



Non-Invasive Blood Glucose Measurement

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Abstract: This paper describes various method of measurement of glucose concentration in the human blood non-invasively. In recent medical practice, the concentration of glucose in blood is measured using an invasive techniques which generally involves puncturing finger. In generic few ml of blood whereas in recent practice less than a drop of blood is taken out and passed through the standard chemical tests to measure glucose concentration. These methods are expensive as well as painful. The frequent finger puncturing causes calluses on the skin and also increases the risk of spreading infectious diseases. So, the development of a non-invasive blood glucose measurement system will be boon to the diabetic patients. This paper describes the method of blood sugar measurement in the human blood non-invasively with various technique. The measurement accuracy of the non-invasive measurement device plays vital role and with noise filtering techniques.

Keywords: Non-invasive techniques, blood glucose measurement, near infrared.

I. INTRODUCTION

Diabetes is a type a metabolic diseases in which the blood glucose (blood sugar) level in human body increases drastically from its normal level. The increase in sugar level is either due to inadequate production of insulin in blood cells or can be because of improper response of body cells to the insulin or can be because of both the reasons. Diabetes can lead to major complications like heart failure and blindness in the human body¹. Hence regular monitoring of glucose level is important. The World Health Organization (WHO) estimated that the number of people with diabetes is more than 200 million.

Diabetes is a state of a body where it not able to produce the quantity of insulin sufficiently required to maintain normal level of blood glucose. So, diabetic patients regulate their blood glucose levels through proper diet as well as by injecting insulin². For the effective treatment of diabetes, patients have to measure the level of blood glucose periodically³⁻⁵. At present, diabetic persons are using invasive figure pricking instrument knows as glucose meter to know the concentration of blood glucose.

In the pathology laboratories, glucose is been measured by puncturing the patient's finger using a lancet to take out a small quantity of blood sample⁶⁻¹⁰. Then the sample of blood will be placed on the strip and is inserted into the blood glucose meter. Inside a glucometer, a series of chemical reactions will take place and as a result of chemical reaction Potassium Ferro cyanide is produced and it reacts with the metals on electrode layer and causes the electric current to flow through the electrodes. More the concentration of glucose in the blood, more the Potassium Ferro cyanide production and more the current through the electrode. This strength of current is used to predict the glucose level present in the blood³.

Development of a non-invasive glucose measurement technique would be a boom for a diabetic patient. The major advantage of noninvasive measurement methods is the relief from pain and comfort due to no finger puncturing. The non-invasive methods of glucose monitoring reduces the difficulties involved in glucose measurement and hence reduces the cost of healthcare. The noninvasive method for glucose measurement like IR spectroscopy is popular from years, but method with a reliable results has not been established yet.

From a last decade or two, lot of research work is going on for the non-invasive blood glucose measurement. The researchers are using various optical methods for the non-invasive measurements which includes near-infrared, photo acoustic spectroscopy, Raman's spectroscopy¹¹, polarization technique and light scattering techniques^{3,12,13}, Trans illuminated laser beam is used to measure glucose concentration by¹⁴. As described by Tang¹⁵, metabolic heat conformation technique can be also used for blood glucose measurement.

In the Near Infrared (NIR) Spectroscopy¹⁶, glucose cells will produce the weakest NIR absorption signals in the human body as glucose is one of the biological component present inside the human body. In measuring the glucose level, the NIR spectroscopy enables the penetration of signals inside the tissue within the range of 1 to 100 millimeters depth. Penetration depth decreases as the signal wavelength value increases Recently few authors incorporated neural network techniques in the non-invasive blood glucose measurement.

This paper is all about the measurement of blood glucose non-invasively by using NIR optical technique which overcomes the problems in invasive measurement like finger puncturing, risk of infection, etc.



The full paper is organized as follows: Section II describes the Principle behind the blood glucose measurement, Section III deals with the system design that includes light wavelength selection, system hardware and experimental analysis. Section IV shows the experimental results of the designed system and Section V concludes the paper.

II. PRINCIPLE OF BLOOD GLUCOSE MEASUREMENT

When a light ray interact with human body tissues, it is attenuated by scattering as well as by absorption by the tissues. Due to the mismatch between the refraction index of extracellular fluid and the cell membrane, light scattering occurs in tissues. Refraction index of extracellular fluid varies with the glucose concentration whereas the cellular membrane index is assumed to be remain relatively constant. Beer-Lambert Law plays a major role in absorbance measurement which states that absorbance of light through any solution is in proportion with the concentration of the solution and the length path travelled by light ray.

Figure 1 shows the description of effect of glucose molecules on the light path. Less glucose leads to more scattering, more path length and hence less absorption whereas more glucose tissues result in less scattering, less optical path length and hence more absorption by the tissues. Due to more absorption in high glucose tissue reflected light is having less intensity compared to tissue with less glucose content.

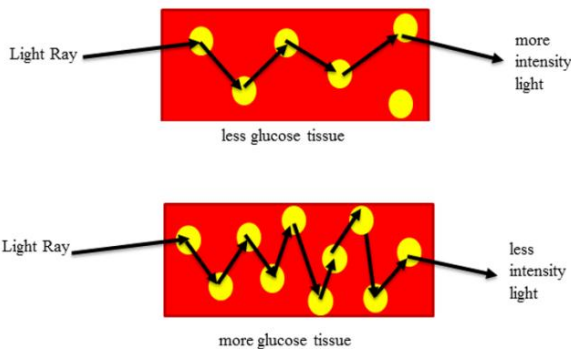


Figure 1 . Effect of Glucose On light Path

Light transport theory describes light attenuation as¹

$$I = I_0 e^{-\mu_{eff} L} \tag{1}$$

where, I is the reflected light intensity, I₀ is the incident light intensity and L is the length of optical path inside the tissue. Attenuation of light inside the tissue depends on the coefficient known as effective attenuation coefficient (μ_{eff}), which is defined as

$$\mu_{eff} = \sqrt{3\mu_a(\mu_a + \mu'_s)} \tag{2}$$

The absorption coefficient (μ_a) is describes as the probability of absorption of photons inside tissue per unit path length and is given by

$$\mu_a = 2.303 \epsilon C \tag{3}$$

ϵ is the molar extinction coefficient and C is the tissue chromophore concentration and the reduced scattering coefficient (μ'_s) is given by eq.4

$$\mu'_s = \mu_s (1 - g) \tag{4}$$

where, g defines the average of the cosine of the scattering angles which has a representative value of 0.9¹ and μ_s defines the scattering coefficient.

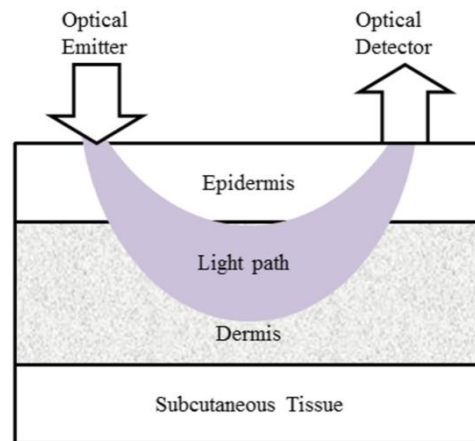


Figure 2. Cross Section of Skin and Light Path

With increase the glucose concentration path length decreases. With the assumption that refractive index of blood cell remains constant (approximately 1.350-1.460) with increase in the glucose concentration scattering properties decreases. From the equations above (1-4) it can be concluded that μ_a also depends on the blood glucose concentration, the increase in the glucose concentration increases the value of absorption coefficient μ_a and hence the effective attenuation coefficient μ_{eff} also increases which in terms results in increase in the attenuation level. Hence from equation (1) it can be concluded that increase in attenuation decreases the intensity of reflected light. Human finger skin tissue consists of epidermis, dermis and subcutaneous tissue layers. When optical signal is sent perpendicularly into the human body part the signal passes through epidermis layer and gets reflected in dermis layer and follows banana shaped path as shown in Figure 2.

III. DIFFERENT NON-INVASIVE TECHNIQUES

A. Bioimpedance spectroscopy

Bioimpedance is a measure of the resistance to electric current flowing through the tissues of a living organism.



The measurement of bioelectrical impedance has proved useful as a noninvasive method for measuring body composition. The impedance spectrum, or dielectric spectrum, is measured in the frequency range of 0.1 to 100 MHz. According to Hillier et al, variations in plasma glucose concentration induce, in red blood cells, a decrease in sodium ion concentration and an increase in potassium ion concentration.

Bioimpedance spectroscopy does not require the use of statistically-derived, population specific prediction models.

The limitation of this technology is that it requires an equilibration process, wherein the user must rest for 60 minutes before starting the measurements.

B. Electromagnetic sensing

Similar to bioimpedance spectroscopy, this technology assesses dielectric parameters of blood. The difference between them is that an electric current is used in bioimpedance spectroscopy, while the electromagnetic coupling between two inductors is used in electromagnetic sensing. The sensor uses electric currents to detect variation of the dielectric parameters of the blood, which may be caused by glucose concentration changes. The frequency range used in this technique is 2.4–2.9 MHz.

Using a specific frequency range can isolate the effect of blood glucose and minimize the characteristics of other substances, such as cholesterol, which might skew readings. Limitation of this method is that Temperature has a strong effect on this form of measurement, because it influences the optimal investigation frequency.

C. Mid-infrared spectroscopy

Midinfrared (MIR) spectroscopy employs the same principles as infrared spectroscopy; in other words, it is the absorption measurement of MIR frequency by a sample positioned in the path of an MIR beam. It is based on light in the 2500–25,000 nm region of the spectrum. Absorption differences when MIR light meets human tissues can be represented by certain modeling techniques in spectral quantitative analysis. A partial least squares algorithm is now normally used for multivariate calibration for these constituents.

Advantage of MIR spectroscopy is that the response peaks of glucose and other compounds are sharper with MIR than with NIR, where they are often broad and weak. Poor penetration is the main limitation of MIR

D. Near infrared spectroscopy

Near infrared (NIR) spectroscopy is located in the wavelength region of 730–2500 nm. The principle is similar to that of MIR spectroscopy. NIR spectra are made up of broad bands corresponding to overlapping peaks: the overtones (ie, first, second, third, and combination overtones), formed by molecular vibrations. It allows blood glucose measurement in tissues by variations of light intensity, based on transmittance and reflectance.

The high sensitivity of the photoconductive detectors is the main advantage of NIR spectroscopy. Water is reasonably transparent to the signal bandwidth used by NIR, which makes it possible to use for blood glucose monitoring. In addition, the measuring signal has high energy compared with MIR spectroscopy. Perhaps even more important, this method is less expensive than MIR. Materials are relatively low in cost, and there is a wide range of commercial products available. These advantages make NIR popular in this research area. Some issue with this method is despite much promising work, researchers still cannot overcome important shortcomings, in particular, the scanning pressure that must be applied, physiological differences not related to blood glucose,

E. Raman spectroscopy

Raman spectroscopy is based on the use of a laser light to induce Raman spectroscopy is based on the use of a laser light to induce oscillation and rotation in human fluids containing glucose. Because the emission of scattered light is influenced by molecular vibration, it is possible to estimate glucose concentration in human fluids. This effect depends on the concentration of the glucose molecules. This technique can measure very weak signals, even in human fluids. The wavelength range of Raman spectrum is considered to be 200 cm to 2,000 cm. Raman spectrum of glucose can be differentiated from those of other compounds in this band. Because the emission of scattered light is influenced by molecular vibration, it is possible to estimate glucose concentration in human fluids. This effect depends on the concentration of the glucose molecules. This technique can measure very weak signals, even in human fluids. The wavelength range of Raman spectrum is considered to be 200 cm to 2,000 cm. Raman spectrum of glucose can be differentiated from those of other compounds in this band

IV. CHALLENGES AHEAD FOR NON-INVASIVE GLUCOSE MONITORING

Various noninvasive technologies have been discussed. Clearly, many research groups are exploring a wide variety of approaches, trying to develop a blood glucose measurement device that can provide stable and reliable results, conveniently and economically.

One of the main reasons is that existing technologies, such as absorption spectroscopy, are relatively poor in signal-to-noise ratio in relation to blood glucose concentration and spectra response. Due to the huge anticipated market for a successful, noninvasive glucose monitoring device, the race for research teams to develop more precise and accurate spectroscopic equipment is heated. Moreover, multivariate training methods are often used in the quantitative analysis that the prediction model is data-dependent, whereas the specificity of measurement is not easy to tackle. Although an improved method is



investigated for quantitative analysis that can enhance the correlation of the spectroscopic properties of the glucose molecule with glucose concentration in blood, more effort should be made to rigorously extend the technique to noninvasive blood glucose monitoring

Moreover, calibration of spectroscopic devices is necessary, because of factors such as light intensity, which may affect the prediction model. As most of the noninvasive technologies are based on some type of optical sensing technique, a time lag may occur between measurements of blood glucose content from different parts of body, which could introduce calibration error. The absorption spectroscopy mainly detects the glucose molecule, and glucose can be found everywhere in the human body. Hence, it is difficult to have a universal prediction model instead of a The absorption spectroscopy mainly detects the glucose molecule, and glucose can be found everywhere in the human body. Hence, it is difficult to have a universal prediction model instead of a single user prediction model, which may need frequent self-calibration. single user prediction model, which may need frequent self-calibration.

V. CONCLUSION

In this review, the latest technologies and devices for noninvasive glucose monitoring have been described. Unfortunately, none of these technologies have produced a commercially available, clinically reliable device; therefore, much work remains to be done. It is relatively simple to measure data and find correlation with blood glucose levels under the controlled conditions of research laboratories. In this review, the latest technologies and devices for noninvasive glucose monitoring have been described. Unfortunately, none of these technologies have produced a commercially available, clinically reliable device; therefore, much work remains to be done. It is relatively simple to measure data and find correlation with blood glucose levels under the controlled conditions of research laboratories: the challenge is measuring these variables in normal environments. This requires understanding the physical and physiological factors that may affect blood glucose measurement. It is important to notice that noninvasive monitoring will never be achieved without vigorous scientific and clinical evidence. At this stage, we are still far away from achieving the goal of noninvasive blood glucose monitoring, with many technical issues yet to be resolved. The challenge is measuring these variables in normal environments. This requires understanding the physical and physiological factors that may affect blood glucose measurement. It is important to notice that noninvasive monitoring will never be achieved without vigorous scientific and clinical evidence. At this stage, we are still far away from achieving the goal of noninvasive blood glucose monitoring, with many technical issues yet to be resolved

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