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# Comparative Study of Different Measurement Sites using NIR Based Non-invasive Glucose Measurement system

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**Abstract**

In Diabetes, self-monitoring of blood glucose is crucial for effective treatment since it can help to identify and prevent unwanted episodes of hypoglycemia and hyperglycemia. Aim of the present work is to design and develop a non invasive gluco-meter using near infrared LED (940nm). Three different designs of probes (arm, finger and ear lobe) were fabricated to measures in-vivo blood glucose. In addition, we also carried out experiments to study the interaction with glucose molecules in solution under plane polarized light. The polarizers were used at three different angles($45^0$, $90^0$ and $180^0$) to know the behavior of glucose interaction with polarized light of 640nm and 740nm with varying concentration of glucose in the solution. The polarization results showed that at $180^0$ the glucose has maximum polarization (1.12) and at $90^0$ and $45^0$ it has comparatively less polarization values 0.9 and 0.35 respectively. The polarization results helped us to design the probes. Therefore, we placed photodiodes at three angles ($45^0$, $90^0$ and $180^0$). The results as expected were better at $180^0$ by showing maximum variation in photodiode voltage output. The results were in the correlation of the polarization studies. A comparative study of three measurement sites has also been carried out. The primary result of current sensor system is promising and with further improvement a robust system for glucose sensing can be realized.


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*Keywords:*
Diabetes; Blood glucose monitoring; hyperglycemia; hypoglycemia; non-invasive glucose monitoring; light emitting diode; photodiode; spectroscopy

## 1. INTRODUCTION

Diabetes is a common chronic disease in nearly all countries worldwide. There are an estimated 382 billion adults with diabetes in 2013. It will become 592 in 2030 according to survey shown by international Diabetes Federation (IDF) . Diabetes or diabetes mellitus is a long-term metabolic pathological condition in which blood glucose level fluctuates outside the normal range (90 to 150 mg/dL) [1]. Diabetes may leads to severe complications such as blindness, amputations, renal disease, cardiovascular diseases and premature deaths. In year 2014 the global health expenditure

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on diabetes was estimated USD 612 billion and expected to become USD 490 billion in 2030. Globally, 12% of the health expenditures spent on diabetes in 2010[2]. The expenditure varies by region, age group, gender and countrys income level. Diabetes is huge and growing problem leading to economic burden on the society. Every seventh second one person dies from diabetes.

At present most of the technologies for measuring blood glucose concentration levels are nominally invasive. It requires finger pricking and extracting a drop of blood which is applied to a test strip where an estimation of glucose is produced by electrochemical or optical methods. This is often painful for the user, it carries risk of spreading infectious diseases. The most of gluco-meters sold in the market usually cost less than 5000 INR and have been discounted greatly because of the purchase of expendable, require test strips that are costly for each measurement. These strips cost approximately 50 INR. This cost is modest cost if only use consumption rate is less. If a diabetic patient use a strip used every day, it costs around 10000 INR per year that he tests only one time a day. Several patients require multiple measurements which would easily have much higher yearly costs. The worldwide market for glucose monitoring products was estimated 180 billion INR in the year 2000[2]. These figures and the revenue shows the need of development of non-invasive device which can promote frequent blood testing and help in control of blood glucose level. Regular blood glucose monitoring plays key role in preventing complications of diabetes[3,4]. This brings about the need for preventive health measures. Therefore there is a need of non-invasive blood glucose monitoring system which can encourage frequent measurement. In the recent years NIRS has come up as a potential technique for non-invasive glucose monitoring[5] due to low absorption and more penetration of Near-infrared (NIR) light into the skin. Many scientists have tried various body sites, i.e. finger, palm, forearm, arm, oral mucosa and tongue, to measure blood glucose non-invasively. Robinson et al.[6] observed transmission NIRS spectra through the finger and reported the average absolute error as 19.8mg/dl. Rong et al.[7] presented non-invasive glucose monitoring through palm. It was shown that results of only single person over a day were satisfactory. Maruo et al.[8] designed the optical fibre probe to get spectra of the forearm. The authors have reported Standard Error of Prediction (SEP) as 32.2mg/dl. It was also observed that the effective optimal path length should be 1.3mm to 2mm for diffuse reflectance measurements. Burmeister et al.[9] observed spectra through various measurement sites: cheek, lower lip, upper lip, nasal septum, tongue, and webbing tissue between the thumb and forefinger it was also reported that the percentage of body fat affects the signal-to-noise ratio of the measurement and must be minimized for reliable glucose sensing. There are many literatures which reveal the feasibility of non-invasive blood glucose measurement using NIR technique. The present work 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. Results and discussion are provided in section IV. Finally section V concludes the paper.

## 2. PRINCIPLE

Glucose is an optically active (chiral) molecule which has ability to rotate the plane of linearly polarized light by an amount proportional to its concentration, the optical path length as well as changing the refractive index of the media, which therefore affects the overall scattering coefficient in a given media. The magnitude of each effect is related to the concentration of glucose. Similarly transmission based estimation is based on principle of Beer-Lambert law which applicable to measurement of the concentration of the absorbing chromophore in a sample[1]. According to this law attenuation of light is directly proportional to the concentration of constituents, thickness of the sample and molar extinction coefficient. The eq. (1) shows the attenuation A, as per Beer-Lamberts law:

$$A = \log\left(\frac{I}{I_0}\right) = \varepsilon C d \tag{1}$$

Where I = intensity of the transmitted light, C = concentration of chromophores (mol L-1), d = path-length of the photon from the source of light to the receiving detector

There is some limitations Beer-Lambert law. It assumes incident radiation to be monochromatic and sample is non-scattering, whereas in case of blood glucose measurements the error is caused due to the scattering property of the tissue. Even the path length d travelled by all photons in tissue is not same. It depends on subjects, the measured region and the wavelength of the light. In a highly scattering medium like biological tissue, photons travel a mean

distance that is far greater than path length d. Differential Path-length Factor (DPF) is used as the scaling factor for path-length correction. The modified Beer-Lambert law incorporates some additional factors:

$$A = \log\left(\frac{I}{I_0}\right) = \varepsilon C d DPF + G \tag{2}$$

Here G is unknown, therefore an absolute calculation of chromophore concentration cannot be derived from eq. (2) The quantitative data for changes in the concentration of chromophores can be derived by using eq(2). Here it is assumed that G has the same value for all chromophores in the medium, by using a differential equation between two chromophores, G is eliminated as shown in eq. (3).

$$\Delta A = \varepsilon \Delta(C)\, dDPF + G \tag{3}$$

In the next section a detailed discussion is presented about the sensor design and methodology used.

## 3. SENSOR DESIGN

Transmittance spectroscopy involves a light source and a light detector positioned on either side of the ear lobe or finger tip or arm. The amount of near infrared light passing through the arm or fingertip or ear lobe depends on the amount of blood glucose in that region. In the current study Near Infrared transmittance is used across the ear lobe, fingertip or arm to measure glucose. The ear lobe was chosen over other model due to the absence of bone tissues and also because of its relatively small path length for the light. Near Infrared (NIR) light is applied onto one side of the ear lobe, while a receiver on the other side receives the attenuated light. This attenuated signal is then sampled and processed. LED (940nm) was used as the light source. Since conventional silicon photodiodes have limited spectral bandwidth, they cannot be used for receiving near infrared light. A photodiode with a high response wavelength of 940nm was used. The light transmitters and receptors around a wavelength of 940nm are relatively low cost as compared to other wavelengths with equal or higher response to glucose. In designing of the system, methods of near-infrared light emission and detection were explored. As suggested by transmission spectroscopy for measuring glucose concentrations is favoured over reflectance. Without access to a spectrometer that analyzes light of wavelengths in the near-infrared spectrum, another option was needed. This brings about the use of photodiodes. Photodiodes are photo-detectors that convert light into current of voltage. Materials used in photodiodes are what determine its properties; most specifically the range of wavelengths of the electromagnetic spectrum the photodiode is capable of outputting a voltage or current. The objective is to develop a non-invasive method for measuring blood glucose concentration levels. Such a method would be pain-free and therefore possibly more desirable amongst a larger population for use with continuous health monitoring. The solution would be using near-infrared light to measure blood glucose concentration levels. Such a method would be painless and would not require tedious amounts of test strips for each measurement. Because it would be painless, it may easily be recommended and used by the general population to monitor their day-to-day health to best adjust their eating habits or exercise.

## 4. RESULTS AND DISCUSSION

### *4.1. Polarization Studies*

Glucose is optically-active (chiral) molecule has the ability to rotate linearly polarized light in proportion to glucose concentration[10]. In the present study initially a polarimetric-based approach attempted to check feasibility of non invasive blood glucose measurement[11]. Spectrofluorimeter (Jasco, FP800) with polarizers is used for the study. Both excitation and emission polarizers were placed in front of source and sample holders. The polarizers were fixed at three different ($45^0$, $90^0$ and $180^0$) angles to excite glucose at different angles. Figure 1(a, b and c) shows average polarization of different concentration of sugar when excited at 640-750nm. The results shows maximum polarization when the light was passed at angle ($45^0$, $90^0$ and $180^0$) for same glucose concentration. The polarization results showed that at $180^0$ the glucose has maximum polarization 1.12 and at ($90^0$ and $45^0$ it has comparatively less polarization i.e 0.9 and 0.35 respectively. Figure 2 shows average polarization of different concentration of sugar at $45^0$, $90^0$ and $180^0$ respectively. The results clearly depicts maximum polarization when the light was passed through $180^0$ as compared to $90^0$ and $45^0$.

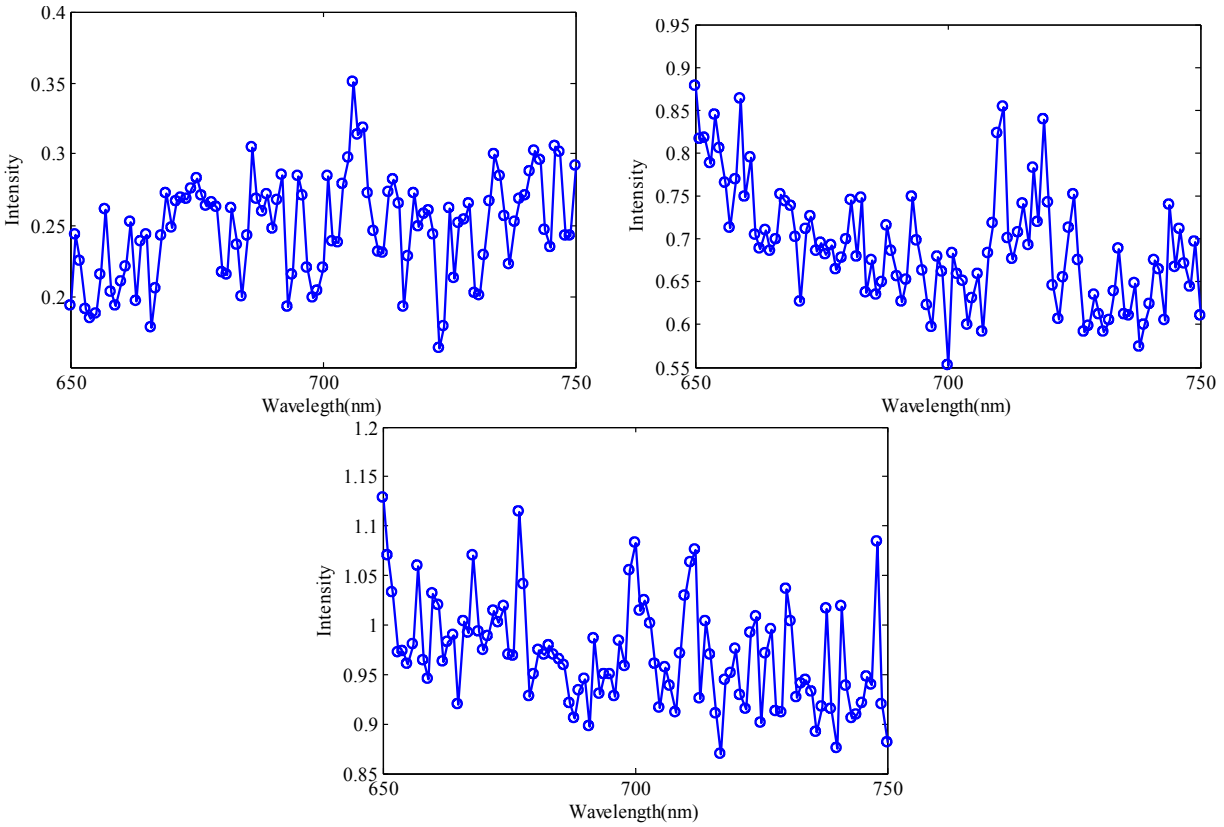


Fig. 1. (a), (b)and (c) Shows average polarization values of glucose at $45^0$, $90^0$ and $180^0$ respectively

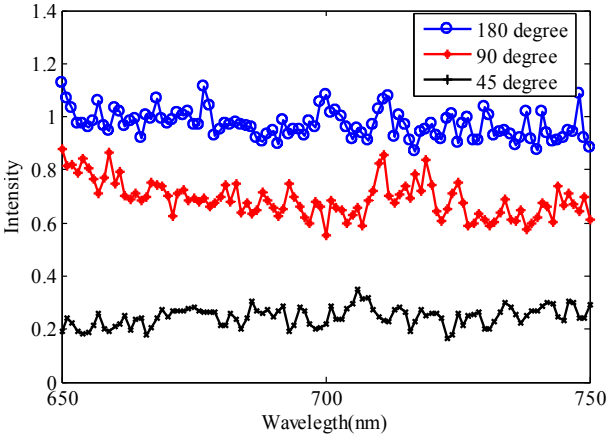


Fig. 2. Shows average polarization values of glucose at 45,90 and 180 respectively

### *4.2. In-vitro experiment and result*

At first, In-vitro test setup is designed to investigate the attenuation of NIR light by glucose concentration. The prototype is designed by placing a LED and an array of photodiodes as shown in fig.3. Three photodiodes D1, D2, and D3 are placed at $45^0$, $90^0$ and $180^0$ angles to demonstrate the effect of variation in glucose concentrations on NIR

light. The path length considered for in-vitro testing is 20mm. The glucose concentration in the samples varies from 40mg/dl to 400mg/dl range. Here buffer solution is considered to demonstrate the effect of glucose concentration on attenuation of NIR light. Initial studies were carried out to show behaviour of light with variation in glucose concentration.

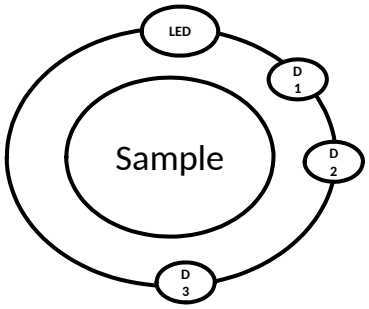


Fig. 3. In-vitro test setup

Table 1. Output of in-vitro test

| Glucose(mg/dl) | 30 deg (mV) | 90 deg (mV) | 180 deg (mV) |
|---|---|---|---|
| 0 | 256.0 | 258.0 | 257.8 |
| 40 | 256.2 | 258.3 | 257.56 |
| 80 | 256 | 259 | 256.06 |
| 120 | 256.07 | 260.6 | 255.09 |
| 160 | 257.08 | 261.4 | 255.05 |
| 200 | 257 | 261.8 | 254.08 |
| 240 | 257.06 | 262.01 | 254.01 |
| 280 | 257 | 262.9 | 253.06 |
| 320 | 257.02 | 262.8 | 252 |
| 360 | 257.6 | 263.1 | 252.1 |
| 400 | 258 | 263.6 | 252.06 |

The refractive index of the solution increases with increase in glucose concentration. This leads to increase in scattering and hence outputs of D1 and D2 photodiodes increased. On the other hand the increase in glucose concentration leads to decrease in transmittance. Therefore the output of D3 photodiodes decreased. Output of photodiodes for different glucose concentrations are shown in the table 1.

### *4.3. In-vivo experiment and Results*

The NIR technique is extended to in-vivo tests on inter subjects as well as intra subjects. In order to test our prototype for in-vivo analysis, ten non-diabetic subjects (age 31.5 ± 7.5 years, BMI 22± 4 kg/m2) are considered for blood glucose measurement under controlled temperature and humidity conditions. Informed consent was obtained from all participants. Three different probes are designed for signal monitoring from finger, ear lobe and arm. For finger and ear lobe LED and sensor are place on opposite side to observe transmitted signal. Whereas in case of arm LED and detector are placed on same side in order to observe diffused reflectance spectra. Block diagram of setup is shown in the figure 4. It is observed from the result that increase in glucose concentration cause decrease in reflective index of blood cells and extra cellular fluids . Transmitted signal increases with increase in glucose concentration and reflected signal decreases. In case of finger and ear lobe, the source and detectors are place at opposite sides of measurement site. The transmitted signal observed at photo detector increases. On the other hand in case of arm source and detector are place on same side. Therefore, scattered signal is observed through forearm. It can be analysed from the table that the signal decreases after having food. It is also observed from table 2 that maximum

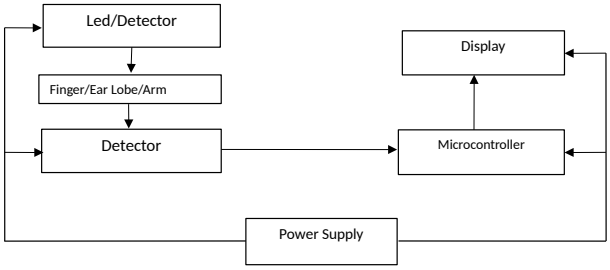


Fig. 4. Shows block diagram of experimental setup

changes observed in case of ear lobe because ear lobe is boneless measurement site with shorter path length. Hence maximum signal observed due to blood glucose changes.

Table 2. Output of in-vivo test

| Subject No. | Ear voltage(mv) | | Arm voltage(mv) | | Finger voltage (mv) | | Commercial gluco-meter(mg/dL) | |
|---|---|---|---|---|---|---|---|---|
| | Before Food | After Food | Before Food | After Food | Before Food | After Food | Before Food | After Food |
| 1 | 1670 | 1882 | 1560 | 1364 | 1675 | 1863 | 111 | 133 |
| 2 | 1642 | 1851 | 1622 | 1558 | 1957 | 1831 | 117 | 139 |
| 3 | 1639 | 1845 | 1527 | 1341 | 1656 | 1866 | 119 | 138 |
| 4 | 1764 | 1942 | 1541 | 1338 | 1771 | 1943 | 105 | 132 |
| 5 | 1673 | 1893 | 1662 | 1453 | 1672 | 1856 | 109 | 130 |
| 6 | 1604 | 1757 | 1429 | 1302 | 1593 | 1788 | 120 | 145 |
| 7 | 1667 | 1871 | 1581 | 1370 | 1675 | 1852 | 105 | 131 |
| 8 | 1703 | 1919 | 1603 | 1407 | 1702 | 1939 | 98 | 133 |
| 9 | 1640 | 1832 | 1510 | 1335 | 1670 | 1830 | 113 | 147 |
| 10 | 1679 | 1885 | 1572 | 1384 | 1690 | 1861 | 116 | 153 |

## 5. CONCLUSION

Preliminary in-vitro prototype for glucose measurement is designed for study the behaviour of light. It is observed that significant scattering and transmittance changes are obtained with variation in glucose concentrations. In vitro experiments show a strong correlation between calculated and actual glucose concentrations. The satisfactory performance of in-vitro prototype provides the motivation to extend the proposed methodology for in-vivo measurement. Three photodiodes were placed at $45^0$, $90^0$ and $180^0$ angles to know the behavior of glucose under plane polarized light. Maximum polarization is observed at $180^0$ as compared to $45^0$ and $90^0$ . Later a prototype was designed for in-vivo blood glucose monitoring. Three probes are designed for arm, finger and ear lobe. Prototype is tested on 10 non-diabetic subjects. A preliminary study shows that the promising results for the development of non invasive blood glucose measurement. Maximum changes observed in case of ear lobe because ear lobe is boneless measurement site with shorter path length. Moreover it is also observed that trend observed in output signal of prototype resembles with that obtained by commercial gluco-meter.

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