Noninvasive Blood Glucose Detection Using Near Infrared Sensor

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***Abstract*— The development of noninvasive blood glucose detector is desired to replace invasive method which is costly and uncomfortable. Near Infrared (NIR) spectroscopy is used to detect blood glucose noninvasively since glucose has specific absorbance spectrum in NIR range, 850nm – 2500nm.LED is utilized as incoherent infrared source to irradiate body surface in wavelength 1550 nm. Penetrated light is then detected by InGaAs photodiode, sensitive for wavelength 850 – 1700 nm. As the measurement sites, earlobe is chosen since it is thin. Photodiode's current is converted into voltage using transimpedance amplifier circuit. In order to minimize high frequency noise, low pass filter is applied consecutively. Early testing is conducted by measuring penetrated light in various concentration of glucose solution with wavelength 1300nm, 1450nm, and 1550nm. Measurement indicates correlation between voltage and glucose concentration. In earlobe testing, light can penetrate tissue with detected voltage, 300mV – 4V depend on the wavelength. Linear approximation and two point equation is applied to the data. This two approach extracts formula that can estimate blood glucose concentration with maximum 30% error. By using two point equation, a specific formula for each person can be obtained.** (*Abstract*)

Keywords*— *Near Infrared (NIR); sensor; noninvasive; blood glucose; photiode.

I. Introduction

Today, finger pricking method is used to measure blood glucose concentration. This method uses colorimetric or amperometric principle and needs strips and needles for each measurement. [1]. Unfortunately, this method needs big cost and creates discomfort because of the periodical needle stick injury. Disadvantages of this method is felt by diabetics who need periodic measurement to maintain safe blood glucose concentration. The development of noninvasive blood glucose detector provides great prospect to comfortable and affordable periodic measurement.

Various studies on noninvasive blood glucose measurement has been performed since the early 90s with various methods: sensing electromagnet, ultrasound technology, infrared spectroscopy, etc. [2], [3]. Noninvasive method used for this development is Near Infrared Spectroscopy. This method is chosen since glucose absorbance spectrum in this range is good enough and relatively comparable to water absorbance spectrum. Water absorbance consideration is important since 70% of human tissue content is water. In addition, the provision of tools and sensors such as LED and photodiode at these wavelengths is relatively easy and affordable compared to other methods.

This paper contains draft interface circuit for near infrared sensor. Infrared ray must be able to penetrate the tissue. At the other side, transmitted light is detected by a photodiode. As the measurement sites, earlobe is chosen since it is thin. It has thinner stratum corneum than other body part so that scatter fewer rays. [4]. This circuit is then implemented and tested. First test is performed on variations of glucose solution, 50mg/dl – 2g/dl. Second test is performed directly in earlobe and the result will be correlated using invasive glucose meter.

II. Theory

A. Glucose NIR absorbance spectrum

Each substance has a unique light absorption spectrum. These properties can be utilized to identify a substance by using light. Glucose has excellent light absorption spectrum at Near Infrared (NIR) range. Figure 1 shows normalized absorbance value of glucose and water. In order to fairly comparing, maximum absorbance value for each must be known.

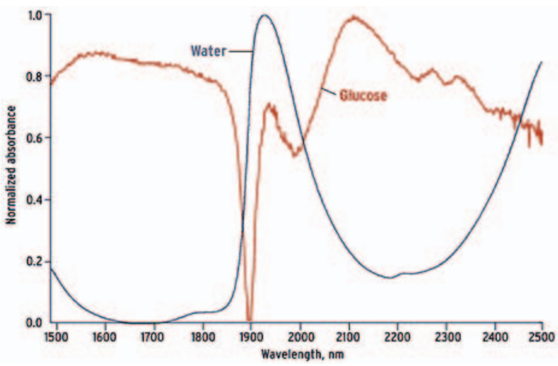


Fig. 1. Water and Glucose Solution Absorbance spectra λ = 1500nm – 2500nm. [8]

Maximum water absorbance is three times higher than glucose absorbance [5]. This means glucose absorbance value is higher than water at a wavelength of 1500nm – 1800nm, especially at ±1660nm when water absorbance is zero. However, the light source for wavelength above 1550nm relatively expensive. Therefore, light alternative under 1550nm with good glucose correlation is taken. Figure 2 shows some wavelength have potential to detect glucose. At 1300nm, concentrated glucose solution less absorbs than pure water. Using this two approach, this paper expects blood glucose levels can be detected using near infrared light, at 1300nm, 1450nm [6], and 1550 nm [7].

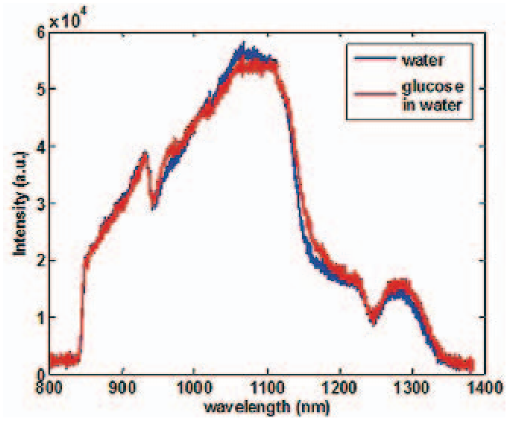


Fig. 2. Water and Glucose Solution Absorbance spectra λ = 800nm - 1400nm [9]

B. NIR Irradiation Effect on Skin Surface

NIR irradiation on skin tissue is scattered due to human body structure. In order to extract information about substance concentration, light must reach blood vessel in dermis [10]. However, some rays will be reflected by outermost skin surface. Some is diffused reflected by substance in the tissue and some is transmitted to the other side. In order to minimize scattering and to make light reach dermis easier, thin tissue is needed. Regarding the requirements, earlobe is the appropriate measurement site [4].

In practice, there's two measurement method for light: transmittance and reflectance. Reflectance measures reflected light which is scattered diffusely from skin surface (diffuse reflectance). Transmittance measures scattered light which go through other side of the tissue. Amount of obtained light depend on tissue thickness and contained substance. Referring to the experiments, transmittance is chosen as measurement method [7].

C. Photiodiode and Interface Circuit

Photodiodes detect light by converting light to electric current due to electron movement in material's PN junction. Produced current is proportional to the optical power and expressed as responsivity in ampere per watt (A/W). Each material has different responsivity towards optical wavelength. Indium Galium Arsenide (InGaAs) is sensitive and has good responsivity to NIR light (λ = 800nm – 1700nm).

Photodiode current is converted to voltage using transimpedance amplifier (TIA) circuit. Photodiode can be configured photoconductive or photovoltaic, such as in fig.3. Photoconductive configuration is utilized in fast light detection. Meanwhile, photovoltaic is used for precision light detection with linear and noiseless output. Photoconductive configuration gives voltage bias to photodiode while photovoltaic not.

Photodiode and its connection to the circuit is prone to noise and signal leakage. Component must generate small noise to keep SNR big. Operational amplifier with JFET input will minimize input bias current so that photodiode current is not disturbed. In order to control noise gain amplifier effect, capacitor is placed parallel with resistor in transimpedance circuit. This can eliminate pole occur from photodiode capacitance effect and minimize high frequency noise gain (see Figure 3).

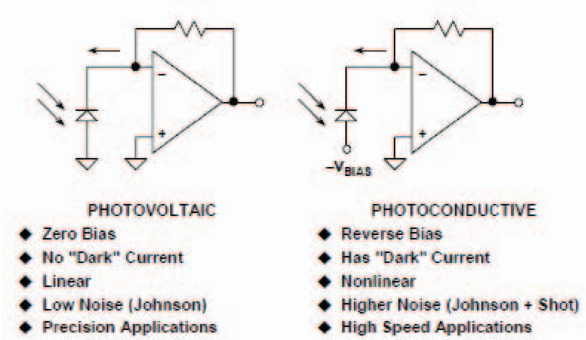


Fig. 3. Transimpedance Circuit [12]

D. Beer Lambert Law

When a light irradiates a substance, it can be absorbed or transmitted. Beer lambert said amount of light that is absorbed by a substance is proportional to the effective path length of the substance (*l*) and the concentration of light absorbing substance (*C*). Absorbance coefficient (□) complete the equation. Absorbance is declared by logarithm of light intensity ratio.

$$A = \log\frac{I}{I_0} = \epsilon.l.C \qquad (1)$$

In glucose solution, there's only two substance to absorb the light: glucose and water. The one that has higher absorbance in a specific wavelength shall be identified by this simple spectroscopy method. Meanwhile, in human tissue it is made off complex substance. A lot of parameter should be taken when applying spectroscopy method in human tissue such as effective pathway length, pigment, etc..

III. Method and Design

A. Component Selection

As light source, NIR LED from Thorlabs is used, with λ = 1300nm, 1450nm, and 1550nm. This LED has narrow spectral wide with peak intensity is around ±10nm from stated wavelength. InGaAs Photodiodes are obtained from ShengShi Optical with sensitivity in λ = 850nm – 1700nm. Responsivity varies for each wavelength from 0.65 to 0.9 A/W. CA3130 from Intersill is chosen as operational amplifier due to its specific application as photodiode amplifier and relatively cheap.

B. Sensor Circuit Design

Transistor is used to enhance and stabilize LED bias current. When using microcontroller to control the lighting, maximum output current from pins is 40mA (ATmega 256). Optical power needed is around 2.5-3mW which can be obtained by forwarding 60mA to LED (see Figure 4).

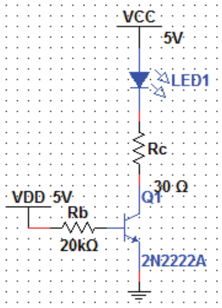


Fig. 4. LED Biasing Circuit using Transistor 2N2222A

Photodiode is interfaced using transimpedance amplifier with photovoltaic configuration. Feedback resistance, R5, is designed as big as possible to compensate small photodiode current. Feedback capacitor, 100 pF, is chosen to minimize noise gain but keeps responsiveness. TIA circuit is followed by RC passive filter to reduce high frequency noise. As anticipation from small voltage output from TIA, noninverting amplifier is added with 2 V_0/V_i amplification (see Figure 5).

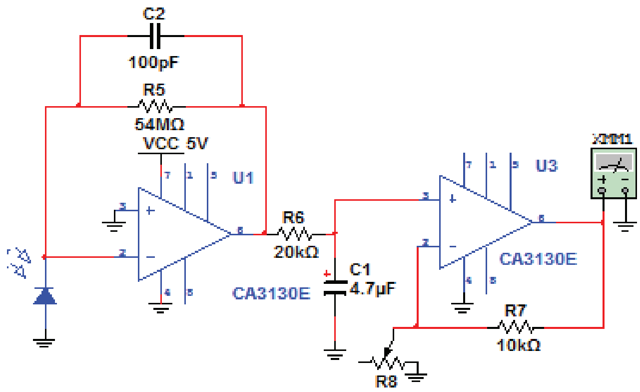
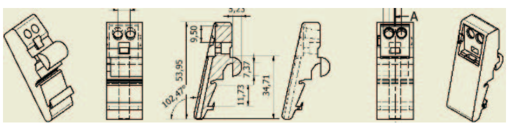


Fig. 5. Photodiode Circuit Design

C. The design of sensor casing

LED is mounted front on photodiode so that the earlobe can be placed in between the component. A custom clamp shaped casing is use to put earlobe in the sensor (see Figure 6). Casing needs to cover the photodiode from unwanted light. Aspects of safety, comfort, and ease of use should be considered which affect the clamp shapes. Clamp's pressure should be maintained so that the blood can flow normally. Four holes is created as places for two LED and two photodiode.


(a)

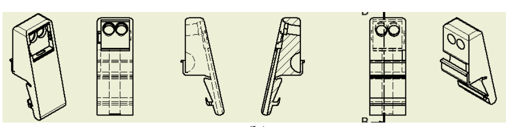

(b)

Fig. 6. Sensor Casing (a) Left side clamp, (b) Right side clamp.

D. Sensor testing on Glucose solution and Earlobe

Sensor sensitivity is tested on various concentration of glucose solution. Glucose solution, 50 mg/dl – 2 g/dl, is made from dextrose powder ($C_6H_{12}O_6.nH_2O$) dissolved in distilled water. Solution is poured in test tube. Test tube is irradiated by NIR light in a simple designed box. LED and photodiode is mounted in the side of the box, facing each other. Photodiode will detect the transmitted light from the tube. Experiment is conducted with three wavelength: λ = 1300nm, 1450nm, 1550nm.

Sensor is also tested in earlobe by clamping it to the earlobe. Photodiode voltage is measured as indicator whether the light transmit the earlobe.

E. Correlation between Voltage and Glucose Concentration

Photodiode voltage is proportional to near infrared light transmittance. It is then correlated with blood glucose concentration. Blood glucose concentration is measured invasively using commercial blood glucometer (EasyTouch GCU) by pricking the finger. Correlation is intended to find blood glucose concentration as a function of photodiode voltage. Two experiments are conducted to get data of blood glucose versus photodiode voltage. At first experiments, ten volunteers, 5 men and 5 women, are involved with variety of age 20-22 y/o. Earlobe voltage and blood glucose concentration are randomly measured without any prerequisite. Photodiode voltage is measured three times for every volunteer.

At second experiment, we examine glucose concentration for one person to remove various factors which influence blood glucose concentration, such as skin color, gender, tissue thickness, earlobe size, etc.. Volunteer is asked to fast to get their minimum glucose concentration. After that we also keeps tracking blood glucose concentration for 15', 30', 60' and 120' after break fasting. This procedure is repeated on the next day. Photodiode voltage in earlobe and blood glucose measurement are measured. A distinct equation is obtained using this experiment.

Two approach is used to get blood glucose concentration formula from these data. First data is correlated linearly and linear blood glucose concentration function of photodiode voltage is obtained. Linear approach is applied based on beer lambert law (1). Light transmittance is calculated using logarithmic function. Meanwhile, for variation of human blood glucose concentration, short variation of photodiode voltage will be obtained. Because of little variation of transmittance ($\frac{I}{I_0}$), we can approximate logarithmic function as linear. This approach is also applied for second data. Another approach is applied using two point equation. Still based on linear approximation of beer lambert equation, equation is formulated using two point from two condition: fasting and 15' after break fasting. This points is inserted to (2).

$$\frac{y-y_1}{y_2-y_1} = \frac{x-x_1}{x_2-x_1} \qquad (2)$$

After getting the equation, the approximation blood glucose concentration is calculated. The difference between actual and approximate blood glucose concentration can lead to sensor accuracy.

IV. IMPLEMENTATION AND TESTING

The circuit (Figure 5) is implemented on epoxy PCB. Sensor casing (Figure 6) is created using 3D printer. Feedback resistance make the output voltage at saturation state (DC, 5V) when the LED is turned on. Capacitor selection affects circuit responsiveness so that 100pF is preferred to larger capacitor. Earlobe clamp is only mounted with led and photodiode. A cable, about 60 cm, is used to connect the component to interface circuit. There is a little AC signal (< 10mV) and DC offset (<10mV) detected.

A. Sensor testing on Glucose solution

Sensor is tested by a various concentrations of glucose solution. Figure 7 – 9 show graphic of glucose concentration versus photodiode voltage for λ = 1300 nm, 1450 nm, and 1550 respectively.

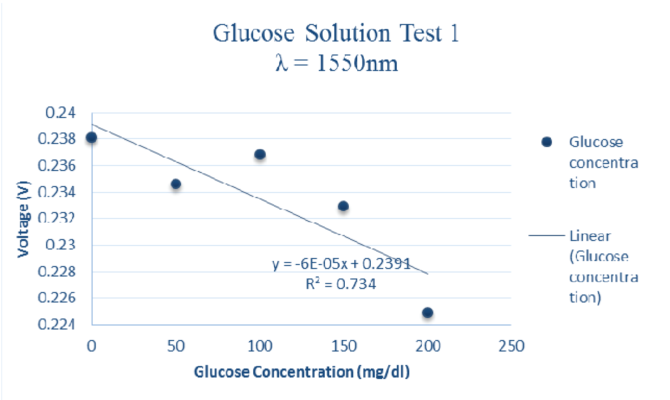


Fig. 7. Glucose concentration and the voltage at λ = 1550nm

From figure 7, it can be concluded generally that there is an inversely proportional relation from photodiode voltage and glucose concentration. By looking this result, we can get glucose sensitivity for the sensor. For each 50 mg/dl increasing of glucose concentration, there is 3 mV raising in photodiode voltage. This is pretty good if we directly compared with blood glucose measurement range. For normal people, it will be around 50 – 250 mg/dl. This means, by assuming glucose solution and blood glucose is identical, we are able to detect blood glucose fluctuating in hundreds to thousand mV range.

For figure 8 and figure 9 it can be concluded that there is a positive correlation between photodiode voltage and glucose concentration. Results for λ= 1450nm is similar to tests in [11] which shows an increasing concentration leads to increasing photodiode voltage. Results for λ= 1300nm is fit with absorbance spectrum in figure 2 which shows concentrated glucose solutions passing more light than pure water. Variation of glucose solution used is different from previous test because short variation (0 – 200mg/dl) can't be detected well so that greater concentration (0 – 14g/dl) is used.

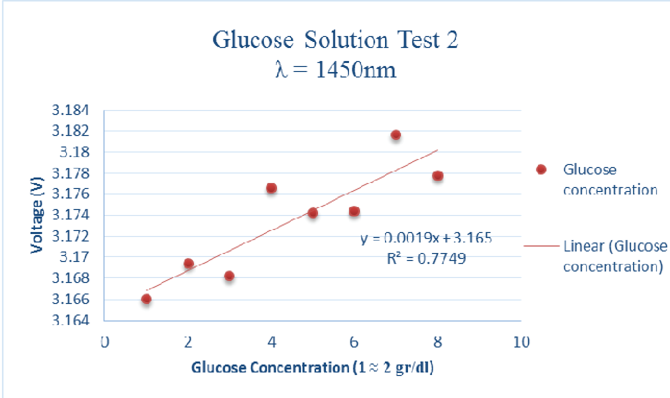


Fig. 8. Glucose concentration and the voltage at λ = 1450nm

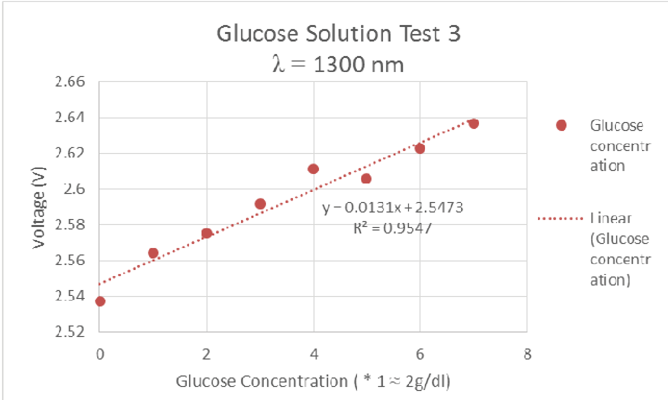


Fig. 9. Glucose concentration and the voltage at λ =1300nm

For both wavelength, every increasing in glucose concentration results in voltage increasing. It means more NIR light detected and less light absorbed by the solution. Meanwhile, when glucose concentration increases, water fraction decreases. This trend shows for this two wavelength the main absorbent is water instead of glucose. The sensitivity over glucose concentration is 700mg/dl for 1 mV (1450nm) increasing and 300mg/dl for 1 mV (1300nm).

Measurement precision is really affected by test tube position in the box since there may be light scattered and influence the photodiode voltage reading.

B. Sensor testing on Earlobe

Table I shows the sensor test result in earlobe. This result is very promising since the light successfully penetrates the earlobe. Detected voltage is in hundreds mV for 1550nm and around 3V for 1300nm and 1450nm.

TABLE I. PHOTODIODE VOLTAGE ON EARLOBE

Wavelength (nm)	Fasting (V)	Break Fasting (V)
1300	3.014	2.961
1450	2.809	2.818
1550	0.676	0.510
Blood Glucose Concentration (mg/dl)	106	166

This value varies when the sensor position on the earlobe moved. The movement of the cable and affect the stability of the voltage produced. Since the test results from glucose solution and earlobes showing 1550nm as the best wavelength for detecting glucose, 1550nm is chosen for the correlation test. A successful work, [7], supports this wavelength usage.

C. Correlation

Data from first experiment is shown by figure 10. By doing linear approximation towards the data, a blood glucose concentration formula is obtained. Reversely proportional relation of glucose concentration and voltage is shown. When using this formula to approximate the blood glucose concentration, 15% error is visited. Applying this formula to other case will result 25 – 30% error. However, this approach is not valid enough since there are a lot of variable not counted. Every person has different parameter that will affect infrared radiation through the skin tissue such as pigment, the effective path length, the body temperature, and skin structure. This experiment try to generalize all factor affecting, but in order to do that we have to collect more samples and adding another sensor to the device. It is also possible if another technique of correlation become more equivalent.

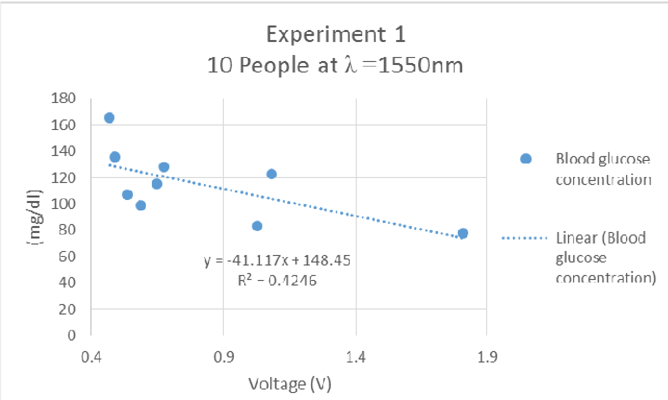


Fig. 10. First Experiment, Linear Correlation Method at λ = 1550nm

Since only one parameter is measured, another experiment is conducted by looking for a specific formula for one person. Procedure of this experiment has been explained previously. Five data is obtained from each day. Two approaches are used to get blood glucose concentration formula: linear correlation and two point equation. By doing linear approximation, a formula (3) is obtained. This formula is checked using the same data to approximate blood glucose concentration. 30% error still can be found.

$$y = -211.36x + 263.34 \quad (3)$$

Two point equation is obtained by inserting two points, the lowest and the highest by fasting and break fasting, as mentioned in table I. This formula is created by assuming linear relationship between blood glucose concentration and light detected. Another parameters which affect blood glucose concentration calculation is assumed as static parameter. By using this equation, we can approximate glucose concentration with 28% error.

$$y = -348.35x + 343.52 \quad (4)$$

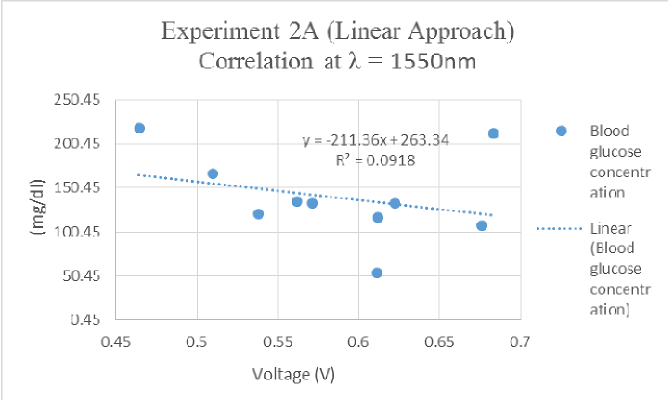


Fig. 11. Second Experiment, Linear Correlation Method at λ = 1550nm

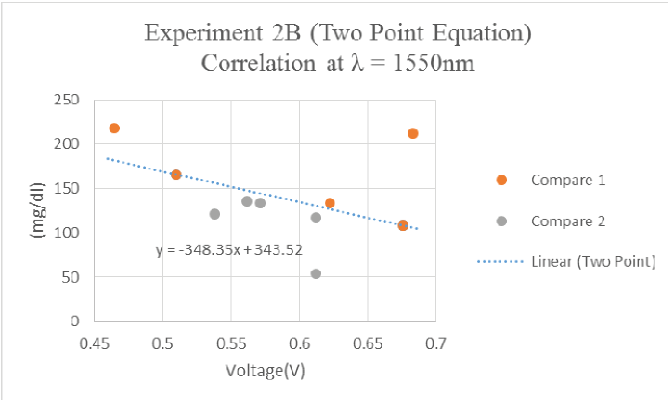


Fig. 12. Second Experiment, Two Points Equation Method at λ = 1550nm

Sensor's position has influence in amount of penetrated light. Different position produce different result. There might be different component structure in every part of the earlobe. Because of that, consistency of measurement sites should be designed in future works.

V. CONCLUTION

NIR spectroscopy has potential as a window to look at the concentration of blood sugar in vitro. Three wavelength tested shows a good detection of glucose by using NIR light. All of them also can penetrate earlobe by current design. Light at 1550nm showing the best glucose detection so that this design can be used for data collection and correlation of blood glucose concentration. However, it is very difficult to extract linear correlation since we only use one parameter and ignore others which may have influence in determining blood glucose concentration. Equation obtained by linear approximation and two point method can estimate blood glucose concentration. This estimation still has error about 30%.

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