Design of a Near-Infrared Device for the Study of Glucose Concentration Measurements

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Abstract

Maintaining healthy blood glucose concentration levels is advantageous for the prevention of diabetes and obesity. Present day technologies limit such monitoring to patients who already have diabetes. The purpose of this project is to suggest a non-invasive method for measuring blood glucose concentration levels. Such a method would provide useful for even people without illness, addressing preventive care. This project implements near-infrared light of wavelengths 1450nm and 2050nm through the use of light emitting diodes and measures transmittance through solutions of distilled water and d-glucose of concentrations 50mg/dL, 100mg/dL, 150mg/dL, and 200mg/dL by using an InGaAs photodiode. Regression analysis is done. Transmittance results were observed when using near-infrared light of wavelength 1450nm. As glucose concentration increases, output voltage from the photodiode also increases. The relation observed was linear. No significant transmittance results were obtained with the use of 2050nm infrared light due to high absorbance and low power. The use of 1450nm infrared light provides a means of measuring glucose concentration levels.

Keywords: Light emitting diode, glucose, blood, photodiode, photodetector, transmittance, spectroscopy

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Dino Sia

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Nomenclature

The following are words used through the report. Their definitions are given.

Absorbance: the ability of a layer of a substance to absorb radiation

Concentration: the amount of component in a given volume

Glucose: a crystalline sugar $C_6H_{12}O_6$.

LED: Acronym for Light Emitting Diode.

MATLAB: Software used for mathematical calculations.

Microcontroller: small computer on a single integrated circuit

Photodiode: A semiconductor sensor used to detect light. Depending upon incident light intensity, current is produced.

Power: the rate at which work is performed or energy is converted

Transmittance: the fraction of radiant energy that having entered a layer of absorbing matter reaches its farther boundary

Wavelength: the distance in the line of advance of a wave from any one point to the next point of corresponding phase

Chapter 1

Introduction

1.1 Background

The continual increase in global population in addition to the expected increases in global obesity and diabetes – more so in North America - suggests that there may also need to be an increase in doctors or health practitioners. In Canada, as of 2007 there were 2.18 doctors per 1,000 people, which although has increased from previous years it is still less other leading industrialized countries [1]. Because health care practice is a highly specialized profession that requires many years of study, such an increase in the number of physicians to accommodate patients may not be easily feasible.

In health care, there are many various instrumentation devices that diagnose patients. These diagnostic devices allow for better implementation of corrective or supportive medical devices and methods of dealing with a wide variety of diseases and disabilities. However, the increasing global population and the poor ratio of doctors per capita, especially in North America, brings forth the concern of being able to provide corrective or supportive methods of treatment for ailments for all of the population.

Such diagnostic, corrective, and supportive devices are widely used throughout health care practice in hospitals, clinics, and even in homes. Their functionality and importance has assisted practicing physicians, therapists, specialists and nurses with daily routine work. However, since a large majority of these instrumentation devices are corrective and supportive, they are used on patients who already suffer from illnesses. This does not necessarily translate to lowered mortality due to illness, nor does it result in a reduced likelihood of

developing illness. Because of the high costs, limited availability, and often the requirement of professional and qualified assistance, such instrumentation devices may not be accessible to all patients. This brings about the importance of preventive care as a means to reduce the likelihood of disease and illness.

In 2004, diabetes contributed 18.4 deaths per 100,000 people in Canada and 20.2 deaths per 100,000 in the United States of America [1]. In 2007, 46.8% of Canadians were reported as either overweight or obese while a staggering 67.3% of Americans were reported as either overweight or obese in 2006 [1]. Instead of spending money on medications or methods to reduce obesity or to cope with the effects of diabetes, perhaps if the focus was on preventing people from becoming diabetic, obese, or both, a lot less money would need to be spent on such health-related issues. Not only could such preventive reduce the amount of people who are obese or have diabetes, but could also benefit health care its allocation of expenses. It may result in more patients per doctor.

Engineering involves the development of products that benefit society. Biomedical engineering focuses on products or devices that are most widely used in health care with a purpose of providing efficient and accurate patient diagnoses and care. The purpose of this engineering project was to address the idea of preventive care as oppose to corrective or supportive care. The goal was to provide suggestion for a device that could possibly be recommended within the health care community that allows patients to monitor their health preventing them from overeating or avoiding high sugar foods. This may perhaps aid in preventing diabetes or obesity and thus improving their quality of life.

The project investigates a possible method of measuring glucose concentrations through the use of near-infrared light by emission from light emitting diodes. The project aims to find a relation between the absorption of near-infrared light and various glucose concentrations. This is a non-invasive

method of measuring glucose concentrations may become a more popular choice for diabetics and in being non-invasive its uses may extend to the general public. In having a large majority of populations able to monitor their blood glucose levels, it may prevent hyperglycemia, hypoglycemia, and perhaps the onset of diabetes.

1.2 Objectives

The objective of this project is to provide a non-invasive approach to measuring and thus monitoring blood glucose concentration levels. As oppose to the current minimally invasive and painful methods of measuring blood glucose concentrations, a non invasive method provides as excellent and perhaps more desirable alternative to present day technologies. To develop such a non-invasive glucose concentration measurement instrumentation device, near-infrared light and its absorption depending on various glucose concentrations will be examined. The use of near-infrared light to measure glucose concentrations does not involve using a lancet to obtain blood samples. Much like how pulse-oximetry is generally used on fingers, a similar approach in measuring blood glucose concentrations from fingers would be easy and more convenient as oppose to taking measurements from other body parts.

An easy and pain-free method of measuring blood glucose concentrations will give people information needed that may help them develop proper or better eating habits and it may allow monitoring to provide information for doctors and physicians to better diagnose patients if any ailments arise. If people eat healthier and exercise more – perhaps as a response to constant high blood glucose concentration readings – the prevalence or possibility of developing diabetes or being obese may lessen. This in turn could lead to lesser doctor visits which may promote a higher doctor per capita ratio. It may also lead to reduced waiting times in hospitals or doctor offices. Deaths due to obesity or diabetes may decrease, but more importantly the quality of life of the general population may

increase. There are many possible positive outcomes from the simple use of blood glucose concentration monitoring among the mass population. There are many corrective or supportive care devices and methods. Preventive care however should not be overseen and perhaps should be a more prioritized focus. A non-invasive blood glucose concentration monitor seeks to address a method of preventive care.

1.3 General Approach

In order to measure blood glucose concentrations, the instrumentation device involves the emission of near-infrared light and detecting an absorbance of the light after it has passed through a specific glucose concentration. A general schematic can be seen in Figure 1.3.1.

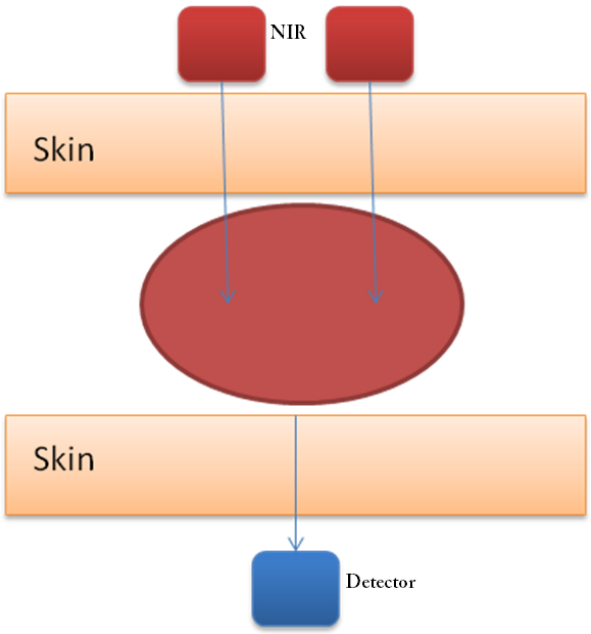


Figure 1.3.1 Schematic Overview of Operation of Non-Invasive Blood Glucose Monitor. NIR are Near-Infrared Emitting Light Sources, Detector detects the amount of light.

In order to implement such an instrumentation device, the chemical and physical properties of glucose in addition to its absorbance at specific wavelengths were examined. In order for the operation of the near-infrared light sources and light detector as well as the analysis of the data, specific compatible hardware and software choices need to be made. Such choices for hardware and software are given in chapter 3.

1.4 Scope of the Project

This project involves the use of near-infrared light and transmittance spectroscopy for the use of measuring glucose concentration levels. Data analysis will be done so as to create a model to best predict glucose concentration levels based on transmittance.

Chapter 2

Literature Review

2.1 Glucose Properties

In order to develop an instrumentation device that is accurate and specific to glucose and its concentrations, the chemical and physical properties of glucose need to be examined. Research papers regarding glucose's reflectance or absorbance at various wavelengths will examined. One research paper [2] examined the prediction of glucose concentrations by near-infrared diffuse reflectance spectroscopy between the wavelengths 1050nm to 2450nm, and determined that with calibration models developed through partial least squares regression, such a method is viable to predict blood glucose concentrations non-invasively.

Table 2.1.1 [3, 4] examines the various wavelengths and spectroscopic characteristics are each of those wavelengths. Figure 2.1.1 [5] shows the absorption spectrum of glucose at near-infrared wavelengths.

Wavelength(nm)	Possible Assign.	description
939	3 ν O-H stretch	a second O-H overtone band
1126	3 ν C-H stretch	a second harmonic C-H overtone band
1408	2 ν O-H	a first O-H overtone band
1538	ν O-H + ν C-H	O-H and C-H combination band
1688	2 ν C-H	a C-H overtone band
2261	ν C-H + ν C-C-H + O-C-H	combinations of a CH stretch and a CCH, OCH deformation
2326	2 ν O-H	a first O-H overtone band

Table 2.1.1 Glucose absorption bands summarized according to the stretch & vibrations of the bonds in the molecule [3, 4].

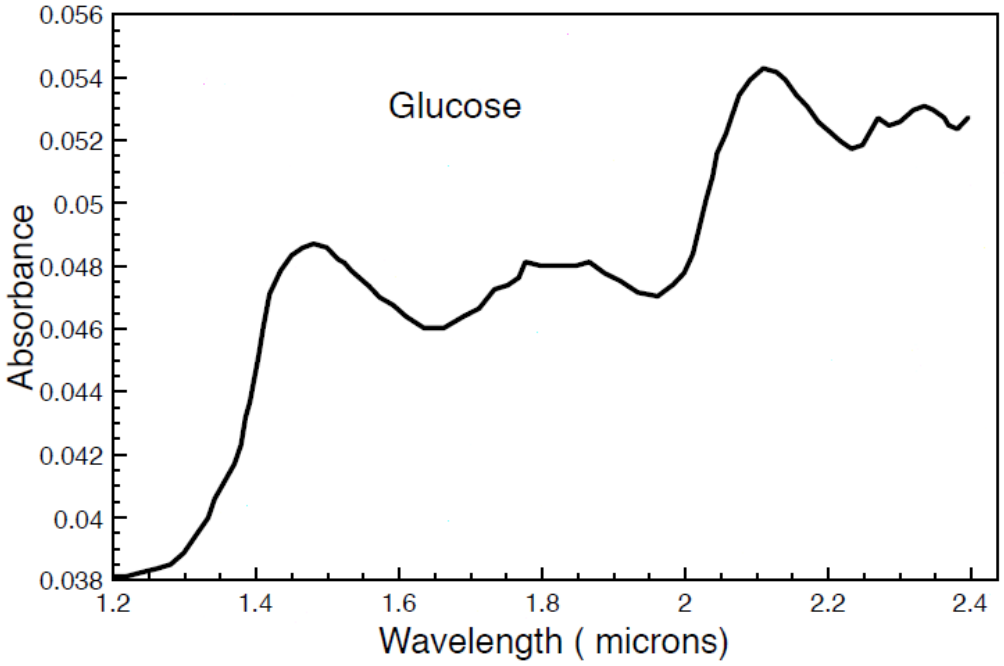


Figure 2.1.1 Absorbance Spectrum of Glucose [5].

Given the above spectrum and absorbance information, a research paper [6] compared the accuracies of different wavelength regions as a means to predict glucose concentration levels – the overtone (1100 to 1850nm) and combination (2050 to 2392nm) bands. These specific regions were chosen because the overtone band contains an absorption peak at 1688nm originated 2*v* of –CH and the combination band has peaks that are combinations of a CH stretch and CCH, OCH deformation [3]. The research paper [6] suggests glucose spectroscopy between wavelengths 1100nm to 2450nm is a possible method of analyzing and predicting glucose concentrations.

2.2 Transmittance versus Reflectance

Glucose determination using near-infrared spectroscopy can be done by taking measurements of either transmittance or reflectance. Transmittance

measurements involve acquiring measurements opposite that of the light source, so as to take readings after light has passed through the substance or subject of interest. Reflectance measurements involve acquiring readings based upon a subject's ability to reflect light. The differences can be seen in Figure 2.2.1.

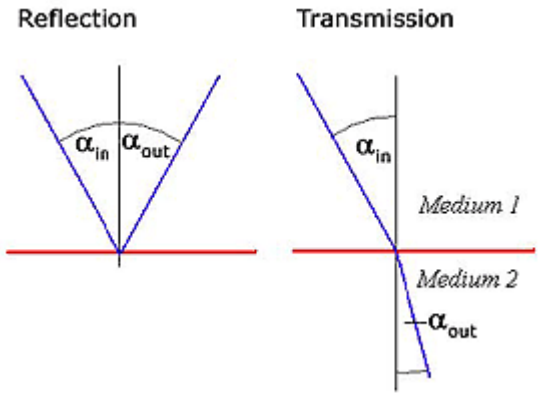


Figure 2.2.1 Transmittance versus reflectance

In order to determine which method of spectroscopy would yield better results, the study [6] was examined. Based on their measurements and investigation comparing glucose concentration analysis determination by reflectance and transmittance, their summary and conclusion suggest the transmittance setup is preferred for glucose monitoring [6].

Chapter 3

Experimental or Design Procedures

3.1 Statement of Problem

Current day technologies for measuring blood glucose concentration levels are minimally invasive requiring a sample of blood in order to obtain a reading. This is often painful for the user and such means to measure blood glucose concentration levels are likely undesired. Additionally, because they require test strips that are costly for each measurement, they may not be easily obtainable for patients. The next problem involves the patients who use it. Non-diabetics have no want or no need to use them. However, with poor eating habits and lack of health monitoring, the onset of diabetes or obesity is more prevalent. It is suggested that if even people who are not ill continuously monitor their health, they may be less likely to succumb to illness in the future. This brings about the need for preventive health measures.

3.2 Methodology of Solution

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.

3.3 Design Considerations

In designing the system, methods of near-infrared light emission and detection were explored. As suggested by [6], transmission spectroscopy for measuring glucose concentrations is favoured over reflectance. According to [2], [5], [6], [7], near-infrared wavelengths in the ranges of 1100 to 1850nm and 2050 to 2392nm are suitable for measuring glucose concentrations by absorbance. Thus, sources of light emission in the ranges of 1100 to 1850nm and 2050 to 2392nm were needed.

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 photodetectors 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. Table 3.3.1 compares 4 different photodiode materials and their respective electromagnetic spectrum wavelength sensitivity. From Table 3.3.1, possible options are photodiodes of indium gallium arsenide or lead (II) sulfide.

Material	Electromagnetic Spectrum wavelength range (nm)
Silicon	190-1100
Germanium	400-1700
Indium gallium arsenide	800-2600
Lead(II) sulfide	<1000-3500

Table 3.3.1 Photodiode Material and Corresponding Electromagnetic Spectrum Wavelength Range [8].

3.4 Parts

Given the requirements of a light source in the range of 1100 to 1850nm closer to 1688nm, a light emitting diode (LED) by ThorLabs (LED1450E) that emits near-infrared light at 1450nm was chosen. Given the requirements of a light source in the range of 2050 to 2392nm preferentially closer to 2261nm, an LED by Thorlabs (LED2050P) that emits near-infrared light at 2050nm was chosen.

The photodiode chosen was the ThorLabs FGA20 as it has an electromagnetic wavelength response range of 1200nm to 2600nm, thus only one photodiode would be needed to obtain measurements from the two LEDs of different wavelengths. The maximum output voltage of the photodiode is 1 volt.

In order to bias the various diodes and obtain voltage measurements from the photodiode, the use of a microcontroller would be very appropriate. A very user friendly and easy to code microcontroller was chosen – the Arduino Duemilanove. It has a maximum output voltage of 5V. It has a maximum input voltage of 5 volts with a built-in analog-to-digital converter with an accuracy of 1024 bits – thus 0.0049 volts per bit. Because the maximum output voltage of the photodiode is 1V and the maximum input to the microcontroller is 5V, a non-inverting amplifier was implemented. The operational amplifier OP491 was chosen. Additionally, various resistors were used.

3.5 Theoretical & Initial Design

The following schematic diagrams show the circuitry for the LEDs and photodiode. Figure 3.5.1 shows the schematic for the LED circuitry for the operation of the LED1450E LED. From the specification sheet of the LED1450E LED [9], it has LED current rating of 20mA and voltage drop of 1.2V. Operation is a 100% duty cycle with a 5V source from the microcontroller. The resistance used is calculated using Equation 3.5.1. This results in an optimal 190Ω resistance. A 1% 200Ω resistor was chosen and used. The higher resistance was chosen so as to not surpass the LED current rating.

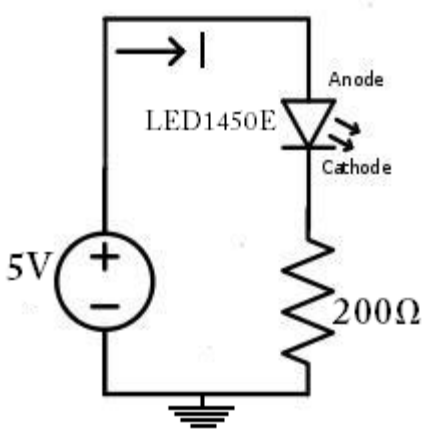


Figure 3.5.1 Circuit for Biasing LED1450E

$$\text{resistance in ohms}(R) = \frac{\text{power supply voltage}(V_s) - \text{LED voltage drop}(V_f)}{\text{LED current rating}(I_f)}$$

Equation 3.5.1 – LED circuit resistor

Similarly, Figure 3.5.2 shows the schematic for the LED circuitry for the operation of the LED2050P LED. From the specification sheet of the LED2050P LED [10], it has LED current rating of 200mA. Operation is a 50% duty cycle with a 5V source from the microcontroller. Assuming a 1V LED voltage drop, the resistance used is calculated using Equation 3.5.1. This results in an optimal 20Ω resistance. A 1% 27Ω resistor was chosen and used. The higher resistance was chosen so as to not surpass the LED current rating.

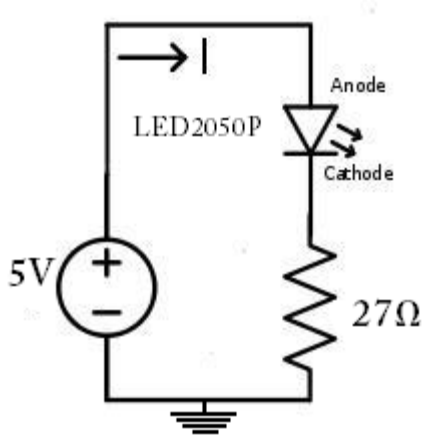


Figure 3.5.2 Circuit for Biasing LED2050P

The specifications sheet of the ThorLabs FGA20 [11] provides Equation 3.5.2 and Equation 3.5.3. The photodiode electromagnetic wavelength responsivity can be seen in Figure 3.5.3 [11] which has also been given by the specification sheet of the photodiode.

$$V_o = P \text{ x } R(\lambda) \text{ x } R_L$$

Equation 3.5.2 – Output Voltage of Photodiode

Where: P is the incident light power at a given wavelength λ

$R(\lambda)$ is the responsivity given by Equation 3.5.3 (which can be read from Figure 3.5.3)

R_L is the load resistor whose placement is shown in Figure 3.3.4

$$R(\lambda) = I_p / P$$

Equation 3.5.3 – Responsivity of Photodiode

Where: I_p is the photocurrent at a given wavelength

P is the light power at a given wavelength

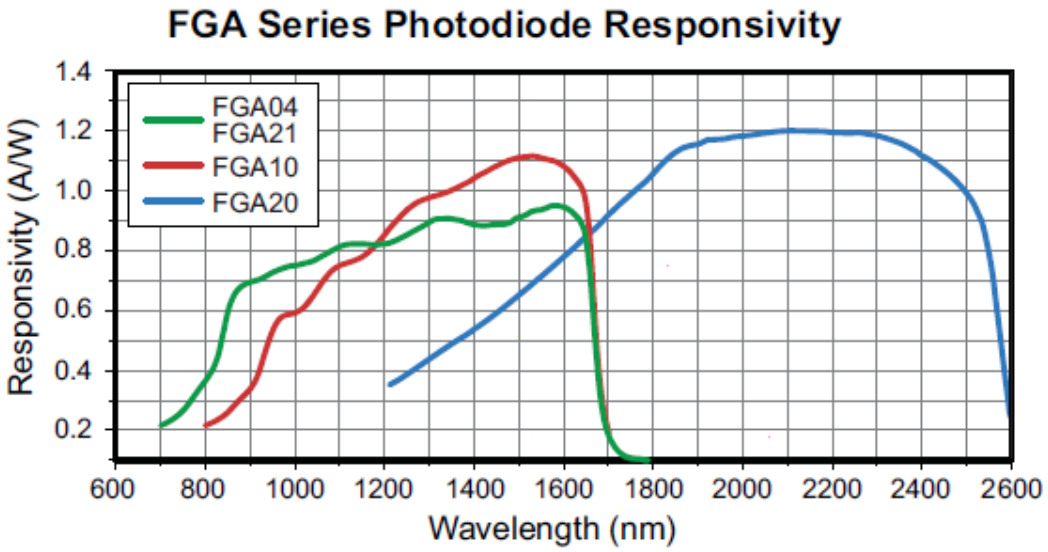


Figure 3.5.3 Photodiode Responsivity

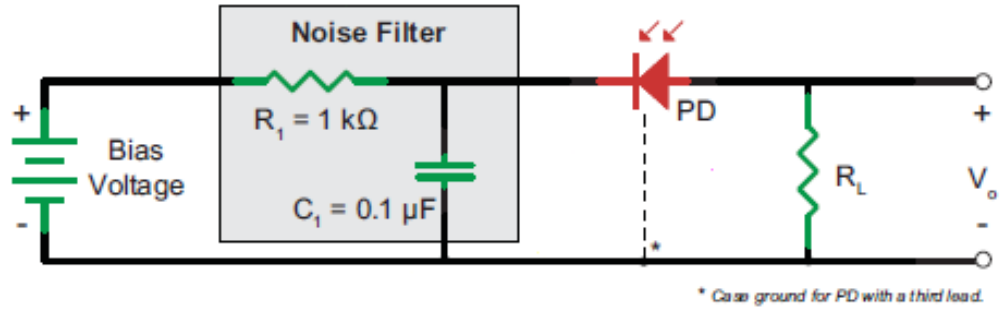


Figure 3.5.4 Recommended Circuit Diagram

From the specification sheets of both LED [9, 10] and the photodiode [11], the resistance load R_L for the suggested photodiode circuit can be calculated. First, calculations were done to calculate R_L using the 1450nm LED. With a power of 2.0mW or 0.002W, a responsivity of 0.6 A/W (as given by Figure 3.5.3 at 1450nm), and V_o of 1V, the calculated R_L is $R_L = 833\Omega$. Then, calculations were done to calculate R_L using the 2050nm LED. With a power of 1.1mW or 0.0011W, a responsivity of 1.2 A/W (as given by Figure 3.5.3 at 2050nm), and V_o of 1V, the calculated R_L is $R_L = 757\Omega$. Comparing both required R_L's, the lower value of $R_L = 757\Omega$ was chosen and thus $R_L = 780\Omega$ ($200\Omega + 200\Omega + 200\Omega + 180\Omega$) was used.

Since the maximum output voltage of the microcontroller is 5V and the recommended bias voltage of the photodiode is 1V, a voltage divider circuit was used (Figure 3.5.5). The following calculations were done using Equation 3.5.4. Since $V_{out} = 1V$ and $V_{in} = 5V$, resistors were chosen as $R_1 = 200\Omega$ and $R_2 = 51\Omega$.

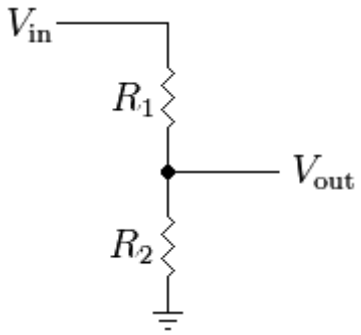


Figure 3.5.5 Voltage Divider Circuit

$$V_{out} = V_{in} [R_2 / (R_1 + R_2)]$$

Equation 3.5.4 V_{out} of a Voltage Divider Circuit

Since the maximum input voltage of the microcontroller, the Arduino Duemilanove, is 5V, a non-inverting amplifier was used. Figure 3.5.6 shows the schematic of a non-inverting amplifier. In a non-inverting amplifier, Vout is given by Equation 3.5.5. Assuming a maximum input voltage of 1V and a desired output voltage of 5V, R_2 / R_1 was selected such that (1 + R_2 / R_1) = 5. R_2 was chosen as R_2 = 200Ω and R_1 was chosen as R_1 = 51Ω.

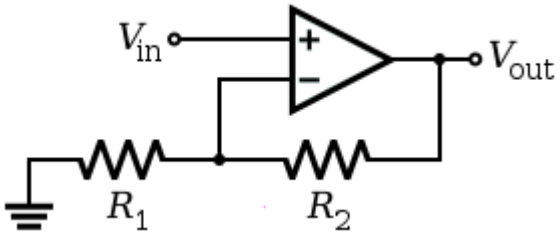


Figure 3.5.6 Non-Inverting Amplifier

$$V_{out} = V_{in} (1 + R_2 / R_1)$$

Equation 3.5.5 V_{out} of a Non-Inverting Amplifier

3.6 Workflow Design

The microcontroller can be powered via universal serial bus (USB) or a voltage between 7 to 12V. For testing and programming purposes, it will be connected via USB. The microcontroller will supply voltages to bias both LEDs and the photodiode. In addition, it will read the output analog voltage from the photodiode and amplifier, and using a 10-bit analog to digital converter it will map input voltages between 0 and 5 volts into integer values between 0 and 1023. This results in a 4.9mV per unit resolution. The numbers between 0 and 1023 can be multiplied by 4.9mV in order to display the analog voltage on the computer. A block diagram of the workflow can be seen in Figure 3.6.1.

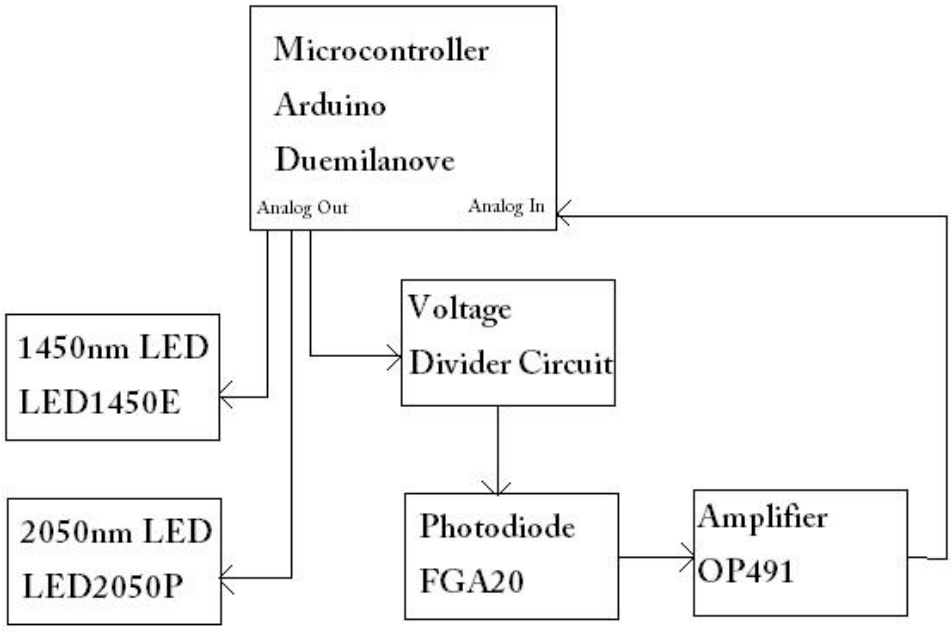


Figure 3.6.1 Workflow Schematic of the System

3.7 Testing & Design Refinements

The goal was also to use parts that are relatively cheap and easily accessible so as provide an affordable solution or alternative to invasive blood glucose testing. Such limitations resulted in the implementation using of LEDs as oppose to perhaps lasers with higher power and a photodiode as oppose to a very expensive spectrometer. The initial idea was to have near-infrared light pass through a thin, easily accessible and convenient part of the body such as the finger.

The microcontroller was programmed to output 5V 100% duty cycles for biasing the LED1450E and FGA20. It was programmed to output 5V at a 50% duty cycle for the LED2050P. The output of the non-inverting amplifier was connected to the analog-in of the microcontroller. The integer value that resulted from the analog-to-digital conversion was multiplied by 4.9 and that resulting output was shown on the computer screen. A multimeter Equus #4320 was used to measure various voltages and currents. The current across the LEDs were within specification and the voltage measurements suggested the LEDs were on. To further determine if the near-infrared LEDs were emitting light, the photodiode was required. By moving the LEDs to emit their light onto the $1mm^2$ area of the photodiode, the measured output voltage of the photodiode increased. This showed the functionality of the LED1450E and LED2050P LEDs and the FGA20 photodiode.

However, the maximum 5V output after the amplifier was not obtained. The gains and R_L were then modified so as to obtain the maximum 5V voltage. First, the R_L value (as seen in Figure 3.5.4) was adjusted to achieve an output voltage as close to 1V as possible. This eventually led to the use of $R_L = 50k\Omega$. Next, the gain resistors of the non-inverting amplification stage were adjusted such that V_{out} (as in Figure 3.5.5) was as close to 5V as possible. This eventually

led to the use of $R_1 = 100k\Omega$ and $R_2 = 3.9k\Omega$. Such changes however resulted in a greater resting voltage of 1.5V as V_{out} from the amplifier. The following refinements are shown in Figure 3.7.1.

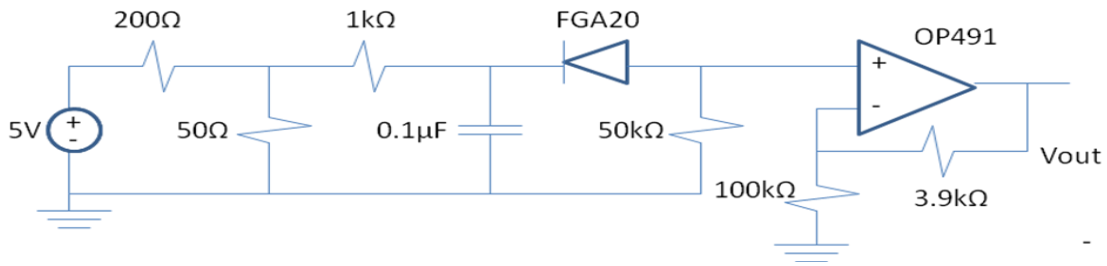


Figure 3.7.1 Refined Photodiode and Amplifier Circuit

Next, testing was done by emitting light through the index finger and trying to obtain a voltage increase output of the photodiode. Regardless of which LED was used, the output voltage of the photodiode did not change. For this reason, test tubes were used and solutions of distilled water and d-glucose were formulated and used for measurement. While voltage increases were found for the LED emitting near-infrared light at 1450nm, no voltage increases were found for the LED emitting near-infrared light at 2050nm. Thus, in order to increase the power of the LED to 28mW, a pulsed response duty cycle of 2A for 1µs every 499µs was used. This involved changing the resistor in Figure 3.5.2 from 27Ω to 2Ω.

3.8 Data Analysis

The output voltage of the photodiode is expected to vary depending on the wavelength of the near-infrared light and the concentration of glucose. Given these various output voltages for the two used wavelengths 1450nm and 2050nm and knowing blood glucose levels are lowest in the morning and highest postprandial, partial least-squares regression analysis will be used to best determine a relationship between output voltages and glucose concentrations. In order to do so, MATLAB will be used and regression analysis will be done. Further info on regression analysis can be found in Appendix A.

Chapter 4

Results and Discussion

4.1 Introduction

Results and measurements obtained from initial through final experimental designs will be presented. There will be discussion regarding these results as well as remedies or suggested remedies to problems encountered to lead to refinements and the final design.

4.2 Initial Design

The initial projected design was to function as shown in Figure 4.2.1.

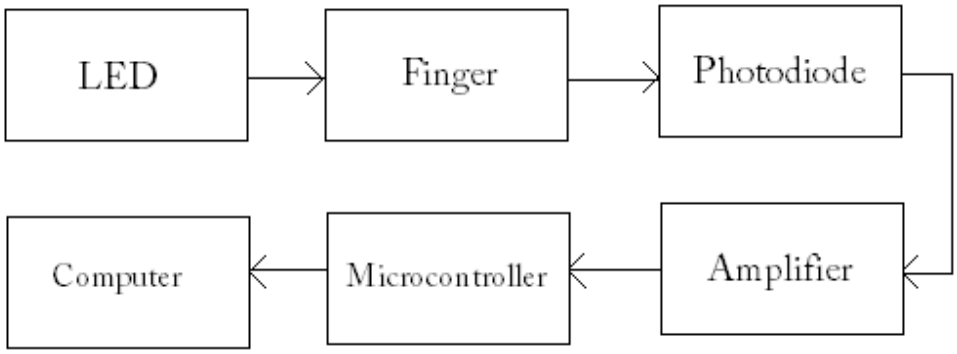


Figure 4.2.1 Initial Projected Functional Design

Without passing the near-infrared light from the LEDs through the finger, this initial design provided voltage outputs between approximately 1500mV (zero infrared light aimed towards the active area of the photodiode) to approximately 4900mV (maximum voltage obtained by aiming infrared light towards the active area of the photodiode). However, with the introduction of the finger to the system, the voltage outputs remained constant at approximately 1500mV without any increase. This suggests that the power emitted by the LEDs is not enough to penetrate the tissues of the finger. Further increasing the amplification of the amplifier stage or increasing R_L in the photodiode circuit resulted in further increased minimum voltage but still zero increase in voltage with the introduction of a finger to the system.

In order to obtain measurements from the system, the finger stage of Figure 4.2.1 was replaced with various test tubes containing solutions of distilled water and d-glucose with concentrations of 50mg/dL, 100mg/dL, 150mg/dL, and 200mg/dL. Such concentrations were chosen as they most closely represent the various blood glucose concentration levels of humans, with 50 to 100 mg/dL being low and average to high, and 150 or 200mg/dL being high and extremely high.

4.3 Refined design

The redesigned functional design is shown in Figure 4.3.1.

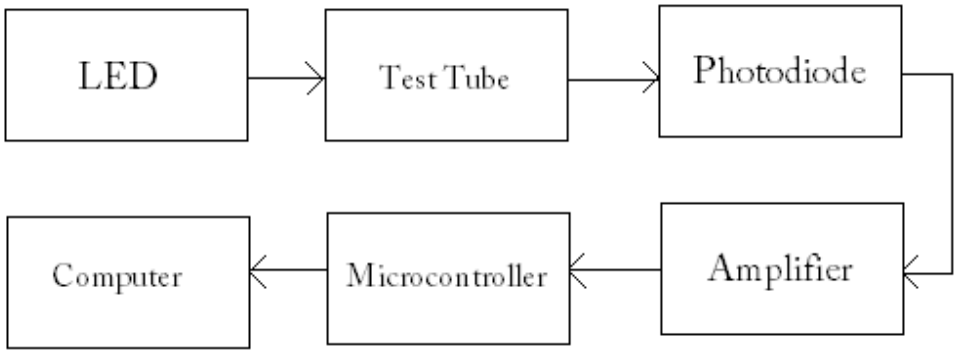


Figure 4.3.1 Functional Design using Test Tubes

Testing was done with lights in the room turned off in order to eliminate possible noise from nearby light sources. For each of the various glucose concentrations contained in the test tubes, the test tube was held in a horizontal position directly above the photodiode. First, the LED1450E was aligned on top of the test tube so as to emit light through the test tube. The angle of the LED was continuously adjusted so as to observe the highest possible voltage reading. Voltage readings from the photodiode were observed. Next, the LED2050P was aligned on top of the test tube so as to emit light through it. The angle of the LED was continuously adjusted so as to observe the highest possible voltage reading. Voltage readings from the photodiode were observed. The voltage readings from each of the test tubes and concentrations are summarized in Table 4.3.1.

Concentration of glucose (mg/dL)	1450nm Minimum Voltage (mV)	1450nm Maximum Voltage (mV)	2050nm Minimum Voltage (mV)	2050nm Maximum Voltage (mV)
50	1616	1651	1548	1563
100	1616	1670	1548	1568
150	1646	1685	1548	1563
200	1680	1720	1548	1563

Table 4.3.1 Photodiode Voltages for Various Glucose Concentrations

Depending on the angle of the LED1450E, the voltage output from the photodiode changed. However, the maximum voltage readings remained the maximum regardless of trial number. This proves the results are repeatable. However as can be seen from Figure 4.3.2 and Table 4.3.2, when comparing the minimum and maximum values for the four tested concentrations there is an overlap of resulting voltages.

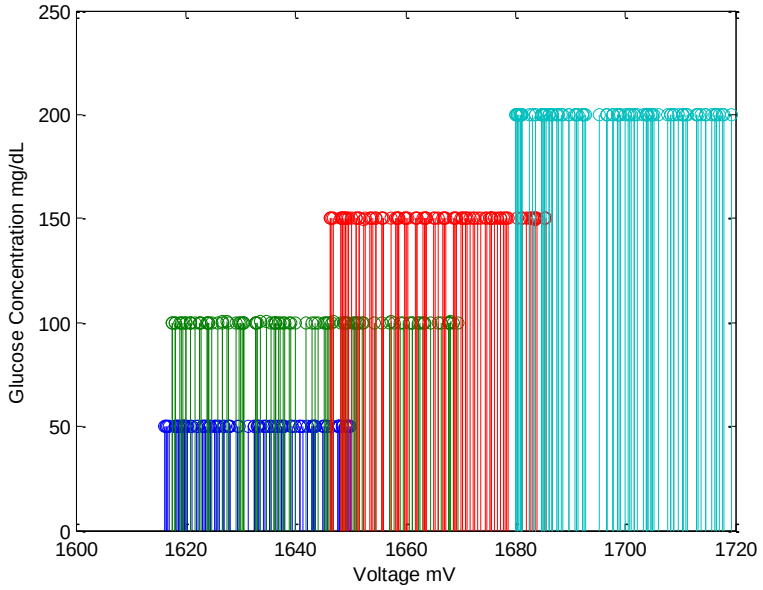


Figure 4.3.2 Glucose Concentration versus Voltage from Photodiode

However, when comparing only the maximum voltages it can be seen that only one maximum voltage corresponds to one glucose concentration (Figure 4.3.3). The relationship appears to be linear – as the maximum voltage increases, the concentration of glucose increases proportionally as well.

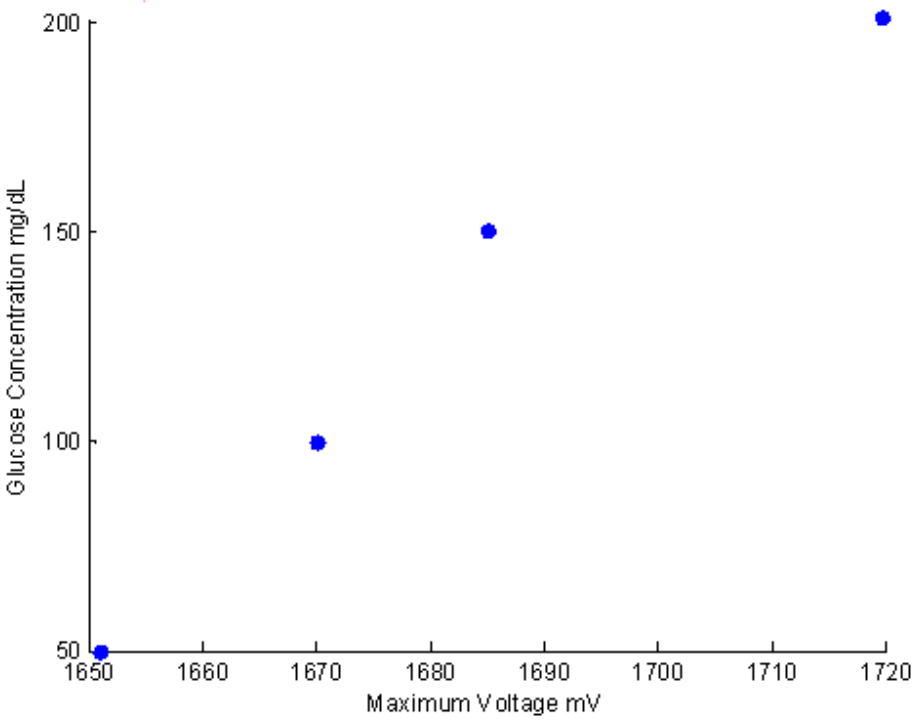


Figure 4.3.3 Glucose Concentration versus Maximum Voltage from Photodiode

When testing the glucose concentrations using the LED2050P, the minimum and voltages for all concentrations were the same. Similarly, the maximum voltages were the same except when testing with the glucose concentration of 100mg/dL. It resulted in a 5mV reading higher than the other concentrations. Because both higher and lower concentrations (50mg/dL, 150mg/dL, and 200mg/dL) yield the same results, the 5mV difference observed by the 100mg/dL concentration can be neglected. Because there were no significant voltage changes noted when using the LED2050P, further refinements to its operation were implemented.

4.4 Refinement of LED2050P Operation

The lack of significant notable results when using the LED2050P as the light source as a means to obtain a voltage from the photodiode depending on various glucose concentrations brought forth the need possibly increase the LED's power. Its initial operation of a 50% duty cycle with a 200mA current resulted in light emission with a power of 1.1mW (Figure 4.4.1). By changing to a pulsed duty cycle of 1µs on and 499µs off with a 2A current (Figure 4.4.2) theoretically results in light emission with a power of 28mW. In order to implement such changes, the resistor in Figure 3.5.2 was changed from 27Ω to 2Ω (Figure 4.4.3), and the microcontroller was programmed to output voltage for 1µs of every 500µs. Testing on the various test tubes containing the glucose solutions was repeated.

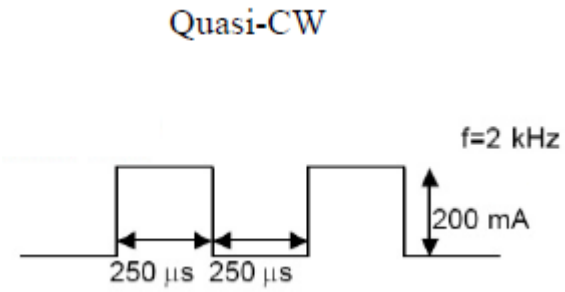


Figure 4.4.1 50% Duty Cycle Current Used for LED2050P Operation Resulting in 1.1mW Power.

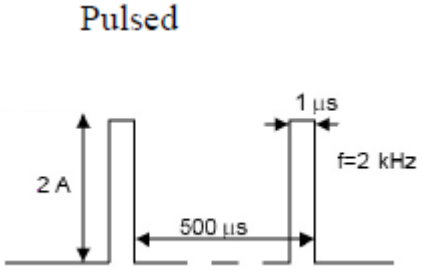


Figure 4.4.2 Pulsed Current Used for LED2050P Operation Resulting in 28mW Power.

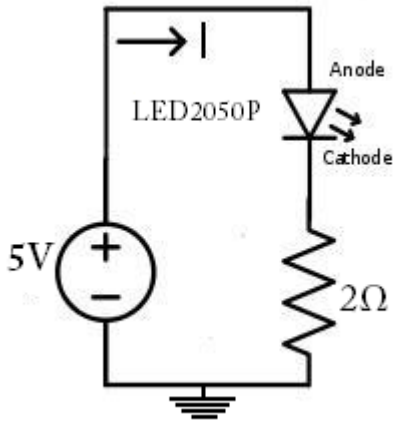


Figure 4.4.3 LED2050P Circuit Design Resulting in I=2A

Again, however, regardless of angle or location of the LED2050P, the minimum and maximum output voltages from the photodiode were not significant in comparison to the minimum voltages, with the minimum voltages being the same for all concentrations. The minimum voltage was also the recorded voltage without the use of an LED. Such results suggest that the absorbance of the solution at 2050nm is high, the power of the LED is inadequate, or both. By examining Figure 2.1.1 it can be seen that the absorption of glucose at 2050nm is indeed higher than at 1450nm.

To confirm this, an empty test tube was used between the LED2050P and photodiode FGA20. Output voltages from the photodiode were significantly above the voltages without the LED. With the introduction of a glucose solution even as low as 50mg/dL, output voltages result in the same voltage as that without the LED. This confirms the premise that the absorbance of glucose is too high and/or the power of the LED is inadequate.

4.5 Data Analysis

Due to the lack of significant results when using infrared light of wavelength 2050nm, data analysis and observations will only be considered with results obtained from using infrared light of wavelength 1450nm. Referring to Table 4.3.1 and Figure 4.3.2, assuming glucose concentrations are not known, it can be seen that between voltages 1616mV to 1651mV, the glucose concentration could either be 50mg/dL or 100mg/dL. Between 1646mV and 1651mV the concentration can be either 50mg/dL, 100mg/dL, or 150mg/dL. In the range of 1651mV to 1670mV the concentration is either 100mg/dL or 150mg/dL. In the range of 1680mV to 1685mV the concentration is either 150mg/dL or 200mg/dL. These overlapping results suggest that it would be difficult to predict glucose concentrations.

With voltage readings of 1670mV to 1680mV there is only one glucose concentration (150mg/dL). When the voltage readings exceed 1685mV, it is clear that the concentration of glucose is 200mg/dL.

To further analyze the results, MATLAB was used. An implementation of the function ‘regress’ was used with the aid of the MATLAB statistics toolbox. Additionally, ‘robustdemo’ was used to develop a best fit model. Figure 4.5.1 shows a 3-dimensional plot of the glucose concentration based on the minimum and maximum voltage readings. Figure 4.5.2 contains the plots of the observed data points as well as a mesh to represent the multiple linear regression. Figure 4.5.3 is the results when using ‘robustdemo’ with the given data points.

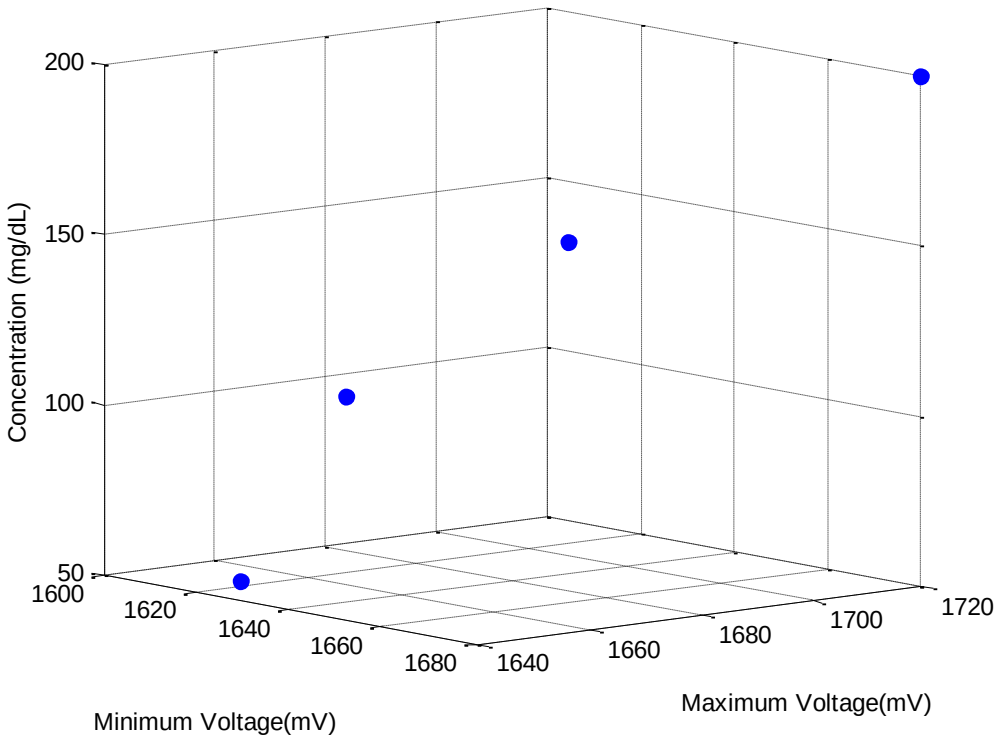


Figure 4.5.1 Glucose Concentration versus Minimum and Maximum Voltages

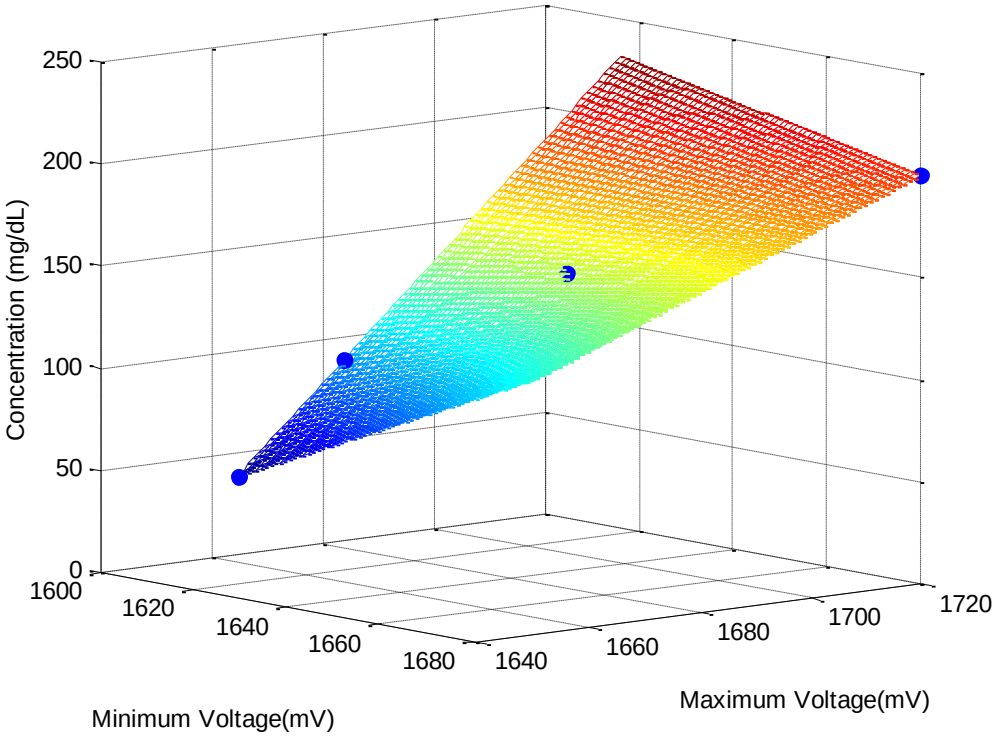
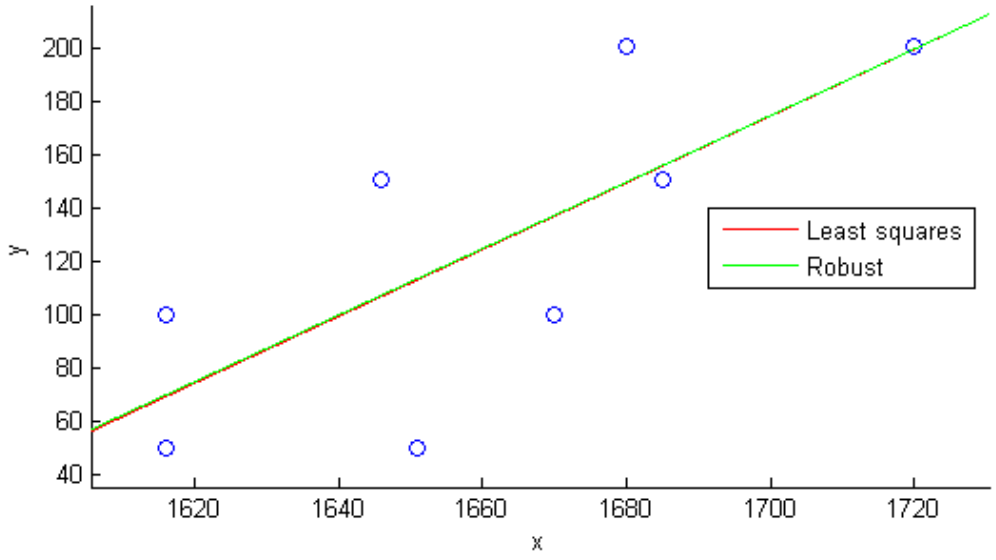


Figure 4.5.2 Glucose Concentration Regression Model & Data Points



Least squares:	Y = -1952.5 + 1.25113*X	RMS error = 43.0358
Robust:	Y = -1940.1 + 1.2438*X	RMS error = 47.1786

Figure 4.5.3 Robust and Least Squares Model

From Figure 4.5.2 it can be seen that as the concentration of glucose is increased, either or both minimum and maximum voltages are also expected to increase. Figure 4.5.3 shows a least squares and robust regression data models. Again it can be seen that as the voltage measurements increase, the expected or predicted glucose concentration increases proportionally. However, given the RMS error of the least squares model being RMS_{error}=43.0358, such measurements are not accurate enough to be used clinically. Additionally, if average glucose levels are between 50 to 100mg/dL and high blood glucose levels are when concentrations are over 100mg/dL, the fit model to such measurements are not adequate to accurately estimate or predict glucose concentration levels.

However, if significant readings or measurements were to be obtained from various electromagnetic wavelengths – especially in the range of 2050 to 2392nm – perhaps regression analysis would have yielded results with less error. The results obtained were that from solutions of distilled water and d-glucose. Such a solution does not account for various substances found in blood nor does it account for substances like flesh or bone.

Because however results were obtained and a linear fit model was found to be suitable for the data observed, using near-infrared at a wavelength of 1450nm does provide a means for measuring and predicting glucose concentrations.

4.6 Error and Possible Areas of Improvement

Possible sources of error that may have yielded such a wide range of minimum and maximum voltage values for various glucose concentrations may the lack of structural support and stability of parts used in the circuit. There were no accurate means of aligning the emitted infrared light with the $1mm^2$ area of the photodiode. Additionally, the test tubes were manually held in place without the

aid of a stabilizing apparatus. To possibly obtain more accurate and precise results, a stable attachment and proper aligning of the emitted infrared light and active photodiode area could have been implemented.

The accuracy of the concentrations of glucose may also have contained error. Preparations of solutions were done using an electronic scale with accuracy to the nearest gram. Test tubes may also have provided sources of error as they are rounded. The use of cuvettes may provide better results.

No readings were obtained from the LED emitting infrared light at 2050nm. Possible reasons may be too high of an absorbance or inadequate power. To obtain better results, lasers at such wavelengths could be used. However, lasers are much more expensive and inaccessible.

Chapter 5

Conclusion and Recommendations

5.1 Project Implementation Summary

The initial problem was the use of minimally invasive methods for blood glucose concentration measurements. To address this problem, this project observed using near-infrared as a possible means to measure blood glucose concentrations. Such implementation would be non-invasive. To implement the use of non-infrared, light emitting diodes that emit light at 1450nm and 2050nm were chosen and used. To detect absorption a photodiode with an electromagnetic sensitivity to electromagnetic light between wavelengths of 1200nm to 2600nm was used. To simulate blood glucose concentrations, solutions of distilled water and d-glucose was used in a test tube. Concentrations of 50mg/dL, 100mg/dL, 150mg/dL, and 200mg/dL were used. Regression analysis was done on the data in order to find a model to best predict glucose concentrations based on voltage readings from the photodiode.

5.2 Conclusions

Using near-infrared light of wavelength 2050nm, minimum photodiode output voltages were the same for all solutions (1548mV). Maximum photodiode output voltages were 1563mV for all concentrations except 100mg/dL which resulted in a 1568mV maximum voltage. Because the minimum voltages were the same for all solutions and 50mg/dL and 150mg/dL resulted in the same maximum voltages, the increased 5mV voltage of the 100mg/dL solution was deemed negligible. Poor results were obtained using the 2050nm LED with a

power of 1.1mW. Further refinements to the operation of the LED were made so as to omit light with a power of 28mW. Again, poor results were obtained even with the increased power output. This suggests the absorption of glucose at 2050nm is too high and/or the power of the LED used was insufficient.

Using near-infrared light of wavelength 1450nm, a linear model was found to best predict glucose concentrations. For a glucose concentration of 50mg/dL the maximum output photodiode voltage was measured as 1651mV. For 100mg/dL, 1670mV. For 150mg/dL, 1685mV. For 200mg/dL, 1720mV. It can then be seen that as glucose concentration increases, the maximum output voltage of the photodiode also increases. This suggests using a near-infrared wavelength of 1450nm and observing transmittance is a possible means to measure or predict glucose concentrations.

5.3 Recommendations

Due to the lack of time and available resources, some ideas of improvement were not implemented. Presented here are suggestions and recommendations for the further development of future implementations or extensions this project. The development of a stable base to hold and align the emitted infrared light with the active area of the photodiode may yield more accurate and precise results. Additionally, a method of stabilizing a test tube between the infrared light and photodiode may be advantageous. A cuvette or similar apparatus for containing a glucose solution may yield more accurate and repeatable results. Also, the use of stronger light sources may yield greater voltage differences for various concentrations. Light sources of 2050nm will need to have higher power output (greater than 28mW). Laser implementation may yield results. For better data analysis, more test concentrations could be used as well as infrared light at many more different wavelengths.

5.4 Final Conclusion

In conclusion, this project has suggested a means for non-invasive glucose concentration testing. With implementation using near-infrared light at a wavelength of 1450nm, there is a relation between glucose concentration and light transmittance. Although not as accurate as present day minimally invasive techniques for measuring blood glucose concentrations, the use of near-infrared light provides a means of non-invasive glucose concentration measurement.

Appendix A: Regression Analysis

Regression analysis is a technique for modeling and analyzing several variables when there is focus on one dependent variable with relationship to one or more independent variables. It provides an understanding on how the typical value of the dependent variable changes when one of the independent variables is changed while other independent variables remain constant.

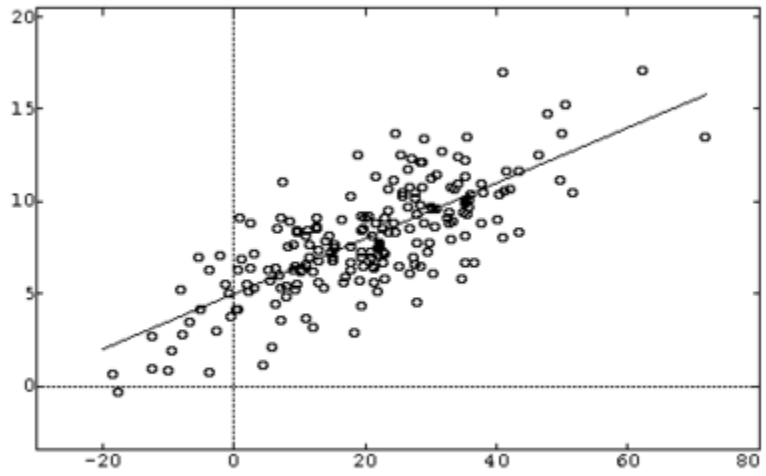
Regression analysis can be used for prediction of a dependent variable given a set of independent variables. It also determines which among the independent variables most closely relates to the dependent variable. Common methods are linear regression and ordinary least squares regression.

Ordinary least squares (OLS) is a simple estimator. The OLS method minimizes the sum of squares residuals, and leads to a closed-form expression for the estimated value of the unknown parameter β.

$$\hat{\beta} = (X'X)^{-1}X'y = \left(\frac{1}{n}\sum x_i x_i'\right)^{-1}\left(\frac{1}{n}\sum x_i y_i\right)$$

Assuming y=Ax+B, given the values of various y for given x, the coefficients A and B are determined to fit the data in a least-squares fit. Such method can be implemented in MATLAB using polyfit(x,y,n) where n is the degree of the polynomial.

The following figure is used as an example. Data points are given and a model is fit to best describe and predict y given x.



A general linear model is given by

$$y_i = \beta_0 + \beta_1 x_{1i} + \cdots + \beta_p x_{pi} + \varepsilon_i,$$

Where coefficients β_i are determined for each independent variable x_i .

Appendix B: Components List & Software

The hardware components used are listed as follows:

Capacitor CFAF-1022-4
IR LED ..... ThorLabs LED1450E
IR LED ..... ThorLabs LED2050P
Microcontroller ..... Arduino Duemilanove
Multimeter ..... Equus #4320
Operation Amplifier ..... Analog Devices OP491
Photodiode ..... ThorLabs FGA20
Resistor 2Ω RDC-2R2-10
Resistor 27 Ω RDC-27R-10
Resistor 51 Ω RDC-51R-10
Resistor 180 Ω RDC-180R-10
Resistor 200 Ω RDC-200R-10
Resistor 1kΩ RDC-1K-10
Resistor 3.9kΩ RDC-3K9-10
Resistor 100kΩ RDC-100K-10

Software used are as follows:

MATLAB, The MathWorks, Inc.
Arduino 0018

Appendix C

Microcontroller Program

```
int ledPinPD = 12;      // photodiode bias digital pin 12
int ledPin2050 = 10;     // 2050nm LED digital pin 10
int ledPin1450 = 8;    // 1450nm LED digital pin 8
int REDled = 2;    // Red LED
int GREENled = 3;  // Green LED
int PDanalogPin = 1;    // photodiode analog read from pin 0
int PDval = 0;          // variable to store the value read
int pulsedurationus = 250;  // 500us pulse, 50% duty cycle
double frequency = 0;   // variable for pulse frequency
double PDvoltage = 0;   // variable to convert PD to voltage
double analogreadtimer = 0;  // variable for reading


void setup()   {
  pinMode(ledPinPD, OUTPUT);
  pinMode(ledPin1450, OUTPUT);
  pinMode(ledPin2050, OUTPUT);
  pinMode(REDled, OUTPUT);
  pinMode(GREENled, OUTPUT);
  digitalWrite(REDled, LOW);
  digitalWrite(GREENled, LOW);
  Serial.begin(9600);  // setup serial
  frequency = 1/((2*(double)pulsedurationus)/1000000);
  pulsedurationus = (int)pulsedurationus;
  Serial.println(frequency);
  Serial.println("Hz");
  Serial.println(pulsedurationus);
  Serial.println("us");
}
```

```
void loop() {

  analogreadtimer += 1;

  digitalWrite(ledPinPD, HIGH);    // set the photodiode on
  digitalWrite(ledPin1450, HIGH);  // set the 1450nm LED on
  digitalWrite(ledPin2050, HIGH);  // set the 2050nm LED on
  delayMicroseconds(pulsedurationus);  // duration 2050nm LED is on

  if ((long)analogreadtimer == ((long)frequency/2)) {
    PDval = analogRead(PDanalogPin);
    PDvoltage = PDval*4.9;

    if (PDvoltage > 1700){
      digitalWrite(GREENled, HIGH);
      digitalWrite(REDled, HIGH);
    } if (PDvoltage > 1616){
      digitalWrite(REDled, HIGH);
    } else {
      digitalWrite(REDled, LOW);
      digitalWrite(GREENled, LOW);
//      PDvoltage = 0;
    }

    Serial.println(PDvoltage);
    analogreadtimer = 0;
  }

  digitalWrite(ledPin2050, LOW);       // set the 2050nm LED off
  delayMicroseconds(pulsedurationus);  // duration 2050nm LED is off

}
```

Appendix D
MATLAB Code for Regression Analysis

```
clc;
clear all;
close all;

x1 = [1616; 1616; 1646; 1680]; % minimum V
x2 = [1651; 1670; 1685; 1720]; % Contains NaN data
y = [50; 100; 150; 200];

%Compute regression coefficients for a linear model with an interactionterm:
X = [ones(size(x1)) x1 x2 x1.*x2];
b = regress(y,X); % Removes NaN data

% Plot the data and the model:
scatter3(x1,x2,y,'filled')
hold on
x1fit = min(x1):max(x1);
x2fit = min(x2):max(x2);
[X1FIT,X2FIT] = meshgrid(x1fit,x2fit);
YFIT = b(1) + b(2)*X1FIT + b(3)*X2FIT + b(4)*X1FIT.*X2FIT;
mesh(X1FIT,X2FIT,YFIT)
xlabel('Minimum Voltage(mV)')
ylabel('Maximum Voltage(mV)')
zlabel('Concentration (mg/dL)')
view(50,10)
```

```
clc;
clear all;
close all;

x=[1616 1651; 1616 1670; 1646 1685; 1680 1720];
y=[50 50;100 100;150 150;200 200];
robustdemo(x,y)

y1=[50;100;150;200];
betahat=y\x;
[b,bint,r,rint,stats]=regress(y1,x);
```

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