



Measurement of glucose concentration in a thin turbid medium by a transmitted Gaussian beam



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ABSTRACT

We show that it is possible to measure glucose concentration in a thin sample containing a turbid medium that simulates optical properties of biological tissue by recording the profile of a sinusoidal reflective grating by means of a laser Gaussian beam. We have described a similar approach for the case of transparent samples in a previous report. Although due to the turbidity of the sample the laser beam is scattered, we show that the probe beam is still sensitive enough to allow the detection of the grating profile. We describe how the changes recorded by the system, when profiling a region of the grating, allow us to determine the concentration of glucose in the turbid medium. We include experimental results.

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1. Introduction

Measurement of glucose concentration in thin turbid media representing optical scattering properties of biological tissue is of major importance. These samples are typically prepared by means of phantoms containing intralipid or nanospheres [1–5]. Techniques to determine glucose concentration in these samples can be classified mainly in two: by transmitted and/or reflected light. When reflective light is used, the techniques are mainly of the type of optical coherence tomography (OCT), refractometric methods and Raman spectroscopy polarization [6–10]. These techniques generally exhibit low sensitivity (signal-to-noise-ratio) thus, requiring high glucose concentrations [8], resulting in imprecise values that require statistical algorithms to improve the estimation of the measurements. In contrast, techniques that use transmitted light are mainly based on the photo-acoustic effect (PA) [9,11–16]. However, the PA signal can vary between measurements, meaning that differences of PA signal can be affected by other factors such as physiological change, temperature and mechanical stability of the sample [13].

In [17] we have described an optical technique for measuring glucose concentration in thin transparent samples. In this report we extend the referred optical technique to measure glucose

concentration in a turbid medium that simulates optical scattering properties of biological tissue.

Phantoms made of 1% intralipid solution are commonly used for experiments that simulate optical scattering properties of biological tissue [18–20]. Our sample has a higher concentration (2.5%) to demonstrate the usefulness of our pure optical technique; this concentration gives optical properties that fall within the range of human breast and skin tissue [21,22]. The maximum width of our sample may be up to 5 mm. Our technique consists in profiling a calibrated reflective grating using a Gaussian probe beam transmitted through the turbid sample. In the next sections we describe our proposal and give our experimental results.

2. Analytical description

Fig. 1 depicts the experimental setup which is based on the homodyne knife-edge detector (KED) [23,24] as done in our previous report for transparent samples [17]. For convenience we briefly describe KED.

The illuminating source is a non-polarized He–Ne laser beam ($\lambda = 632$ nm). The laser beam is directed towards a beam splitter (BS). The beam reflected by BS is transmitted through a focusing lens (L) and directed towards the surface of the grating through the turbid sample (S). The reflective grating is a commercially available holographic grating with a sinusoidal profile. The beam reflected by the grating propagates again through the sample and

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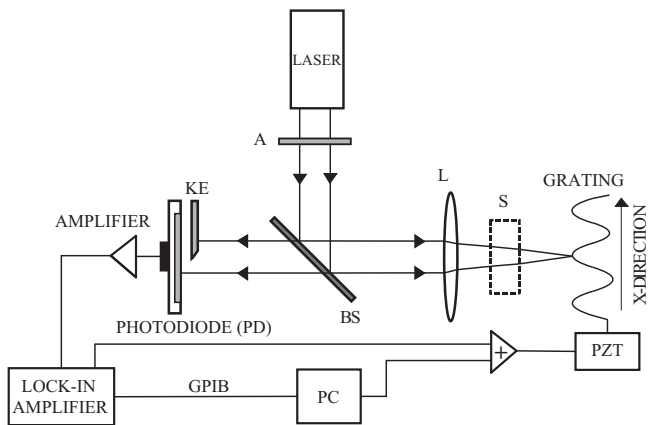


Fig. 1. Experimental setup of the KED.

through the focusing lens and is directed to a photodiode (PD) partially blocked by a knife-edge (KE). The turbid sample is in a glass container with dimensions $5.0 \times 5.0 \times 5.0$ mm. An attenuator (A) limits the incident power light at the surface under test to avoid damaging of the grating surface due to excessive heating. The focusing lens is a $100\times$ objective microscope, with 1 cm working-distance to allow the placement of the sample. Initially, the lens and the grating are adjusted to focus the Gaussian beam when the sample is a liquid transparent medium as described in [17]. When the transparent sample is replaced by the turbid one, the transmitted light is scattered; we show below that the lens is still useful under this condition, allowing us to detect the grating profile.

In [23,24] it is shown that, when the sample is not placed in the optical path, or equivalently, when the sample is a virtual one with refractive index equal to one the power collected by the photodiode is given by,

$$P_{out}(x_0, y_0) = -i \frac{8 P_0 \delta_0}{\lambda r_0^2} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \exp\left(-2 \frac{(x-x_0)^2 + (y-y_0)^2}{r_0^2}\right) \times \text{erf}\left(i \frac{x-x_0}{r_0}\right) \frac{\partial}{\partial x} h(x, y) dx dy, \quad (1)$$

where $h(x, y)$ represents the surface profile of the grating considered in a plane (x, y) , P_0 is the beam power which is constant. The semi-width of the Gaussian probe beam is represented by r_0 and focused at (x_0, y_0) , λ is the wavelength of the illuminating source. In Eq. (1) the partial derivative of the height distribution appears as a consequence of a first order expansion due to the vibration of the grating, with small amplitude δ_0 as described in [23,24]. $\text{erf}(\cdot)$ is the error function and $i = \sqrt{-1}$. It is possible to calculate the double integral in Eq. (1) in a closed form, taking into account that $h(x, y)$ represents a one-dimensional sinusoidal function with period Λ , we obtain,

$$P_{out}(x_0, y_0) = \frac{8\pi^2 \delta_0 P_0}{\lambda \Lambda} \exp\left(-\frac{\pi^2 r_0^2}{2\Lambda^2}\right) \text{erf}\left(\frac{\pi r_0}{\sqrt{2}\Lambda}\right) \left[h_0 \sin\left(\frac{2\pi}{\Lambda} x_0\right) \right]. \quad (2)$$

Eq. (2) demonstrates that the power collected by the photodiode is proportional to the local vertical height of the grating, the term in square brackets. Thus, in order to record the vertical profile over a determined region, it is necessary to perform a linear scan.

A plot of Eq. (2) for the two different gratings used in our experiments, 600 and 300 lines/mm is depicted in Fig. 2 for a constant local vertical height.

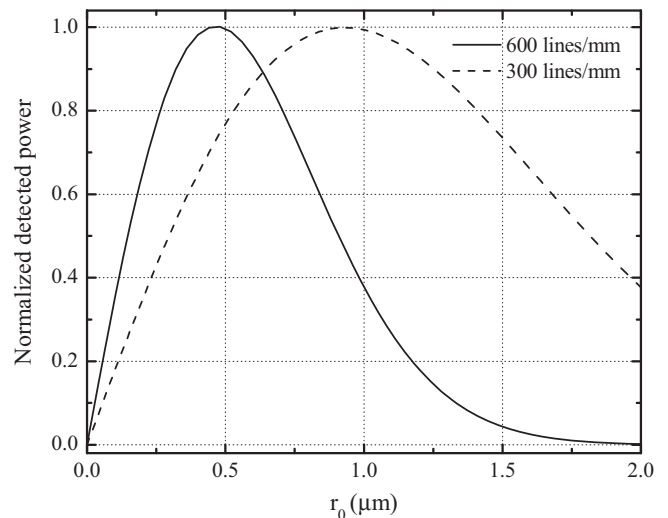


Fig. 2. Normalized detected power as a function of r_0 according to Eq. (2) for gratings 600 and 300 lines/mm.

It can be noticed from Fig. 2 that for both gratings the amplitude of the detected power decreases for $r_0 > 1 \mu\text{m}$. In our experiments larger semi-widths are attained.

Eq. (2) is the key of our proposal; however, before describing how it is applied to determine glucose concentration in turbid media, it will be useful to refer to our previous report [17] for measuring glucose concentration in thin transparent samples. In the referred report it is described that a linear relation between the semi-width and the concentration is expected for low concentration values, as the beam is well focused, and the surface under test is in the Rayleigh region where small changes result linear. Experimentally, it was shown in the reference, that for a thin transparent sample (< 5 mm) increasing glucose concentration (c) of the sample results in a linear increase of r_0 ; this linear relation holds well in a range up to 10 g/dl. It should be noticed however, that a linear function between r_0 and c , does not imply a linear relationship between the detected power and c as stated by Eq. (2). When a turbid media substitutes the transparent media, as it will be seen below, a linear relationship is found, contrary to the transparent case.

The measuring procedure is as follows. First, the system is adjusted to best focusing conditions with a sample with zero glucose concentration (smallest r_0 value). Then, a scan of a region of the grating is recorded. Next, the same region of the grating is recorded for different glucose concentrations. As indicated, increasing c in the sample results in a linear increase of r_0 ; thus, due to the exponential term in Eq. (2) the heights of the vertical profiles recorded will decrease. This effect can be appreciated in the plot of Fig. 2.

Eq. (2) further shows that the collected power is also a function of the period of the grating Λ .

Its effect can be visualized in the following way. The system is first adjusted to a minimum r_0 for $c=0$. Then, as indicated, as in our case $r_0 > 1 \mu\text{m}$, the recorded profiles will exhibit maximum height; increasing c will result in reducing the vertical heights of the recorded profiles. Let us now consider two particular cases of reducing the vertical profiles to 75 and 50% with respect to the case $c=0$. The 600 lines/mm grating will require defocusing values of 1.08 and 1.19 μm respectively; these values correspond to samples with concentrations of 0.3 and 0.9 g/dl respectively. In contrast the grating of 300 lines/mm will require higher defocusing, 1.47 and 1.81 μm , corresponding to higher concentrations 4.5 and 7.5 g/dl [17]. Table 1 summarizes these results.

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