GLUCOSE SENSOR UTILIZING SILICON PLANAR TECHNOLOGY

NSF Summer Undergraduate Fellowship in Sensor Technology
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ABSTRACT

A glucose sensor using silicon and platinum was designed and fabricated. The interaction of glucose oxidaise and glucose produces proteins which have dielectric properties that produce an electrical output measured through the bonding pads of a sensor. The sensor consists of two layers of platinum: one porous layer that serves as an area for the reaction to take place, and a second layer that consists of two bonding pads. The sensors were placed in solutions of different glucose concentrations. Their resistance was measured and it was found that in a solution of less concentration, the resistance was greater. We also researched non-invasive ways of measuring glucose. Technologies used included Raman spectroscopy, near-infrared spectroscopy, photo-acoustic spectroscopy and mid-infrared spectroscopy.

1. INTRODUCTION

The body's inability to produce insulin is referred to as diabetes. One type of diabetes, diabetes mellitus, requires patients to inject insulin, sometimes up to seven times a day. By injecting the body with insulin, a diabetic person assists the cellular uptake of glucose; otherwise, glucose levels can rise above normal levels. Diabetes affects over 100 million people worldwide and over 14 million in the United States.[1] It is also ranked as the seventh leading cause of death in the United States.[2] The quality of life for people suffering from diabetes mellitus is greatly reduced by having to extract blood from one's body in order to measure glucose levels. Also, diabetes can lead to severe complications such as blindness, kidney failure and heart failure. Finding a continuous and, hopefully, non-invasive way of measuring the amount of glucose in the blood is essential in improving the quality of life of these people. Although this would not keep people from having to inject with insulin, it would get rid of the extraction of blood by wounding the skin. This, coupled with an implantable insulin pump, would require no involvement of the patient. This research concentrated on manufacturing a sensor that would measure the concentration of glucose in a continuous manner and on researching different non-invasive ways of measuring glucose.

1.1 Enzyme Sensor

For purposes of this research, a biosensor was used. A biosensor is an analytical device that utilizes biological material. There are two kinds of - antigen and enzyme. We

used an enzyme biosensor. An enzyme reaction needs to occur close to the sensor so that the material generated can be disseminated throughout the sensor. Once the material diffuses to the sensor, an electrical signal is produced.[3] This signal is then analyzed. The concentration of the material can be determined by the information received. The oxidation of glucose produces proteins, which contain dielectric properties that can be measured easily. Glucose oxidaise enables the oxidation of glucose to take place (see Figure 1). Immobilized glucose oxidaise on a sensor produces the following reaction:

$$\text{Glucose} + O2 \rightarrow \text{Gluconic Acid} + H2O2$$

Ions are produced because of this reaction. As a result, the conductivity at the surface of the sensor changes. Therefore, the greater the concentration of glucose, the lower the resistance. This type of sensor is an impedance-based sensor that detects gases such as hydrogen and ammonia produced by the glucose reaction.[4]

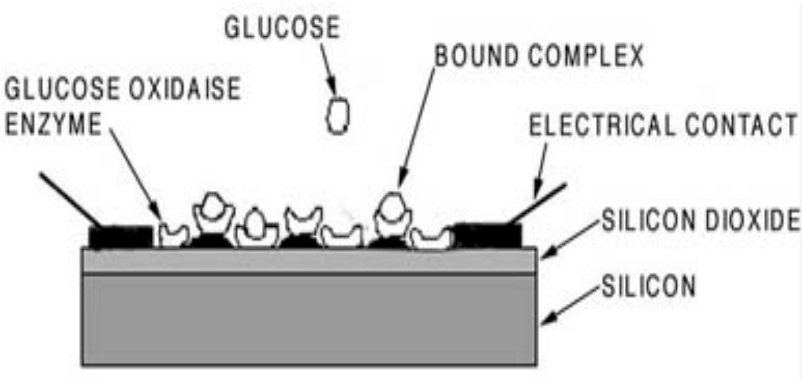


Figure 1: Glucose enzyme sensor

2. EXPERIMENTAL PROCEDURE

2.1 Mask Design

AutoCad was used to design the mask for this sensor, which consisted of two layers. The first layer contained an ultra-thin, discontinuous film (see Figure 2) while the second layer consisted of the bonding pads for the devices (see Figure 3). The ultra-thin film overlapped with the bonding pads. The overlap served as the connection between the membrane and the bonding pads (see Figure 4).

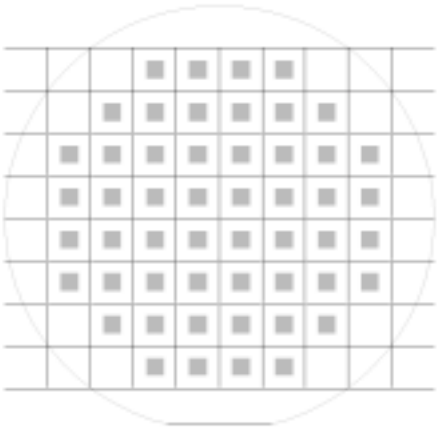


Figure 2: First layer (Ultra-thin Platinum film)

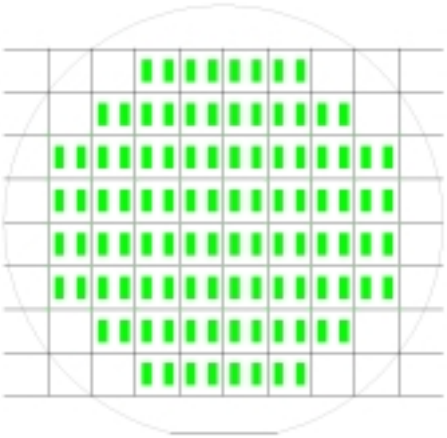


Figure 3: Second layer (Bonding Pads)

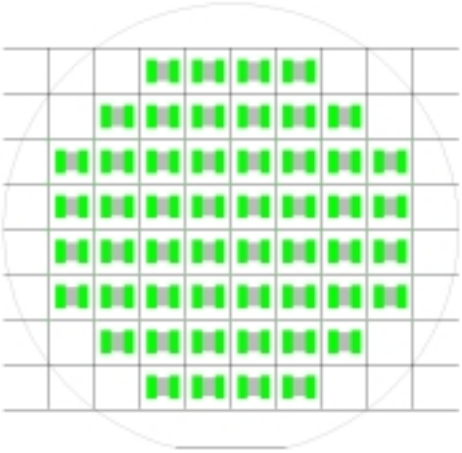


Figure 4: Mask design

2.2 Mask Fabrication

The Autocad design was then converted into another format that could be read by the printing machine. The design is printed on a glass plate, which in itself, is the mask. The plate is then developed much like a photograph is developed.

2.3 Sensor Fabrication

This sensor consists of platinum on silicon oxide. To deposit the platinum on the silicon sputtering and electron-beam, evaporation were used. In sputtering, a substrate (in this case silicon wafers) is placed in a vacuum with argon gas. Voltage is passed through a cathode or target (platinum). Argon contains positive ions and it is these ions that are accelerated and impact the target, displacing platinum and depositing it on the substrate.

During e-beam evaporation, the wafers are placed in a vacuum and an electron beam is used to evaporate material (platinum). The material is then deposited on the wafers
A two-inch diameter wafer was used in fabricating the sensor. The wafer was oxidized in order to isolate the silicon and prevent it from acting as a conductor. An oxidation layer of 1000 angstroms was created (see Figure 5). The wafers were first sanitized and then placed in a furnace at 1100°C. Wet heat was used for the oxidation.

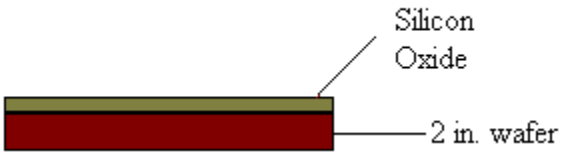


Figure 5: Silicon oxide layer

In our first try to build the sensor, we decided to use the lift-off process in depositing the first layer of platinum. During the lift-off process, positive photoresist is spread on the wafer. The wafer is then exposed to UV light on the mask aligner using the first layer mask. This wafer is then developed, leaving on it the parts of the wafer that were exposed and removing the parts, in this case the squares, which were not exposed (see Figure 6).

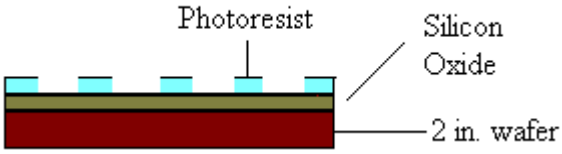


Figure 6: Lift-off process

The wafer was then placed in the sputtering machine. A 25-angstrom layer of platinum was deposited over the whole wafer, then the photoresist was removed, leaving on the wafer only the platinum that was not on the photoresist. At first, this method seemed to work, so we proceeded to place the bonding pads. The wafer was put back on the sputtering machine. A 1000-angstrom layer of aluminum was deposited on the wafer. On this first try, we decided to use aluminum for the bonding pads instead of platinum since it is usually much easier to work with. Positive photoresist was then placed on it. The wafer was exposed and then developed. During developing, the aluminum clearly did not hold. It was torn off and so was the platinum layer. Our technique was then altered.

On our second try, we used the same process as the first layer but we e-beamed the second layer, hoping the bonding pads would adhere better. However, the process did not work. The thermal coefficients of expansion of platinum and aluminum are very different. We believe this difference caused too much stress to build up, while developing (the material could not handle the stress). We then decided to use platinum for both layers.

By eliminating the lift-off process and reversing the order of the layers, we finally succeeded in fabricating the sensors. We got wafers with a fresh layer of oxide, and sputtered 1000 angstroms of platinum on them to take the place of the second layer. We also sputtered 1000 angstroms of silicon as a mask in order to protect the platinum and prevent it from being peeled off (see Figure 7).

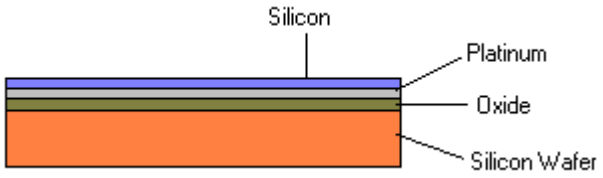


Figure 7: Silicon mask

Photolithography was used to etch the platinum and silicon into the bonding pads (see Figure 8).

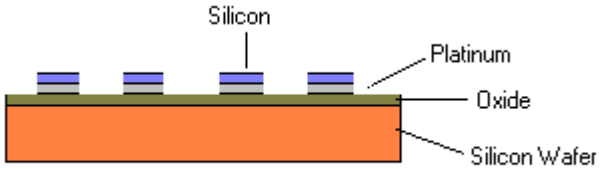


Figure 8: Etching of the bonding pads

We then e-beamed the 25-angstrom layer of platinum, which was to be the ultra-thin platinum film. We found that sputtering the thin film on the bonding pads did not achieve continuity. The bonding pads are 40 times thicker than the ultra-thin film; therefore when the film, which is overlapping with the pads, is placed on the pads, continuity is not possible (see Figure 9).

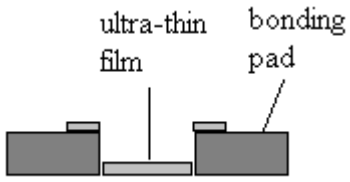


Figure 9: Discontinuity of ultra thin film

Using e-beam instead increased the chances of side coverage and, therefore, the chances of continuity (see Figure 10).

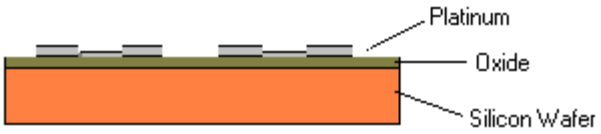


Figure 10: Final Product

Because a 25-angstrom layer of platinum is not visible to the naked eye, an image of the layer was taken with an atomic force microscope (see Figure 11). A difference in height, or a step, is visible in the image. This shows that there is platinum on the surface.

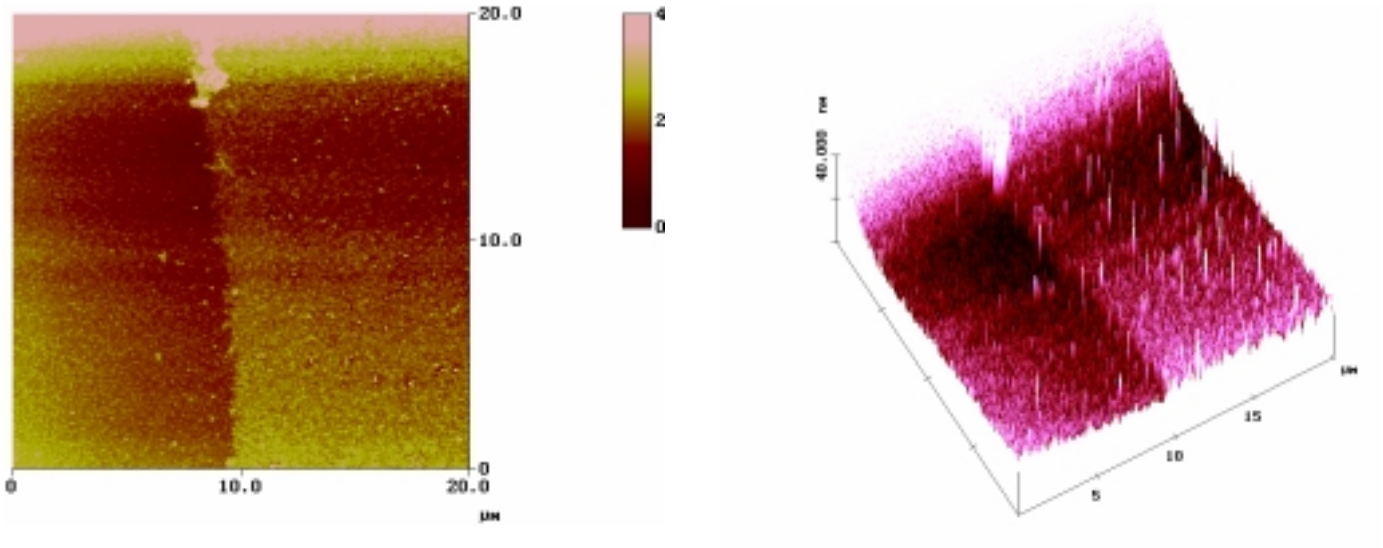
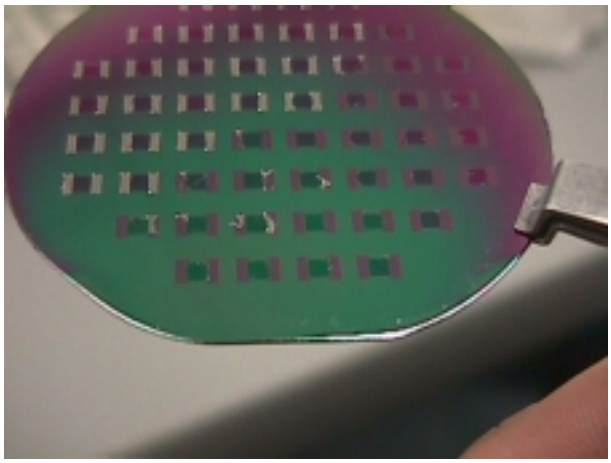
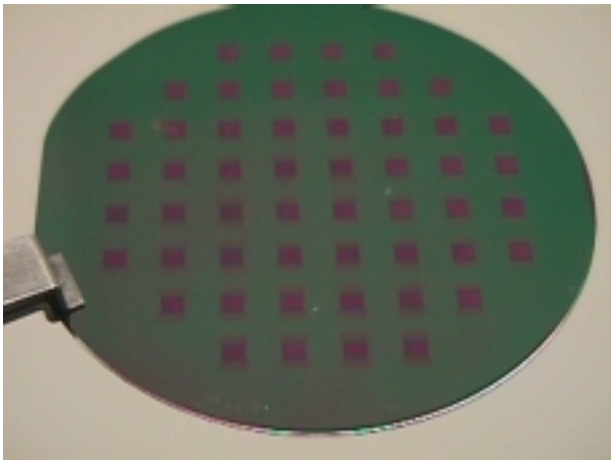


Figure 11: Picture of 25-angstrom layer taken with an atomic force microscope.

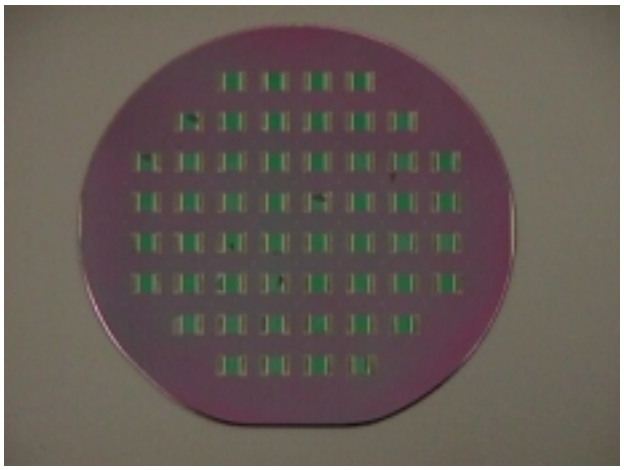
After a few tries, this method proved to be somewhat effective. The sensors were still very sensitive and prone to be damaged. Some sensors did not adhere, while others did but did not possess continuity. Our outcomes are shown in Pictures 1-3. The three wafers shown in the pictures were made at the same time.



Picture 1: Half of the sensors did not adhere.



Picture 2: None of the sensors adhered.



Picture 3: All of the sensors adhered.

We took the wafer with the most visibly complete sensors and measured impedance. The measurements showed that, in fact, the sensors were functional. Measurements achieved are shown in Table 1.

In KΩ

1	2	3	4	5	6	7	8	9	10	11	12	13
5.33	5.13	6.23	8.99	107.5	5.72	4.22	4.98	45.38	474.18	4.25	4.81	33.42

14	15	16	17	18	19	20	21	22	23	24	25
419.36	72.86	4.60	24.48	7.37	10.41	110.78	8.53	5.26	16.53	690	6.45

27	28	29	30	31	32	33	34	35	36
11.37	8.01	101.7	310.8	18.35	40.71	20.94	33.05	106.6	8.42

Table 1: Initial resistance of sensor

These measurements were acquired from the sensors that adhered to the wafer. A higher resistance is seen on the membranes that had extra platinum pieces on them. Membranes that were scratched or damaged showed discontinuity or a resistance of 0Ω and were therefore not useful. In general, resistances between 4 KΩ and 8 KΩ imply that the sensor is effective. Anything greater was due to extra pieces of platinum lying on the membranes. These sensors were therefore thought to be non-functional.

2.4 Testing

The reaction of the sensors to different concentrations of glucose was tested. To do this, glucose needs to be immobilized on the sensor. This was achieved by physical absorption at a solid surface. This method requires the surface to be placed in a concentrated solution of enzymes.[3]

We began the glucose immobilization by soaking the sensors for 48 hours in a glucose oxidase immobilization solution. The solution consisted of glucose oxidase and a sodium bicarbonate buffer. The pH of the buffer was adjusted to 9.3 by adding sodium hydroxide. The pH is optimum for the reaction to take place. After soaking for 48 hours, the sensors were rinsed in a sodium acetate detergent solution (pH 5.3). This solution was made with the sodium acetate buffer and Tween 20, an enzyme detergent. Rinsing the sensors in this solution removed unbound enzymes before testing.[3]

Measurements were taken using a probing microscope and an impedance analyzer. The first resistance measurements were taken after soaking the sensors in the sodium acetate buffer. The resistance for this solution was very low. Three solutions with different concentrations of glucose were then made. The different concentrations were of 100mM, 25mM and 10mM. After each concentration was tested on the sensors, the sensors were rinsed in the sodium acetate buffer. The general trend in the graph shows

that the higher the concentration of glucose is, the lower the resistance. Higher concentrations of glucose imply a greater conductivity is present; therefore, the resistance is less. A lower concentration leads to less conductivity and more resistance.

The average difference in resistance between the 25mM glucose solution and the 100mM glucose solution was of 7.97 MΩ while the difference between the 10mM solution and the 25mM solution was of 1.49 MΩ. Although some errors were encountered in some sensors, the trend is pretty consistent throughout the graph. From these results we can see that the sensors did in fact work, although their accuracy is unknown. In order to determine this more extensive testing needs to be done.

Measurements of only 14 sensors were achieved in the testing part of this research. Of the three wafers seen in Pictures 1-3, 156 sensors were expected although less than half of those actually adhered to the wafers. Of the ones that adhered, only a few were useful and only 14 survived through the testing. The results in the testing of these 14 sensors are shown in figure 12. This shows that these sensors are very delicate and not as effective as is necessary in measuring glucose in humans.

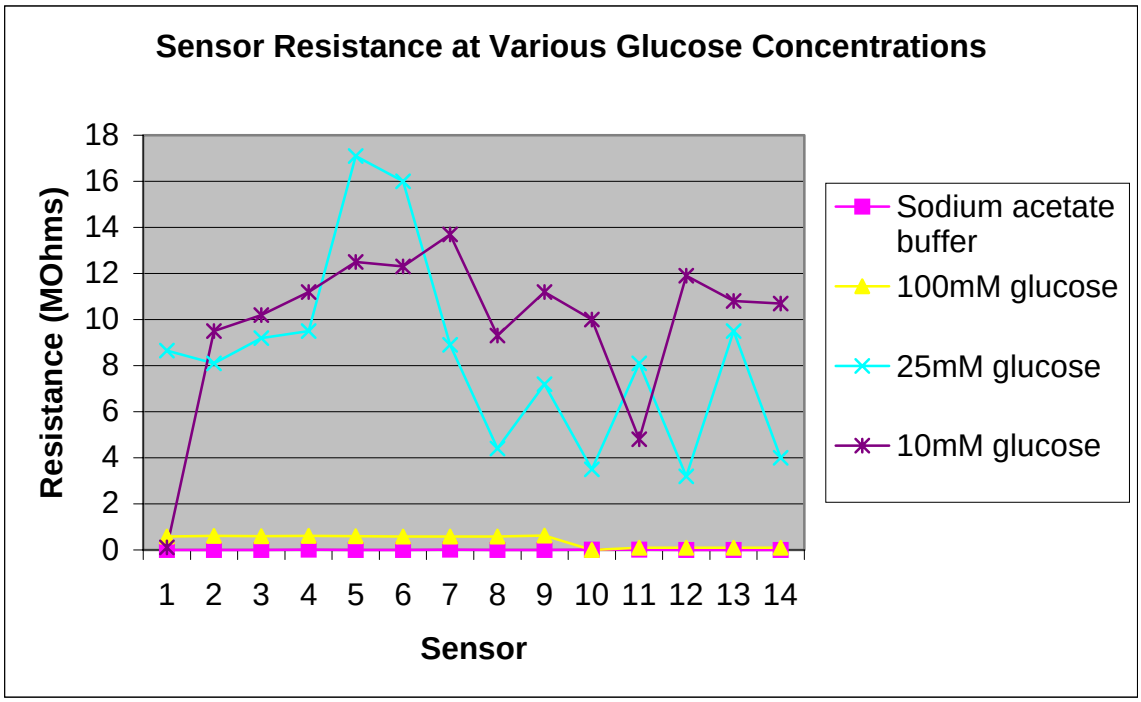


Figure 12: Graph of sensor resistances at various glucose concentrations.

3. FURTHER DEVELOPMENTS

The purpose of fabricating a glucose sensor was to get acquainted with different techniques to measure glucose levels. After this was done, we concentrated on researching non-invasive ways that glucose could be monitored continuously. Many different technologies may be applied in developing such a device. In general, non-

invasive glucose monitoring techniques can be classified as subcutaneous, dermal, epidermal and combined dermal glucose measurements.[5]

3.1 Raman Spectroscopy

In Raman spectroscopy, laser light is used to vibrate molecules. It then measures the scattered light produced. For each material, different wavelengths are produce leading to different spectrums. Because a unique spectrum is created from different materials, it is easy to discern what the material is. In measuring glucose, a device would be designed that would find its spectrum (see Figure 12) and determine the concentration of glucose. Raman spectroscopy can be used throughout the body, although the eye is a more effective location to determine the concentration of glucose. Not only is the interior of the eye optically accessible, but also in comparison with blood throughout the body, the aqueous humor of the eye has less Raman-active substances to complicate the overall spectrum and its analysis.[6] Although this technology seems promising, some problems include instability in the laser wavelength and intensity, errors due to other material in the tissue sample and long spectral acquisition times.[5]

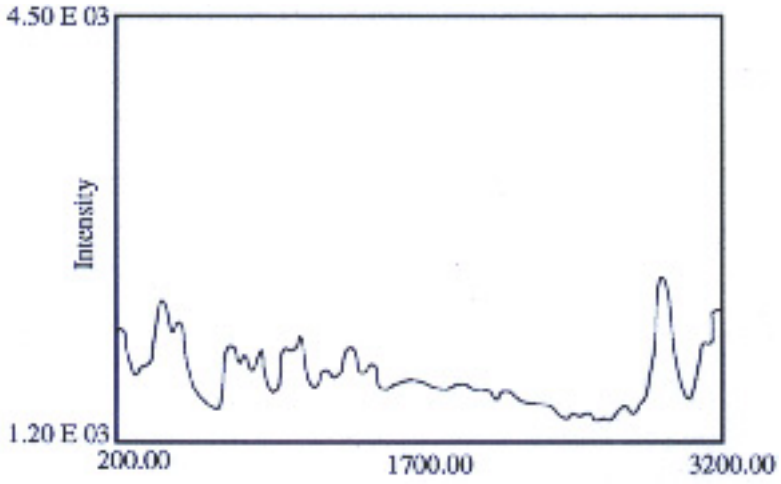


Figure 12: Raman spectrum of a 50% glucose solution. [7]

3.2 Near Infrared Spectroscopy

Near-infrared spectroscopy measures the wavelength of the absorption of mid-infrared light sample. This information is then compared to already known information about the material being tested.[8] One problem with this method is that the infrared absorption is restricted to compounds with small energy differences.[9]

3.3 Other Methods

Other methods studied include Photo acoustic Spectroscopy and Mid-Infrared Spectroscopy. In other studies, the suction of fluids through the skin used. The sample acquired is then analyzed for glucose concentrations.

4. CONCLUSION

After many attempts, the final attempt at fabricating a platinum glucose sensor worked. The method of choice is still not completely effective. Many complications surged along the process, most noticeably the fragility of the sensors and their inability to adhere to the silicon surface. Although sensors were produced, this method could not be used in an industrial matter. The method would have to be modified in order for the product to result in a greater percentage of useful sensors.

Still, a glucose sensor fabricated using the method of choice in this research, would only be useful as an implantable device. Implanting a silicon sensor is not possible as of today. The body perceives this sensor as a foreign body and cuts off the oxygen supply to it, causing damage to the body and the sensor. This is why a non-invasive way of measuring glucose is needed. Non-invasive glucose monitoring is in its early stages as of now. The accuracy achieved by already developed devices is not medically acceptable. Only by dedicating more time to the research of this matter can an effective non-invasive glucose-monitoring device be developed.

5. ACKNOWLEDGMENTS

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