ISSN 1846-6168 (Print), ISSN 1848-5588 (Online)
https://doi.org/10.31803/tg-20210212112152

Original scientific paper
Received: 2021-02-12, Accepted: 2022-03-28

Analyzing the Human Blood Glucose Level Trend (Up or Down) by Using Optical Polarization

Ercan Mengüç*, Selçuk Helhel

Abstract: Large amount of people having diabetics in the world, and it is increasing very rapidly. Diabetics should to check their blood glucose level at least four times a day. When controls are not done regularly, risk of hypoglycemia and hyperglycemia may arise. There are ongoing researches for developing non-invasive methods as an alternative to finger piercing, which is the most commonly used and painful method for patients. In this study, although a physical glucometer design has not been completed yet, it has been demonstrated which wavelength ranges and which parameters can be used for non-invasive device. Most importantly an empirical relationship has been established between the level of blood sugar and de-polarization disturbance seen in circularly polarized light. The proposed equation can estimate the blood glucose level based on de-polarization information with an average error rate of 1%.

Keywords: blood glucose; depolarization; glucose; non-invasive; polarization of light; tissue

1 INTRODUCTION

In diabetes, pancreas cannot produce enough insulin or produced insulin cannot be used effectively. Diabetes is divided into two categories as Type-1 and Type-2. Type 1 diabetes (previously known as insulin-dependent) is characterized by insufficient insulin production and requires daily need of insulin. Type-2 diabetes have a combination of insulin secretion disorders and insulin resistance. Type-2 represents more common diabetes disease.

Hypoglycemia and hyperglycemia are two negative sides of diabetes that need to be avoided. Those can be under control by regular measurements. Diabetics have to keep their blood sugar levels under control. To achieve this, patients must measure their glucose level up to 6 times a day. There are three different methods to detect blood glucose level. These are invasive, minimally invasive and non-invasive. The most widely used method is an invasive one and in that method some blood is taken out of the body with a needle and measurements are made. This way comparatively expensive and they are not practical for kids' usage. In second method; there is still a needle which also embedded in the patient's body. At third method measurements are taken without taking blood out of the body. Therefore, patients do not feel pain.

It is a known fact that the light is a special form of an electromagnetic wave. Light that falls on human body is absorbed, scattered, reflected or transmitted. Mentioned light events contain information about medium.

Increased glucose ratio makes blood more homogeneous and the polarization information observed from medium is high enough. That homogeneity causes less scattering and absorption events; this situation typically results in stable polarization information. It is proved/shown by using analysis and graphics at section 3. Proposed empirical model can predict blood glucose levels concerning the polarization distortion with an average error rate of 1%.

Different methods and techniques on non-invasive glucose level measurements have been studied during the past. But there is no commercial product has produced in market yet. According to the literature and market review, studies are mostly at the beginning phase [1]. In literature; one may find optical techniques [2-4]; MIR (middle infrared), NIR (near-infrared) and Raman spectroscopy techniques [5-7]; techniques using electromagnetic field measurement [8-10]; bio-impedance technique [11, 12]; photo-acoustic method [13]; non-enzymatic sensor applications for determining glucose level [14]; and techniques based on polarization measurements [15-17]. All methods have problems such as insensitivity to glucose measurement and accuracy.

Before analysis, optical properties of human skin and blood are added to optical design platform. All simulations are performed on optical simulation program. During simulation, changes in the flow rate, fluidity and temperature changes of the blood are ignored. In real life, these parameters must be studied and checked furthermore, since these parameters vary from person to person. Parallel to high technological developments, it is expected to that this technology will be miniaturized and will start to be used by patients. Most important aspect of the proposed method makes it possible to predict whether or not the diabetic patient trends of hypoglycemia or hyperglycemia. Furthermore, it is possible to produce pre-warning alarm for patients if the predetermined values are reached.

Details of polarization techniques are given in Section 2, design methods and modeling are in Section 3, results are in Section 4 and conclusion is given in final section.

2 POLARIZATION INFORMATION

When any optically active sample is exposed to a polarized light, some rotational changes occur in polarization information. Rotational change is called optical de-polarization. These changes (optical depolarization) can be measured by polarimeter and provide important information about chemical and physical structures of substances [18, 19]. Change of polarization information from circular to elliptical state allows us to calculate the de-polarization ratio. So we can estimate the trend of blood glucose level either increasing or decreasing. For this aim, model is generated in the simulation platform. In simulation, optical

properties of both blood and skin are added in the model. Circularly polarized light at 600-800 nm wavelength region is sent to the modeled biological tissue and elliptical polarized light is obtained on the other side of the tissue.

Fig. 1 shows the structure of a typical polarimeter. It consists of two polarizers such that one of them is stationary and the other one is rotating. When polarized light passes through an optically active substance, initial polarization state changes rotationally. These rotational change indicates that activity of the optical substance. This activity allows us to determine the molecular size, concentration and purity of the substances.

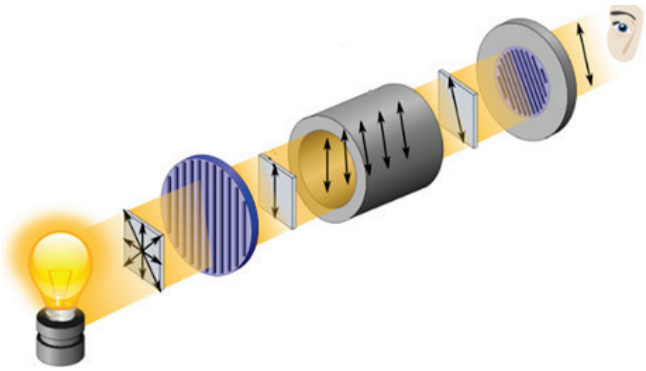

Figure 1 Polarization measurement

Most biological tissues have an anisotropic structure. Because tissues have organic and inorganic molecules with different refractive index values in same environment. Different refractive indices are caused important property called birefringence that distorts polarization information. De-polarization information manifests itself as a phase delay at tissue output. 90% of the phase delay in tissues with a depth of several hundred micrometers is thought to be the result of birefringence.

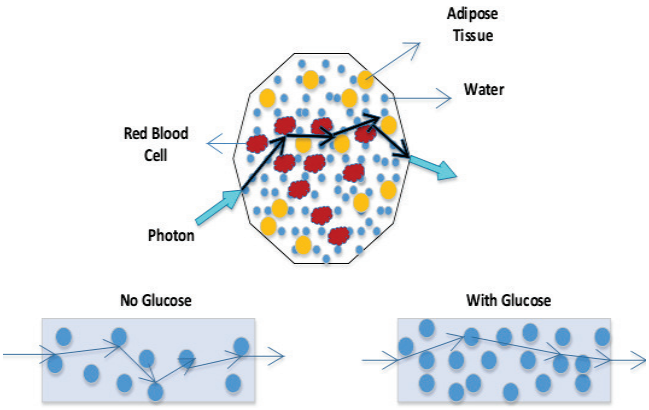

Figure 2 Photon movement

In Fig. 2, it is possible to see how glucose changes the propagation of the light. It is predicted that as the glucose level in the environment increases, both the possibility of light scattering and the optical path decrease, and therefore absorption event in environment decreases. The resulting de-polarization rate increases due to poor absorption. It means that polarization information is preserved. Therefore, if glucose ratio is high enough, de-polarization event within the tissue will be poor and polarization information at tissue outlet will be quite similar to the original polarization information. Mentioned situation is proved by simulation analysis and showed in section 3.

Blood is a structure consisting of plasma and blood molecules. Plasma consists of water, proteins, glucose, and other water-soluble substances, and it constitutes approximately 55% of blood. Although there is an increase in glucose level in blood plasma, hemoglobin concentration, absorption coefficient and refractive index values of blood molecules stay constant. Increased glucose level in blood only changes the density of plasma [21]. The most important change here is the reduction of the refractive index difference between blood molecules and blood plasma. Thus, possibility of scattering and absorption events in blood is reduced. That's why, obtaining polarization information will be easier [21-23].

First step to calculate the de-polarization information is creating simple models of biological tissues. All data is obtained from literature to create models of both human blood and skin. While creating the models, blood flow rate, viscosity and temperature parameters were neglected, and the values of the healthy person dates are used. Polarization measurements of the light passing through the tissue are made in the optical design program. Polarization analysis functions and Stokes parameters of the program are used. Finally, biological model is illuminated with a circularly polarized light wave and an elliptical polarized light wave is obtained at the other side of tissue.

Polarization ellipse used in the optical design program takes into account only E_x and E_y components, while neglecting the E_z component. Polarization ellipse is shown in Fig. 3.

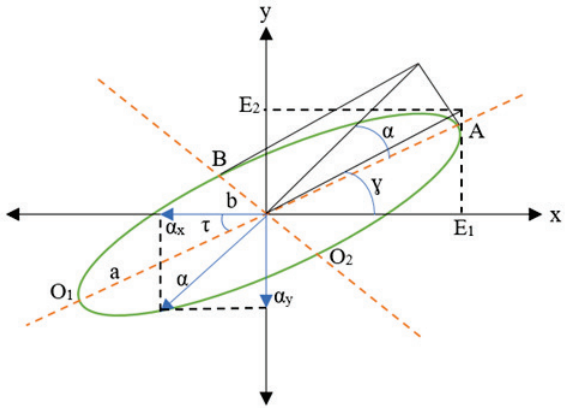

Figure 3 Polarization ellipse

After the polarized light wave is sent to the optically active substance simulator runs the polarization state analysis feature by investigating each photon present in the light. Depending on the type and concentration of the molecules circular polarization information is de-polarized and converted to elliptically polarized light.

Degree of elliptic polarization is calculated by using Eq. (1) and Eq. (2). Amount of rotation in conversion from

circular polarization to elliptical polarization varies depending on the molecular concentration of the particles. For any de-polarization event in optically active substances, the ɣ value shown in Eq. (1) and the δ value in Eq. (2) are the best coefficients used to express the polarization state. Alternatively, α and τ can also be used to describe the polarization state [2].

$$\gamma = \frac{1}{2}\cos^{-1}\cdot\left[(\cos 2\alpha)\cdot(\cos 2\tau)\right], \tag{1}$$

$$\delta = \tan^{-1}\left[\frac{(\tan 2\alpha)}{(\tan 2\tau)}\right]. \tag{2}$$

3 MODELLING AND TESTİNG

600-800 nm wavelength region is considered to be suitable for optical estimation of blood glucose level. In the mentioned region, changing in plasma-derived de-polarization information is negligible and the initial polarization information is largely preserved. Thus, changes in this region are only expected due to glucose levels. The reasons for choosing this region are given below;

1) Absorption and scattering coefficients arising from blood molecules and plasma in the 600-800 nm region are low and the anisotropy factor is in the range of 0.98 and 1.
2) Hemoglobin covers approximately 40 - 50% of the total blood amount and the absorption value from hemoglobin is low in this region.
3) Refractive index mismatch value of hemoglobin between glucose and other molecules is low. In addition, after about 600 nm the refractive indices of Oxy and de-oxy hemoglobin are approximately equal and it's overlapped. This shows that the saturation of blood with oxygen will not affect the measurement results.
4) Approximately 50-60% of blood consists of plasma. ~90% of plasma consists of water. In this region, water-related absorption and scattering events are low.
5) Low absorption coefficients caused by epidermis layer.

Optical coefficients of human skin and blood are obtained from the literature and inserted to the optical design program. The aforementioned expectations have been satisfied. Absorption and scattering parameters from blood molecules and plasma are less in this region. Besides, the anisotropy factor is observed as 0.98-1 in the 600-800 nm range. Therefore, light in this wavelength region will mostly be affected by glucose levels.

The performance tests are given to prove either the mentioned wavelength region is suitable or not. When a circularly polarized light at 100 nm wavelength is sent through an optical environment where there is no biological tissue in the model, there is no depolarization event (100% transmission) at the outlet (Fig. 4).

Optical properties of biological tissues are added into the model for observing their effects, and transmission ratio drops down to 12.86% concerning initial conditions (Fig. 5). Fig. 5 shows that the photon has lost its energy by encountering to high absorption and scattering at the specified wavelength.

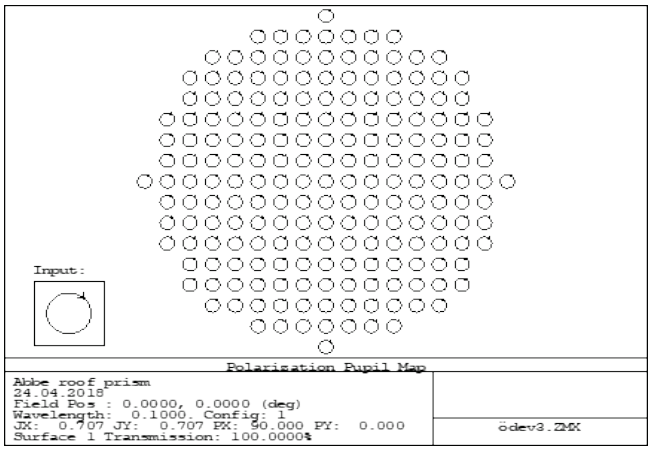

Figure 4 Circularly polarized light at 100nm wavelength

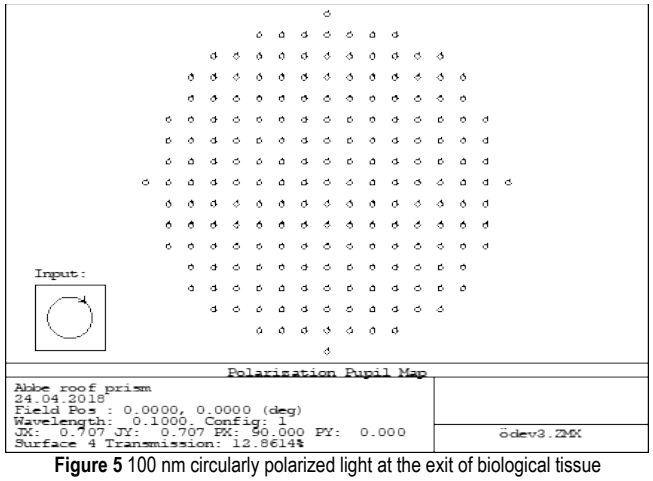

Figure 5 100 nm circularly polarized light at the exit of biological tissue

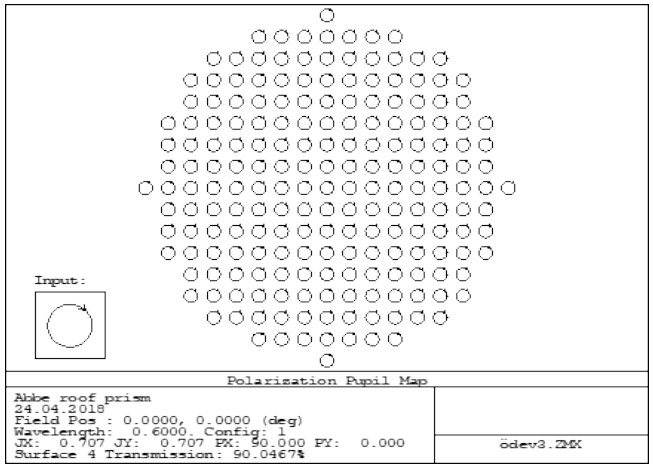

Figure 6 600 nm circularly polarized light at the exit of biological tissue

For the next step, applied wavelengths are changed to 600 nm and 800 nm. At 600 nm and 800 nm, transmission values increase up to 90% and 94%, respectively (Fig. 6 and Fig. 7). These results prove the accuracy of the items described at the beginning of Chapter 3 and tell us we may

use this wavelength interval. As obtained from Fig. 6 and Fig. 7, de-polarization level in this wavelength region is low and polarization information is high enough to make the analysis. In this way, changes in glucose level can be observed more easily only in this region. Other components that can be mask the change in the polarization information that is not sourced by glucose are less in mentioned region.

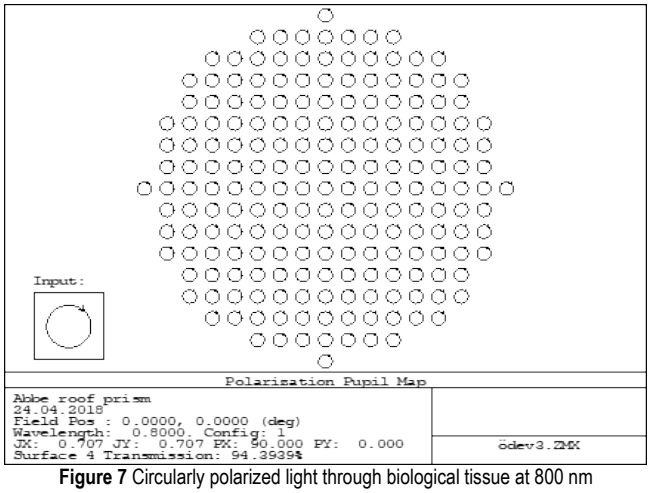

Figure 7 Circularly polarized light through biological tissue at 800 nm

Finally, by combining all results 600-800 nm region seems suitable for operating wavelengths. Afterward, de-polarization information will obtain with respect to different glucose level.

4 RESULTS

By using optical design program, polarization information that transmitted through the tissue at different glucose ratios in the 600-800 nm region is measured. Eq. (1) and Eq. (2) are used to calculate degrees of polarization.

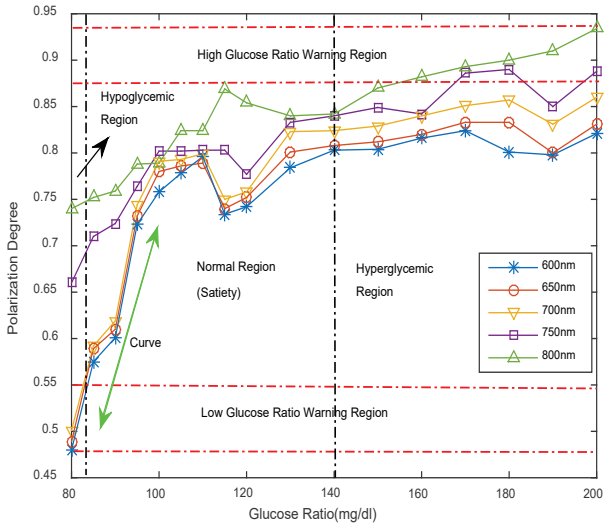

Figure 8 Polarization degree for different wavelength concerning different glucose level (80-200 mg/dl)

Finally, different degrees of polarization state are obtained for different wavelengths. Fig. 8 shows the change in polarization degree according to five different wavelengths and varying glucose level. The treated wavelengths are 600 nm, 650 nm, 700 nm, 750 nm, and 800 nm. Normally, glucose level above 120 mg / dl is considered high, especially in Type-1 patients, this value can be up to 180 mg/dl. Therefore, this expanded region can be used to derive a mathematical model. From these graphs, it is seen that the wavelengths of 600 nm, 650 nm, and 700 nm are very close to each other. And it can be established linear relationship for a glucose level between 80 mg/dl and 100 mg/dl (Green line in Fig. 8).

Tab. 1 demonstrates average mean error and median error of five different wavelengths. Minimum errors of the median specified in Tab. 1 are shown in bold. Minimum errors are at 600 nm, 650 nm, and 700 nm. With help of Table 1, 600 nm, 650 nm, and 700 nm are grouped for generating mathematical models. Also smoothing function is applied on plots. The proposed mathematical model is expressed in Eq. (3). Coefficients of Eq. (3) and their meanings are tabulated in Tab. 2.

Table 1 Calculated Mean and Median Errors

Wavelength	Mean (rmse)	Median (rmse)
$error_{600\ nm}$	0.0441	0.0275
$error_{650\ nm}$	0.0351	0.0169
$error_{700\ nm}$	0.0259	4.85e-04
$error_{750\ nm}$	0.0344	0.0586
$error_{800\ nm}$	0.0696	0.0935

$$P(x) = a_1 \cdot \mathrm{e}^{-\left(\frac{x-b_1}{c_1}\right)^2} + a_2 \cdot \mathrm{e}^{-\left(\frac{x-b_2}{c_2}\right)^2}. \quad (3)$$

Table 2 Coefficients of Eq. (3)

x	Glucose Ratio (mg/dl)	SSE	0.002514
$P(x)$	Polarization Degree	R-square	0.9851
a_1	0.8646	Adjusted R-square	0.9783
a_2	0.2053	RMSE	0.01512
b_1	179.7	b_2	102.2
c_1	115.4	c_2	27.21

In Fig. 9, measured values and the response of the proposed model are shown together. It is seen that proposed model is quite sensitive and has the potential to respect the glucose level [24, 25].

In addition, an equation is created in range where the glucose level is 80-100 mg/dl only to prevent situations caused by the hypoglycemic state. This equation is showed at Eq. (4). Because, as seen in Fig. 8 (green line), this region has a linear relationship with the glucose level and degree of polarization. A sensor using this relationship can be designed much more easily.

$$y = 0.0144 \cdot x - 0.65 \quad (4)$$

where x = glikoz oranı and y = polarizasyon derecesi.

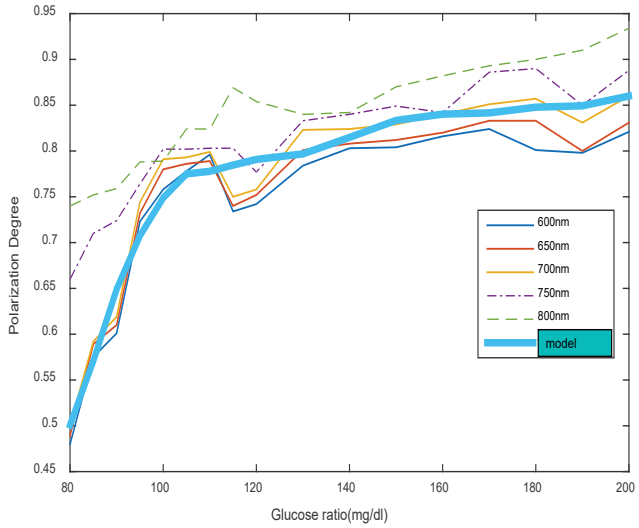

Figure 9 Fitting curve obtained from the median curve of the sum of curves of different glucose and wavelengths

5 CONCLUSION

In this study, estimation of human glucose level is investigated. By using polarization techniques light transmitted through modelled biological tissue is examined. Skin, blood, and glucose models are used in the optical design program. Skin, blood, and glucose are created by using optical coefficients (absorption, scattering, reflection, transmission, and anisotropy) obtained from various sources in the literature.

Optical method is proposed to estimate the glucose level in human blood and a potential working wavelength window is proposed. This window is between 600 to 700 nm. It is shown by simulation results that window is suitable. In order to determine this window most accurately, all components of blood and skin such as hemoglobin, melanin, skin, and plasma must be taken into consideration. Effects of these components can be examined in further academic studies.

A mathematical model predicting the trending tendency of increasing and decreasing glucose levels is proposed. The proposed mathematical (empirical) model can predict blood glucose levels despite the polarization distortion with an average error rate of 1%. This proposed mathematical model makes it possible to create a monitoring and warning system for diabetic if it is integrated with sensor. It will be possible to predict whether the diabetic patient tends hypoglycemia or hyperglycemia. So, it is possible to produce pre-warning alarm for the patient if the predetermined values are reached.

In future, firstly, obtained results taken from this work must be done in vivo. Secondly, all this work can be turned into a portable device that patients can use. Finally, focusing on concepts related to how to increase accuracy, how to eliminate distorting effects, how to set up a powerful calibration model, how to increase low SNR rates, and how to design miniature device.

5 REFERENCES

[1] Purvinis, G., Cameron, B. D., &. Altrogge, D. M (2011). Noninvasive Polarimetric-Based Glucose Monitoring: An in Vivo Study. *Journal of Diabetes Science and Technology, 5*(2), 1-10. https://doi.org/10.1177/193229681100500227

[2] Khalil, O. S. (1999). Spectroscopic and Clinical Aspects of Noninvasive Glucose Measurements. *Clinical Chemistry, 2*(45), 165-177. https://doi.org/10.1093/clinchem/45.2.165

[3] Cote, G., Fox, M., & Northrop, R. (1992). Noninvasive Optical Polarimetric Glucose Sensing Using a True Phase Measurement Technique. *IEEE Transactions on Biomedical Engineering*, *7*(39), 752-756. https://doi.org/10.1109/10.142650

[4] Waynant, R. & Chenault, V. (2010). Overview of Non-Invasive Fluid Glucose Measurement Using Optical Techniques to Maintain Glucose Control in Diabetes Mellitus, Food and Drug Administration. Center for Devices and Radiological Health, 1-6.

[5] Klonoff, D. (1997). Noninvasive Blood Glucose Monitoring. *Diabetes Care, 3*(20), 433-437. https://doi.org/10.2337/diacare.20.3.433

[6] Liu, J., Liu, R., & Xu, K. (2015). Accuracy of Noninvasive Glucose Sensing Based on Near-Infrared Spectroscopy. *Applied Spectroscopy, 11*(69), 1313-1318. https://doi.org/10.1366/14-07728

[7] Khalil, O. S. (2004). Non-Invasive Glucose Measurement Technologies: An Update from 1999 to the Dawn of the New Millennium. *Diabetes Technology & Therapeutics, 5*(6), 660-697. https://doi.org/10.1089/dia.2004.6.660

[8] Gabriel, S., Lau, R., & Gabriel, C. (1996). Dielectric Properties of Biological Tissues: II. Measurements in the Frequency Range 10 Hz to 20 GHz. *Phys. Med. Biol*, 41, 2251-2269. https://doi.org/10.1088/0031-9155/41/11/002

[9] Kuang, W. & Nelson, S. (1998). Low-Frequency Dielectric Properties of Biological Tissues: A Review with Some New Insights. *American Society of Agricultural Engineers, 1*(41), 173-184. https://doi.org/10.13031/2013.17142

[10] Domnin, K., Cherevatenko, G., & Aksenov, E. (2014). Angular Measurements of Light Scattered by the Glucose Containing Biological Tissues and Their Phantoms. *Journal of Physics: Conference Series, 541*(012041), 1-6. https://doi.org/10.1088/1742-6596/541/1/012041

[11] Caduff, A., Dewarrat, F., Talary, M., Stalder, G., Heinemann, L., & Feldman, Y. (2007). Non-invasive Glucose Monitoring in Patients with Diabetes: A Novel System Based on Impedance Spectroscopy. *Biosens & Bioelectron, 22*(5), 598-604. https://doi.org/10.1016/j.bios.2006.01.031

[12] Mazady, A. (2010). Non-invasive Glucose Meter. Electrical and Computer Engineering Department the University of Connecticut, no. Storrs, CT 06269-2157, 1-13.

[13] Schiavon, M., Dalla, M., & Cobelli, C. (2018). Modeling Subcutaneus Absorbtion of Fast-Acting Insulin in Type 1 Diabetes. *IEEE Transactions on Biomedical Engineering, 65*(9), 2079-2086. https://doi.org/10.1109/TBME.2017.2784101

[14] Xin, J. & Mohammed, A. (2020). Generalized Modeling Framework of Metal Oxide-Based non-enzymatic Glucose Sensors: Concepts, Methods, and Challenges. *IEEE Transactions on Biomedical Engineering, 67*(3), 679-687. https://doi.org/10.1109/TBME.2019.2919462

[15] McNichols, R., Cameron, B., & Cote, G. (1999). Development of a Non-invasive Polarimetric Glucose Sensor. Biomedical Engineering Program, vol. Texas A&M University, 1-3.

[16] Firdous, S. & Ikram, M. (2004). Polarized Mueller Matrix Analytical Model for Glucose Measurement in Vitro, Experimental / Laboratory Studies. *Turk J. Med. Sci*, 35, 149-155.

[17] Jang, S. & Li, H. (2010). A New Method for a Non-Invasive Glucosesensing Polarimetry System. *International Journal of Engineering Research & Innovation, 1*(2), 36-42.
[18] Helhel, S., Khamidov, I., Kahya, G., Bayar, C., Kaynar, S., & and Gumerov, R. (2015). Double-wedged Wollaston-type polarimeter design and integration to RTT150-TFOSC; initial tests, calibration, and characteristics. *Experimental Astronomy, 39*(3), 595-604. https://doi.org/10.1007/s10686-015-9468-8
[19] Helhel, S., Khamidov, I., Kahya, G., Bayar, C., Kaynar, S., & Gumerov, R. (2014). Design of TFOSC Compatible Polarimeter for Polarimetric Observations. *Piers 2014* Guangzhou: Progress in Electromagnetics Research Symposium, Guanzhou.
[20] Yadava, J., Rania, A., Singha, V., & Murarib, B. (2015) Prospects and Limitations of Non Invasive Blood Glucose Monitoring Using Near-infrared Spectroscopy. *Biomedical Signal Processing and Control*, 18, 214-227. https://doi.org/10.1016/j.bspc.2015.01.005
[21] Bykov, A. & Kirillin, M. (2009). Chapter 3, Monte Carlo Simulation of Light Propagation in Human Tissues and Noninvasive Glucose Sensing. *Handbook of Optical Sensing of Glucose, Taylor and Francis Group*, 65-94. https://doi.org/10.1201/9781584889755.ch3
[22] Genina, E., Bashkatov, A., & Tuchin, V. (2009). Chapter 21, Glucose-Induced Optical Clearing Effects in Tissues and Blood. *Handbook of Optical Sensing of Glucose*, Taylor and Francis Group, 657-691. https://doi.org/10.1201/9781584889755.ch21
[23] Zhernovaya, O., Sydoruk, O., Tuchin, V., & Douplik, A. (2011). The Refractive Index of Human Hemoglobin in the Visible Range. *Physics in Medicine and Biology*, 56, 4013-4021. https://doi.org/10.1088/0031-9155/56/13/017
[24] Menguc, E. (2018). *Modelling of Glucose Level in Living Biological Tissues by Using Optical de-polarization Relationship*. Akdeniz University, Antalya, Institute of Natural Sciences.
[25] Mengüç, E. & Helhel, S. (2018). A Review on Measurement Methods of Non-invasive Blood Glucose Level. *International Conference on Advanced Technologies, Computer Engineering and Science (ICATCES'18),* Safranbolu, Turkey, 250-256.

Authors' contacts:

Ercan Menguc, PHD student
(Corresponding author)
Akdeniz University,
Department of Electrical and Electronics Engineering,
Dumlupınar Bulvarı, Antalya, Turkey
+90-05455562077, ercanmenguc@gmail.com

Selcuk Helhel, Professor
Akdeniz University,
Department of Electrical and Electronics Engineering,
Dumlupınar Bulvarı, Antalya, Turkey
+90-05055052239, selculhelhel@akdeniz.edu.tr