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Measuring and Analysis of Blood Glucose Using Near Infrared Spectroscopy

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Abstract: - Blood tests can help a physician to detect early on certain diseases that a patient suffers. A rapid analysis, performed by modern techniques, such as the near-infrared spectroscopy (NIRS) method, by spectroscopic analysis, can reduce the time of blood determination and analysis so that it can be prescribed to a patient as soon as possible. To reach glucose, the absorption wave must cross three layers of skin and the constituent elements of the blood. The element studied in this case was blood glucose, because too much amount leads to diabetes.

Keywords: - non-invasive workflow algorithm, blood measuring methods, monitoring, skin measuring absorption, blood glucose, near infrared, absorbtion.

I. INTRODUCTION

Blood testing is one of the most important routine methods used by physicians to diagnose a patient's health or disease progression at a given time. These blood tests can help the doctor diagnose the functionality of certain internal organs such as the liver, heart, kidneys etc., to observe and prevent the appearance of diseases such as anemia, diabetes, or to check and evaluate certain prescribed treatments. This paper aims to analyze the blood by the near-infrared (NIR) absorption and reflection method, taking as a case study the analysis and monitoring of blood glucose, cholesterol or hemolithogram. Raman spectroscopic applications were used in the early 1970s for blood-related investigations of hemoglobin structure. Subsequently, additional applications were developed along with improvements and innovations in Raman spectroscopy instruments and techniques. Each of the five sections (hemoglobin and red blood cells, white blood cells, platelets, plasma and serum and whole blood) contains a chronological overview of the research.

II. THEORY

Blood tests generally help the doctor to diagnose and monitor patients. In this sense, in the chapter iv, we list below some useful blood tests that can help the doctor in diagnosing a patient, detecting diseases and establishing a treatment to help the patient. Blood is made up of many constituents that make it difficult to accurately analyze certain substances. But in order to have a blood test, the near-infrared spectroscopic wave must pass through the skin layers. The blood consists of plasma (55%) and formed elements (45%). Plasma contains 7% protein, 91% water and 2% other solutions.

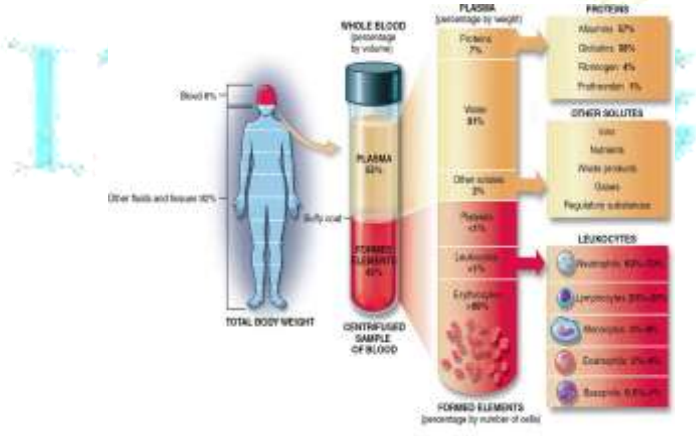

Fig. 1. Blood constituents [1]

The formed elements contain: platelets <1%, leukocytes <1% and erythrocytes> 99% as can be seen in Fig. 1 above.

But in order to reach the blood, the infrared wave must pass through several layers of the body. The first layer is the skin that has three substrates: epidermis, dermis and hypodermis. The epidermis is the outermost layer of the skin and the first layer that will hit the infrared wave. In this sense, part of the infrared wave is suppressed in the epidermal layer at a depth of 0.7 ~ 1.3 µm. There is a dermal-epidermal junction between the epidermis and the dermis. The epidermal layer is located on the surface that in fact it is a layer of non-vascularized epithelium and is separated from the dermis by a junction. The dermal layer is the second layer of the skin, having no net limitation to the next layer, the hypodermic one [1].

Therefore, the absorption radius will have to cross three layers of the skin, each layer having its absorption rate, and in addition it will have a refraction or loss rate of the wave[2]. The cutaneous organ is therefore composed of the ectodermal leaf, the one from which the epidermis and the appendages develop, and from the mesodermal leaf, precursor of the dermis.

The epidermis is an epithelial tissue, which contains a variable number of cells and is devoid of blood vessels. It has a protective role of the tissues and is coated with the following substrates:

- Basal layer: it has a photoprotective role due to melanin;
- The thorny layer: it is made up of polyhedral cells through which the nutritional lymph circulates;
- The granular layer: where keratohyaline cytoplasm predominates;
- The glossy layer: made up of cells rich in glycogen and fat, representing that epidermal barrier to water and other chemicals;
- The horny layer: it is the film or lipo-protein coating of skin acid (pH);

Derma is the connective layer of skin separated from the epidermis by the basement membrane. The dermis is composed of two layers: a superficial layer made of dermal papillae and a deeper and thicker layer called the dermis and made of collagen, elastic and crosslinked fibers [17]. Derma is rich in water, salts, proteins, lipoproteins or glucose. So, we can say that we can also find some glucose in this layer. This is actually glucose that passes through the blood and is consumed by the dermal layer through perspiration. A higher amount of this glucose indicates a normal transfer from the blood vessels to the dermal cells. The lack of this glucose indicates that it is not consumed and continues to reside in the blood [22].

Hypoderma is the layer composed of fat cells, lipocytes, which contain triglycerides separated by conjunctival septa that contain nerves and blood vessels. This is the layer where the spectroscopic one approaches the capillary vessels and their own test.

III. RESEARCH

To reach the blood vessels, the infrared light must pass through the skin. From the main source a part of the NIR wave will be reflected and only a part will be absorbed.
Before reaching the skin, the NIR wave will have to pass through the adipose tissue, which consists of perspiration and vasodilation. These fat cells are the first elements that will oppose the passage of light through the skin tissue.

The first result will be an infrared wave that will be strongly reflected. The incident light beam and the reflected light beam will be coplanar. The ray of incident light (φ_i) is the energy value that will pass on, and the ray of reflected light (φ_r) is the reflected ray that will be lost. This reflection can be mitigated by arranging an enclosed space that redirects the reflected rays back into the test environment. Only that this reflection can be controlled just on the surface, within human tissues this light will no longer be able to be controlled as well, because it is in an uncontrollable biological environment (Fig. 2).

$$\varphi = \varphi_i - \varphi_r \qquad (1)$$

where:

- φ - absorption radius;
- φ_i - incidental radius;
- φ_r - reflected radius;

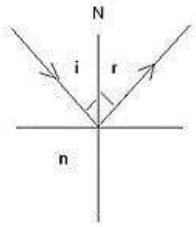

Fig. 2. Reflection infrared

According to Lambert's law, the reflection is more intense as the surface is smoother and the reflection angle is perpendicular to the test surface.

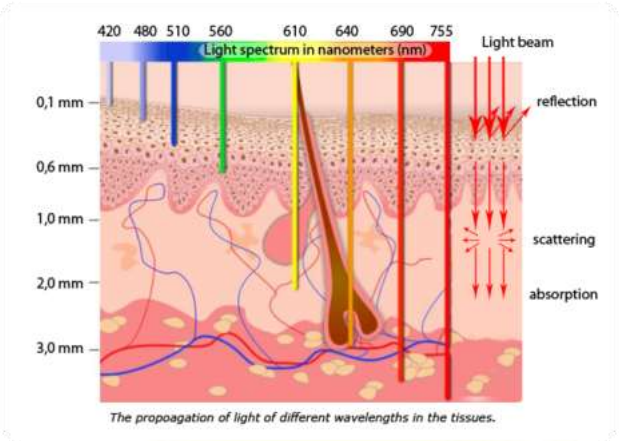

Fig. 3. Skin length wave [14]

As can be seen in the figure above Fig. 3, the near infrared wave must cross in the first epidermal layer ~ 0.6mm, in the second layer, the dermis, the length of the cross-section is between 0.6 ~ 2.0 mm, and in the third layer between 2.0 ~ 3.0 mm. The total cross section is approximately ~ 3mm [15].

There are three types of blood vessels:

- Arteries: it transports blood from the heart to the capillaries;
- Capillaries: they exchange water and substances between blood and tissues;
- Vein: transports blood from the capillaries to the heart;

The anatomy of a blood vessel, is composed largely of plasma (55%) and elements formed (45%). Plasma is formed in most of the water. The infrared wave could easily pass through this plasma without having too much absorption.

The highest absorption of the NIR wave will have it in the constituent elements of the blood, of which are the red cells, erythrocytes that are 99%, white cells - lymphocytes and platelets, which together are 1%.

In this sense, the absorption rate of the spectroscopic wave will have the highest absorption in the formed elements, and especially in erythrocytes.

Capillaries have a different structure from arteries and veins. In general, all blood vessels have the same structure:

- The tunic penetrates the innermost layer of a blood vessel;
- The media tunic is the middle layer which ensures the resistance and elasticity of the blood vessels;
- The external tunic is the layer that protects the blood vessels through collagen and fiber [22];

Arteries are the blood vessels that carry oxygenated blood to the capillary. Oxygen exchange occurs in capillaries and post-capillaries. The capillary walls are very thin, being made up only of the intimate tunic (Fig. 4).

The diameter of this wall is large enough to allow the red blood cells to pass to reach the exchange vessels, where the exchange of nutrients, oxygen and waste between blood and tissues is done.

The capillaries are of three types: continuous, fenestrated and discontinuous. The most permeable are the discontinuous capillaries, which allow even the erythrocytes to pass through the capillary wall (Fig. 4).

Veins are blood vessels that carry blood from the capillary to the heart, deoxygenated blood. The connection between capillaries and veins is made through venules which, by branching, are transformed into veins.

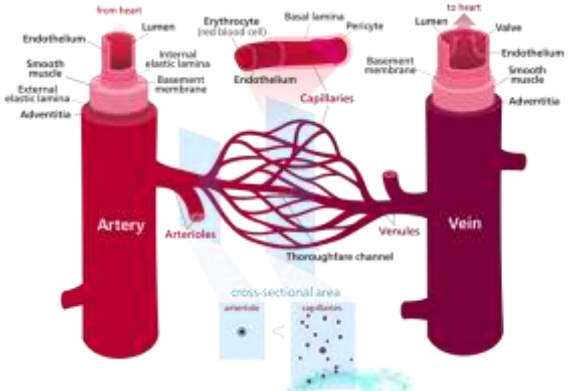

Fig. 4. Cross sectional area vessels blood [12]

The walls of the veins are smaller than those of the arteries and the lumen is larger. Blood pressure is the force of blood that flows through the wall of a vessel and is given by the equation:

Blood pressure = flow * resistance (2)

It is measured in Hg (millimeters of mercury) and occurs during the systolic period. The highest pressure is in the aorta and decreases as it spreads throughout the body. The absorption rate is at its highest point when blood pressure pushes the blood throughout the body. Our goal is to measure absorption through three levels: skin, blood vessels and blood constituents, in our case glucose.

The exchange of gases, nutrients and wastes between blood and tissues is done in the capillary, which is surrounded by lymph and interstitial fluid. Oxygen is transferred from the blood into the liquid through diffusion, and the carbon dioxide passes into the blood.
For the tests that we will approach, we are interested in the rate of absorption in the capillary [16]. The size of the capillaries is between 5 ~ 10 microns in diameter. Oxygen, carbon dioxide, nutrients and waste are exchanged through the thin walls of the capillaries. The blood flow to the capillary is controlled by structures called precapillary sphincters. These structures are located between arterioles and capillaries and contain fibers that allow them to contract. When the sphincters are open, blood flows freely to the capillary beds of the body tissue. When the sphincters are closed, blood is not allowed to flow through the capillaries. Fluid exchange between capillaries and body tissues occurs at the capillary bed.

In order for the spectroscopic wave to reach these capillaries and to measure for example glucose from blood, it must pass through the three layers of the skin, where the absorption rate will be more than half the value.

IV. METHODS AND RESULTS

A. Methods

To measure the study element, in our case blood glucose, we considered all the layers through which the NIR test wave passes. The first layer covered is the skin, where the absorption is very high due to the resistance of the constituent elements of the skin. The following standard elements for measurement and testing were used:

- wavelength with variation 610 ~ 960 nm;
- the amount of glucose used in the test;
- sampling time;
- the limits of the absorption values;

The electric light beam when it passes through the skin tissue will have a very high absorption rate and the photoelectric signal will be diminished. The values of the infrared wave remain constant at the beginning, the change of these values being caused only by the circulation of the arterial blood. When blood flow increases in

the blood vessels during the systolic period, we have a maximum absorption of near infrared light, which means that the photoelectric signals will have a lower intensity.

For tests was used the Qwiic sensor AS7263, the version for absorbance. This sensor also has the variant for colorimetric measurements, Qwiic AS726. AS7263 is the NIR version of the spectral sensor capable of measuring 610, 680, 730, 760, 810 and 860 nm of light, each with a maximum detection error of 20nm. The 6 light channels have the following wavelengths:

R = 610nm; S = 680nm; T = 730nm; U = 760 nm; V = 810nm; W = 860nm;

AS7262 is the NIR version of the spectral sensor capable of measuring and transmitting on 6 channels the values for:

V = purple; B = blue; G = green; Y = yellow; O = orange; R = red;

The following results were obtained on the thumb according to Table 1:

TABLE I STANDARD REFERENCES ABSORBANCE

	R-610	S-680	T-730	U-760	V-810	W-860
Sample1	7797.68	3150.99	874.13	416.04	387.01	291.97
Sample 2	7894.71	2573.4	897.28	424.99	305.84	296.62
Sample 3	8011.66	3247.07	901.92	427.98	388.00	298.95
Sample 4	7888.06	3186.12	882.23	419.0	389.98	294.29
Sample 5	7739.20	3184.05	874.13	415.04	392.95	290.80
Sample 6	7937.24	3175.79	882.23	420.02	391.96	295.46

Therefore, we will have to calculate the absorption rate through the three layers of skin: epidermis, dermis and hypoderma, as well as absorption through the structure of a capillary vessel. We will first have the absorption formula through the skin:

$$\Delta_n = (\varepsilon + \delta + \chi) - \varphi_n \qquad (3)$$

where:

- φ_n is the radius of total incidence through the three layers of skin;
- ε is the rate of absorption through the epidermis;
- δ is the absorption rate through the dermis;
- χ is the rate of absorption through the hypodermis;

After crossing the layers of the skin, the spectroscopic wave will have to pass through the capillary, and implicitly through the blood. Here we will calculate the absorption rate through the capillary wall and through the blood constituents. Glucose will have a higher absorption rate than the other constituents.

To calculate the rate of absorption through the capillary, we must find out the absorption through the capillary wall and then through the blood, which consists of plasma (55%) and elements formed (45%).

$$\beta_n = (\pi + \lambda) - \varphi_n \qquad (4)$$

where:

- φ_n is the radius of total incidence through the blood and capillary wall;
- π is the rate of absorption through the capillary wall;
- λ is the rate of absorption through the blood;

Therefore, the rate of absorption by blood glucose would be given the sum over a given interval of time:

$$\int_0^n \Gamma - (\Delta_n + \beta_n)\, dx \qquad (5)$$

where:

- Γ = it is the rate of glucose uptake;

B. Results

A normal blood glucose on an empty stomach should be between 70-108. Between 120-180 would be at the limit, between 215-250 the blood sugar is high and over 350+ would be dangerously high for a patient. If we calculate the values on the W-860 nm channel in this case, we have set some reference values:

- $\Delta_n = 80$
- $\beta_n = 80$
- $\varphi_n = 40$

In this case glucose will be on each sample:

TABLE II VALUES (GLUCOSE / SAMPLE

W-860		Γ
Sample1		91.97
Sample2		96.62
Sample3		98.95
Sample4		94.29
Sample5		90.80
Sample6		95.46

For graphical monitoring and for a more adequate visualization of glucose, we have developed an application software, that will discuss in future, that synchronizes with the heartbeat and when the blood flow is maximum.

V. CONCLUSIONS

The analysis and monitoring of blood elements can help us to detect many diseases, such as glucose, when they may be in abnormal quantities. The problems encountered were generally related to the accuracy of the measurements through the three layers of the skin, the blood vessels, especially the capillaries, and not ultimately through the blood and its constituent elements. We started from a normal reference value, to measure the absorption spectroscopic wave deviations and to observe the absorption rate caused by glucose. One of the problems that the measurements could deceive is the presence of glucose in the skin layers, which would mislead the absorption rate. Besides these challenges, there are differences in the texture of the skin that differ from the person by thickness or age.

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