Angular measurements of light scattered by the glucose containing biological tissues and their phantoms

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Abstract. Method of optical polarimetry is well known, but earlier it was mainly used to low scattering media. In this paper we consider the possibility of measuring the glucose concentration by detecting polarization of the backscattered laser light. Dependencies of the degree of polarization and of the optical rotation on the registration angle were received. Furthermore, the significant impact of the wavelength and the power of probing beam on the degree of polarization was shown.

1. Introduction
The development of noninvasive and continuous or repeated methods of monitoring blood glucose concentration is one of the priorities of modern biomedical diagnostics. Due to the urgency of the problem, a number of methods of non-invasive measurement of glucose concentration in the blood are developing. However, none of the existing methods has not yet reached the stage of commercial production, so research in this area continues.

Recently, several key areas in the optical measurement of glucose concentration in tissues have seen progress, such as: infrared spectroscopy; Raman spectroscopy, polarimetry and fluorescence spectroscopy. Furthermore, the preliminary positive results were obtained by the methods of optoacoustics and optical coherence tomography [1]. One of the most perspective methods is polarimetry of backscattered light. Polarimetry has been used for investigation the optically homogeneous mediums, earlier polarimetric measurements in turbid media considered to be impossible. However, a number of researchers [2, 3] have shown that laser light backscattered by turbid media (which includes most of biological tissues) can have sufficient degree of polarization for the corresponding measurements. Furthermore it is known that change in the glucose concentration in biological tissues affects their optical properties. One of the dominant effects is reducing of the scattering coefficient with increasing glucose concentration. The scattering coefficient of biological tissue is determined by the difference in refractive index of the extracellular fluid and the cellular membranes. Increasing the concentration of glucose in the extracellular fluid leads to an increase its refractive index, which in turn reduces the total scattering coefficient of the tissue. As a result, the photon path length varies, and hence the polarization of the scattered light is also changed. In connection with this, we determined the objectives of this work: to develop a method of measurement of glucose concentration in biological tissue and their phantoms based on turbid polarimetry.
2. Methodology

The light entering a turbid medium, including the majority of biological tissues, is repeatedly scattered and absorbed, which results in the broadening of the laser beam and its attenuation during propagation through the medium. Volume scattering is the main cause of the significant diffuse light propagation in the backward direction [4]. For each observation point of the scattered light at the tissue surface, the ensemble of the effective optical paths that light travels from the source to this point was characterized by different optical paths. The corresponding trajectories occupy a spatial region, having a «banana» shape. The analytical expression for the photon path distribution of such shape was derived [5]

\[ P(x, y, z) = \frac{z^2 \exp\left[-k((x^2 + y^2 + z^2)^{3/2} + ((r - x)^2 + y^2 + z^2)^{3/2})\right]}{[x^2 + y^2 + z^2]^{3/2}[(r - x)^2 + y^2 + z^2]^{3/2}}, \]  

(1)

where the source is placed at the origin (0, 0, 0) and the detector is placed at (r, 0, 0), x and y are directed along the surface, z – normal to the surface, \( k = \sqrt{3\mu_a^s \mu_a^r} \), \( \mu_a^s \) – absorption coefficient, \( \mu_a^r \) – reduced scattering coefficient, \( \mu_s^r = \mu_s (1 - g) \), g – anisotropy factor. Particularly, the most likely path (center line of the “banana” region) in the case of the weak absorption limit, \( kr < < 1 \), can be defined as

\[ z_0(x) \approx \left( \frac{1}{8} \left( (x^2 + (r - x)^2)^2 + 32x^2(r - x)^2 - x^2 - (r - x)^2 \right)^{1/2} \right)^2. \]

(2)

At \( x = r/2 \), the central line of the “banana” region reaches a maximum depth of \( z_0^{\text{max}} \approx \frac{\sqrt{2}r}{4} \). For the strong absorption limit \( kr >> 1 \),

\[ z_{\text{med}}(x) \approx \left( \frac{2x(r - x)}{(3\mu_a^s \mu_s (1 - g)r^2)^{1/2}} \right)^{1/2}, \]

(3)

reaching the maximum value \( z_{\text{med}}^{\text{max}} \approx \sqrt{r/2k} \) at \( x = r/2 \).

On the other hand, if we consider the vector nature of the light and characterize the photon by its Stokes vector \( S = (I, Q, U, V) \), then the motion of such a photon in the scattering media can be described by a sequence of variation in the Stokes vector associated with the photon. Each scattering event is accompanied by a variation of the Stokes vector for this photon. The new Stokes vector \( S_{n+1} \) can be defined as

\[ S_{n+1} = M_\varphi(\theta)M_\mu(\phi)S_n, \]

(4)

where \( M_\varphi(\theta) \) – Muller matrix of the scattering particle, \( M_\mu(\phi) \) – matrix, that describes the rotation of the Stokes vector around the axis, specifying the direction of the photon’s propagation before interaction [6]. Thus, the plane of polarization of the photon is rotated. Since this rotation is relatively random, the detected photon will be randomly polarized and, hence, the detected light will be partially depolarized, where the degree of polarization will decrease with the increasing order scattering.

The change in the concentration of glucose in turbid media leads to a number of processes, that affect its light-scattering properties, herewith, the scattering coefficient and the polarization of the scattered light vary. Below, there are the dependencies of the refractive index (5), scattering coefficient (6) and the anisotropy factor (7) on the glucose concentration in the intralipid (sterile fat emulsion for intravenous infusion) solution, which along with suspension of the microspheres and the milk solution used to simulate biological tissues [7].
\[ n = 1.325 + 1.515 \times 10^{-6} \cdot C_{gl}, \]  
\[ \mu_s = (1 - 0.0022 \cdot C_{gl} / 18) \cdot \mu_{sm}, \]  
\[ g = (1 + 0.000007 \cdot C_{gl} / 18) \cdot g_m, \]

where \( C_{gl} \) [mg/dl] – glucose concentration, \( g_m \) \& \( \mu_{sm} \) – scattering anisotropy factor and scattering coefficient of intralipid solution, respectively, before the glucose is added. Apparently, the increase in the glucose concentration of such media leads to a decrease in the difference between the refractive index of scatterers and the media \( \Delta n = n_s - n_{medium} \), which in turn will decrease the reduced scattering coefficient: \( \mu_s^{'} \downarrow \).

On the other hand, the addition of glucose to human blood leads to a slightly different effect. The optics of whole blood is mainly determined by the optical properties of the red blood cells and plasma. Increasing the concentration of glucose in the blood leads to an increase in the reduced scattering coefficient \( \mu_s^{'} \uparrow \). This effect is related to the penetration of glucose into the red blood cells and its reaction with hemoglobin inside cells [8].

Furthermore, glucose, due to its chirality, has the ability to rotate the polarization plane of the linearly polarized light passing through the solution. The angle of rotation is directly proportional to the concentration of the optically active molecules, the length of the interaction layer and a constant of the substance, called the specific rotation. The resulting angle is defined as

\[ \varphi = \alpha_{\lambda} L C_{gl}, \]

where \( \alpha_{\lambda} \) has the dimension [deg•dm\(^{-1}\)•g\(^{-1}\)•l] and represents the specific rotation at wavelength \( \lambda \), \( L \) – length of the sample in dm, \( C_{gl} \) – concentration in g/l. This angle becomes significant, due to the fact that the photon pathlength in turbid media is considerable (1).

Thus, the growth of the glucose concentration in turbid media will alter the polarization of the scattered light, as a result of changing the scattering coefficient and the optical chirality of the glucose molecules. Moreover, it was shown in the Ref. 9 that for different detection angles the optical rotation and the degree of polarization would be different for the same glucose concentration. The experimental study [9] has shown that in the forward direction glucose chirality makes the greatest contribution to the optical activity, and in other directions optical activity is dominated by scattering effects. Therefore we can discuss the optimal choice for the detection angle of the scattered light from the standpoint of the maximum sensitivity to changes in glucose concentration.

3. **Experimental setup**

The spatial distribution of the light backscattered by turbid media were investigated. To conduct this study we developed a laboratory set (figure 1), consisting of: laser with a polarizer fixed on it, and the cuvette or a holder for samples, photodetector, which position could change relative to the direction of probe beam, rotating analyzer was installed on the photodetector. Furthermore, the significant impact of the wavelength and power of probing beam on the degree of polarization was noticed. Therefore, a semiconductor laser with a wavelength 650 nm was used as the light source, which power was regulated to achieve a maximum degree of polarization.

Experiments were conducted on solutions of milk, human blood and the human finger pad. The cow's milk was used for creation of the human skin phantom. In milk the fat globules and colloidal protein particles (casein micelles) act as scatterers. Such media can be used as a biological tissue phantom, as is strongly scattering with scattering anisotropy factor \( g > 0.7 \), i.e. close to tissues.
4. Results
Experiments with solutions of milk and human blood shown that the dependences of the parameters of the scattered light on the registration angle $\theta$ are symmetric with respect the probe beam axis. The figure 2 shows the dependences of the light intensity (voltage on the photodiode), degree of polarization (DOP) and optical rotation of light scattered by milk solution (1:4 with distilled water) and solution of human blood (1:1 with NaCl solution) on the registration angle for different glucose concentrations in the solutions.

The experimental results show that the intensity (figure 2 a, d) and degree of polarization (figure 2 b, e) of the light decrease with increasing angle $\theta$, and the optical rotation increases (figure 2 c, f) for both samples. Increasing the concentration of glucose causes a slight change in the intensity for the solution of milk (figure 2 a) and a substantial increase for the solution of human blood for all registration angles (figure 2 d), which is the result of reduced scattering coefficient increased. The degree of polarization evenly decreases with increasing glucose concentration for milk (figure 2 b), while for the blood the dependence is more complex (figure 2 e). The optical rotation increases in the case of milk for all registration angles (figure 2 c) and vice versa decreases for the blood at all angles (figure 2 f), but the most significant absolute change for both samples was observed at the minimum values of $\theta$, i.e. closest to the opposite direction.
Figure 2. Angular dependences of the characteristics of light backscattered by the solution of milk (a-c) and solution of human blood (d-f) for two glucose concentrations: voltages on the photodiodes versus registration angle \( \theta \) (a, d), degree of polarization versus registration angle \( \theta \) (b, e), optical rotation versus registration angle \( \theta \) (c, f). The symbols are data points; the lines are guide for the eye.

Preliminary measurements on the human finger pad shown that the angular dependences of the intensity, the degree of polarization and optical rotation were asymmetrical relative to the axis of the probe beam and were relatively complex function of the registration angle. However, the greatest degree of polarization was observed closer to the opposite direction as for the samples described above, indicating the prospect of such method of measurement for \textit{in vivo} experiments.

5. Conclusions

In this paper, the angular dependences of the parameters of backscattered polarized light in the glucose containing biological tissues and their phantoms was considered. In the experiments we studied a 20\% solution of milk, a 50\% suspension of human blood and the skin on the human finger.
The dependencies of the intensity, degree of polarization and of the optical rotation on the registration angle were received for different glucose concentrations using created experimental setup. The experimental results shown that the angles closer to the opposite direction are most preferred for measuring the parameters of polarized light scattered by biological tissues. The obtained results should be considered when creating a non-invasive blood glucometer based on optical polarimetry. An example of such a sensor is the differential optical polarimeter, which working principle and test results were described in [10, 11].

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