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An Assessment of Pain-Free Blood Glucose Level by Noninvasive Methods

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ABSTRACT

Introduction: Diabetes mellitus is the kind of metabolic disease that affects millions of people around the world. Diabetics must have a constant awareness of their blood glucose level to keep their physics in healthy condition.

Objective: In this paper, a comprehensive discussion on current methods which are performed for blood glucose measurement and exploration on the current implementation of noninvasive glucometer strategies through linear regression is represented.

Methods: Linear regression models are generated through One-to-One and weighted average correlation of individual input parameters. Thirty-eight samples are incorporated in the analysis, here Density in 'kg/m^3', Pressure generated by Blood Test in 'Pa' and Absorption in 'AU' is considered as Input parameters and Glucose Concentration in 'mg/dL' as an output parameter. R-Square is performed to understand the best fitting between observed and predicted Glucose Concentration levels. In the end, the weighted average prediction is also done for the correlation.

Results: By comparing the observed value, the linear regression predicted the optimal glucose concentration (mg/dl) with 0.9794 R-Square value. And from the prediction process, it was observed that Density to Glucose Concentration result with 100% best fitting, Pressure to Glucose Concentration result with 99.99% best fitting, Absorption to Glucose Concentration result with 97.95% best fitting and Weighted Average to Glucose Concentration result with 99.8% best fitting.

Conclusion: Arrived direct correlations are very much useful to create new products for monitoring blood glucose level continuously under non-invasive conditions.

Key Words: Metabolic, Glucose, Blood, Noninvasive, samples, Linear Regression

INTRODUCTION

People with diabetics are tasked with monitoring their blood glucose levels at frequent intervals within the day to ensure the blood glucose levels within the permissible range.[1] Based on this measurement, diabetics can inspect their health to make sure of their life safety.[2-4] The most familiar method of measuring the glucose content is by blood sampling and testing with glucometers. This is done through pricking their skin in fingers many times in a day. This inconvenience can be rectified by the way of noninvasive glucose monitor systems.[5] A special type of sensor is introduced here to obtain the accurate value of blood glucose level without collecting blood samples.

Blood Glucose measuring techniques have three categorization[1] (i) Invasive (ii) Minimal Invasive and (iii) Noninvasive as shown in figure 1. This paper illustrates on various contents of noninvasive glucose monitoring systems with the following classes, (a) Diabetes and its impact (b) Invasive glucose measurement strategies which are currently in use (c) Traditional strategies on noninvasive glucose measurement (d) New approaches in noninvasive glucometers and (e) Conclusions regarding the feasibility methods.

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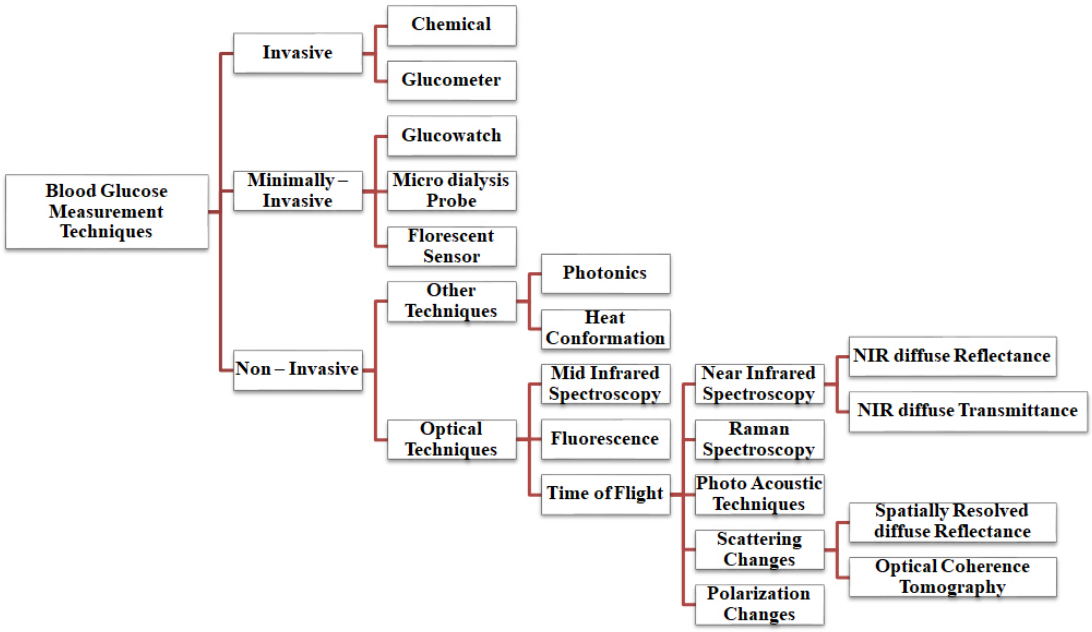

Figure 1: Blood Glucose Measurement Techniques

DIABETES AND ITS IMPACT

"Diabetes" is the kind of autoimmune disease results due to the loss of the ability of the pancreas to produce adequate quantity and quality of insulin required to break down the glucose content. In the digestive system, carbohydrates are break down into glucose which is then utilized by the cell for energy conversion. To use this glucose, cells need insulin. If required insulin is not present in the cells then it results with excess glucose in the blood stream. Generally two types of diabetes, Type 1 is Insulin Dependent Diabetes Mellitus occur in childhood due to genetic predisposition and Type 2 is Non-Insulin Dependent occurs later in life due to obesity and other relevant factors.

If blood sugar is left unregulated over a time leads to accelerated complications like a greater risk of stroke.[1,3] Now a day, there is a need for minimization of the complications associated with diabetes and respective health care cost. So the appropriate glucose measurement method is always in demand to keep the people under healthy condition.

INVASIVE GLUCOSE MEASUREMENT STRATEGIES

At present there are two main methods are followed under Invasive glucose measurement, the first one is called an A1C test. This simple lab test is conducted through a small amount of blood sample drawn from the person. This test helps to find the average glucose level in the blood for the past three months. For diabetics, this test is recommended at least twice in a year which helps to measure the risk level. The scale measurement followed in A1C test is 12, 11, 20, 9, 8, 7 and 6corresponding to the average glucose level of 345, 310, 275, 240, 205, 170 and 135 respectively.

The test procedure is, pricking of patient finger to collect blood sample with a help of lancet, then dropped into a strip and optical meter is used to measure the blood glucose content level. Based on the type of sensor, healthy condition is measured for blood glucose level as prescribed in Table 1.

Table 1: Blood Glucose Level[2]

Healthy Condition	Plasma Sensor (mg/dL)	Glucometer (mg/dL)
Before Meals	90-130	80-120
1 to 2 Hours After Meals	< 180	< 170

Another mode of invasive glucose measurement is based on different site inspection like the upper arm and forearm, but the accuracy is not up to the level of pricking method. Another method is MINIMED monitoring system, it is known as invasive continuous monitoring system[3], here a small plastic catheter is inserted under the skin to measure the blood glucose level continually and sometimes it is used to inject insulin at the risky situation. These methods have their discomfort like fainting at sight and anxiety towards regular usage. To overcome this kind of distress, preferably noninvasive methods are considered.

TRADITIONAL STRATEGIES ON NONINVASIVE GLUCOSE MEASUREMENT

The main objective of noninvasive glucose measurement is to avoid pain and discomfort, piercing of skin and tissue deterioration. Many strategies are applied to reach these requirements; some of the inventions are commercially available is

illustrated in Table 2. Two different techniques are used for the development of the product (i) Reverse Iontophoresis – Electrical current-based (ii) Spectroscopy – Interaction of Light-based.

Table 2: Commercially Available Non-invasive Invention

Name of the Invention	Type of Technique	Demerits
GLUCOWATCH by Animas Corporation[6]	Reverse Iontophoresis (Electrical Current)	i. Skin Irritation / Burn due to Continuous Electrical Charge ii. Less Accurate detection of hypoglycemia iii. The requirement of Blood Sample for Calibration
SENSYS GTS by Sensys Medical, Inc[7]	Near-infrared spectroscopy (Interaction of matter in light)	It changes in a pattern according to texture, colour, and temperature of person's skin
OPTISCAN by Biomedical Corporation[8]	Mid-infrared spectroscopy (Interaction of matter in light)	The need of 120 mL blood sample for the result, so not an invasive

Non-invasive applied by Photoacoustic spectroscopy, here beam of light is performed. Optical energy generated from the light capable of developing an acoustic pressure wave. This wave helps to find glucose concentration through the microphone. A linear response is perceived by Mckenzie et al., based on the light source and glucose concentration.[9] Later the research created by incorporating piezoelectric transducer and a laser pulse measurement through an optical fibre.[10] The transducers are capable of detecting the photoacoustic pulse with high accuracy.[3]

Another strategy followed is Scatter changes of a blood sample based on the refraction index. Light refraction measured under abdomen is observed as accurate site indication of blood glucose level. The scatter method requires calibration process, so it is mandatory to take into account of signal shift due to location factors.[4]

NEW APPROACHES IN NONINVASIVE GLUCOMETERS

Few recent geometry methods are available based on reverse iontophoresis and fluorescence. Fluorescence method is achieved by using a contact lens. These methods are continuous and non-invasive by incorporating carbon nanotubes and metabolic heat conformation. Under Metabolic heat confirmation method, body heat and oxygen supply are measured through a sensing device.[11] In 19thcentury, elevated tear glucose levels were first introduced.[12] Blood glucose level can be monitored through the tears. Boron acid doped lens is deficient with electron which can be easily reached back by the presence of glucose. This change will be reflected in fluorescence spectral which is directly related to blood glucose level.[11] A related study found that these lenses are comfortable to use continuously for long run.[13]

Other new approaches are based on the sugars leaching, pH response, sensitivity, polarity and comfortability.[5,12] Leaching is known as the process of extraction of specific materials from a carrier and converts into a liquid. From the literature, it was found that leaching will cause about eight percentage changes in the fluorescent intensity.[11] GlucoScope and Glucoview are the products invented under non-invasive glucometer in the year 2003. GlucoScope is a small pair of binoculars used to measure the blood glucose level based on the fluid which is associated in the anterior chamber of the eyes. Gluco-view is the kind of disposable contact lens used to measure the glucose level in the tears by changing the respective colour spectrum.[14] All these products are having a drawback of collecting the data for prediction which significantly affect the calibration process.

MATHEMATICAL CORRELATION

During the research the diabetes data base is collected from UCI machine learning repository for testing. This trial and error is done with the help of linear regression model. The predicted measurement of glucose concentration is correlated by the followingequations.

$$y1 = b1(1) + b1(2)*x1 \quad (i)$$

$$y2 = b2(1) + b2(2)*x2 \quad (ii)$$

$$y3 = b3(1) + b3(2)*x3 \quad (iii)$$

$$ya = [y1 + (0.9999*y2) + (0.9795*y3)] / (1+0.9999+0.9795) \quad ....(iv)$$

Where,

x1= density kg/m^3 - (Input Parameter)

x2= pressure generated by BT (Pa) - (Input Parameter)

x3= Absorption (AU) - (Input Parameter) and b1, b2, b3 are the arrived coefficients

Here 38 samples are taken into consideration for trial and error calibration. The expected output value is represented as y_1, y_2, y_3 and y_a. Linear regression is collectively done by relating individual input parameter and output parameter as detailed in Figures 2(a) – 2(d). Finally, the weighted average prediction is also done for the correlation. By comparing the observed value, the linear regression predicted the optimal glucose concentration (mg/dl) with 0.9794 R-Square value. Table 3 elaborates on input and output parameters used for the regression analysis.

Table 3: Samples of human blood parameters (Input & Output Parameters)

Description	Minimum	Maximum	Average
Density(kg/ m3)	1104.06	1230.18	1165.34
Pressure generated by BT(Pa)	-4330.9	-4325.3	-4328
Absorption(AU)	6.778	20.361	12.988
Glucose Concentration(mg/dl) – Observed	54.055	180.182	115.34
Glucose Concentration(mg/dl) – Predicted under Density (y1)	54.055	180.182	115.34
Glucose Concentration(mg/dl) - Predicted under Pressure (y2)	54.044	177.244	113.676
Glucose Concentration(mg/dl) - Predicted under Absorption (y3)	54.048	165.353	104.937
Glucose Concentration(mg/dl) Predicted under Weighted Average (ya)	54.049	174.26	111.317

From the prediction process from figure 2, it was observed that Density to Glucose Concentration result with 100% best fitting, Pressure to Glucose Concentration result with 99.99% best fitting, Absorption to Glucose Concentration result with 97.95% best fitting and Weighted Average to Glucose Concentration result with 99.8% best fitting. These direct correlations are very much useful to create a new product for monitoring blood glucose level continuously under non- invasive.

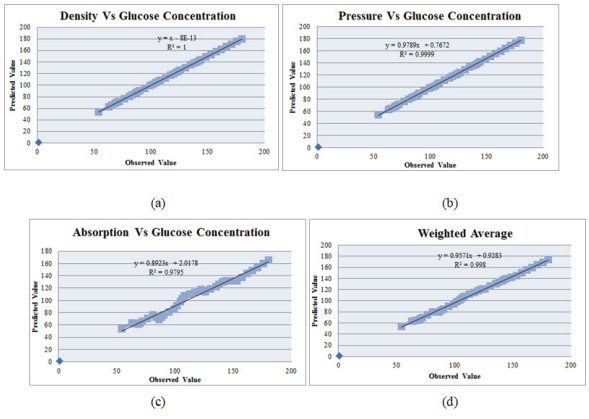

Figure 2: Correlation between Predicted and Observed Blood Glucose Concentration (a) Density Vs Glucose Concentration (b) Pressure Vs Glucose Concentration (c) Absorption Vs Glucose Concentration (d) Weighted Average Vs Glucose Concentration.

CONCLUSION

A detailed report on diabetes with its impact, invasive glucose measurement strategies, appropriate traditional strategies followed in noninvasive glucose measurement and inventions about new approaches are presented. The research is still ongoing to find an alternative for finger pricking even after crossing a decade, to reach utmost accuracy and comfortability. Some useful and hopeful approaches are already made from the different research which enhances the possibility of achieving those products. Regression correlation is analyzed here to find the relationship between blood glucose concentrations with density, pressure and absorption. Precisely this will help to invent the portable noninvasive product at low cost as possible.

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