

**Optics Letters**

**A Theoretical Analysis of a New Polarimetric Optical  
Scheme for Glucose Sensing in the Human Eye**

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Abstract: The challenging task of in vivo polarimetric glucose sensing is the identification and selection of a scheme to optically access the aqueous humor of the human eye. In this short communication an earlier approach of Coté et al. (G.L. Coté, M.D. Fox, and R.B. Northrop, "Noninvasive Optical Polarimetric Glucose Sensing Using a True Phase Measurement Technique," IEEE Transactions on Biomedical Engineering, vol. 39, no. 7, pp. 752–756, 1992) is theoretically compared with our new optical scheme. Simulations of the new scheme using the eye model of Navarro, suggest that the new optical geometry can overcome the limitations of the previous approach for in-vivo measurements of glucose in a human eye.

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Non-invasive detection of blood glucose levels in humans is an ambitious goal for managing diabetes. Several optical techniques have the potential of avoiding the disadvantages of the commonly used fingerstick method, and thus enable a more frequent determination of glucose levels.<sup>1</sup> In particular, polarimetry applied to the aqueous humor of the eye can be one such method.<sup>1-3</sup> This technique uses the property of glucose to rotate the plane of polarization of linearly polarized light according to the Beer-Lambert law:<sup>4</sup>

$$\alpha = [\alpha]_{\lambda, pH}^T \cdot \ell \cdot c \quad (1)$$

where  $[\alpha]_{\lambda, pH}^D = 4.562 \text{ degrees}\cdot\text{cm}^2/\text{g}$  is the specific rotation of glucose,  $\ell$  the optical pathlength through the sample and  $c$  the glucose concentration. Knowing the pathlength  $\ell$  inside the sample, the glucose concentration  $c$  can be calculated by observing the rotation  $\alpha$  that the glucose molecules induce to linearly polarized light. The aqueous humor in the anterior chamber of the eye has been shown to reflect glucose levels typically found in the serum.<sup>5</sup> Thus, an estimation of the blood glucose level can be obtained through a polarimetric measurement performed in the anterior chamber of the eye. Côté attempted glucose detection by passing a beam of linearly polarized light tangentially through the aqueous humor and by observing  $\alpha$  on the other end.<sup>3</sup> However, no commercial device exploiting this simple optical working principle has so far been realized. We believe the major reason for this could be that the accurate determination of optical path traversed by an incident light-beam ( $\ell$ ) remains critical due to the limitations imposed by the corneal shape.

In this letter, we start by briefly describing the approach of Côté<sup>3</sup> and then by introducing a simple axial geometry we will arrive at the new scheme that exploits the Brewster-reflection of circularly polarized light off of the lens of the eye.<sup>6-8</sup> These methods for optically accessing the aqueous humor are analyzed theoretically with respect to their geometric and electromagnetic properties of light propagation and applied to a simulation, implemented in Matlab®, based upon the eye model of Navarro.<sup>9</sup> We assume a linear, isotropic and homogeneous ocular media having an average refractive index.

The transmission and reflection Jones matrices reported in Eqs. (2) and (3) have been calculated by using the Fresnel equations for propagation between media of different refractive indices,

whereas, to describe the effects of glucose on the electric field we use the Jones matrix shown in Eq. (4).<sup>11</sup> In Eqs. (2) and (3),  $n_i$  and  $n_t$  are the refractive indices of the incident and traversed medium, whereas  $\theta_i$  and  $\theta_t$  are the incident and refractive angles, respectively. In Eq. (4), the arguments of the cos and sin functions represent the rotation angle due to glucose as shown in Eq. (1).

$$T = \begin{bmatrix} \frac{2n_i \cos(\theta_i)}{n_i \cos(\theta_t) + n_t \cos(\theta_i)} & 0 \\ 0 & \frac{2n_i \cos(\theta_i)}{n_i \cos(\theta_i) + n_t \cos(\theta_t)} \end{bmatrix} \quad (2)$$

$$R = \begin{bmatrix} \frac{n_t \cos(\theta_i) - n_i \cos(\theta_t)}{n_i \cos(\theta_t) + n_t \cos(\theta_i)} & 0 \\ 0 & \frac{n_i \cos(\theta_i) - n_t \cos(\theta_t)}{n_i \cos(\theta_i) + n_t \cos(\theta_t)} \end{bmatrix} \quad (3)$$

$$Rot = \begin{bmatrix} \cos([\alpha]_{\lambda, pH}^T \cdot \ell \cdot c) & \sin([\alpha]_{\lambda, pH}^T \cdot \ell \cdot c) \\ -\sin([\alpha]_{\lambda, pH}^T \cdot \ell \cdot c) & \cos([\alpha]_{\lambda, pH}^T \cdot \ell \cdot c) \end{bmatrix} \quad (4)$$

In the Navarro model the refracting surfaces of the human eye are described by centered quadric surfaces, which were fitted to the anatomical data. All surfaces show rotational symmetry along the optical axis so that the optical system of the eye shows rotational symmetry as well. The present work is limited to a simplified two-dimensional representation of the eye applying a cross-section of the Navarro eye that contains the optical axis. Thus, the quadric surfaces are reduced to quadratic relations of the form:

$$x^2 + (1+Q)z^2 - 2Rz = 0 \quad (5)$$

where the space variable  $z$  defines the optical axis and forms a two-dimensional Cartesian coordinate system with the space variable  $x$ .  $Q$  and  $R$  are the asphericity and the radius of curvature, respectively. Therefore, the first three curves of the eye profile, representing anterior cornea, posterior cornea and anterior lens, are given by:

$$z(x) = \frac{R - \sqrt{R^2 - (1+Q) \cdot x^2}}{1+Q} \quad (6)$$

where relevant parameters of the model are given in table 1.

In the tangential approach of Coté<sup>3</sup> to optically access the eye, incident linearly polarized light is passed tangentially through the aqueous humor, as shown in figure 1(a). Because of the refraction at the cornea, an incident light beam has to impinge the anterior cornea at a minimum distance  $x_{min}$  from the ocular axis to achieve this tangential path. Applying the simulation, this minimum distance is determined to be  $x_{min} = 5.45$  mm. Since the average cornea in an adult human eye has a diameter of only 10 to 11 mm, the tangential path is theoretically not possible to achieve.

The axial access (along the optional axis of the eye) to the aqueous humor of the eye could be an alternative approach. This is schematically shown in figure 1(b), in which a linearly polarized

incident light beam propagates through the cornea and the aqueous humor to the lens. Part of the beam is reflected back and propagates again through the aqueous humor, the cornea, and out of the eye, where it can be detected. Beam propagation of incident and detected light are both along the optical axis and therefore the arrangement for an experimental setup can be extremely simplified. Applying matrices in Eqs. (2) to (4) and assuming an incident linear polarization state perpendicular to the plane of refraction, the mathematical formulation can be expressed as:

$$\bar{E}_o = T_{ca} \cdot T_{hc} \cdot Rot \cdot R_l \cdot Rot \cdot T_{ch} \cdot T_{ac} \cdot \bar{E}_i = C \cdot \bar{E}_i \quad (7)$$

where

$$C = \frac{16 \cdot n_c^2 \cdot n_h \cdot (n_h - n_l)}{(n_c + 1)^2 \cdot (n_c + n_h)^2 \cdot (n_h + n_l)}$$

$\bar{E}_i = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$  and  $\bar{E}_o$  are the incident and resulting electric field,  $n_i$  are refractive indices and the subscripts  $a$ ,  $c$ ,  $h$ , and  $l$  stand for the media air, cornea, aqueous humor, and lens, respectively. While the incoming light beam propagates through the aqueous humor, its polarization state is rotated by glucose. At the lens, the beam is reflected and the  $s$ -component of the electric field undergoes a phase shift of  $\pi$ , while the  $p$ -component does not. This is equivalent to mirror the polarization state at the  $p$ -axis. Since the direction of rotation by glucose is constantly correlated to the direction of light propagation, the rotation of the polarization state is nulled when the reflected light beam crosses the aqueous humor again to leave the eye. This is expressed by Eq. (7), which is independent of glucose concentration. Therefore, this approach does not allow to measure the glucose concentration.

To circumvent this problem, we propose a new approach to access the aqueous humor of the eye. (see figure 2(c)) which works as follows: Part of the incident circularly polarized beam is reflected off the lens at the Brewster's angle ( $\theta_B$ ). According to data reported in table 1  $\theta_B$  can be calculated to be  $46.72^\circ$ . This reflection yields a purely linearly polarized reflected beam, orientated perpendicularly to the plane of refraction. On its way out of the eye the polarization state of this beam is rotated by the glucose molecules in the aqueous humor and thus carries the concentration information. Mathematically, this can be expressed as:

$$\vec{E}_o = T_{ca} \cdot T_{hc} \cdot Rot \cdot R_1 \cdot Rot \cdot T_{ch} \cdot T_{ac} \cdot \vec{E}_i = C \cdot \vec{E}_i \quad (8)$$

but this time,  $C$  is a  $(2 \times 2)$  matrix.

The distance between the entrance point of the incident beam from the ocular axis is  $x_i = 3.12$  mm, and the incident angle is  $\phi_i = 55.4^\circ$ . These values are not critical to achieve in a human eye. Using Eq. (8) we calculated the angular orientation of the polarization with respect to the perpendicular to the plane of refraction as a function of the glucose concentration. Figure 2 shows the results obtained from this simulation. The results show excellent theoretical linearity with the slope of  $-1.68 \cdot 10^{-2}$  mdegrees-dl/mg. The negative sign is due to dextrorotatory effect of glucose, i.e., the polarization state is rotated clockwise. Calculation shows an optical pathlength in the aqueous humor after the lens reflection of  $\ell = 3.63$  mm. Using this value in Eq. (1), the expected slope should amount to  $-1.66 \cdot 10^{-2}$  mdegrees-dl/mg. The difference between the slopes appears because of the refraction of the reflected beam at the cornea. As the  $p$ - and  $s$ -components of the electric field have different transmission coefficients, the polarization state performs a

small additional rotation at each interface. Both, the humor-cornea interface and the cornea-air interface introduce a clockwise rotation, in which the effect of the latter dominates.

Reflection off the lens induces a loss of optical signal that reduces the signal-to-noise ratio. To evaluate the relative output power, we neglected the absorption and scattering effects. From the electric field  $\vec{E}_o$  obtained by Eq. (8), the relative power of the output beam can be calculated summing the square of its two components. This procedure yields a relative power of the output beam of about two percent with respect to the power of the incident beam. For a wavelength of 632.8 nm and for an exposure time of 10 sec, ANSI standards<sup>12</sup> recommend a maximum optical power entering the eye of 200  $\mu\text{W}$ . Therefore, in this working condition, we could expect an output optical power of about 400 nW which, considering that the intensity signal should be mainly sinusoidal, could be detected by a low-noise detector with a signal-to-noise ratio better than 1000.

In conclusion, our scheme of identifying and selecting an optical path using Brewster reflection off the ocular lens is demonstrated theoretically. This optical geometry has the potential in becoming the basis for future instrumentation for in vivo and non-invasive polarimetric glucose sensing, through the eye.

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Table 1. Parameters of the Navarro eye model.

Surface	Radius (mm)	$Q$	Medium	$d$ (mm)	$n$
Cornea (anterior)	7.72	-0.26	Cornea	0.55	1.367
Cornea (posterior)	6.5	0	Aqueous	3.05	1.3374
Lens (anterior)	10.2	-3.1316	Lens	4	1.42

$R$  = radius of curvature  
 $Q$  = asphericity  
 $d$  = thickness of medium  
 $n$  = refractive index.

## Figure captions

Figure 1. Different schemes to optically access the aqueous humor of the eye: a) tangential path approach of Coté et al, b) axial alignment, c) new scheme, (this paper), using Brewster reflection off the lens.

Figure 2. Relative azimuth angle of the resulting light polarization for different glucose concentrations for the new scheme, which applies Brewster reflection off the lens (fig. 1(c)). The angles are reported with respect to the azimuth angle of polarization directly after the reflection off the lens ( $\theta = 90^\circ$ ).

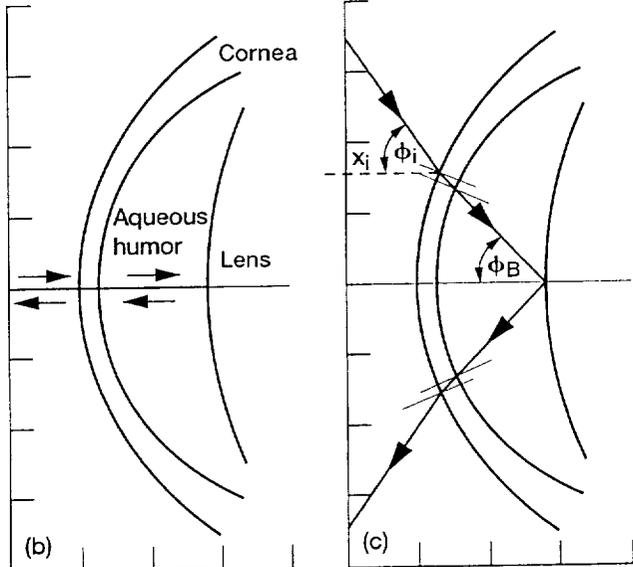
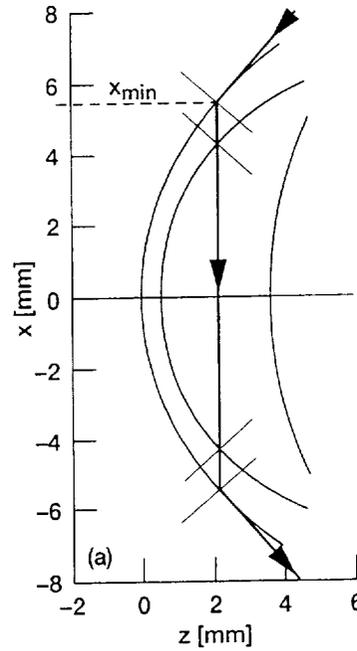


Figure 1.—Different schemes to optically access the aqueous humor of the eye: (a) tangential path approach of Côté et al, (b) axial alignment, (c) new scheme, (this paper), using Brewster reflection off the lens.

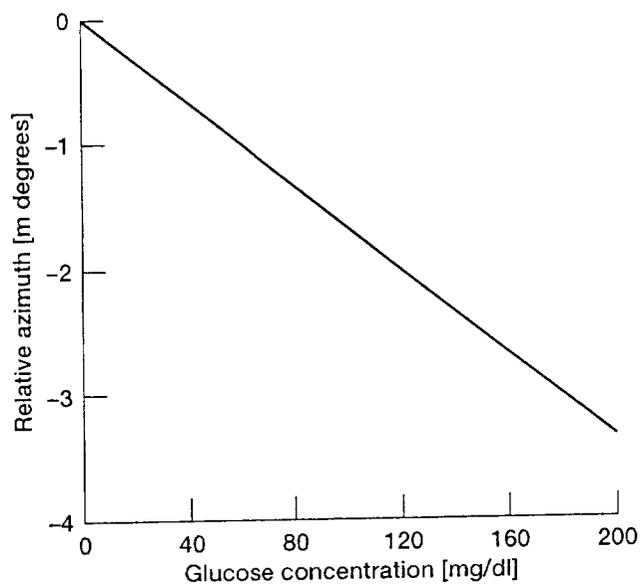


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