازما والدم غير المتجلط لأشخاص متطوعين. إذا كلل النجاح لهذة التقنية الجديدة فسوف تصبح جهازا جديداً لفحص الدم باستخدام الليزر.