Development of a Spectroscopic Device for Non-Invasive Blood Glucose Testing

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***Abstract*— The glucose level in the human blood is an important factor which characterize the condition of a patient with diabetes mellitus. Non-invasive glucose monitoring is a very urgent task, which has not yet found a convenient and inexpensive solution. Recent studies have shown that a spectroscopic method based on measurements of absorbed light passing through the blood-containing organs of the patient opens up the most opportunities for the realization of a non-invasive determination of the glucose level in the blood. Nevertheless, the implementation of this method faces certain difficulties associated with the need to ensure high sensitivity of the method, its speed, as well as the allocation of the fraction of absorbed light, for which glucose is responsible. The method can be implemented only with carrying out complex of calculations and preliminary experiments verifying the results. This report is devoted to set of calculations that ensure the efficiency of the method. This complex includes the calculation of the light source that allows to carry out multiple measurements of light intensity on a large number of wavelengths with a transition time from one wavelength to another not exceeding tens of microseconds. In addition, the complex includes the calculation of the optimal optical scheme that minimizes light losses during measurements, as well as the calculation of the distribution of absorbed light between the various absorbing components constituting the blood-containing organ through which light passes.**

Key words*— *diabetes mellitus; non-invasive method; light source; wavelength switching

I. INTRODUCTION

The light entering the biological tissue undergoes numerous scattering and absorption events propagating through the tissue. Biological tissues are heterogeneous in composition with spatial changes in optical properties. Scattering occurs at the place where is a spatial change in the refractive index [1].

The depth of light penetration into biological tissues depends on how much the tissue absorbs light.

Most tissues are sufficiently weak absorbers to provide a significant penetration of light into the therapeutic range in the range of 600 to 1300 nm. Inside the therapeutic range, scattering occurs together with absorption, so that the propagating light becomes diffuse. The tissue absorption is a function of the molecular composition. Molecules absorb photons when the photon energy corresponds to the interval between internal energy states, and the transition between quantum states obeys the selection rules. In the treatment of absorption, transitions between two energy levels of the molecule, which are well defined at the appropriate wavelengths, can serve as a spectral imprint of the molecule for diagnostic purposes [1, 2]. The proposed method is based on a polychrome light source with a controlled spectrum. Its application will allow to measure the absorption of light at 30 or more wavelengths (nowadays light absorption is carried out at 1–2 wavelengths). This method will ensure a more reliable and accurate the concentration testing of glucose in the blood.

II. PECULIARITIES OF THE MATHEMATICAL MODEL OF THE LIGHT INVESTMENT

The main difficult for obtaining correct data in implementing the spectroscopic method is a fact that the wavelength band of light absorbed by glucose significantly overlaps with the absorption band characteristic of water. As a result, it arises the difficult task of determining the light proportion, for the absorption of which water is responsible. This problem can be solved by multiple photometry at many arbitrarily chosen points of the spectrum within the absorption of light by glucose and water overlaps.

Meanwhile, all modern spectrometric schemes of glucometers provide illumination of the sample with monochromatic light with a constant wavelength or with two or three wavelengths in succession.

As already noted, spectrometric methods for determining glucose in the blood, based on the study of light absorption, are considered the most promising for constructing a noninvasive glucometer. At the same time, it should pay attention to the fact that light during the application of spectrometric methods is absorbed not only by glucose, but also by other absorbing agents - water, epidermis, melanin, other components of the blood. Thus, one of the most important tasks that should be solved in concept development of a technical hardware-software module of a spectrometric non-invasive glucometer is the task of determining the absorbed light fraction which glucose is present in the blood. One possible solution to this problem is to sequentially measure the absorption of light over many wavelengths, corresponding to the number of absorbing agents [3].

An important fact is that the spectral characteristics of all absorbing agents (glucose, water, melanin, other impurities contained in blood and tissues) are well known or can be easily measured using standard spectrophotometers. This allows us to

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obtain additional information for successive measurements of the light absorption at different wavelengths. To measure at the *i*-wavelength of the spectral range, we can write equation

$$k_{i1}x_1 + k_{i2}x_2 + \ldots + kx_N = I_i \,, \qquad (1)$$

where k_{ij} are the known light absorption coefficients at the i-wavelength for the *j*-absorbing agent, x_j is the unknow concentration for the *j*-absorbing agent, and Ii is the result of measuring the intensity of the absorbed light at the *i*-wavelength.

If measurements are made at N wavelengths within the spectral range of the device, then for each of the measurements one can write such an equation with N unknowns. Thus, it is possible to obtain a system of N linear equations with N unknowns, which can be quickly solved by using not too complicated software. One of the solutions of this system of equations is the concentration of glucose in the blood.

Let us consider an elementary idealized version, when only two absorbing agents participate in the absorption process, for example, water and glucose. Such an option is easy to implement experimentally, since a simple solution of glucose in distilled water can serve as a breakdown for measurements. For this variant, the system of equations can be written as follows

$$\begin{cases} \mu_w k_{1w} n_w + \mu_g k_{1g} n_g = I_{1i} - I_{1d} \\ \mu_w k_{2w} n_w + \mu_g k_{2g} n_g = I_{2i} - I_{2d} \end{cases}, \qquad (2)$$

where indices 1 and 2 refer to two wavelengths on which measurements are made, the indices w and g refer to water and glucose, respectively, the molar mass of the substance, k is the absorption coefficient of the substance at a given wavelength, and n is the amount of matter. The value of I corresponds to the light intensity, and the indices i and d correspond to the incident and detected light.

The next step is to complicate the light absorption model by adding new absorbing agents, for example, hemoglobin and oxyhemoglobin. For four absorbing agents, the system of equations is the expression

$$\begin{cases} \mu_H k_{1H} n_H + \mu_w k_{1w} n_w + \mu_o k_{1o} n_o + \mu_g k_{1g} n_g = I_{1i} - I_{1d} \\ \mu_H k_{2H} n_H + \mu_w k_{2w} n_w + \mu_o k_{2o} n_o + \mu_g k_{2g} n_g = I_{2i} - I_{2d} \\ \mu_H k_{3H} n_H + \mu_w k_{3w} n_w + \mu_o k_{3o} n_o + \mu_g k_{3g} n_g = I_{3i} - I_{3d} \\ \mu_H k_{4H} n_H + \mu_w k_{4w} n_w + \mu_o k_{4o} n_o + \mu_g k_{4g} n_g = I_{4i} - I_{4d} \end{cases} \qquad (3)$$

where indices 1–4 relate to the four wavelengths on which measurements are taken, the indices H and o refer to hemoglobin and oxyhemoglobin, respectively.

The experiment described by formula (3) can be performed using a control blood sample, and its results will give materials for calibration of the module being developed.

The system of equations (4) is linear and can be solved by changing the variable

$$\begin{cases} n_w = \frac{(I_{1i} - I_{1d}) - (\mu_o k_{1o} n_o + \mu_g k_{1g} n_g + \mu_H k_{1H} n_H)}{\mu_w k_{1w}} \\ \mu_H k_{2H} n_H + \mu_w k_{2w} n_w + \mu_o k_{2o} n_o + \mu_g k_{2g} n_g = I_{2i} - I_{2d}, \\ \mu_H k_{3H} n_H + \mu_w k_{3w} n_w + \mu_o k_{3o} n_o + \mu_g k_{3g} n_g = I_{3i} - I_{3d} \\ \mu_H k_{4H} n_H + \mu_w k_{4w} n_w + \mu_o k_{4o} n_o + \mu_g k_{4g} n_g = I_{4i} - I_{4d} \end{cases} \qquad (4)$$

Expressions (3) and (4) refer to the case when the light absorption is carried out only by blood components, that is, with an invasive method for determining the composition of glucose in the blood. For the case of non-invasive determination, it is necessary to add to the system of several equations that consider the absorption of light by other absorbing components that are not part of the blood. In order to determine which components should be taken into account, it is necessary to determine the place of measurement on the human body and to find out which layers are to pass the probing radiation beam.

III. Limitations in the Implementation of the Experemental Module

Based on the requirement that light pass through areas that are as much as possible saturated with blood, we chose the earlobe as a part of the body of the patient on which measurements will be taken. In this case, the light will pass through the skin, fatty layer and blood vessels. In the composition of the skin, absorption provides melanin, as well as, to a lesser extent, the stratum corneum of dry nuclear-free cells and epidermal material, including fibrous proteins-keratin. Collagen has an important absorbing role in the subcutaneous lipid layer. In addition, the lipid layer exerts a strong scattering effect on the light flux. In order to minimize the effect of the scattering effect, it is necessary that the aperture of the entrance range of the photodetector in the clip, put on the earlobe for measurement, significantly exceeds the aperture of the probing beam of light.

Based on the foregoing, a non-invasive device for determining blood glucose should measure light absorption at one to two dozen wavelengths in succession in a very short time, preferably in the same phase of the cardiocycle. The latter condition is since the reproducibility of the measurement results is due to the reproducibility of the measurement conditions. If we assume that the duration of the cardiac cycle phase is 50–100 ms, then the measurement time, including the switching time from one wavelength to the other, should be several tens of times smaller and be 1–4 ms. This speed can be achieved by using the light source with a programmable wavelength, in which the fine tuning of the wavelength is realized by the acousto-optic tunable filter (AOTF). Acoustic-optical tuning allows to achieve the speed of switching the wavelengths, determined by the time of passage of the wave front of the acoustic wave through the aperture of the light beam. If we assume that for the AOPF we use a Bragg cell based on a tellurium dioxide crystal (TeO2), which makes it possible to achieve maximum diffraction efficiency and to minimize light losses, then a transverse slow acoustic wave propagating in the crystallographic direction [4] will cross the light beam aperture in a time of the 10 μs order.

If it is assumed that a time of 20 μs is sufficient to perform a single measurement, then for a time intended for measurement at one wavelength (only 30 μs), the light absorption measurement can be performed several dozen times, which is sufficient for the collection of statistics and noise level estimation. Thus, it can be considered that a polychromatic light source with a program-controlled spectrum described above provides the necessary speed for non-invasive formation of a blood glucose measuring device based on the spectrometric method.

IV. Conclusion

From the foregoing, it can be concluded that the proposed concept of a technical solution for experimental module for the diagnosis of blood sugar without blood sampling includes the use of a polychromatic light source with a programmable spectrum, measuring absorption at several dozen wavelengths (the exact number of wavelengths N will be determined in in the course of experiments with by a model of a light source with a controlled spectrum), as well as solutions of a system of N linear equations in which the unknowns are the parts of light, various absorbing agents of the illuminated portion of the patient's body. Thus, it becomes possible to determine the fraction of light absorbed by glucose, and after normalization, the determination of the glucose content in the blood.

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