Near-infrared LED based Non-invasive Blood Glucose Sensor

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Abstract — **Diabetes is a metabolic pathological condition of concern, which affects vital organs of body if not diagnosed and treated on time. Regular monitoring of blood glucose is important to avoid complication of diabetes. Commonly used glucose measurement methods are invasive which generally involves finger puncturing. These methods are painful and frequent pricking cause calluses on the skin and have risk of spreading infectious diseases. Therefore there is need to develop a non-invasive monitoring system which can measure blood glucose continuously without much problem. The present work is focused on development of non-invasive blood glucose measurement sensor system using Near-infrared (NIR) technique. Initially in-vitro glucose measurement prototype is developed using continuous wave (CW) from NIR LED (940 nm) to check the sensitivity of the system for different glucose concentrations. Later a Sensor patch was designed using LED and a photodiode to observe diffused reflectance spectra of blood from the human forearm. Diffused reflectance spectra of the subjects obtained with this technique was also compared with commercially available invasive finger tip gluco-meter. The results are promising and show the potential of using NIR for glucose measurement.**

Keywords: Non-invasive method; Diabetes; Near-infrared spectroscopy; Diffused reflectance spectra

I. INTRODUCTION

Diabetes is metabolic disorder in which blood glucose fluctuates from its normal range (90-140mg/dl). Insulin is a hormone produced in body to regulate blood glucose level naturally. Under some pathological failure, body is not able to produce insulin or body cells become unable to use insulin. Poor management of diabetes can lead to serious health problems such as cardiovascular diseases, damage of blood vessels, stroke, blindness, chronic kidney failure, nervous system diseases, amputation of foot due to ulceration and early death [1]. The number of diabetic people is increasing across the world due to population growth, unhealthy diet, obesity and lack of physical activity. According to International Diabetes Federation (IDF) 382 million people suffering from diabetes in 2013, an alarming figure which is set to reach 592 million by 2035[2]. Only in India, about 65 million people suffer from diabetes, making it the 'Diabetes Capital' of the world. China, India and USA are among the top three countries suffering from diabetes. According to world health organization (WHO), every year 35 million people die because of diabetes [3].

At present none of the available methods can cure diabetes completely. Occurrence of complications can be prevented by keeping blood glucose levels in the normal range. Regular glucose monitoring, diet plan, insulin shots and oral medications are the foundation of diabetes treatment. Regular blood glucose monitoring is the key step in efficient management of diabetes to control blood glucose. Most of commercially available glucose measurement devices are invasive. Diabetic patients need to monitor their blood glucose two to three times a day. The invasive methods are painful, have high recurring cost and danger of spreading infectious diseases. Non-invasive methods are more desirable and excellent alternatives to these devices. Enhancing glucose measurement techniques to allow easy and continuous monitoring has received a lot of attention from both academic and industrial researchers over the past three decades. Non-invasive glucose monitoring could make millions of people more relaxed and comfortable about blood glucose testing. Thus it is necessary to develop a non-invasive blood glucose method which can provide painless, convenient and cost effective glucose monitoring to diabetic patients. Non invasive monitoring system will be a major breakthrough in the area of treating diabetes patients. Various optical non-invasive techniques have been explored for development of glucose measurement system. Optical methods are one of the painless and promising methods that can be used for non-invasive blood glucose measurement. Near-infrared (NIR) is one of the most widely explored optical techniques [4] because of its high penetration in skin. This technique has been applied on various body parts: finger, palm, arm, forearm, earlobe, check etc. Maruo et al. [5] designed the fibre optical probe to get spectra of forearms of type 1 diabetic individuals. The authors have reported that the results have good correlation between the predicted and reference glucose values at 1600 nm. Shu-Jen et al. [6] utilized reflectance signal in higher overtone region, where absorption of glucose is negligible. Temperature is modulated between 22 and 38 °C.

This paper presents a possible design and development of a sensor system to detect blood glucose non-invasively using Near-infrared (NIR) radiation. The subsequent section

describes the principle of glucose measurement using NIR method. System details are presented in section III along with the criteria of selection of wavelength and sensor. Results and discussion are provided in section IV. Finally section V concludes the paper.

II. PRINCIPLE OF GLUCOSE MEASUREMENT

As the radiation interacts with biological tissue, it is attenuated by absorption as well as scattering. The attenuation of light can be described by light transport theory:

$$I = I_0 e^{-\mu_{eff} L} \quad (1)$$

In equation (1) I is the reflected light intensity, I_0 the incident light intensity, L is the optical path-length in tissue, and the term μ_{eff} is defined in equation (2) in terms of absorption coefficient μ_a and reduced scattering coefficient μ_s'.

$$\mu_{eff} = \left[3\mu_a(\mu_a + \mu_s')\right]^{1/2} \quad (2)$$

$$\mu_a = 2.303\varepsilon C \text{ cm}^{-1} \quad (3)$$

Equation (3) shows relation of absorption coefficient (μ_a) to the tissue chromophore concentration (C), where ε is molar extinction coefficient. Value of μ_a changes with variation in glucose concentration.

$$\mu_s' = \mu_s[1 - g] \quad (4)$$

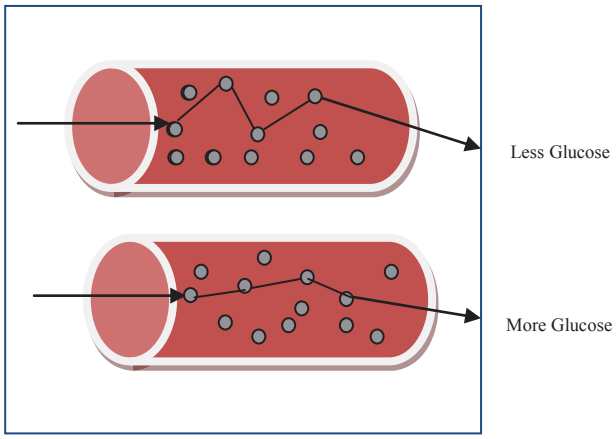

Figure 1 Schematic description of affect of glucose on light path. More glucose results in less scattering consequently less optical path and less absorption [8].

Equation (4) shows expression for reduced scattering coefficient where g is anisotropy factor and μ_s is scattering coefficient. Variation in glucose concentration affects the intensity of light scattered from tissue. Light scattering involves the change in refractive index mismatch of extra cellular fluids (ECF) and membrane of cells. The value of refractive index of ECF (n_{ECF}) is approximately 1.348-1.352. Whereas refractive index of blood cells (n_{cell}) is approximately 1.350-1.460 [7].

With the addition of glucose concentration in blood, value of n_{ECF} increases and n_{cell} is relatively assumed to be constant which leads to decrease in the scattering properties of tissue. This leads to a smaller scattering coefficient and consequently shorter optical path. Thus with the increase in glucose concentration, scattering properties of skin decreases [8]. Fig. 1 shows the Schematic description of affect of glucose on light path.

III. SENSOR DESIGN

a) Selection of wavelength and transducer material

Near-infrared Spectroscopy (NIRS) uses the light in 750-2500 nm region which interrogates the tissue with low-energy radiation. No specific reagents are required for measurement, so repetitive analysis can be performed at low cost. NIR radiation in 700-1100nm is considered as therapeutic window, as it allows the glucose measurement up to the depth of few mm under the skin. Glucose has absorption peaks at 939nm, 970nm, 1197nm in higher overtone region, 1408nm, 1536nm, 1688nm, 1925nm in first overtone region and 2100nm, 2261nm, 2326nm in combination region [9]. For present design NIR LED at 940nm wavelength (TSAL5300) is used. Although glucose has less absorption at 940nm as compared with first overtone and combination region, but due to minimum attenuation of optical signal by other constituents such as water etc, desired depth of penetration can be achieved at this wavelength. LED based sensor system is preferred for present work as it overcomes all the limitations of LASER. As LASER have higher construction cost, larger space for making the instrument and more instrument space for cooling. In comparison LED is smaller in size, lower cost, requires less power, no extra circuit is required for cooling, and causes less damage to tissue. Thus LED based system would be low cost and portable alternative to LASER based systems. Photodiodes is used to detect the attenuation of radiation due to changes in the glucose concentration. Monolithic photodiode/preamplifier 8-pin DIP package (OPT101, Texas instruments) is used to detect the attenuated light.

b) In-vitro testing

In-vitro test setup is designed to investigate the attenuation of NIR light with variation in glucose concentration. The in-vitro prototype is designed using LED at 940nm and a photo diode. Photodiode is placed in opposite direction to the LED to get transmitted signal. The problem of stabilizing the photodiode is overcome by fixing the setup in a closed box. However variation in the output voltage is also minimized by making the LED supply current constant. Samples are prepared by dilution of 40 mg/dl dextrose glucose in each step to make variation of glucose form 40mg/dl to 400mg/dl. For in-vitro measurement total ten readings are taken to investigate the affect of variation in glucose concentration on NIR radiation.

c) In-vivo experiment

The schematic of cross section area of skin layers and light path length is shown in fig. 2. Outer most layer of skin is

epidermis and middle layer is dermis. Inner most layers are the subcutaneous layer which contains fat. Dermis layer contains most of blood vessels. To measure glucose level radiation must penetrate in this layer. The diffused photons illuminate a banana-shaped region of the penetrated tissue to a maximum depth d/2 from the surface of the skin where d is the distance between source and detector [5]. Maruo et al. [5] suggested that average optimal path length for glucose measurement through forearm should be more than 1.3mm.

In-vivo sensor patch is designed to observe diffused reflectance spectra of forearm. The sensor patch is designed by placing NIR LED (950nm) and a photodiode at 4mm distance from each other. During the experiment, subjects are asked to sit in relaxed position and not allowed to move during optical measurement. Sensor patch is placed on inner side of forearm for measurement of glucose. The measurement using diffuse reflectance spectra through forearm is collected for this experiment.

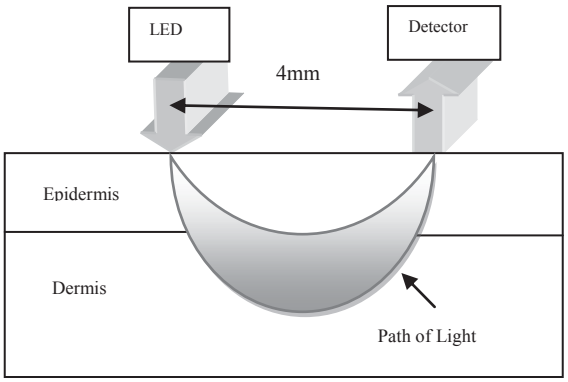

Fig. 2. Schematic of cross section area of skin layers and light path

d) Block Level Description

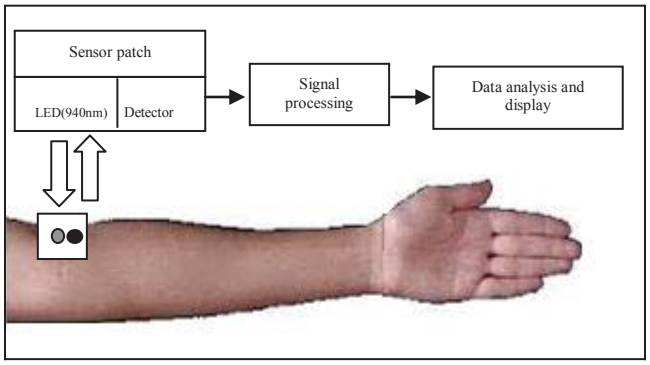

Fig. 3 Block diagram of the prototype

Block diagram of *In-vivo* prototype is shown in fig. 3. Low pass filter of cut off frequency 10Hz is designed to remove high frequency components and 50Hz power line interference. High pass filter of cut off frequency 0.5Hz is used to remove baseline drift or low frequency signals.

IV. RESULTS AND DISCUSSION

For in-vitro experiment different glucose concentration is prepared in distilled water followed by addition of 40mg/dl glucose and the attenuation in NIR radiation is observed by placing the sensor path on the test tube wall. As the glucose concentration increases, output of photodiode decreases. In-vitro results are shown in fig. 4.

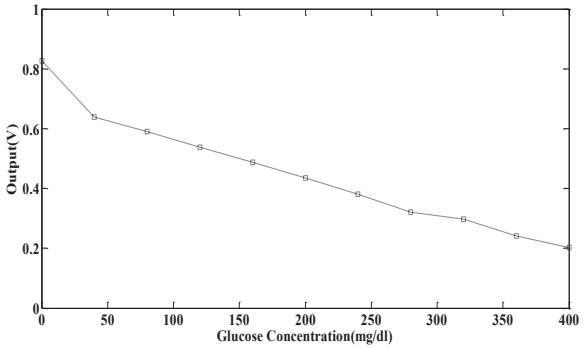

Fig.4. In-vitro result showing decrease in transmittance with increase in glucose concentration in aqueous solution

Overall transmitted signal decreases with increase in glucose concentration due to the absorption of radiation by glucose. Thus an in-vitro study shows the strong correlation between optically measured signal and actual glucose concentrations.

Later In-vivo experiment using sensor patch and signal conditioning unit are designed to acquire diffused reflectance spectra through inner side of forearm. To investigate the sensitivity of sensor patch, seven non-diabetic subjects (4 male and 3 female) between 25 and 35 years age are considered. The signal is taken before meal and after meal from each subject. The data obtained from the commercially available gluco-meter and NIR sensor patch for seven subjects before and after meal are shown in the table 1 and 2 respectively.

TABLE 1 Glucose concentration before meal

Subject	Average voltage (V) NIR Sensor	Glucose mg/dl
A	2.4745	84
B	2.578	91
C	1.827	94
D	2.522	100
E	2.510	112
F	2.758	89
G	2.12	98

TABLE 2 Glucose concentration after meal

Subject	Average voltage (V) NIR Sensor	Glucose(mg/dl)
A	2.178	131
B	2.27	123
C	1.55	120
D	2.272	138
E	2.195	141
F	2.231	128
G	1.805	135

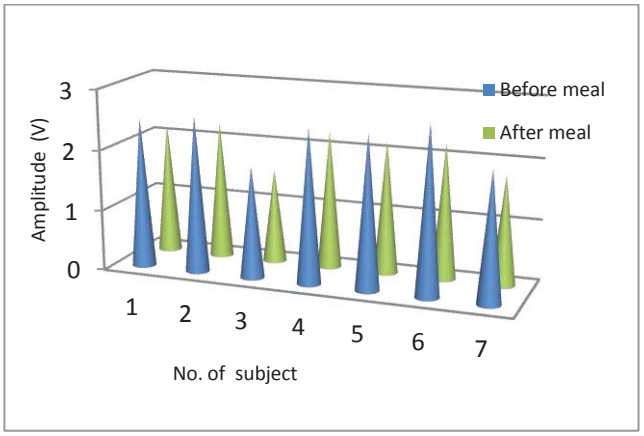

Fig.5. Before and after meal In-vivo result using NIR sensor patch showing difference in the output signal

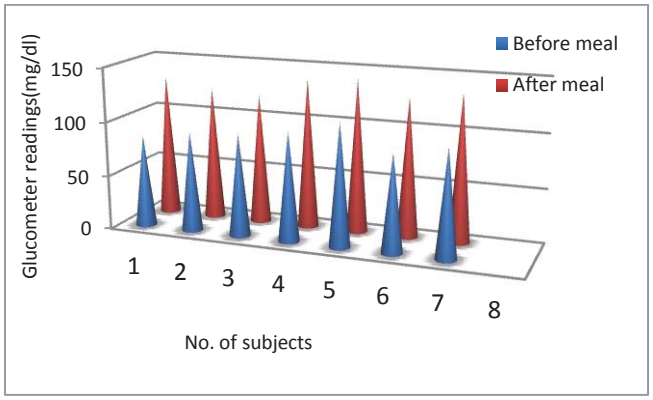

Fig. 6. Before and after meal result using gluco-meter

For validation of *In-vivo* experiment, data acquired by proposed prototype is compared by simultaneously measuring the subject's blood glucose with the help of invasive finger tip gluco-meter (Dr. Morepen, Gluco one BG3). There is decrease in the signals amplitude observed after meal as compared with before meal. It is due to the reason that there is decrease in refractive index between n_{ECF} and n_{cell} as the glucose concentration increases.

The fig. 5 and 6 shows a significant difference in the blood glucose before and after meal using designed sensor patch which is in accordance with commercially available gluco-meter readings respectively.

The results obtained by current sensor prototype are encouraging. The obtained result shows the prospects of the non-invasive blood glucose measurement system based on diffused reflectance through forearm. The performance of the proposed method can be improved by reducing the error caused by positioning of sensor patch on forearm in each measurement. Moreover with the use of suitable signal processing methods to remove interferences by other biological chromophores (proteins, lipids, water etc) can improve the results.

V. CONCLUSION

In the present work prototype for non-invasive glucose measurements using Near-infrared LED based sensor is developed. In-vitro and In-vivo experiments are carried out using the prototype and results obtained as output signal of prototype is comparable with commercially available glucometer. The result shows the feasibility of the development of non-invasive blood glucose measurement system based on diffused reflectance through forearm. In future the performance of the proposed method can be improved by reducing the positioning error and by the use of suitable signal processing techniques to remove interferences.

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