

Challenges & Countermeasures in Optical Noninvasive Blood Glucose Detection

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Abstract:

This paper describes the critical and necessary points required for the design and development of the noninvasive blood glucose monitoring device. The lifestyle quality of the Diabetic patients will improve with the noninvasive technology due to its tight monitoring over the fluctuations in higher or lower blood glucose levels. Noninvasive blood glucose detecting techniques will provide increased patient compliance with pain free, low cost blood glucose monitoring. Optically based noninvasive techniques have brought improvement in this area. Various noninvasive methods have been emerged for noninvasive blood glucose detections, present paper describes their methods, significance and limits. All these technologies are based on the selectivity of the analytical information, instrumental signal to noise ratios, specific properties of the measurement sites and instrumental efficacy for the blood glucose specific signal acquisitions.

Keywords: Noninvasive, Blood Glucose, signal to noise ratio, higher or lower blood glucose levels.

I. INTRODUCTION

Diabetes mellitus a metabolic disorder, refereed as the imbalance of the controlled regulation of blood glucose in our body. In the year 2000, above 17 crores of the world populations were diagnosed with Diabetes and projected near to the 40 crores around the year 2030 [1,2]. To detect the level of the blood glucose, the concerned Diabetic patients need to examine his/her blood sample by piercing (invasive method) the body area related. Invasive method requires blood samples which is painful and costly. It provides initiations of patient's mental agony related puncturing pain and incomppliance started after daily use on a routine basis. This problem hinders the tight management of blood glucose and hence diabetic condition prevails [3]. The noninvasive blood glucose monitoring technology efforts to provide better life for diabetic patients by improving their compliance for tight blood glucose monitoring, with lower risks of medical complications and mortality related with this metabolic disorder. With this noninvasive technology, the continuous blood glucose monitoring will be possible at a large scale. For these reasons, at present the noninvasive blood glucose detection is the most burning and demanding topic in the medical science and its related areas [2, 3, 6].

This paper is oriented as follows: Section I provides the information about the prevalence of the diabetes mellitus and noninvasive blood glucose monitoring techniques. Section II depicts the modern optical technology based methods. Section III describes about the challenges and countermeasures for noninvasive blood glucose monitoring. Section IV illustrates the principles involved in the measurement concerned. Section V depicts the projected methodology. Section VI deals with the conclusion and afterward the references were noted.

II. THE MODERN OPTICAL TECHNOLOGY BASED METHODS

A. Polarization method: The optical phenomenon, where a plane polarized light passes a medium composed of chiral molecules (optically active like glucose), the polarization plane of the light is rotated by a certain angle, which is proportionate to the concentrations of the chiral molecules (like glucose) presence [4,5,12]. The polarization changing property of the glucose molecules is targeted for the non-invasive blood glucose detections [5, 12]. **Significance:** Polarization method involves the use of visible light, which is available abundantly in nature. Additionally the small devices for optical measurements are readily available at present day scenario [1-3, 4, 5, 12]. **Limits:** The optical properties of the skin is largely scattering in nature. The scattering property of the skin depolarizes the light. As a result, the detection of blood glucose through polarimetry produces erroneous results [4, 5, 12].

B. Optical Coherence Tomography (OCT): In this technology the super luminescent light is used to generate a low coherence light. The sample and the moving arm are associated with an interferometer. The reference arm is loaded with a mobile mirror and a light sensor for the acquisition of the respective interferometric signals [2]. The light backscattering from the sample tissues is conjugated with the light reflecting from the reference arm falls on the photo sensor. The delay correlation between the two signals is calculated to provide the output signal [3]. The movement of the reference arm mirror of the interferometer provides tissue scanning up to a depth of 1mm. The sample arm mirror movement is related with tissue surface scanning [2, 3, 7]. This dual mode (depth, tangential) of tissue scanning yields images of 2-D quality with good resolution property. The refractive index properties of the tissue scatterers, the body's interstitial fluid plays a vital role in determining the tissue optical properties.

Significance: The variation in glucose concentrations varies the refractive index of the tissue which in turn regulates the scattering coefficients. For this reason OCT signal can provide assessment about the glucose content in the tissue [2, 7]. **Limits:** The OCT signals are generated during the movement of the reference and sample arm. These movements may be subjected to motion artifacts related issues. In OCT method the extreme change in skin temperatures generates erroneous results. However error is negligible in minute skin temperature changes [3, 7].

C. Fluorescence Technology: Human tissues generate fluorescence when illuminated by light at fixed frequencies. A laser beam of 308nm when directed on glucose solution, the fluorescence phenomenon is observed in the spectral ranges between 340 to 400nm with highest peak near to 380nm [2, 3]. **Significance:** Light in the range of Ultraviolet to Visible can be used for blood glucose detection through fluorescence technology. **Limits:** Ultraviolet light along with fluorescence, it produces a very strong tissue scattering properties. The fluorescence property of the human tissues varies not only with glucose variation but also with other skin optical properties [2, 3].

D. Ocular Spectroscopy: This spectroscopy technique uses a specific glucose sensitive hydro gel within specially designed contact lenses. Boronic acid based derivatives were introduced in this technology. The chemically strong covalent bonds were formed by the chemical reaction between the glucose concentration in the tears and the boronic acid derivatives. When a laser based light source is used, the resultant reflected light changes its color based on the magnitude of the glucose binding with the derivative molecules. The spectrometer is used for detecting the respective color changes [2, 4, 11]. **Significance:** The aqueous humor under the cornea with lower scattering properties of the human eye serves as the measurement area for this technology [2, 3, 4, 10, 11]. **Limits:** Glucose concentration varies in blood and tears over a marginal time period. Contact lens usage provides unpleasant experiences to some patients and moreover it can be subjected to contact lens related severe eye infections [2, 3, 4, 10, 11].

E. Infrared spectroscopy: For noninvasive blood glucose detections, near and mid infrared spectroscopy is largely useful [2, 3]. **Near infrared spectroscopy (NIR):** When a beam of infrared light is directed over a tissue part, the light undergoes certain phenomenon known as absorption, reflection and scattering, etc [2,3,8,9]. The information about the blood glucose concentrations could be obtained by using both the transmission and reflection property occurred due to light tissue interactions. The changes in the resultant wave property are picked up the application of suitable photo sensors for noninvasive blood glucose detections [8, 9]. **Significance:** Generally the near infrared light usually describes the light tissue interactions between the spectral ranges from 760nm to 2500nm. As NIR spectroscopy suffers lower penetrations profile inside the tissue with the increase in its wavelength, it is widely used for tissue depth analysis up to maximum of 100mm starting from 1mm. **Limits:** The absorption profile of blood glucose molecules overlaps with the water molecule absorption profiles. It is even more complicated when other molecules (like proteins, fats, blood components, etc) exhibits the same phenomenon. Both the internal and external factors like body blood pressure, body heat, water content, various protein proportion contents, atmosphere dependent barometric pressures, day and night temperatures, different weather conditions, produces variability in the blood glucose measurement accuracy and precision [2,3,8,9,13].

Mid-IR spectroscopy: The electromagnetic spectral range from 2500 to 10,000nm comes under the Mid-IR spectroscopy. The mode of operation and the working technique for Mid-IR spectroscopy is similar to that of NIR spectroscopy. Mid-IR is composed of larger wavelengths with higher absorption profile compared to that of the scattering one [2, 3]. For this reason, Mid-IR is applied for noninvasive blood glucose detection in the reflection mode [8, 13]. **Significance:** The Mid-IR blood glucose band profiles are more clear and distinct as compared to NIR [9, 13]. **Limits:** Lower tissue penetration profile [10, 13].

F. Raman spectroscopy: When a laser light is focused over a liquid sample, it triggers the vibration and rotation phenomenon in that sample [2, 3, 17-19]. The scattered light that it emits is proportionate to the molecular oscillations, which is influenced by the amount of optically active entity present in that sample [15-19]. For this property, the Raman spectroscopy is employed for noninvasive blood glucose detections. Raman spectrum exhibits between 200 to 1800 cm^{-1} [15-19]. In this spectral band glucose detection property of Raman spectroscopy is clear and sharp. The overlapping spectrum is largely minimized in that region, as obtained during NIR spectroscopy [2, 3, 15-19]. **Significance:** The interventions from illumination and fluorescence are quite acceptable [17-19]. Single wavelength based laser LEDs are useful due to their low cost and large availability [2, 3, 15-19]. Newly advanced Raman Spectroscopy such as surface enhanced Raman spectroscopy is used successfully for non invasive blood glucose detections [17-19]. **Limits:** Fluctuations phenomenon in the LED laser spectra along with its variation in magnitude of operations occurs repeatedly. Noise addition from the other glucose similar molecules exists. Usually larger amount of time is required for Raman spectroscopy in acquiring a specific spectral signal [17, 18, 19].

III. CHALLENGES & COUNTERMEASURES IN EFFICIENT NONINVASIVE BLOOD GLUCOSE DETERMINATIONS.

Accurate determination and their specific mode of action directs towards the applicability of a technology, explicitly for a certain problems. Precision and analysis of the resultant wavelength is the key for smooth functioning of the noninvasive blood glucometer [2, 3, 21].

(i) The spectroscopic data obtained from the output signal must be embedded with blood glucose related informative signature bands. The necessity of this type is mandatory, irrespective of the methods utilized for noninvasive blood glucose determinations. Various statistical tools can be employed to examine the blood glucose related correlations, model robustness, chemical selectivity, calibration based measurements, etc. In this objective, the statistical tool like multivariate approaches yields very good results [2, 3, 20, 21].

(ii) The instrumental efficacy, reliability is adequately required for precise detection of blood glucose related specific band signatures without being influenced by the surrounding noisy environment. The instrumental limits for blood glucose detection are confirmed by the application of signal to noise ratios measurements. Various experimental tissue mimicking phantoms like Intralipid, etc. were used to define the blood glucose detection capability and its role over signal to noise ratios. The novel engineering principles must be engaged to design and develop such a high level performing device [14, 20, 21].

(iii) The optical and inbuilt tissue characteristics of the human body parts play a major impact over accurate noninvasive blood glucose determination, for the desired clinical interpretations. The in-depth tissue dimensions, optical properties, body heat, molecular orientations of various body fluids etc. constitutes the physical and chemical properties which hinders the process of noninvasive blood glucose determinations [14, 20, 21].

(iv) The dimensional characteristics of the target tissue matrix must be thick enough to provide adequate analyte concentrations for the proper signal generations which can be distinguished easily from the surrounding noise. The biological tissues with extreme scattering properties yield a poor quality signals with compromised signal to noise ratios [14].

(vi) The spectroscopy techniques generally include the target substances for light interactions and analysis of the resultant light wave characteristics for result interpretations. The degree of light tissue interactions pattern depends up on the type of the spectroscopy utilized. The interaction with the various skin layers is important in skin spectroscopy experiments. Similarly, for glucose concentration determinations, the interstitial fluids must be studied. The concentration of the glucose in the interstitial fluid resembles the similar concentration in the whole body blood under normal circumstances. Various physical and chemical factors influence the balance of the blood glucose concentrations [2, 3, 20, 21].

Good calibrations techniques and its stability for various conditions is an essential factor for the successful noninvasive blood glucose determinations.

The critical parameters are listed as follows:

1. To record good quality of output signals with low signal to noise ratios.
2. Robust calibration procedures for the experimental models.
3. Rigidity to produce repeatable and consistent results.
4. The output results as well as experimental process must be less sensitive towards internal or external factors [2, 3, 20, 21].

These factors are countless and always target oriented. Problem solving approach is needed for the noninvasive blood glucose measurement procedures [2, 3, 20, 21].

IV. PRINCIPLE OF MEASUREMENT

Generally the light wavelengths between 780nm to 2500nm are defined as near infrared regions. Similarly the ranges from 2500nm to 2500nm are called as mid infrared regions [2, 3, 20, 21].

The glucose (C₆H₁₂O₆) molecule possesses hydroxyl and methyl groups in its chemical structure. The hydrogen based functional groups are sensitive in the infrared regions. The absorption patterns of glucose and water molecule in the infrared region based on their chemical characteristics are shown in the figure 1. The first and second overtone absorption of the glucose molecule is in the region of 1500nm to 1899nm and 1100nm to 1300nm respectively. These overtone absorption phenomenons provide the application of infrared spectroscopy for noninvasive blood glucose determinations [2, 3, 20, 21].

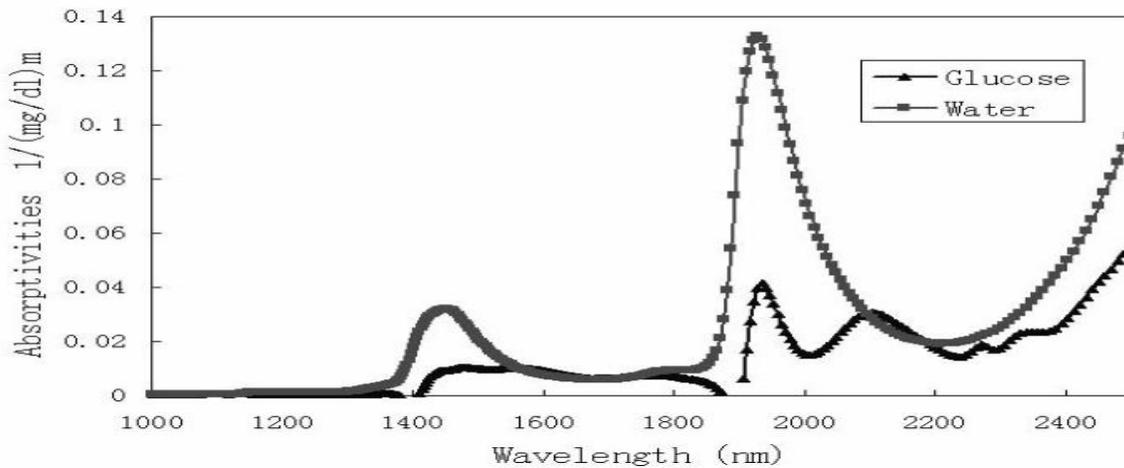


Figure.1. The absorption curves of glucose and water at near and mid infrared region of the wavelength spectrum. Adapted from the reference [20].

Inherent characteristics of the measurement samples, used to vary the amount of intensity on the light path by a definite wave number of the wavelength. The famous Lambert-Beer Law is utilized for assuming the light absorption as (A) and the wave number as (ν), this phenomenon is expressed as follows:

$$A(\nu) = -\log I(\nu) / I_0(\nu) \quad (1)$$

Here (I₀) denotes the light intensity of the adjacent medium, (I) indicates to the amount of light intensity at the definite wave number (ν) for the measurement samples [22].

V. PROPOSED METHODOLOGY

In recent time various optical based principles have been proposed for noninvasive blood glucose monitoring. NIR & MIR spectroscopy based noninvasive techniques for determining the blood glucose concentration had been demonstrated by many research groups and excellent progress has been made in past few years [2, 3]. For noninvasive blood glucose determination numerous optical techniques have emerged with promising results [2, 3]. The near and mid infrared spectroscopy based approaches have shown exceptional quality in acquiring blood glucose related signals for non invasive blood glucose predictions [20, 21].

Figure 2. depicts the sketch of a proposed noninvasive blood glucometer. The light source unit provides light in the infrared region. It is being focused on the human finger tip. The output transmitted signal is received by the infrared light sensitive detector. The ADC block provides the digitization of the received analog signals. Amplifier is introduced to magnify the feeble bio-signal. The advanced microprocessor based circuitry helps in quantifying the blood glucose related information and after suitable signal processing and conditioning the desired blood glucose level is displayed on the display board.

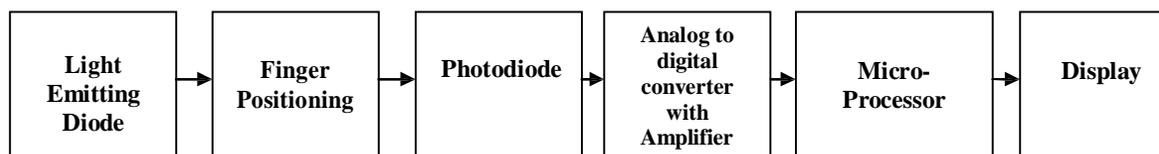


Figure 2. Block diagram of the proposed system.

VI. CONCLUSION

The noninvasive blood glucose technology yields a novel edge for continuous blood glucose monitoring, increased patient compliance, blood free measurements, reduces work load over hospital workers, tight diabetic control regimen. It can provide efficient cross check and control over fluctuating higher or lower blood glucose levels. Additionally it can trigger alarm system to indicate abnormal hyper or hypo glycemic conditions in case of severe emergency.

This paper represents the problems and countermeasures required for noninvasive blood glucose measurements. The blood glucose induced signals are very feeble and overlapped by other molecules present in the blood medium. To overcome such difficulty, the idea for hybrid technology is evolved now days for providing optimal solutions towards the noninvasive blood glucose detections techniques and calls for further problem oriented research in this field.

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