A Portable Non-Invasive Glucose Monitoring Device

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A Portable Non-Invasive Blood Glucose Monitoring Device

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***Abstract*— Diabetes is known as one of the life threatening diseases in the world that occurs not only among adults and elderly, but also among infants and children. Blood glucose measurements are essential for diabetes patients to determine their insulin dose intake and continuous monitoring is vital to ensure that glucose level is always within the normal range. The commonly used methods to measure glucose level in blood are invasive which are high in accuracy but are usually painful and has higher risk of infections. As an alternative, non-invasive techniques are introduced to develop pain free glucose measuring methods. In this paper, a portable non-invasive blood glucose monitoring device is developed using near infrared sensors. Besides being able to detect glucose concentration in blood, the device is also able to display the glucose level and the required insulin dose, corresponding to the body mass index (BMI) of the user. Several in vitro and in vivo experiments proved the reliability of the device. Results of the experiments proved that the device is reliable in glucose detection with 4% - 16% accuracy compared to the common invasive finger-prick method.**

I. Introduction

Diabetes Mellitus is one of the common life threatening diseases in the world. Malaysia is ranked 10^{th} in the world with the highest number of population with diabetes (World Health Organization, (WHO), 2013). The number prevalence increases every year due to the changes of human's lifestyles. The main cause of diabetes mellitus is still unrevealed, but it is closely related to body weight, gender, diet, genetic and physical activities[1]. There are many known factors that can develop complications in diabetic patients The effects of diabetes can only be seen between six (6) to twelve (12) months after having continuous high level of glucose in blood, which can further lead to other major health problems such as kidney failure, heart disease, blindness, stroke and neuropathy. For example, the possibility of leg amputation in smoking diabetic patients is higher than ordinary smokers due to blockage of blood vessels which can further lead to a more serious heart disease. Addition to that, excess of alcohol consumption in diabetic patients can cause nerve damage and high blood pressure, high blood fats and excess weight gain[1].

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Blood glucose measurement are categorized into three techniques; invasive, minimally invasive, and non-invasive[2]. Invasive techniques in glucose measurement devices are widely used as it has high measurement accuracy. The most common and inexpensive invasive technique is finger prick which requires blood extraction from the finger by using a lancet (small, sharp needle)[2]. The blood sample will be used to measure blood glucose level using a glucometer. Some common practices allow the blood extraction to be obtained from other sites of the body such as the upper arm, forearm, base of the thumb and thigh. However the reading of blood glucose level might vary compared to the reading obtained from the fingertip[3].

Schichiri *et al*. (1985) were the first to introduce the minimally invasive technique by the development of subcutaneously implantable needle-type electrodes The use of subcutaneous implantation technique was able to avoid infection problems such as septicemia, fouling with blood clots and embolism[4]. In 2006, Dachao Li *et al*. (2006) from Tianjian University of China had proposed a new approach of measuring blood glucose level using ultrasonic by combining interstitial fluid transdermal extraction with the surface of plasma resonance detection[6]. Another approach using electrochemical detection was proposed by Jui *et al*. (2011) from the National United University of Taiwan. The application used an electrochemical sensor which consisted of a potentiostat with a glucose test strip and an automatic test system[5]. Results showed that these techniques were able to measure the glucose concentration in blood accurately. Even though minimally invasive techniques help to reduce the pain and risk of infections, it is still not desirable for some diabetic patient as these methods involve direct contact with the tissue. Besides that, the measurement are sometimes not accurate due to noise and artifacts resulted from the patient's movement and the reaction between electrodes and other reactants in blood[7].

The latest technology which is non-invasive has been introduced as an alternative to reduce pain during the blood extraction and insulin injection. Various methods have been introduced such as infrared, photoacoustic, ultrasound and fluorescence to detect glucose in the blood[7][15][16]. Most of the results showed a good correlation between non-invasive and invasive techniques[2]. The major reason for continuous research efforts in the field of non-invasive blood glucose measurement is that it is the only way to develop a pain free glucose monitoring system. Instead of extracting blood, other fluids such as the saliva, sweat, urine or tears can be used as an alternative to measure glucose concentration. Besides that, glucose level can also be measured through direct measurement of body tissues such as the skin, tongue, aqueous humor of the eyes and oral mucosa[7].

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The latest research regarding measurement of the glucose level in sweat was conducted by Oscar *et al*. (2013). The approach uses the electronic nose technology which implemented thirty two (32) metal oxide semiconductor (MOS) sensors, operating at different temperatures to detect the glucose level in sweat[8]. Another research group from New Jersey has been applying the non-invasive technique using Raman spectra to detect glucose in porcine eyes[9]. Glucose solution was injected into the porcine eyes and the concentration was controlled. Afterwards, the Raman spectra were measured using a compact spectroscopic system with a laser excitation wavelength at 785 nm. From the results, both approaches proved to have high viability in glucose detection[8][9].

Among the available methods of non-invasive technology are absorbance spectroscopy, photoacoustic spectroscopy, polarimetry, fluorescence and dielectric spectroscopy[10][15][16][17]. Absorbance spectroscopy is the most commonly used method as it allows light to be reflected, scattered and transmitted when its focused on biological tissues, which depends on the structural and the chemical composition of the sample[10].

Diabetic patients should continuously monitor their glucose levels at a normal range. A self - monitoring system is required to ensure their glucose levels is always within the normal range and it may also help in maintaining their diet and physical activities. One of the earliest portable non-invasive blood glucose devices was introduced by Arlene Duncan *et al*. (1995) which used pulsed laser photoacoustic spectroscopy to detect the glucose concentration in blood from the finger[15]. Another approach of a portable glucose sensor was developed by J.R. Blanco *et al. (*2006) who designed a low cost portable potentiostat for amperometric biosensors. The device measures the Faradaic current that originated by the electronic interchanges between specific substance and biological recognition system which was present on the electrodes and kept at an appropriate potential[16]. In 2013 Takahashi *et al.* has developed a portable glucose monitoring system by using implantable fluorescent-hydrogen sensor, wearable photo detector, microcontroller, wireless device and software for transdermal. The experiment was conducted by attaching the portable device to the rat's ear and fluorescent intensity was measured for three (3) days[17]. Both approaches applied non-invasive technique to measure the glucose levels and shown to be reliable and accurate in measuring glucose level in blood[16][17]. The reported researches proved that the implementation of non-invasive techniques were appropriate to develop portable non-invasive glucose monitoring systems.

In this paper, the design of a portable non-invasive glucose blood monitoring device using the absorbance principle is proposed. The proposed device is designed to be able to detect glucose level in blood using near infrared sensors and also to determine the required insulin dose corresponding to the body mass index (BMI) of a user The design of the device is not only intended for diabetic patients but are also for non-diabetic patients, to help maintain a normal blood glucose level for a healthy life style.

II. METHODOLOGY

Figure 1 illustrates the block diagram of the proposed portable non-invasive glucose monitoring system.

A. Hardware Implementation

The main hardware components in the system include a transmitter (LED1550E), a photodiode (FGA10), an operational amplifier (OP491), microcontroller (Arduino Uno) and a liquid crystal display (LCD) keypad shield.

The NIR detection circuit (as shown in Figure 2(a) and 2(b)) consists of a transmitter circuit and a receiver circuit with both transmitter and receiver positioned side by side and points to a reflective surface. Both transmitter and receiver operate at 5 V and are powered by the Arduino microcontroller. The receiver circuit (as shown in Figure 2(b)) consists of a photodiode, a noise filter and an operational amplifier. A low pass filter is connected to the voltage source to reduce the noise frequency from the source.

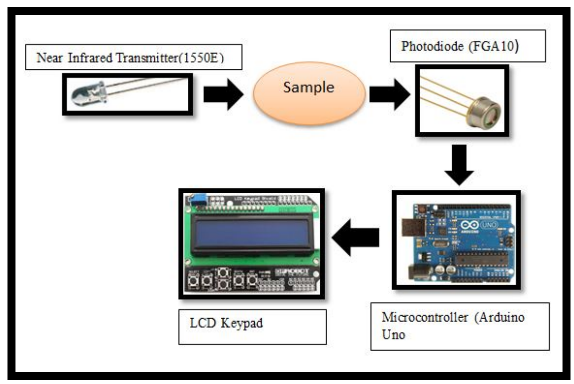
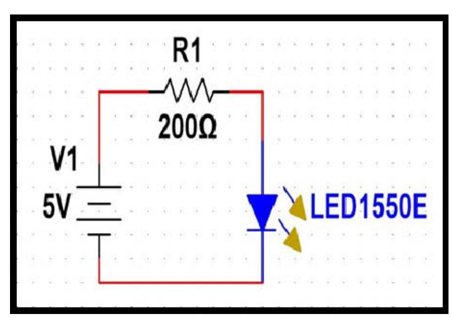
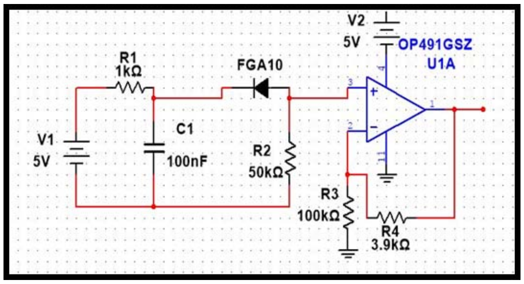


Figure 1: Block diagram of the portable non-invasive blood glucose monitoring device

The FGA10 photodiode is suitable to be used with the transmitter as it has a wavelength sensitivity which is within 800 nm-1800 nm. The photodiode is used to measure continuous wave fiber light source and converts the optical power received from the transmitter to an electrical current value. The value of the output voltage depends on the intensity of the infrared signal it receives, which is between 0 V to 5 V. An operational amplifier is used to amplify the output signal. Figure 3.4 (b) shows the complete schematic diagram of the detection circuit.



(a)



(b)

Figure 2: Schematic diagram of the NIR detection circuit. (a) Transmitter circuit. (b) Receiver (photodiode) circuit.

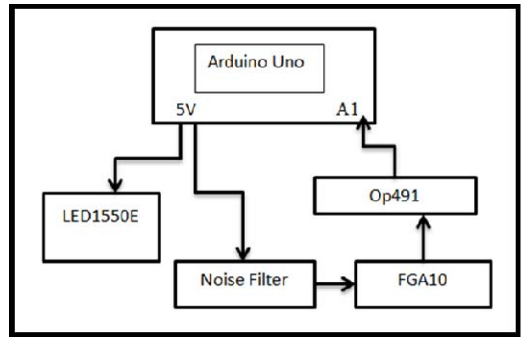
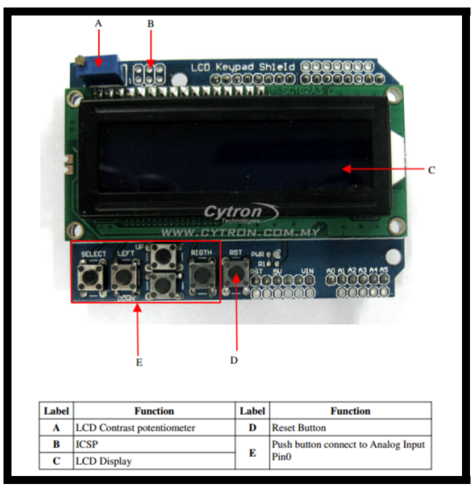


Figure 4: Block diagram of the Arduino microcontroller and the detection circuit

The LCD keypad shield, as in Figure 3 is developed to be used with any compatible Arduino boards. It consists of six (6) momentary push buttons and a 2x16 LCD screen. Pins 4 to 9 of the main Arduino board are used to control the LCD display, while pin 8 and 9 are used for Register Select (RS) and Enable pin. The LCD keypad shield is used to enter the height and weight of a user and the screen to display the measured glucose concentration and required insulin dose of a particular user .



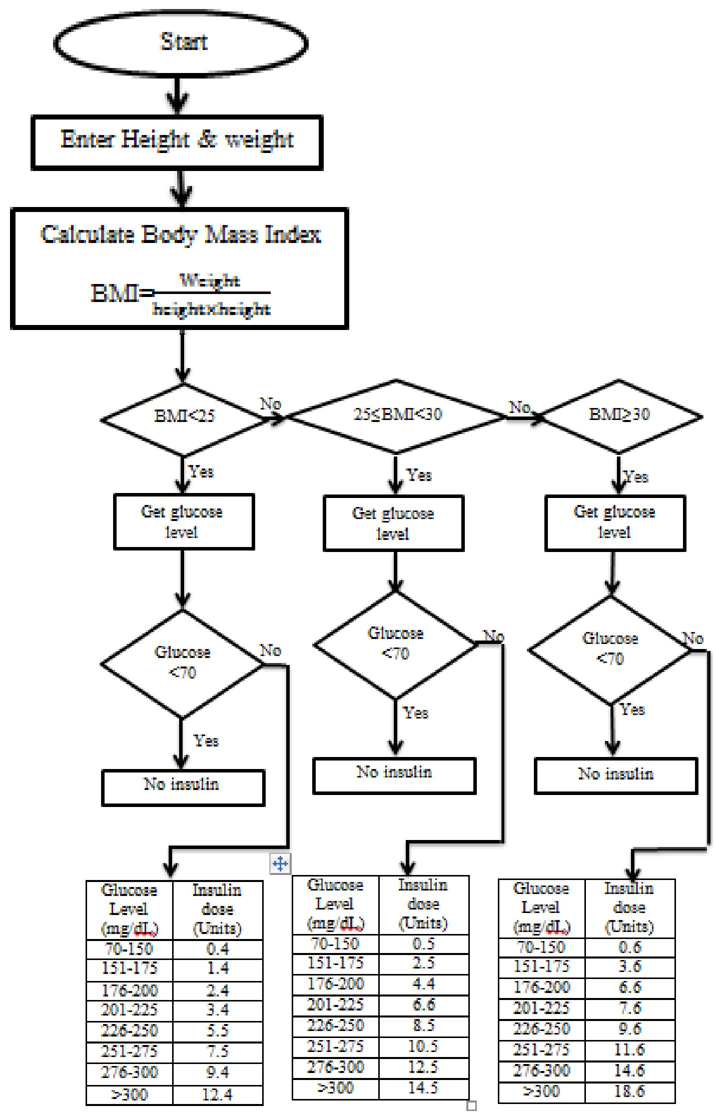
Label	Function	Label	Function
A	LCD Contrast potentiometer	D	Reset Button
B	ICSP	E	Push button connect to Analog Input Pin0
C	LCD Display		

Figure 3: LCD Keypad shield

B. Software Development

The main focus of the software development is on the algorithm design of the microcontroller. The control system of the device uses the Arduino Uno which is a microcontroller board based on Atmega328 with fourteen (14) digital input and output pins. It can be powered by a (5 V-12 V) battery or by a serial connection to the computer. The microcontroller supplies voltages to bias both transmitter and photodiode. The output of the photodiode and amplifier are connected to the analogue pin of the microcontroller. The block diagram of the Arduino and the detection circuit is show in Figure 4.

The algorithm for the microcontroller is designed to calculate the concentration of glucose as well as the required insulin dose, corresponding to the body mass index (BMI) of the user. The output voltage obtained from the photodiode is used as a parameter to determine the glucose concentration by using a mathematical equation acquired from the glucose calibration experiments. Figure 5 illustrates the algorithm of the glucose and insulin calculations for three (3) different BMI groups; underweight (BMI < 25), normal (25 ≤BMI ≥30), and overweight (BMI > 30). The data are based on subcutaneous insulin order set of Banner Good Samaritan Medical Centre, Phoenix[14].



Glucose Level (mg/dL)	Insulin dose (Units)
70-150	0.4
151-175	1.4
176-200	2.4
201-225	3.4
226-250	5.5
251-275	7.5
276-300	9.4
>300	12.4

Glucose Level (mg/dL)	Insulin dose (Units)
70-150	0.5
151-175	2.5
176-200	4.4
201-225	6.6
226-250	8.5
251-275	10.5
276-300	12.5
>300	14.5

Glucose Level (mg/dL)	Insulin dose (Units)
70-150	0.6
151-175	3.6
176-200	6.6
201-225	7.6
226-250	9.6
251-275	11.6
276-300	14.6
>300	18.6

Figure 5: Algorithm of the glucose and insulin calculations for three (3) body mass index (BMI) groups

Two (2) sets of experiments were conducted to determine the relationship between glucose concentration and the sensor's output voltage. Several glucose solutions of different concentrations ranging from (10 mg/dL - 320 mg/dL) were prepared by dissolving glucose (dextrose monohydrate) in 1 dL of distilled water. The glucose solutions were prepared in tinted amber reagent bottles to avoid from being affected by light. For voltage measurements, 30ml of glucose solutions for each concentration were placed into a cuvette and positioned as shown in Figure 6. In addition, a reliability test was carried out by comparing the glucose concentration measurements from four subjects using invasive techniques (Accu-Check) and the proposed device.

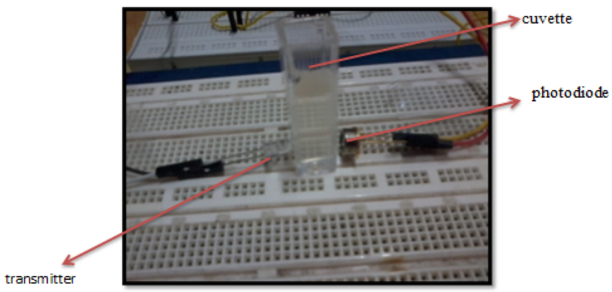


Figure 6: Glucose calibration experimental setup

III. RESULTS & DISCUSSION

A. Glucose Concentration Calibration Curve

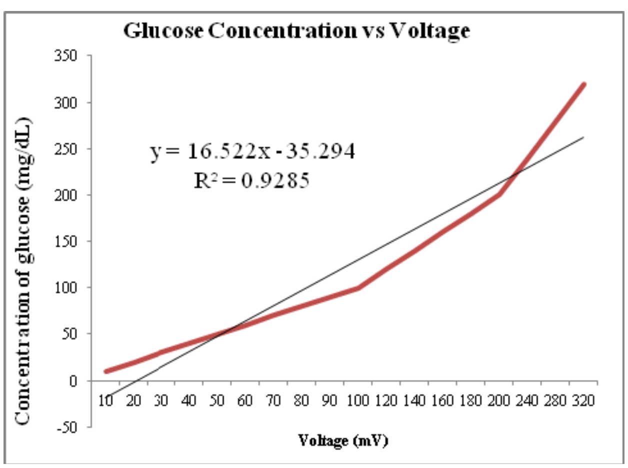


Figure 7: Relationship between glucose concentration (mg/dL) and voltage (V)

Results from the calibration experiments show that the output voltage of the sensor increases in direct proportion with increase of glucose concentration as shown in Figure 7. The relationship between glucose concentration and voltage is linear as described in (1);

$$y = 16.522x - 35.294 \quad (1)$$

where y is the glucose concentration (in mg/DL) and x is output voltage (in V).

The R^2 value (regression value) obtained from the graph in Figure 7 is 0.9285 which shows a good correlation between both (glucose concentration and voltage) variables. This proves that the linear relationship between glucose concentration and voltage is significant.

B. Device Operation

The operation of the system starts once the transmitter in Figure 8 transmits an infrared signal which is exposed to the glucose solution or blood sample. The glucose molecule in the glucose solution or blood sample reflects the infrared signal to the receiver (photodiode). The photodiode receives the infrared signal which is converted to an equivalent voltage value. The Arduino Uno microcontroller, uses these voltage value as a parameter to calculate the glucose concentration and determine the insulin dose needed corresponding to the user's body mass index (BMI). Finally, the measured glucose concentration and insulin dose will be displayed on the LCD screen.

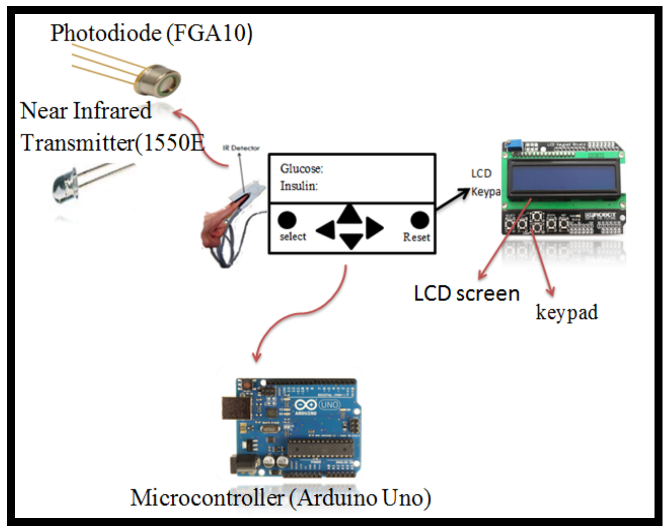


Figure 8: The portable non-invasive glucose monitoring device

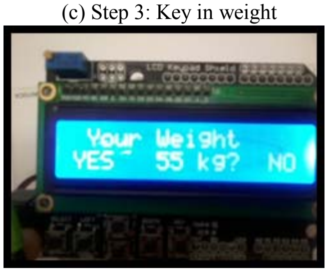
The device is developed using a near infrared sensor with a peak wavelength of 1550 nm and Arduino Uno as a microcontroller. From a research conducted in McMaster University, it was found that NIR with higher wavelength (2050 nm) was able to penetrate deeper into the body tissue. However, too high of observance may cause other substances in the blood to interfere with the infrared signal[11]. In their experiments, the results obtained using NIR of 1450 nm proved that the NIR which was less than 2000 nm is more appropriate when implemented using Arduino.

The device requires the user to key in their height and weight using the push buttons as shown in Figure 9(a). Once the height and weight are entered, the BMI for the user will be calculated and shown on the LCD screen. To proceed to the next process, the user will need to press the SELECT button. At this stage, the sensor will start to be activated and a "READY" message will be displayed on the screen as in Figure 9(f). Once the glucose concentration is measured, the device will calculate the required insulin dose corresponding to the BMI and display the measured glucose concentration in mg/dL and insulin dose needed in Units as shown in the last step. The user is able to repeat the measurement by pressing the RESET button. The working displays on the LCD screen are shown in the steps below:

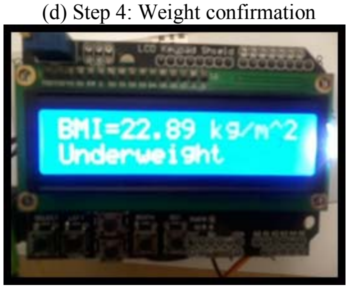
(a) Step 1: Key in height

(b) Step 2: Height confirmation

(c) Step 3: Key in weight



(d) Step 4: Weight confirmation



(e) Step 5: Determine body mass index

(f) Step 6: The activation of NIR sensor

(g) Step 7: Glucose concentration and insulin dose display

Figure 9: Step by step operational flow of the device

C. *Invasive vs Non-invasive Reliability Tests*

A reliability test was conducted on four (4) subjects using both invasive technique with the finger-prick method (Accu-Check) and the non-invasive technique with the portable device. Blood glucose measurements from both methods were compared in Table 1. The percentage difference for each measurements between the two techniques were calculated as in (2),

$$\%\ Error = \frac{Glucose_{invasive} - Glucose_{non\text{-}invasive}}{Glucose_{non\text{-}invasive}} \times 100\% \qquad (2)$$

where $Glucose_{invasive}$ is the glucose reading from the invasive technique (Accu-Check) and $Glucose_{non\text{-}invasive}$ is the glucose reading from the non-invasive technique.

TABLE.1: COMPARISON OF BLOOD GLUCOSE CONCENTRATION MEASUREMENTS USING INVASIVE (ACCU-CHECK) AND NON-INVASIVE METHOD

Subjects	**Glucose Concentration Measurements (mg/dL)**		**Percentage Difference (%)**
	Accu Check	**NIR Sensor**	
1	108	113.15	4.70
2	98	114.31	16.64
3	98	113.15	15.46
4	103	116.75	13.3

Results from the reliability test showed that, there is a good glucose measurement agreement between the two methods (Accu-check and NIR Sensor), which is proved from the low percentage difference (4%-16%) when both glucose measurements of the same subjects were compared. The slight differences may be due to several factors which include the calibration curve which was obtained from glucose solutions measurement only and does not contain any other substances as in real blood. The physical factor of different users may also effects the measurements as each user has different skin thickness which effects the penetration of the infrared signal[7]. Another factor might be due to the infrared signal being scattered to the surroundings and less will be received by the photodiode[12].

IV. CONCLUSION

The developed portable device was able to detect different glucose concentration and determine the required insulin dose for different BMI measurement. The detection sensor was developed using a near infrared sensor with a peak wavelength of 1550 nm and a photodiode (FGA10)..

In-vitro experiments were conducted to determine the relationship between glucose concentration and voltage. Results showed that these two variables have a strong linear relationship; voltage increases as glucose concentration increases. The percentage difference obtained from the reliability test was less than 20%, which proved that the non-invasive technique implemented in the device is reliable to be used to measure glucose in blood. The portable non-invasive blood glucose monitoring device is not only beneficial for diabetic patients, but also for normal people to keep their glucose level at normal range to maintain a healthy lifestyle.

As a recommendation for future improvements, to ensure that most of the infrared signal is focused, the transmitter can be designed to be mounted to an optical rod[13]. By doing so, the signal can be directed towards the receiver (photodiode) without being scattered to the surroundings. As for the consistency of the output voltage, the sensor should be kept fixed by using any aid of stabilizing apparatus[11]. Besides using the absorbance technique, the reflection technique can also be considered as another technique to design the device as it is also able to provide accurate measurements in glucose detection. Further researches with the help of clinical experts can be conducted to determine the relationship of insulin dose, body mass index and glucose level in blood using patients as subjects. To obtain a more realistic blood glucose calibration, a solution that mimics real blood in the human body may be used.

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