Non-Invasive Glucose Measurement Techniques using Near-Infrared Spectroscopy

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Abstract:-The paper describes the various Blood Glucose measurement made non-invasively using the concept of Near-Infrared (NIR) Spectroscopy. NIR has been the recent trend of measurement as far as non-invasive technique is preferred. The various non-invasive glucose measurement techniques are discussed in which NIR plays a vital role.

Index Terms: NIR Spectroscopy, Noninvasive, Plethysmograph, Regression Equations

I. INTRODUCTION

Blood Glucose testing is a cornerstone for effective Diabetes Management. Diabetes is a growing health concern these days..It is a metabolic disorder in which the blood glucose levels tend to fluctuate from its normal range which is 90 to 140 mg/dl. The human body regulates the glucose level in the blood by means of a hormone called Insulin. Diabetes is the state in which the body is not able to produce insulin or cannot make use of those being produced; which is classified into Type I and Type II. respectively. According to World Health Organization (WHO), every year 35 million people die because of Diabetes [1]. At present, there are no methods available that can permanently cure Diabetes. Regular glucose monitoring, diet plan, insulin shots and medications are the techniques that can keep diabetes under control, out of which regular glucose monitoring is more efficient. The amount of glucose in the blood provides the information regarding the diabetic condition. A person suffering from diabetes can have either a raised or lower levels of glucose count. Thus the Blood Glucose level helps in making decisions regarding the food and physical activity. The current measurement gadgets are based on the Invasive technique. The commercial available ones are the Glucose meters which requires direct blood samples by means of pricking ;which inevitable brings pain and infection to the patients. In order to avoid the disadvantages of invasive method, a quite number of non-invasive techniques are experimented.

II. GLUCOSE IN HUMAN BODY

D-Glucose is the molecule which is present in the body whose chemical formula is $C_6H_{12}O_6$. The human blood consists of this molecule in the water base of plasma. The glucose concentration in the blood can vary between 60- 160 mg/dl [2]. The arterial and the capillary blood taken from the fingertip will have an identical glucose content when compared with the glucose level of the venous blood which is lower. The blood glucose is also present in other bi-fluids such as interstitial fluids, saliva, sweat and urine.

Glucose permeates the Red Blood Cells (RBC) via passive diffusion. RBC works as buffer to control the blood plasma glucose concentration. When the glucose concentration of plasma increases, the water moves from Interstitial Fluid (ISF) to plasma and the glucose then diffuses to ISF where it forms the energy source for the cells. Apart from the plasma and ISF, there are other blood transporters present in the cell membrane.

III. NON-INVASIVE TECHNIQUES

The Non-Invasive glucose measurement technique does not require any blood samples which means no pricking. The different technologies are listed below:

- Mid Infrared (MIR) Spectroscopy
- Bio impedance Spectroscopy
- Fluorescence
- Raman Spectroscopy
- Near Infrared (NIR) Spectroscopy

A. Mid Infrared (MIR) Spectroscopy

Mid Infrared Spectroscopy light is concentrated around 2500-1000 nm range [3]. Compared with the NIR, it has a poor input. It has strong ro-vibrational molecular transitions. The fundamental vibration bands have stronger line strengths than the overtone and the combinational bands of visible and Near Infrared. Some absorption bands are so strong thus leading to complete absorption and no spectra.

B. Bio Impedance Spectroscopy

The method provides the measure of the resistance offered to the electric current flowing through the tissues of an organism. The impedance spectrum is measured in the frequency range of 0.1 to 100 MHzThe measurement provided by the bioelectric impedance is useful as a non-invasive technique for measuring body composition.

C. Fluorescence

This technique makes use of fluorescence reagents to identify the presence of glucose molecules in blood. It is very sensitive with little or less damage being done to the body. However, its short life and bio-compatibility are still a concern for its popularity.

D. Raman Spectroscopy

The Spectroscopy technique makes use of a light source preferably a laser light to induce oscillation and rotation in human fluids which contains glucose. Since the emission of the scattered light is influenced by the molecular vibration, the estimation of glucose concentration is made possible.

E. Near Infrared (NIR) Spectroscopy

Near Infrared has a wavelength of 750-2500 nm. It consists of broad bands which corresponds to overlapping peaks. The blood glucose measurement inthe tissue is made by employing variations of light intensity based on transmittance and reflectance.NIR spectroscopy permits glucose estimation in tissues in the scope of 1–100 mm of profundities, with a lessening in entrance profundity for expanding wavelength values [4].The Beer-Lambert's Law provides a mathematical formulation for the calculation of absorbance of a sample from the concentration and the thickness of the sample [5]. The absorbance value is also related to the transmittance. The Beer-Lambert's Law is a combination of two laws that forms a mathematical model for expressing the light absorbed by matter, and how the intensity of transmitted light decreases exponentially as concentration of the substance in the solution increases. The transmittance is related to the optical depth and the absorbance (A) as in [6]

$$A = \varepsilon cl \quad (1)$$

which can be also given by:

$$OD = LOG_{10}\frac{I_0}{I} = \varepsilon cl \quad (2)$$

Where OD – Optical density
I_0 - Light intensity of incident light
I – Light intensity of the transmitted light
E – Extinction coefficient
C – Concentration of blood glucose
l – Length of light path through solution

IV. VARIOUS NIR SPECTROSCOPY DESIGNS OF BLOOD GLUCOSE MEASUREMENT

The various non-invasive NIR based glucose measurement methodologies are:

A. Blood Glucose Measurement System using Glucose Sensor

The proposed system comprises of six segments which involves a Glucose Sensor, Power Supply, Voltage Divider , Voltage Regulator, Microcontroller and a LCD.A power supply of 12V is given to the sensor[7].The sensor transmits the signals and obtain the infrared beams through the fingers. Voltage Divider circuit partitions the 12V to yield the required 5V. The microcontroller is to process and display the result in the LCD. The prototype is based purely on the absorbance transmittance photometry, from which the absorbance is based on the Beer-Lambert's law.

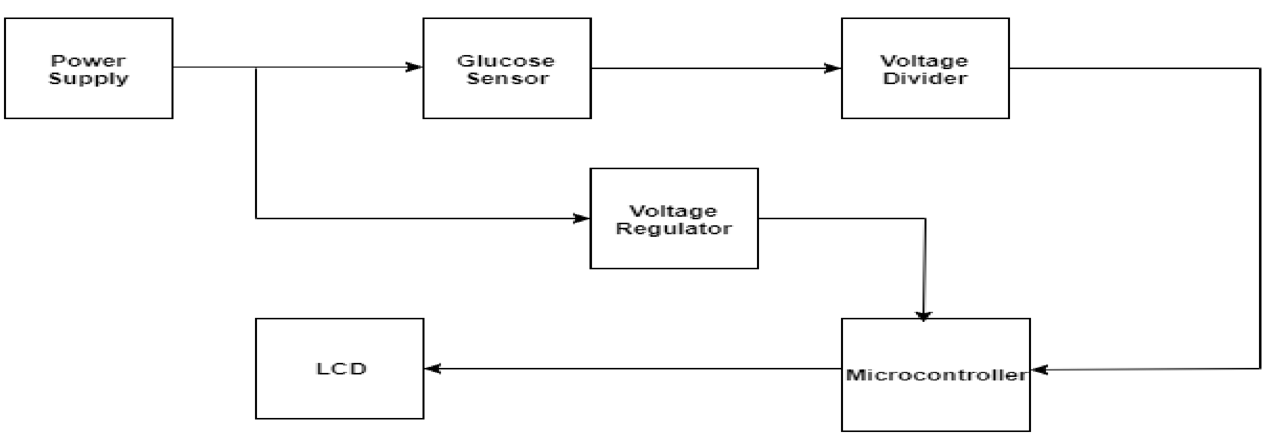

Fig1: Blood Glucose System using Glucose Sensor

The values obtained non-invasively are compared with the ones obtained through commercial glucose meters [7]. The results obtained through non-invasive technique almost matches with the invasive measurement, thus making the system more feasible.

B. Glucose Estimation Based on Near Infrared Laser Diode Spectroscopy

The prototype includes a finger plethysmograph to estimate the resistivity of the blood which is related to the amount of glucose in the blood. The hardware part consist of a Laser Diode which is of the wavelength of 650 nm , a Laser Driver, two Voltage Regulators, a 9V Step-down Transformer , Bridged Rectifier, two Photo detectors, an Amplifier, Analog to Digital Converter, Arduino Uno as the Microcontroller and a LCD to display the signal intensity[8]. The right index finger of the subject is placed between the laser source and the photo detectors, to measure the signal intensity V. The laser diode used is of a He-Ne red one. The regression equations are considered to obtain the best fitting model and to estimate the values to correlate the validity of the device. The technical principle is to implement the existing photoplethysmograph principle of the pulse oximeters to estimate the glucose concentration. The Laser beam is directed towards the tissue where the light is being absorbed and scattered. Out of the total scattered radiation, a portion of it is allowed to impinge on the photo detector.

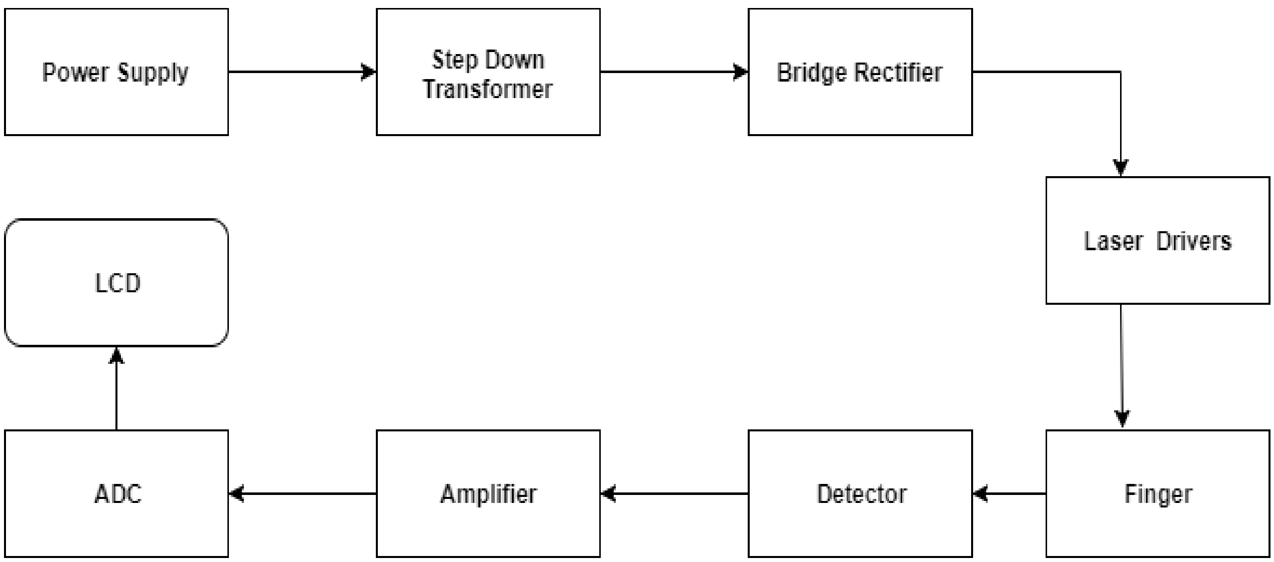

Fig 2. Glucose Estimator Based on Laser Diode

Since the basic principle is based on absorption and scattering, the interaction of the skin layer is considered. The human skin is a multilayered organ and the absorption depends on the melanin content. The wavelength of the laser diode is chosen in such a way that it can provide the best absorption of glucose in the near infrared region without much absorption of water and hemoglobin from the tissues and it can penetrate deeper into the tissues. The absorption window of NIR ranges between 650 nm to 1350 nm for human tissues. The laser tissue interaction provides the optical characteristics of the biological tissues and the changes that can occur in the optical and electrical parameters of the blood. The regression equation is also considered in order to correlate the data with the measurement obtained from the finger plethysmograph.

C. Optical Based Glucose Monitoring Sensor Prototype

The prototype is of a low cost non-invasive spectroscopy based glucose monitoring system which is based on invitro and in vivo experiments conducted. The components used are a 3mm T-1 Infrared emitting Diode of wavelength 950 nm, a Silicon PIN Photodiode, Opto semiconductors in the range of 350 nm to1100 nm, ADC, a Microcontroller [9]. The diode forms the light source. Initially the sample thickness is measured which in fact is located between the NIR light source and the detector. The output from the sensor is obtained for converting using the ADC module. The absorbance and the concentration values are calculated using a Data processing algorithm. The reference value is obtained using a multiplier function which in fact is the previous obtained value. The data thus obtained is parsed to Lab VIEW using the Lab VIEW interface for the Arduino module.

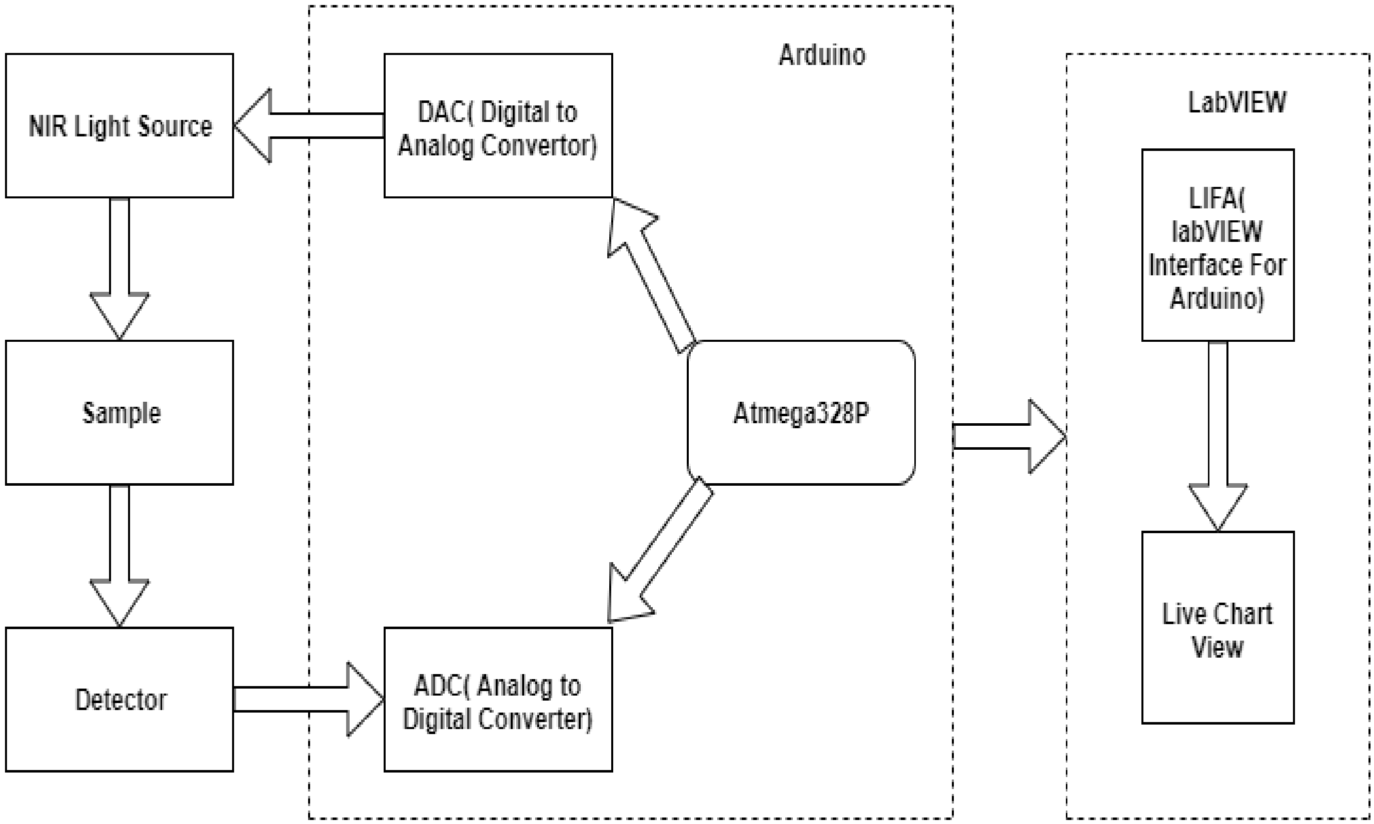

Fig 3. Optical Based Glucose Sensor

The invitro experiment is done using a higher concentration solution of glucose (111mMol) .The NIR Spectra is measured from it. A high precision measuring tube of 50 ml is used to measure the glucose powder and the distilled water. Two aqueous glucose solutions with the same concentration are used for the experiment. A reference reading is considered. With each increment to the initial solution, the concentration of the solution too increased which is to obtain a set of readings whose average value is taken at the end. The increase in the concentration increases the output voltage [9], thus stating a linear behavior between the output voltage and the concentration. Then vivo experiment is done on the index finger. The spectroscopy is initiated when the human tissue is placed between the source and the detector circuit. The calibration process is done considering both invasive and non-invasive values to get the value of the molar absorptive coefficient. The system can be prototyped with low manufacturing and maintenance cost which can in fact provide a promising future for NIR non-invasive techniques.

D. Glucose Monitoring System Based on Distributed Multi-Sensors Information Fusion of Multi wavelength NIR

The system involves a near infrared multi wavelength noninvasive blood glucose monitoring system with distributed laser multi sensors [10].The monitoring accuracy is based on the multi- sensor information fusion model on Back Propagation Artificial Neural Network (BP-ANN). The Root Mean Square Error of the Prediction (RMSEP) for the non-invasive glucose measurement is taken as 0.088mmol/L and the Correlation Coefficient (CC) is 0.94.The prototype includes 3*3 laser diode arrays operating at output powers of 5mw [7]. The measurement region is chosen between 1400-1800 nm. The measurement site is exposed outside and to decrease the influence of outside factors, individual difference like age, gender are considered low. The system has six channels of laser-driving and photo – amplification circuit. It also consists of a photodiode feedback circuit to operate the laser with an output power of 5mw. The spectral signal obtained is amplified and is transferred to plug seat JP2-1 which is connected to the Analog to Digital (A/D) Convertor .The A/D Convertor supports the Lab View Drive which displays the data from the amplified signal.

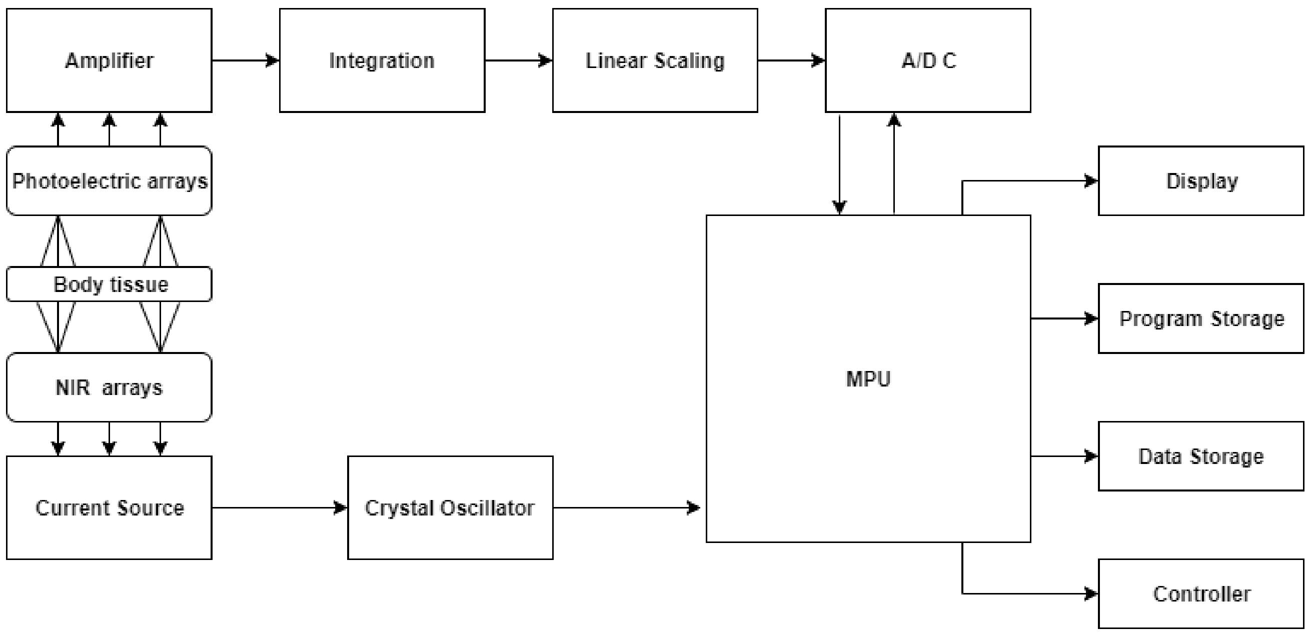

Fig 4. Glucose Monitoring System Based on Distributed Multi-Sensors Information Fusion.

The BP-ANN being a supervised learning network has two phases of positive transmitting processing and error reverse transmitting processing. A 3 layer BP-ANN is considered to model fuse multisensor information and to predict the blood glucose concentration. The Least Square Error Function is taken as the error function for the training of BP. The prediction done by the Lab View includes 8 measurement options and the corresponding blood glucose prediction program will be launched on selecting. A glucose sample experiment is also done along with the non-invasive technique , each done with a single ,two and three wavelengths. In the case of glucose sample, the samples are taken in a 5mm quartz cell and the temperature is maintained at 37^0 C. Two sets having 20 samples are taken with varying concentrations ranging from 10 to 200 mg/dL.

In the case of non-invasive, the glucose tests are done on volunteers at certain time before and after meal with atime gap of half an hour. After the glucose measurement, the multi sensors were attached to the measurement sites to get the spectra information [11]. A total of 142 samples were taken out of which 122 couples of glucose absorption spectra were obtained. The model yielded RMSEP of 0.08mmol/L and CC of 0.9315 using three wavelengths, thus stating that BP-ANN decreases the prediction error.

E. Blood Glucose Monitoring and Detection of a Meal

The proposed Glucose Monitor (GM) consists of three modules [12].The first part is the near - infrared module. When the near-infrared light is transmitted through fingers, based on the received near-infrared light signals the concentration of blood glucose level is obtained. Near infrared module consists of a near-infrared LED transmitter, a near-infrared receiver and signal amplifier. The second part of the Arduino is the main control chip, which is responsible for the processing of received blood glucose signal. The Arduino provides an Integrated Development Environment (IDE) that is capable of running on all major operating systems and has support for a simplified C/C++ programming language [13]. The third part is the LCD to display the result of Arduino processing.

The data thus obtained is used for the Meal Detection Algorithm (MDA) which is used as a part of an artificial beta-cell [14] .The meal challenge can be met, in principle, by three different approaches. The first one is the feed-forward control approach in which the user of the artificial beta-cell informs the controller about the occurrence of a meal by clicking a button to initiate an insulin bolus. The second way uses a feedback control, where the algorithm responds only if there is sufficient rise in glucose. The third approach is based on discrete meal detection; which triggers an insulin bolus using continuous feedback from a GM. The glucose Rate of Change (RoC) is estimated by two different methods; based on real-time glucose measurements sampled at 1-min intervals. The first approach gives the calculation of glucose RoC using a three-point (current and two previous samples) backward difference [15].The second approach is based on optimal estimation theory, using a Kalman filter [16].The proposed algorithm for meal detection is divided into five stages. The first stage is data acquisition, in which the last 5-min reading from the GM is conveyed to the algorithm. These data are processed in parallel by a RoC component and a Kalman filter estimation algorithm. In the second stage, the RoC estimation is broken into backward difference RoC based on the raw data and backward difference estimation based on the glucose estimation from the Kalman filter.

The estimated RoC is then compared with a threshold value that corresponds to a meal-related rise in glucose and is screened to minimize false-positive detections. Thus, four separate inferences of the actual RoC can be generated. As a safety measure, a meal declaration will not be issued if such a declaration is issued 15–20 min earlier, and a night safety condition prevents any meal announcement during the night. This condition can be adjusted depending on the lifestyle of an individual patient.A voting algorithm is also implemented to minimize the risk of an unnecessary insulin bolus. A meal flag will be sent only if two of three methods or three of four methods consistently detect a meal in the same 5-min time window and the controller will receive a meal flag thus resetting the algorithm for the next data point.

V. CHALLENGES AHEAD FOR NON-INVASIVE GLUCOSE MONITORING

The major difficulties faced by the non-invasive technique includes the indirect way of measurement and the calibration issues[17].The indirect way of measurement makes them vulnerable to low signal to noise ratio; which can be combated by considering a comprehensive evaluation of measurement which covers various physical and chemical tissue parameters [18]. Being non-invasive, which is an indirect technique of measuring glucose, a time lag can occur between the measurements of blood glucose content from different parts of body, which can be repaired using an algorithmic approach. Device calibration is a concern when user- friendly and usability concept is considered. A user –oriented approach by implementing the system through a mobile app has completely made it popular and will yield a higher subject satisfaction in future.

VI. DISCUSSION

Non-invasive glucose monitoring technique through NIR can hold a greater promise for a better, uniform and accurate prototype for managing diabetes. The previous review typically describes the development of various glucose monitoring devices using NIR .Further the challenges faced by the non-invasive technique has been considered.

VII. CONCLUSION

The non-invasive technique is a growing trend and it has viewed quite enough research for the development of a non-invasive glucose monitoring using NIR, the complexity and the indirect measurement still remains a concern for its successful development. Although, some of the devices discussed have made a considerable progress in the concerned area, thus creating a possibility for painless, accurate measurement. Yet, it requires effort to improve the performance and the usability to illustrate its benefits.

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