The optical and electrical non-invasive methods of measurement for glucose concentration in biological liquids

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Abstract. The article describes the radio-wave and optical methods of determining glucose concentration. The radio-wave method is based on the use of a sensor with a resonant frequency that is displayed when in contact with highly lossy materials and with an extended near-field zone in the resonance area. The optical method is based on studying the influence of glucose concentration (0–20 mmol/l) in bidistilled water on absorption spectra in the range of 190-1000 nm. The article presents the results of the experimental test of the near-field sensor with the pre-produced biological media imitating the human body tissues, and the results of the optical method demonstrate the possibility to measure the concentration with the use of an optical emitter with a wave length of 830 nm.

1. Introduction

Diabetes mellitus is one of the three diseases most frequectly leading to incapacitation of the population and death. According to the World Health Organization (WHO), in 2010 the number of diabetic people equaled 284.6 million people , which is 6% of the population aged between 20 and 79. In Russia, in 2010 there were registered over 9.6 million diabetic patients. According to the WHO prognosis, for the period between 2010 and 2030, the number of deaths from diabetes will double [1].

The way to fight the disease is to follow a strict diet with regular self-control of the blood glucose concentration. However, the modern invasive glucometers have a number of disadvantages, such as: painful procedure of finger stick, threat of infection penetration when doing the procedure in non-sterile conditions, as well as the high cost of consumables. All these disadvantages have led to the necessity to develop a new type of glucometers that would not require a blood sample to determine the glucose level. This type of devices was called a non-invasive glucometer. The most well-known non-invasive methods of blood glucose determination are: Raman spectroscopy, impedance spectroscopy, near infrared spectroscopy, photoacoustic spectroscopy, etc. The Raman spectroscopy [2] is based on measuring scattered light. The impedance spectroscopy is based on measuring resistance when the radiation frequency is changed. Measurement of glucose level requires several sensors placed in the vein area on human arms [3]. The near infrared spectroscopy is based on transmission of near infrared radiation through the vascular area of the body (a finger, an ear lobe, etc.). In this case, the glucose concentration is calculated on the basis of the obtained spectral information [4]. All measurements in the near infrared spectroscopy are based on passing of light radiation through or depthward the sample and measuring the intensity of (passed or reflected) beam. Spectrometers for measuring in the near

infrared spectroscopy have an adequate light source (such as a high stability quartz tungsten lamp), a monochromator or an interferometer, and a detector. Regular monochromators are optoacoustic tunable filters, diffraction grids, or prisms. Spectroscopy in the middle infrared region is based on light absorption by glucose molecules [5]. This method uses a light beam passing through a crystal contacting the skin, thus guaranteeing that the electromagnetic field created by reflected light reaches the dermis (the skin layer that contains the largest amount of glucose). There is a technology based on ultrasonography – photoacoustic spectroscopy [6]. This method is based on an acoustic response of an activated liquid with the use of laser light. This method is similar to spectroscopy in the middle infrared region. There are also other, less known methods for determination of blood glucose level [7].

2. Experiment

Determination of glucose solution absorption in bidistilled water 20 mmol/l, 10 mmol/l, 5mmol/l, and 0 mmol/l. The solution concentration is chosen so that the density on the maximum band was within the optimal range of photometric measurements (0.3–1.5 of optic density). The solutions are prepared in measuring flasks according to the exact sample weight. For standard measuring cells (l = 1 cm) and values of $\varepsilon=10^3$–10^4, regular solution concentrations are about 10^{-2} mol/l. The process of solution preparation is shown on Figure 1.

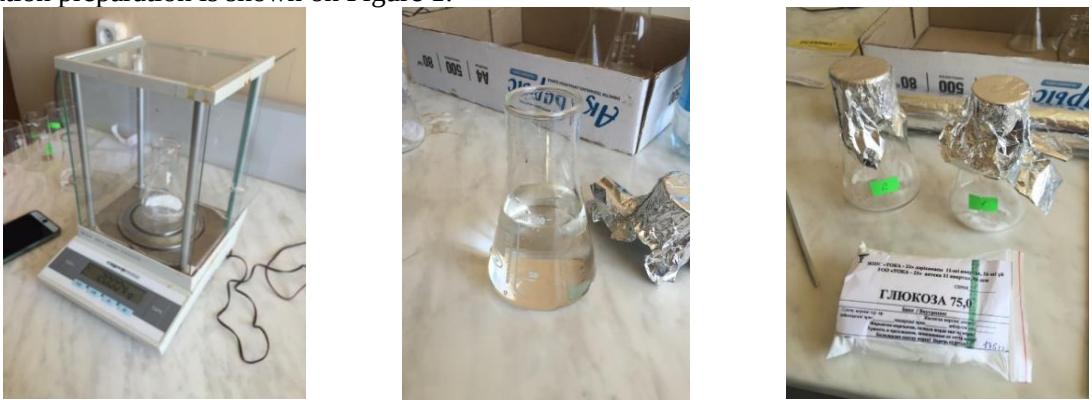

Figure 1. Solution preparation.

Both cells with the solution are placed inside, and parameters are set (Figure 2) with the help of the software installed on a personal computer.

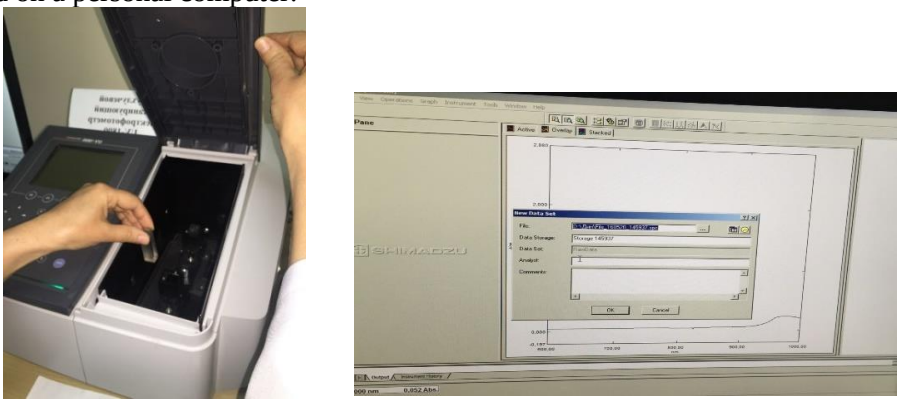

Figure 2. Cell installation and parameter setting.

The results of measurements are glucose solution absorption values within the range of 190 to 1.000 nm, 190 to 450 nm, and 600 to 1.000 nm. The series of absorption spectra measurements conducted on glucose solutions showed dependence of absorption level with the wave length of

825.5nm (peak 3); on all other peaks no changes were detected. Figure 3. shows absorption spectra changes that are detected when glucose concentration is changed. It is evident that the absorption level increases with the increase of glucose concentration.

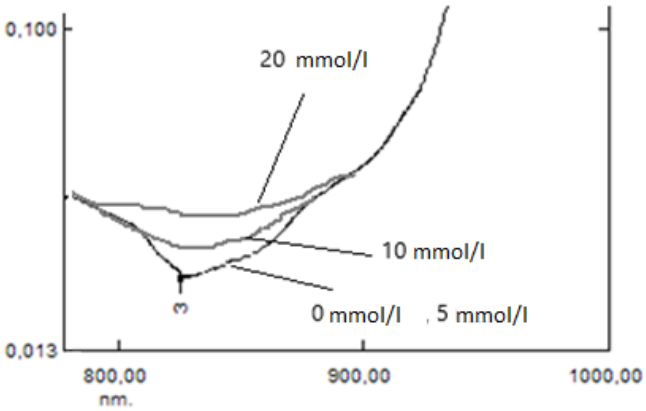

Figure 3. Absorption spectra for solutions with glucose concentration of 0 mmol/l, 5 mmol/l, 10 mmol/l, and 20 mmol/l.

Table 1 shows the results of optical measurements of absorption levels on glucose (3) and water (1) peaks. The detected glucose absorption peak allowed conducting tests of absorption levels in glucose solutions for the same concentrations with monochromatic light-emitting diode irradiation with the wave length of 830 nm (which is necessary for production of a portable glucose level meter).

Table 1. Glucose solution absorption.

Device	Concentration / Wave length, nm	0 mmol/l	5 mmol/l	10 mmol/l	20 mmol/l
Light-emitting diode I/Io	825.5	0.036	0.037	0.053	0.067
Spectrophotometer	976	0.247	0.255	0.255	0.255
	825.5	0.033	0.035	0.039	0.052

Production of a sensor was based on a calculated model [8]. The sensor is a combined split antenna based on a flexible substrate RO3003; it was produced 25mm in diameter with a 50-Ohm port brazed to it. This sensor has high penetration of electromagnetic waves into highly lossy media due to the near field length. Production of a biological phantom was based on graphite, polyurethane, and acetone [9,10]. This structure is sufficiently strong, which allowed creating thin materials, such as horny layer, epidermis, and capillary layer. The mentioned layers are the thinnest. The produced material was measured with the use of the previously developed method for measuring plane-layered materials [11,12]; charts of the real part of frequency-dependent dielectric permittivity were plotted for each material (Figure 4). As the charts show, the values of the real part of dielectric permittivity are similar to the materials demonstrated in modelling.

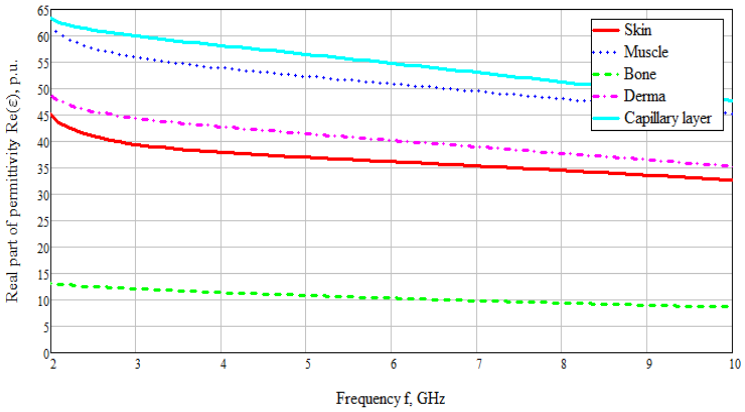

Figure 4. Real part of dielectric permittivity of the model materials and phantoms.

The differences in the values of real part dielectric permittivity were in average 1-2 relative units. The used data allowed creating a phantom of human biological tissues. The created region is forearm, since there is a large diameter vein there. Each layer is produced separately in molds of different thicknesses. Subsequently, each layer was cut to similar parts sized 150×150 mm (Figure 5). The size was chosen according to the size of antennas for blood glucose concentration measurement [13].

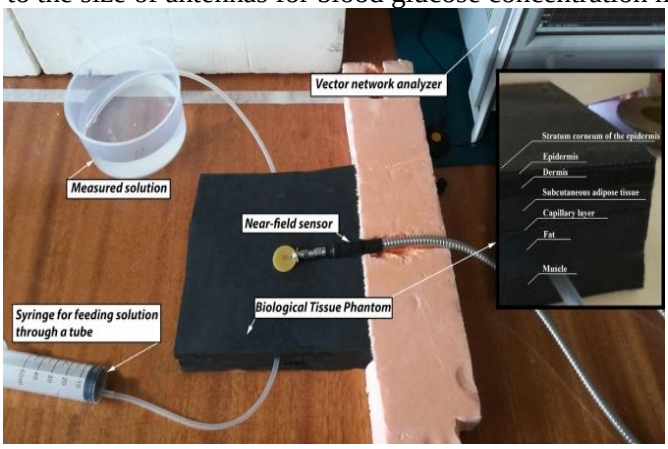

Figure 5. The graphite-based phantom and the measuring installation for determination of concentration in normal saline.

For determination, an installation based on a vector network analyzer was assembled. (Figure 5). A silicone tube with the internal diameter of 5mm was used as a venous vessel. A syringe with normal saline and the necessary glucose concentration was placed inside the tube, and when pressed, the liquid passed through the tube thus modelling blood flow inside the human veins. This choice allowed changing glucose concentration without physical effect on the antenna and thus conducting more accurate measurements.

The experimental research showed that the maximum amplitude difference is within the frequency range of 1.45–1.55 GHz. Based on the obtained results, the curve of reflected signal S11 to different glucose concentrations in normal saline was plotted (Figure 6). The dots show the data obtained experimentally on frequency 1.53 GHz. It is evident that in minimal glucose concentration the obtained values line up in a regressive curve. Also, the concentration of 10 mmol/l coincides with the regression curve. For concentrations of 7 and 9 mmol/l, the values differ from the supposed ones. This deviation is associated with the nonlinear behavior of dielectric permittivity values in low frequencies [14].

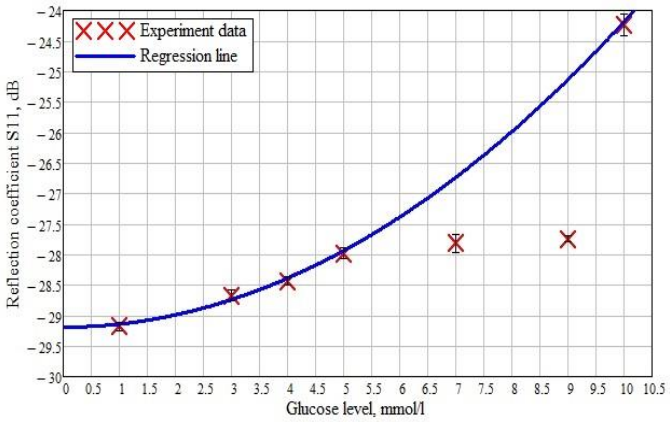

Figure 6. Dependence of the reflected signal on glucose concentration in normal saline in frequency of 1.53 GHz.

3. Conclusion

This thesis described the sensor based on a combined split antenna with an extended near field with high penetration depth of electromagnetic field. The reflected signal from an arm model with superficial veins was measured. The sensor demonstrated high reflected signal response in small changes of glucose in water solution. The obtained data show the possibility to determine blood glucose with high accuracy. The average reflected signal data variation with a 1 mmol/l change equaled 0.1–0.15 dB, which is a high value for a small glucose level change.

Also, there were conducted experimental measurements of glucose level in biological liquids by NIR-methods in the range of 190 to 1100 nm in solutions with different glucose concentrations — 20 mmol/l, 10 mmol/l, 5 mmol/l, and 0 mmol/l, and spectra of those solutions were obtained.

However, due to the fact that glucose concentrations in these solutions are low, similar curves of solution absorption spectra were obtained. A possibility to measure glucose concentration at λ=830nm was demonstrated.

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