Calculational-experimental Method of Non-invasive Determination of Glucose Concentration in Human Blood

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Abstract— Diabetes mellitus is one of the most common diseases, which today is considered incurable and accompanies a person all his life. To avoid further complications, people with diabetes must adhere to a special regime of life and nutrition and periodically take samples of their blood "for sugar." Therefore, the importance of developing a device and a method for non-invasive determination of glucose in the blood is obvious.

Our method relates to spectroscopic methods and is based on measuring the intensity of absorbed light as it passes through the blood-containing organ of a person at certain wavelengths. Such methods have been developed for a long time, but until now, it has not been possible to solve the problem of isolating the fraction of light absorbed by glucose. The report considers the possibility of determining the fraction of light absorbed by glucose by multiple measurements of the total intensity of absorbed light on a large number of wavelengths in the near-infrared region of the spectrum, and also processing the experimental data obtained by means of a specially developed mathematical apparatus for this purpose, including the formation and solution of the system linear equations with the number of unknowns not less than the number of light absorbing components in the blood-containing organ, through which the light transmits.

We estimate the method by determining the convergence of the solution of the system of equations, and formulate the requirements for the refinement of the spectral characteristics of the absorption of some of the absorbing components.

Key words— diabetes mellitus; noninvasive method; system of linear equations; convergence of solutions

At present, diabetes is one of the most common diseases, which today is considered incurable and accompanies a person all his life. In order to avoid further complications, people with diabetes are forced to adhere to a special regime of life and nutrition and periodically take samples of their blood "for sugar," or rather, to determine the amount of sugar. Naturally, sampling of blood (or biomaterial) is accompanied by some difficulties, such as; it is necessary to have constantly not only a glucometer, but also special test strips, and also to ensure sterility during such an operation. Since it is necessary to check the concentration of sugar in the blood is not one, but several times a day, piercing each time a finger-also causes a number of inconveniences. Therefore, the importance of developing a device and a method for non-invasive determination of glucose in the blood is obvious.

Now in the scientific literature it is possible to find a large number of more or less substantiated by the principles of action and construction of devices that allow you to determine the concentration of glucose in the patient's blood without blood sampling. These proposals can be divided into two large groups - based on non-optical methods and based on optical methods.

One of the simplest methods is the method of comparing the temperatures measured in various organs of the patient's body [1]. The method is based on a linear relationship between the concentration of glucose and the temperature difference between insulin-dependent and insulin-independent parts of the body. The concept of the method is that some organs of the human body absorb glucose without the help of insulin, i.e. are insulin independent. These include cells of the brain, lens, retina, nerve endings. To feed other tissues and organs with glucose insulin is required. With a lack of insulin in the body, the blood glucose level rises, which leads to increased work of insulin-independent body tissues, accompanied by heat release and increased temperature. In this case, insulin-dependent tissues will not get enough glucose, and their biological activity will be reflected in lower temperatures.

Another example of a non-optical non-invasive method for determining glucose is based on measuring the concentration of acetone, exhaled by a person that correlates with the glucose content [2]. Acetone is present in the exhaled air constantly at 1–3 mg/m3; the concentration of acetone in urine is semiquantitative and has a small diagnostic value.

Note also the investigation of Indian scientists who created a method for determining the glucose content from the plethysmogram signal with verification using the electromagnetic method [3]. The method involves the use of a multi-sensor system and processing of the data obtained using multidimensional linear regression and artificial neural network technologies. The achievement of high accuracy is impeded by fluctuations in skin moisture and body temperature.

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Optical methods for determining blood glucose among non-invasive methods are considered the most promising [4]. These methods include photoacoustic, polarimetric, spectroscopic methods, as well as methods of Raman spectroscopy and optical coherence tomography. However, the most promising optical methods are spectrometric. They allow to receive certain information about the content of various impurities in the blood, including glucose. Studies in this area are conducted quite widely and a considerable research experience has already been accumulated [5, 6].

Our method refers to spectroscopic methods and is based on measuring the intensity of absorbed light as it passes through the human blood-bearing organ at certain wavelengths [7]. Although this method has long been known, it has not yet been possible to solve the problem of glucose-absorbed light amount selection. The report considers the possibility of determining the fraction of light absorbed by glucose by multiple measurements of the total intensity of absorbed light on a large number of wavelengths in the near-infrared region of the spectrum, and also processing the experimental data obtained by means of a specially developed mathematical apparatus for this purpose, including the formation and solution of the system of linear equations with the number of unknowns not less than the number of light absorbing components in the blood-containing organ through which the light transmits. One of the main tasks is also the creation and improvement of a mathematical model for determining the concentration of a needed substance.

A Bouguer–Lambert–Beer law was selected as a basis for determining the fraction of absorbed light in the blood, (1).

$$I_0 = I(l)\bullet e^{k_\lambda l} \text{ , where} \tag{1}$$

I_0 – intensity of light, at the entrance to the substance;

$I(l)$ – intensity of light, at the exit of the substance;

k_λ – absorption coefficient of the substance;

l – thickness of substance.

Since in general this law is used only for a single-type substance (more precisely for a substance that has a certain thickness), it has been modified. Namely, our formula has become:

$$I_0 = I\bullet e^{k_m\bullet n_m + k_p\bullet n_p + ... + k_z\bullet n_z} \text{ , where} \tag{2}$$

k_m – absorption coefficient of a substance of type m at the i-th wavelength in the layer l_0 (dimensionless number);

n_m – is the concentration of a substance of type m, distributed over the thickness of the layer l_0.

After a certain transformation, we get a simple linear equation:

$$k_m\bullet n_m + k_p\bullet n_p + ... + k_z\bullet n_z = \ln\frac{I_0}{I} \tag{3}$$

Then, for the case of solution of glucose and water, the light absorption fraction formula has the form:

$$k_w\bullet n_w + k_g\bullet n_g = \ln\frac{I_0}{I} \text{ , where} \tag{4}$$

g – glucose,

w – water.

Since any substance has its own absorption coefficient at certain wavelengths, and taking into account that there is no concept of the thickness of substance in the solution, our formula makes it possible to measure the percentage component of any substance in a given solution.

Naturally, some substances can have the same absorption coefficients at certain wavelengths; to avoid this, it is proposed to conduct multiple measurements. As a consequence of multiple measurements, we have entire groups of systems of equations. The more systems, the more accurate the result. However, this fact increases the time of solving these systems, which is not always a feasible solution. The main feature of the non-invasive method is not only obtaining the results without sampling the biomaterial, but also a rapid calculation.

Some substances at certain wavelengths have a maximum absorption coefficient, and others, at the same wavelengths, have minimal absorption coefficient, and even tends to zero. Hence, under certain conditions, we can neglect certain substances at certain wavelengths, which makes it possible to greatly simplify the solution of systems of equations.

As mentioned before, the main proof of our theory is to verify the convergence of systems of equations. Since the Gaussian method is the most common method for determining the convergence of a system of linear algebraic equations, we used them.

A good example for a quick check of the correctness of our theory is that the total percentage of all substances in the solution is 100%. And since blood is a compound substance and the whole biochemical composition of the blood is still not known (and some people have minor differences in the composition), the total percentage should not exceed 90–97%.

In the general sense, the convergence of systems of equations is the definition of intersections of planes at one point. However, we have not the coordinates of the plane (not the equations of the planes), but the coordinates of the functions, where the value of the absorption coefficient of the substance at the *i*-th wavelength is plotted along one axis, and the intensity of the absorbed light at the *i*-th wavelength is plotted along the other axis. Since we are looking for the concentration of our substance, and it is immutable – the functions will converge at one point. Since our system is inhomogeneous (the free coefficients are not equal to 0), it is suggested to solve it by the Gauss method, that is, by the method of successive elimination of variables, when, with the aid of elementary transformations, the system of equations is reduced to an equivalent system of triangular form, from which successively, (by the number), all the variables of our system of equations are found.

After calculating the amount of glucose in the blood in percentages, we translate it into mol/liters and output the result.

In conclusion, we note that the light beam will pass not only through the blood, but also through the skin and tissues. We must take into account the substances that are in them. For example, in earlobes, absorption in such components as melanin, epidermis and proteins contained in tissues should be taken into account. Accordingly, the number of equations of the system and the number of wavelengths on which the measurements are made will be increased. It will also be necessary to take into account the scattering of light by proteins, which will require additional calculations and, possibly, affect the design of the device for bringing the probing beam of light and the output of the transmitted beam. In general, since practical investigations of the optical transmission of blood and biological fluids have not yet been carried out with respect to the proposed method, in the future, it may be necessary to adjust and adapt them. Nevertheless, such corrections should only affect the list of components considered and their components in the formula, but not the formula itself.

Thus, we created a mathematical apparatus and an algorithm for determining the concentration of the test substance in solutions, suitable for the stable and rapid operation of a non-invasive glucometer.

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