

Design and Development of Non-Invasive Prototype to Measure Pulse Rate, Blood Glucose and Oxygen Saturation Level in Arterial Blood

Nazo Haroon

Department of Mechatronics Engineering, CEME
National University of Sciences and Technology (NUST)
Islamabad, Pakistan
nazoharoon78@mts.ceme.edu.pk

Mohsin Islam Tiwana

Department of Mechatronics Engineering, CEME
National University of Sciences and Technology (NUST)
Islamabad, Pakistan
mohsintiwana@gmail.com

Abstract—The article is dedicated to propose a system which can measure heart rate, blood glucose and oxygen saturation ratio non-invasively with maximum possible accuracy. The design is easy to use, real time and pain free. Preliminary results are acquired on a prototype amplification and filter circuitry, a sensor consisting of two LEDs red (660 nm) and near infra-red (940 nm) as transmission spectrums and an Arduino controller board. Fingertip photoplethysmographic (PPG) signal analysis is done. Furthermore, results have been compared to commercially available pulse oximeter and measurement accuracy of $\pm 3\%$ for pulse rate and $\pm 1\%$ for oxygen saturation is observed. In non-invasive glucose measurement, accuracy plays a vital role. Hence, a 3 day clinical trial is conducted in a hospital for various diabetic and non-diabetic test specimens of different ages. Total 132 specimens were analyzed during the trial period and results are compared with the Beckman coulter AU-480 chemistry analyzer present in the pathology laboratory of the hospital. Clarke Error Grid (CEG) analysis depicts 94.70% of the readings (of all 3 days) fall in the clinically accepted zone A. The Absolute Relative Differences (ARDs) yield mean and median error values of 9.51% and 8.05%, respectively.

Keywords—Pulse oximeter; photoplethysmography; absolute relative difference; non-invasive; chemistry analyzer

I. INTRODUCTION

Diabetes mellitus is a chronic disease in which a body fails to produce sufficient amount of insulin required by the body. Insulin is an enzyme produced by pancreas in the body. Insulin helps to provide energy via blood glucose to various body cells. The method of measuring the blood oxygen saturation is known as Pulse Oximetry. Measuring of blood oxygen saturation ratio (SpO_2) leads to examine the patient's organism capacity to acknowledge the oxygen requirements of various organs. On the other hand, the SpO_2 ratio also aid in determination of influence of a patient's respiratory system. People suffering from different cardiac diseases are advised to regularly monitor their heart rate and oxygen saturation ratio to ensure the stable condition of human cardiovascular system. To keep oneself healthy, where we do care about essential nutrients required for body, arterial blood plays vital role since, it contains the blood oxygen saturation ratio information. The conventional techniques available in market are invasive and pain causing. Conventionally, the oxygen

saturation was measured by sampling the arterial blood with the use of a blood gas analyzer [1]. The commercially available glucometers in the current market, getting famous, are also of invasive type. One has to prick their fingertip every time they check glucose. All sorts of invasive testing strips are expensive disposable consumables. Hence there was a need to propose a non-invasive (NI), pain free and user friendly method which can cater solution to all said problems.

People suffering from diabetes mellitus may undergo hyperglycemia and hypoglycemia, leading to exhibit irregular high and low glucose levels, respectively. Diabetes mellitus (DM) is classified into three main categories. In type 1 DM, body doesn't produce insulin that is why patients suffering from type 1 DM take insulin for the rest of their life. Type 1 is also termed as Insulin Dependent Diabetes Mellitus (IDDM). Mostly people develop type 1 diabetes in early 40's, in their child hood or in teenage years. In Type 2, human body doesn't produce enough insulin as per the body requirements or in other case cells in the body do not respond to it which is usually termed as insulin resistance. Type 2 is also called as Non-Insulin Dependent Diabetes Mellitus (NIDDM). People usually develop type 2 DM after 40's or in their adulthood. Patients suffering from type 2 diabetes are advised to take dose regularly, continuously monitor their blood glucose and do exercise as per doctor directives. Approximately, 10% of all diabetic cases belong to type 1 and rest of 90% belongs to type 2. People who are fat and have obesity plus overweight problems, tend more to suffer from type 2 diabetes [2]. Third type of DM is gestational diabetes which affects females during their pregnancy. Females possessing this type of DM may face failure of enough insulin production in their body because of high levels of glucose. Perhaps, proper diet, medication and exercise yield better controlling of the said disease.

Table 1 shows the summary of some non-invasive (NI) techniques used to measure blood glucose and achieved accuracy. Ilana Harman-Boehm et al. describes a non-invasive blood glucose measurement method for diabetic and non-diabetic patients using three independent techniques i.e. ultrasonic, electromagnetic, and thermal. Results are compared with Bayer glucometer for diabetic and non-diabetic people.

TABLE I. SUMMARY OF NI TECHNIQUES USED AND ACQUIRED ACCURACY

Sr. No.	Authors	NI Techniques	Accuracy	Reference
1.	Ilana Harman-Boehm et al.	Combination of three independent technologies i.e. ultrasonic, electromagnetic and thermal technique.	Mean %ARD=29.9% Median %ARD=19.9% 50% results lie in zone A	[3]
2.	Ilana Harman-Boehm et al.	Combination of three NI methods: ultrasonic, electromagnetic and thermal.	Mean %ARD=22.4% Median %ARD=15.9% 60% results lie in zone A	[4]
3.	Jan Lipson et al.	Raman Spectroscopy.	53% results lie in zone A	[5]
4.	Md Koushik Chowdhury et al.	Amplitude modulated ultrasound and infrared technique.	85% results lie in zone A	[6]
5.	Caduff et al.	Ultrasonic reflection and laser doppler fluxmetry (LDF) technique.	56% results lie in zone A	[7]
6.	Chen et al.	Optical signal pulsatile microcirculation (OSPM) technique.	100% results lie in zone A	[8]

The mean and median Absolute Relative Differences (ARDs) were 29.9% and 19.9%, respectively. Clarke error grid analysis shows that 92% of the readings fell in the clinically acceptable zones A and B, with 50% in the A zone [3]. Later on, to get more accuracy they performed some more trails on two different days with targeted diabetic patients of type 1 and type 2. For day 1, they were able to get ARDs mean and median 22.4% and 15.9%, respectively. And for day 2 results the ARDs mean and median were 23.4% and 16.5%, respectively. Clarke error grid (CEG) analysis shows 96% of the readings (on both days 1 and 2) fall in the clinically accepted A and B zones, of which 60% are within zone A [4]. Jan Lipson et al. describe requirements for calibration in NI glucose monitoring by Raman Spectroscopy. Results have been evaluated for 30 tests specimens and obtained a median absolute relative difference of 92% of the data in the clinically accepted Clarke zones A and B with typically 53% in zone A [5].

Md Koushik Chowdhury et al. describes error grid analysis of reference and predicted blood glucose level for results obtained from 10 adult human volunteers (2 normal and 8 pre-diabetic) in fasting and random mode. Non-invasive measurement is done by using Amplitude Modulated Ultrasound and Infra-red (940 nm) sensor. Results have been compared to invasive glucometer Accu-check and Clarke and Parker error grid analysis is done. Both grids show the overall (Normal & Pre-diabetic patients) 85% results lie in clinically accepted zone A. Individually, for normal test specimens 87.50% and for pre-diabetic patients 84.375% data points lie in zone A [6].

Caduff et al. describes the environmental temperature effects on thickness of skin and microvascular flow of blood in various diabetic and non-diabetic test specimens.

13 diabetic and 7 non-diabetic test specimens have been evolved during the study performed in a chamber where temperature and humidity were kept controlled. Ultrasonic technique was used to measure skin thickness and laser Doppler fluxmetry was used to evaluate microcirculation at lower forearm. Clarke error analysis shows 93% of the values situated in the high performance zones (56% and 37% in the A and B zones, respectively) [7]. Chen et al. analyzed the variations in the spectrum of light transmitted through the fingers of 15 diabetic patients, based on the signals from pulsatile microcirculation. The measurements were very accurate when done in a stable environment, with 100% of the values situated in the A and B zones of the Clarke's Error Grid, when compared with a classical glucometer [8].

Furthermore, some electrical methods were also proposed with acceptable results but their effect on the skin of diabetic patients was reddening, irritation and minimal burns [9]. Hence, the goal of the paper is to propose a method which is promising to resolve patient's health issues whilst measuring pulse rate (PR), SpO₂ ratio and blood glucose non-invasively with maximum accuracy by keeping the design as simple as possible. Fingertip photoplethysmography (PPG) signal analysis of near infra-red (NIR) spectrum is done with the help of an amplification and filter circuitry and an algorithm is established which performs all the mathematical formulas calculation and interprets the sensor's data to yield the said parameters. Fig. 1 represents the block diagram of the non-invasive pulse rate, oxygen saturation and glucose measurement system. PPG signal is extracted from the hardware and further processed via micro controller Arduino UNO board and algorithm is developed which performs all calculations and displays the final PR, SpO₂ and glucose values on the laptop screen.

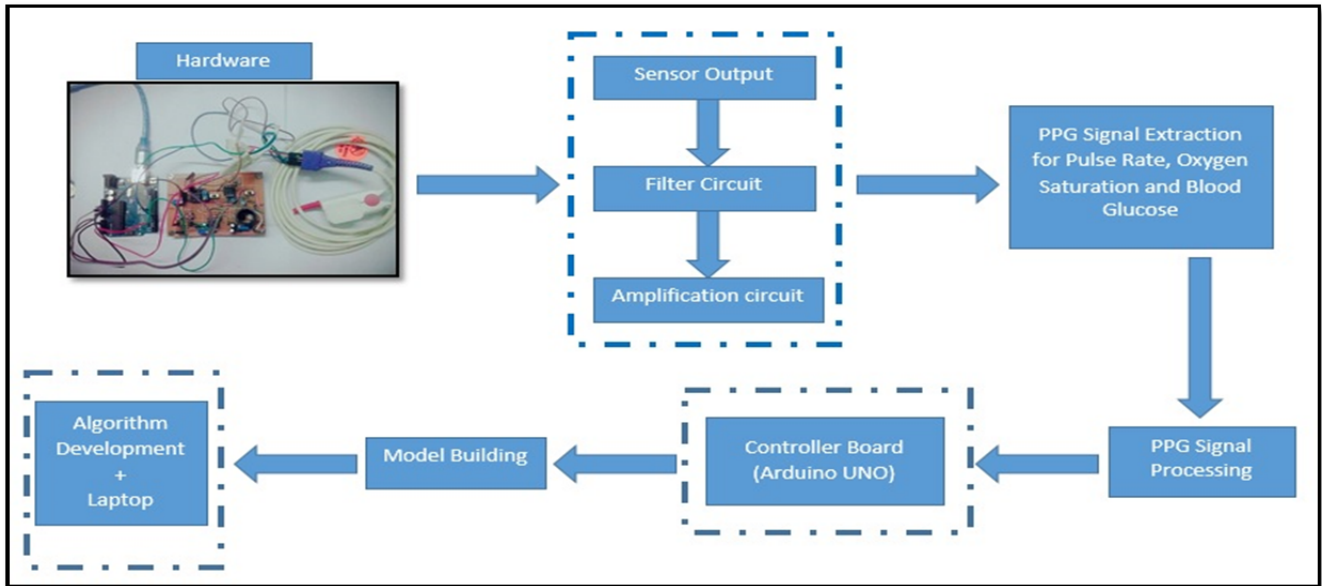


Fig. 1. Block diagram of non-invasive pulse rate, oxygen saturation and glucose measurement system.

II. METHODOLOGY

A. Principle of Pulse Oximetry

As far as pulse oximetry is concerned, there are two methods to find SpO₂ ratio which are transmittance oximetry and reflectance oximetry. For proposed method, transmittance oximetry is used in which light source and detector, both are mounted on the opposite sides. When light is being emitted, it passes through the fingertip tissues and falls on the light detector present at the other end.

Since, oxygen is coined to hemoglobin in the arterial blood that is why photoplethysmography (PPG) signal analysis is necessary to notice the optical changes in the absorbed signal and its absorption characteristics are compared to make decisions about pulse rate (PR) and SpO₂. This follows Beer Lambert's law as shown in "(1)" [10]. Over here, I_{out} is the transmitted light intensity via fingertip, I_{in} is the incident light intensity, ϵ is the molar absorptivity, C is concentration level to be measured and L is optical path length.

$$I_{out} = I_{in} e^{-\epsilon cl} \quad (1)$$

A fingertip pulse sensor probe, Nellcor DS 100A is being used, consisting of two LEDs having different wave lengths i.e. red and infrared, 660 nm and 940 nm, respectively. The fingertip PPG signals analysis shows DC and AC components. The DC component doesn't change with time and it shows light absorption via finger's skin, bone, muscles and venous blood while the AC component gives information about the arterial blood and its pulsatile nature depicts that it changes with time with respect to heart beat. Fig. 2 depicts the schematic design for blood oxygen saturation level measurement. The algorithm manipulates the sensor's output data, analyzes the PPG signal's AC and DC components and implements the following "(2)" for calculating blood oxygen saturation level.

$$\text{Oxygen Saturation} = \frac{AC \text{ Red} / DC \text{ Red}}{AC \text{ IR} / DC \text{ IR}} \quad (2)$$

B. Pulse Rate Measurement

Pulse rate waveform is obtained by using a basic signal conditioning circuit consisting of cascade low and high pass filters as schematic depicts in Fig. 3. High frequency and power line noise is eliminated by using a low pass filter. However, low frequency noise and baseline drift is removed by using a high pass filter of cut off frequency 0.5 Hz. Small variations in the signal acquired by the photodetector are converted into square pulses to calculate heart rate which can be seen in Fig. 4. The reason of doing this is to get the precise pulse rate value from the PPG pulse wave form as shown in Fig. 5.

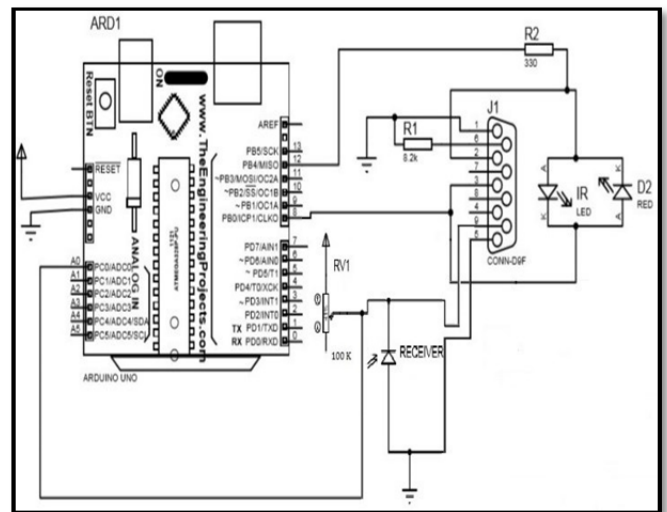


Fig. 2. Schematic to find blood oxygen saturation level.

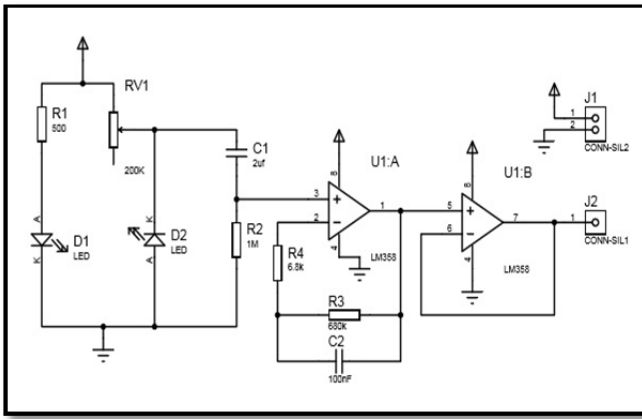


Fig. 3. Schematic to get pulse waveform.

C. Wavelength Selection for Glucose

Near infrared is one of the mostly used optical technique for glucose measurement. To deal with tissues having low energy radiation, normally the Near Infrared Spectroscopy (NIRS) is used. The NIR spectrum ranges from 750 to 2500 nm region. The range, 700 to 1100 nm wavelength is usually called as therapeutic window because it allows maximum penetration depth up to few millimeters under the skin. In higher overtones, glucose has absorption peaks at different wavelengths such as 939 nm, 970 nm and 1197 nm [11]. For proposed method, NIR LED having wavelength 940 nm is used. At this wavelength, minimum attenuation is offered by some constituents present in human body such as plasma, hemoglobin and deoxyhemoglobin molecules and water to the emitted light signal which yields better results.

D. PPG Analysis and Analytical Modeling for Glucose

Fig. 7 depicts the schematic diagram for blood glucose measurement. Sensor used for non-invasive glucose measurement gives better signal output and has high signal to noise ratio. Signal acquired from sensor is filtered via paired low and high pass filter with cut off frequencies 10 Hz and 0.5 Hz, respectively. The fundamental working principle is based on Beer Lambert's law as already described in "(1)". Fig. 6 depicts the protocol followed by microcontroller to get the final glucose value.

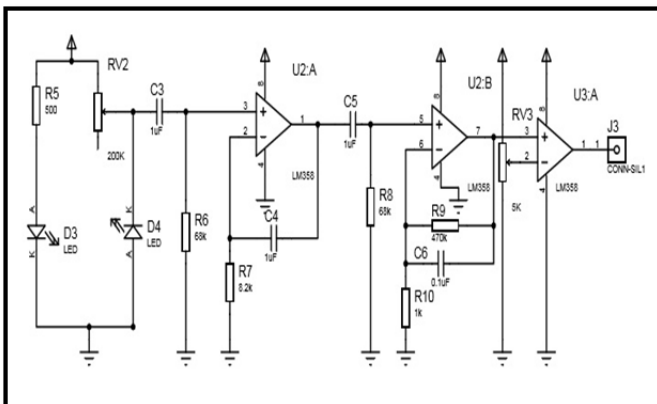


Fig. 4. Schematic to calculate pulse rate.

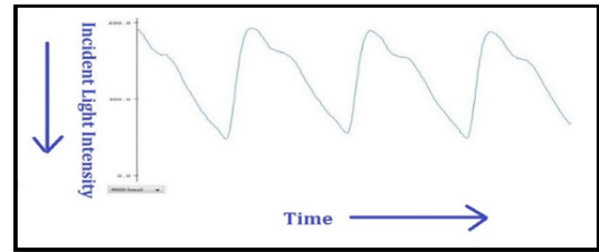


Fig. 5. Noise free filtered PR wave.

Once filtered signal is acquired from hardware and fetched to Arduino then intrinsic molecular properties have been administered such as near infrared light absorption characteristics, molar extinction coefficients calculations and optical path length, transmitted and incident light intensity determination. Arduino's interrupts are used to get those intensities, simultaneously. Algorithm evaluates the transmittance and optical density as shown in "(5)", "(6)", "(7)" and "(8)", performs mathematical modeling and takes the mean of the optical density values which are taken at different times i.e. t , $t+1$ and so on as shown in "(3)" and "(4)". Addition and subtraction of the mean value in the experimental values helps to overcome the error. Furthermore, experimental values are fetched in a linear curve fitting equation to perform linear regression as depicted in "(9)" to get the best glucose values. That equation yields the error less predicted values to the reference values by best fitting the curve. Closer to the curve line, less erroneous results would be and vice versa. Intensities attained from sensor are fetched to microcontroller and rest of the transmittance and absorbance calculations, linear regression, curve fitting and analytical modeling is done by coding Arduino sketch software. All of the equations used in the algorithm are mentioned below:

$$OD_{\lambda} = \left(\log \frac{I_o}{(I_N (t_i))} \right) \quad (3)$$

$$OD'_{\lambda} = \left(\log \frac{I_o}{(I_N (t_{i+1}))} \right) \quad (4)$$

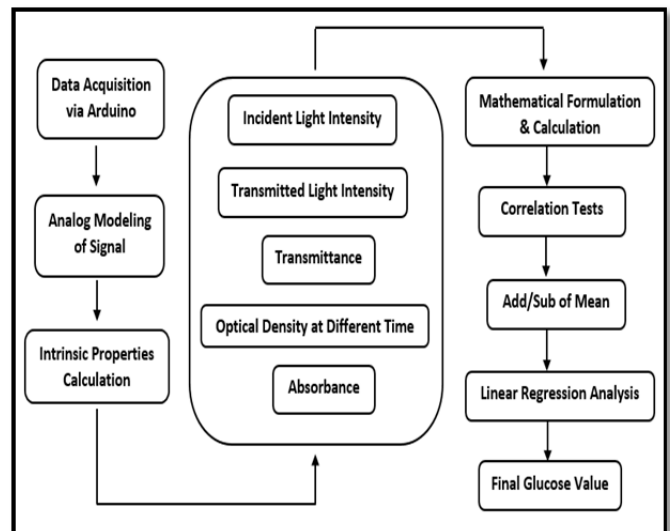


Fig. 6. Protocol followed by microcontroller for glucose measurement.

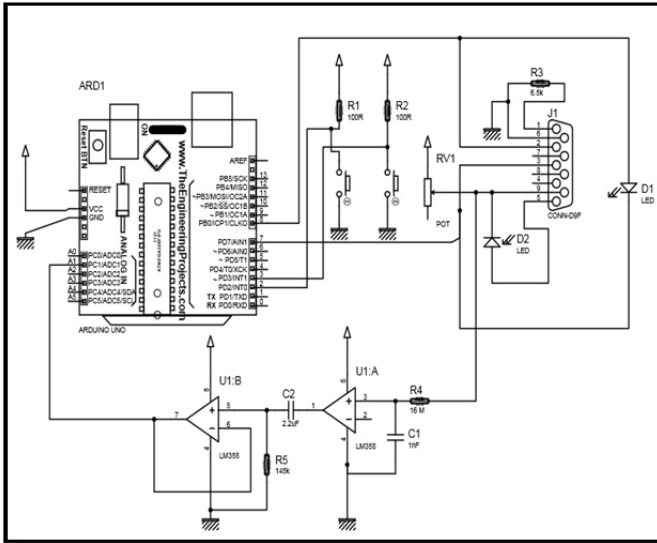


Fig. 7. Schematic to find blood glucose level.

$$A = a(\lambda) C L \quad (5)$$

$$A = \epsilon C L \quad (6)$$

$$\%T = \frac{I_N}{I_0} * 100 \quad (7)$$

$$A = 2 - \text{Log}_{10}[\%T] \quad (8)$$

$$Y_p = 1.1599\mu - 0.9643 \quad (9)$$

Over here; OD_λ = Optical density, A = absorbance, $a(\lambda)$ = wavelength dependent coefficient, T = transmittance, I_N = transmitted light intensity, I_0 = incident light intensity, Y_p = predicted glucose value and μ = experimental input values, ϵ , C and L are already explained in “(1)”. For finding the exact finger thickness, special sized rings have been used for every test specimen. The diameter of the ring yields the thickness of the fingertip, since light reaches to the receiver from the source by passing through the fingertip. Hence, thickness of finger is the ultimate measure of the path length.

III. RESULTS

Initially results have been acquired and compared to commercially available fingertip pulse oximeter which finds out the blood oxygen saturation level and pulse rate as per IEC60601-1-2 standards. Experimental study involves readings of 3 females and 4 males and their result comparison of PR and SpO_2 level with the commercially available pulse oximeter. The overall measurement accuracy of $\pm 3\%$ for pulse rate and $\pm 1\%$ for blood oxygen saturation level is being observed as can be seen in Table 2.

A. Clinical Trials of Glucose

For blood glucose level measurement, a 3 day clinical trial is performed in the pathology LAB of Holy Family Hospital (HFH), Pakistan. Experimental study of all 3 days can be seen in Table 3. A total of 132 test subjects were analyzed during the study, consisting of various diabetic and non-diabetic patients. Total 49, 57 and 26 test specimens were analyzed on day 1, 2 and 3, respectively. Out of which 14, 12 and 6 test

specimens were analyzed in fasting mode on day 1, 2 and 3, respectively and 35, 45 and 20 in random mode on day 1, 2 and 3, respectively. Study involves total 13 type-2, 4 hypoglycemic and 4 gestational diabetic patients.

The Clarke Error Grid (CEG) analysis is done by using MATLAB and graphically expressed as shown in Fig. 8, 9 and 10. Fig. 8 depicts the CEG of all 3 day results. The points lying in zone A are those which follows the International standards Organization (ISO) latest accuracy criteria and have maximum error equal or less than 15%. From CEG, the respective blood glucose level determining accuracy dependent values are classified into different zones. For example zone A: 94.70%, zone B: 4.54%, zone C: 0.00%, zone D: 0.76% and zone E: 0.00%, respectively as shown in Fig. 8. The Absolute Relative Differences (ARDs) yield mean and median values of 9.51% and 8.05%, respectively.

Fig. 9 shows the non-diabetic and diabetic result values of all 3 day data. For non-diabetic patients, the blood glucose level determining accuracy dependent values are classified into CEG zones as; zone A: 100.00% and zone B, C, D and E = 0.00%, respectively as shown in Fig. 9(a). CEG zones for diabetic test specimens are classified as; zone A: 66.67%, zone B: 28.57%, zone C: 0.00%, zone D: 4.76% and zone E: 0.00%, respectively as shown in Fig. 9(b). CEG analysis of diabetic patients involve 3 females suffering from hypoglycemia, 10 females of type 2 diabetes, 3 males of type 2, 1 male suffering from hypoglycemia and 4 females of gestational diabetes. The Absolute Relative Differences (ARDs) of non-diabetic patients yield mean and median values of 9.51% and 8.05%, respectively and the ARDs of diabetic test specimens yield mean and median values of 19.53% and 13.94%, respectively.

Fig. 10 depicts the fasting and random mode readings of diabetic and non-diabetic test specimens of all 3 days. For fasting mode, the blood glucose level determining accuracy dependent values are classified into CEG zones as; zone A: 90.63% and zone B: 6.25%, D: 3.13%, C and E = 0.00%, respectively as shown in Fig. 10(a). CEG zones for random mode of diabetic and non-diabetic test specimens are classified as; zone A: 96.00%, zone B: 4.00%, zone C, D and E = 0.00%, respectively as shown in Fig. 10(b). The ARDs of diabetic and non-diabetic test specimens in fasting mode yield mean and median values of 11.20% and 9.67%, respectively and the ARDs of random mode yield mean and median values of 8.97% and 7.60%, respectively.

The invasive LAB chemistry analyzer installed in HFH is Beckman Coulter AU-480. It is a fully automated spectrophotometer, principally based on beer lambert law. Blood glucose levels were analyzed through Endpoint-2 method at a primary source wavelength of 340 nm. First centrifuged serum is placed into chemistry analyzer. A reagent is added in serum which develops a particular color. When visible light is passed through it, change in wavelength is observed. Instrument measures that change and is further calibrated, for glucose reagent, with standard known valued calibration samples. Once reagent is calibrated, a standard curve is generated. Instrument saves that curve for a limited period of time and any unknown glucose sample can be correlated to get the exact glucose value.

TABLE II. TEST RESULTS FOR PULSE RATE AND BLOOD OXYGEN SATURATION LEVEL

Test Results for Blood Oxygen Saturation & Pulse Rate											
Test Specimens	Red Signal AC	Red Signal DC	IR Signal AC	IR Signal DC	Oxygen Saturation SpO ₂	Experimental Results		Commercial Pulse Oximeter		Percentile Error (%)	
						Percentile Ratio %SpO ₂	Pulse Rate (BPM)	Percentile Ratio %SpO ₂	Pulse Rate (BPM)	For SpO ₂	For PR
Female	0.132648	2.867513	0.143050	2.911167	1.002698	98.82	96	99	98	1	2
Male	0.140478	2.960407	0.136369	2.909504	1.012417	99.78	92	98	95	1	3
Male	0.141121	2.981010	0.132315	2.800910	1.002106	98.77	76	99	79	1	3
Male	0.115522	2.876572	0.126881	3.129680	0.99059	97.63	74	98	77	1	3
Male	0.140626	2.992310	0.141052	3.041881	1.01349	99.89	80	99	83	0	3
Female	0.143212	2.782269	0.1364210	2.653834	1.00132	98.69	98	98	99	0	1
Female	0.140612	2.994382	0.140532	3.043337	1.01319	99.86	93	99	96	0	3

TABLE III. SUMMARY OF IN VIVO EXPERIMENTAL STUDY SUBJECTS OF GLUCOSE

Days	Test Specimens	Fasting/ Random		Male/Female		Age (years) (min to max)	Diabetic	Non-diabetic
Day 1	49	Fasting	14	Male	3	30 to 40	N/A	3
				Female	11	18 to 37	3-Hypoglycemia	8
		Random	35	Male	7	23 to 74	1-Type 2	6
				Female	28	18 to 40	1-Type 2	27
Day 2	57	Fasting	12	Male	N/A	N/A	N/A	N/A
				Female	12	24 to 70	4-Type 2	8
		Random	45	Male	2	25 to 30	1-Hypoglycemia	1
				Female	43	21 to 65	4-Type 2	39
Day 3	26	Fasting	6	Male	2	57 to 69	2-Type 2	N/A
				Female	4	21 to 35	N/A	4
		Random	20	Male	1	10	N/A	1
				Female	19	21 to 38	4-Gestational 1-Type 2	14

The latest ISO 2013 proposes a narrower accuracy range for high blood glucose levels for commercially available glucometers. According to that standard, results at or above 75 mg/dL must possess the measurement accuracy of $\pm 15\%$, previously it was $\pm 20\%$ and for results below 75 mg/dL, the

acceptable range is $\pm 15\%$ which is same as per USFDA (United States Food and Drug Authority) standard. Hence, obtained experimental results follow the ISO and USFDA standards until glucose value reaches to 230 mg/dl. Up to this value, ARD remains 15% but afterwards error gets more than 15%.

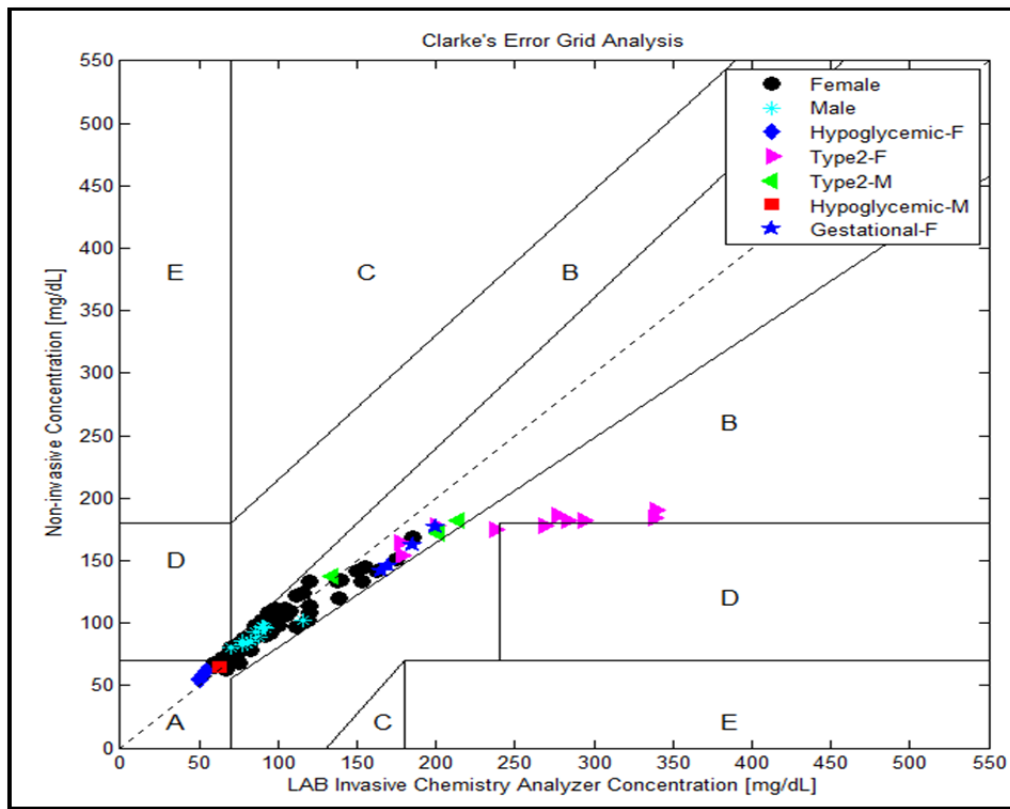


Fig. 8. Clarke Error Grid (CEG) analysis of the LAB invasive chemistry analyzer (x-axis) and non-invasive blood glucose concentration (y-axis) of test specimens of all 3 days experimental study.

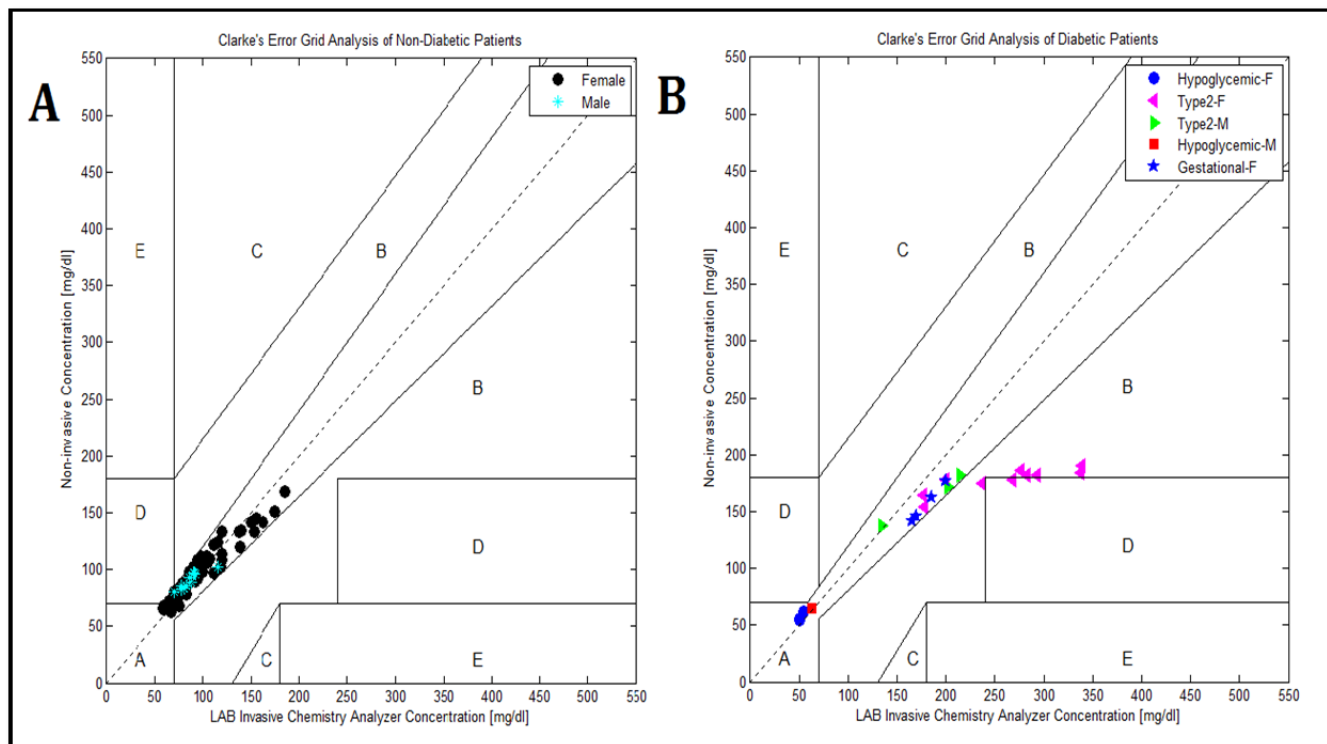


Fig. 9. (a) Clarke Error Grid (CEG) analysis of non-diabetic test specimens; (b) Clarke Error Grid (CEG) analysis of diabetic test specimens.

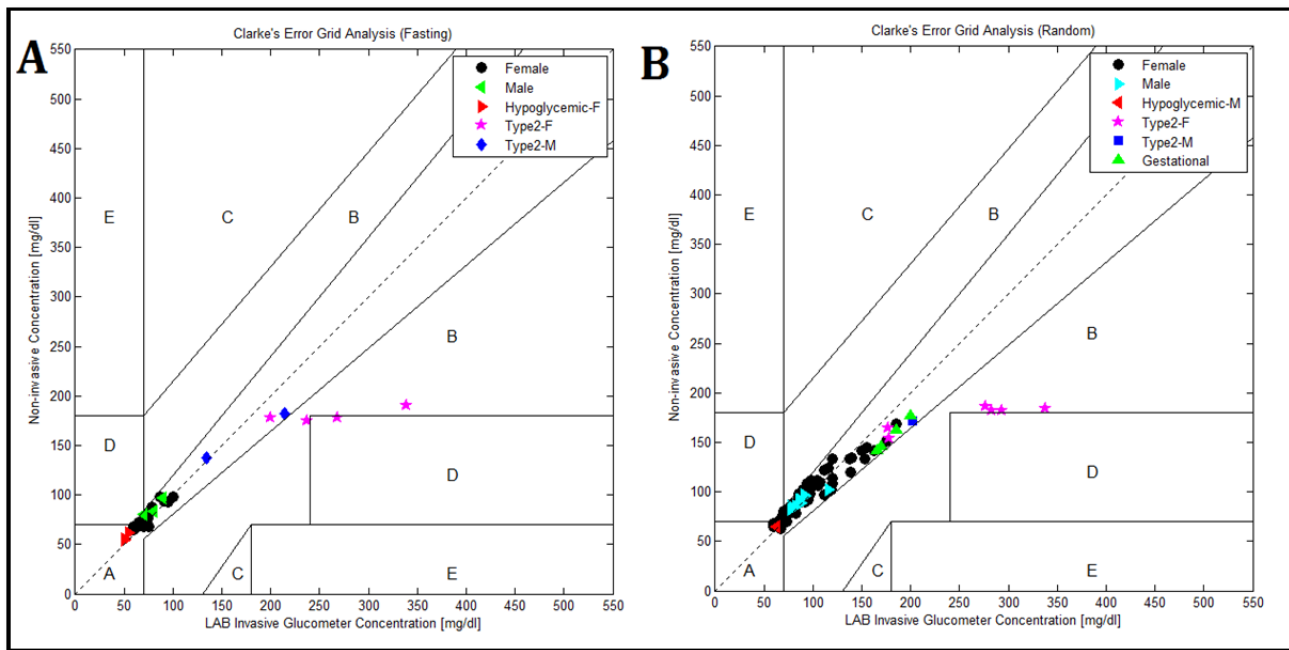


Fig. 10. (a) Clarke Error Grid (CEG) analysis of diabetic and non-diabetic test specimens in fasting mode; (b) Clarke Error Grid (CEG) analysis of diabetic and non-diabetic test specimens in random mode.

IV. CONCLUSION

Previously, much research has been done regarding non-invasive blood glucose monitoring followed by fusion of diverse techniques but all suffer from inaccuracies. Conventional devices available in market are invasive, pain causing, require puncturing of skin and expensive too because every single time a new test strip and needle is required to check the glucose level. In human body, there are other analytics which affect the absorption spectrum of glucose. Water influence is dominant among all other substances. Overlapping water absorption peaks, proteins, or other blood components, and especially from varying amounts of blood and tissue in the optical path are major cause of erroneous measurements. Thus, previously proposed glucose monitors were not proven to be practical, precise, and/or economical. However, the proposed prototype is simple and reliable. Results are compared with invasive chemistry analyzer Beckman Coulter AU-480. The acquired mean and median absolute relative difference values are 9.51% and 8.05%, respectively. The CEG analysis shows the measurement accuracy of 94.70% which refers to the results falling in clinically accepted zone A. This prototype is not feasible for clinical purpose for diabetic patients having high glucose levels because it gives more than 15% error to those measurements. Thus, in future, some other transduction method needs to be incorporated in the design to get more accurate results for high glucose values.

ACKNOWLEDGMENT

I would like to thank ALLAH almighty, my kind supervisor and friends who helped me out during my research phase.

REFERENCES

- [1] H. M. Sami, B. S. Kleinman, V. A. Lonchyna, "Central venous pulsations associated with a falsely low oxygen saturation measured by pulse oximetry," *J Clin Monit*, vol.7, pp.309-312, 1991.
- [2] M. C. Pande, A. K. Joshi, "Non-Invasive Optical Blood Glucose Measurement," *International Journal of Engineering Research and Applications (IJERA)*, Vol. 3, ISSN: 2248-9622, Issue 4, Jul-Aug 2013, pp.129-131.
- [3] Harman-Boehm, Ilana, et al. "Noninvasive glucose monitoring: a novel approach." (2009): 253-260.
- [4] Harman-Boehm, Ilana, et al. "Noninvasive glucose monitoring: increasing accuracy by combination of multi-technology and multi-sensors." *Journal of diabetes science and technology* 4.3 (2010): 583-595.
- [5] Lipson, Jan, et al. "Requirements for calibration in noninvasive glucose monitoring by Raman spectroscopy." *Journal of diabetes science and technology* 3.2 (2009): 233-241.
- [6] Chowdhury, Md Koushik, et al. "Error Grid Analysis of Reference and Predicted Blood Glucose Level Values as Obtained from the Normal and Prediabetic Human Volunteers." *American Journal of Biomedical Engineering* 5.1 (2015): 6-14.
- [7] Forst, T., et al. "Impact of environmental temperature on skin thickness and microvascular blood flow in subjects with and without diabetes." *Diabetes Technology & Therapeutics* 8.1 (2006): 94-101.
- [8] Chen, Chung-Sen, et al. "Noninvasive blood glucose monitoring using the optical signal of pulsatile microcirculation: a pilot study in subjects with diabetes." *Journal of diabetes and its complications* 22.6 (2008): 371-376.
- [9] Smith, John L. "The pursuit of noninvasive glucose: hunting the deceitful turkey." Last accessed May 2 (2011).
- [10] G. Maruf, Azmal, A. Al-Jumaily, "Continuous Measurement of Oxygen Saturation Level using Photoplethysmograph Signal", *Intl. Conf. on Biomedical and Pharmaceutical Engineering, ICBPE* 2006.
- [11] O. S., Khalil, "Spectroscopic and clinical aspects of non-invasive glucose measurements", *Clinical Chemistry*, vol. 45, no.2, pp.165177, 1999.