Proceeding Paper

Non-Invasive IR-Based Measurement of Human Blood Glucose [†]

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Abstract: Non-Invasive blood glucose monitoring using infrared (IR) light is considered to be a useful and reliable tool for measuring blood sugar levels during daily activities. IR-based glucose monitoring depends on the variant absorption levels of IR light waves by blood with high or low levels of glucose solution. This paper introduces a low-cost finger probe to measure glucose based on Arduino and embedding a Clarke error grid with fuzzy logic. An electronic blood glucose meter was designed and implemented in a non-invasive and painless manner based on an infrared sensor. The electrical signal expressing the level of glucose in the blood with a mathematical equation was used to calibrate and map the physical and electrical values. The final numerical value was validated with the Clarke error grid by implementing fuzzy logic (FL). The designed device was tested on 30 subjects with 15 diabetes subjects. The results show the high significance of results at points where the FL was able to determine an error range of less than 10% of measured glucose within the same range of the reference measurements. The proposed method of using FL with a Clarke error grid gives more confident and precise outputs in cases of this kind of portable device.

Keywords: glucose monitoring; mid-infrared probe; fuzzy logic

1. Introduction

Diabetes mellitus is an intractable chronic disease in which abnormal glucose metabolism occurs due to a partial or complete deficiency of insulin secreted by the pancreas [1]. Uncontrolled blood sugar levels or glycemia can lead to health complications for patients. In fact, blood sugar levels in healthy people change before and after a meal. Generally, pre-meal glucose blood sugar concentration is 70–100 mg/dl. Diabetes is diagnosed when blood glucose levels are approximately 126 mg/dL (7 mmol/L) during fasting and 200 mg/dL 2 h after eating [2]. Chronic hypoglycemia, a drop in blood sugar, can induce diabetic coma if it drops too quickly. This can lead to brain damage and even death [3].

In order to prevent and avoid the complications associated with the change in the amount of glucose in the blood and the proper monitoring of the development of the dis-ease by health care personnel in order to control the disease effectively, patients need to monitor their blood sugar regularly. In reality, the majority of patients cannot feel the change in their glucose level unless, it is very high or very low, without taking a sample. According to the American Diabetes Association, patients with type 1 undergoing intense therapy should test their blood sugar 4–5 times a day, but those with type 2 require only two measurements per day [4]. Unfortunately, the blood glucose monitoring devices that are available in the market only offer a limited number of measurements per day, while a diabetic needs continuous real-time glucose monitoring (CGM) to be informed in case of severe hyperglycaemia or hypoglycaemia. This is especially true for insulin-dependent

patients [5]. In addition to that, conventional glucometers require patients to prick their finger each time a measurement is taken to obtain the amount of blood needed for the sensor to work. These pricks are so painful and affect the fingers in the long term to such a degree that some people reduce the number of measures just to avoid pain. Therefore, it is clear that an ideal CGM device should be non-invasive, portable, accurate, inexpensive, easy to use, and not require extensive calibration. Mid-infrared (IR) radiation, with a wavelength range from 2500 nm to 25 μm, offers the highest selectivity for low-concentration compounds in complex organic media. In principle, most approaches using mid-infrared rely on the strong absorption of water in living tissue. Diffuse reflectance spectroscopy can access glucose molecules from the epidermal layer, whereas photothermal detectors can provide information from depths of 20–100 μm [6].

A number of portable non-invasive blood glucose monitors have been developed that have demonstrated excellent blood glucose measurement and monitoring capabilities [7,8]. Most non-invasive devices require frequent calibration, but current research that works on developing non-invasive devices is finding that the calibration process, its duration, complexity, and effectiveness are detrimental and not periodically possible. In recent years, great efforts have been made to reduce or even eliminate the frequency of calibration [9,10]. This paper presents a fuzzy logic-based calibration system to map the output voltage of IR sensor and Arduino controller into reliable glucose concentration using Clarke error grid. In this study, the fuzzy logic is responsible about estimating the error tolerance using the output voltage from Arduino controller and the estimated glucose concentration.

2. Theoretical Background

As light rays traverse the tissues of the human body, they are subject to several phenomena such as scattering, absorption, reflection, and refraction. These phenomena provide evidence of irreconcilable refraction and reflection between the inside and outside of the cell and through the fluid. Theoretically, the detection should remain nearly constant, but it can change as the concentration of glucose molecules changes, and Pierre-Lambert's law states that the amount of light absorbed by a substance depends on the concentration and length of the way the light passes through a medium. Increased absorption in tissues containing many sugar molecules reduces optical density through those tissues compared to less dense tissues. A wavelength of 940 nm has been found to be clinically acceptable as it has low absorption and as the intensity of light passing through blood vessels is not lost to the absorption of sugar molecules [6]. The resulting optical density relationship after absorption is given by Equation (1):

$$I = I_0 e^{-\mu_{eff} L} \tag{1}$$

where:
    I: is the corresponding optical density.
    I_0: is the transmitted optical density.
    L: length of path crossed by light.
    μ_{eff}: is the coefficient of loss within tissue, defined by Equation (2):

$$\mu_{eff} = \sqrt{2\mu_a(\mu_a + \mu_s')} \tag{2}$$

A change in light density after absorption eventually appears as a change in voltage, which leads to a change in the output shown as blood glucose percentage after being processed and calibrated.

3. Materials and Methods

3.1. Hardware Design

3.1.1. IR Transmitter and Receiver

We used infrared sensors to measure the sugar in blood vessels. These sensors have the advantage of generating an analog voltage signal that corresponds to the intensity of the received light. An infrared sensor generally consists of a sensor and a photoreceptor and converts the receiving train of pulsed IR into an analogue output voltage that is later used as input for the Arduino platform. The sender and receiver were obtained from the TP808 photocoupler element. This is highly sensitive, consisting of infrared diodes and NPN phototransistors with a high sensitivity indicated by 980 nm wavelength and 30 mW.

3.1.2. Amplifiers and Filters

The Lm358 amplifier was used for this purpose. A non-inverting amplifier formula was used to calculate the gain from the following Equation (3):

$$G = 1 + \frac{R2}{R1} \tag{3}$$

A passive low-pass filter RC (C = 10 uF, R = 330) was connected after the amplifier to remove unwanted signals such as power supply noise.

3.1.3. Final Monitoring Circuit

The final monitoring circuit (Figure 1) was implemented using the previous IR circuit and Arduino Uno controller to convert the analog input from the IR sensor into digital values.
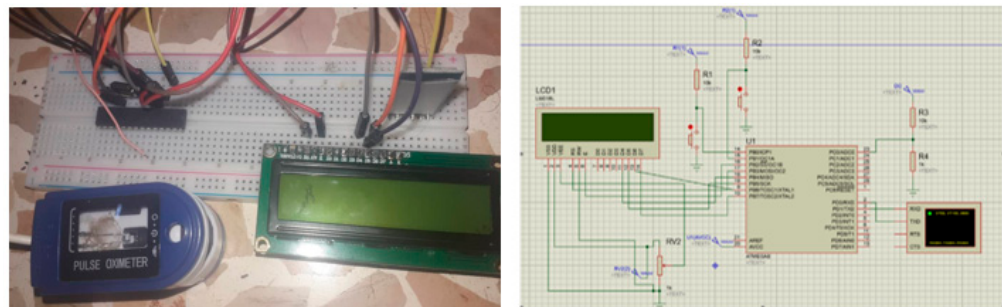

Figure 1. The implemented portable glucose monitor in this study.

3.2. Fuzzy Logic with CEG

The Clarke error grid, which is approved for clinical evaluation, was used as a marker of differences between test glucose measurement techniques and intravenous blood glucose baseline measurements [11]. This method uses a Cartesian scheme in which values are predicted by displaying the method under examination on the *y* axis, and the values received from the reference method on the *x* axis. The country region represents an ideal match between the two, while the points below and above the line indicate the exaggerated estimates and reduced actual values, respectively. Region-A (acceptable) represents glucose values that deviate from the 20% reference value or lie within the blood glucose range (<70 mg/dL). Values within this range are clinically correct, and thus correct clinical diagnosis can be made on their basis. Region-B (benign defects) is above and below region-A. This range represents values that deviate from the baseline after increasing by 20%. Values within zones A and B are clinically acceptable, but values within regions are included. Regions-C and -E are potentially bad and their use can lead to clinically significant errors.

In this study, the horizontal axes of CEG (Figure 2a) represent the output voltage of Arduino based on preliminary calibration process. The main objective of this methodology is to find the expected error tolerance of glucose concentration, which represents the

confidence interval of the estimated glucose value. To estimate the error in the observed glucose, FL (Figure 2b) was used to evaluate the output voltage from Arduino and the average accuracy of measured voltage based on CEG's areas (in scale of [0 to 1]).


(**a**)   (**b**)
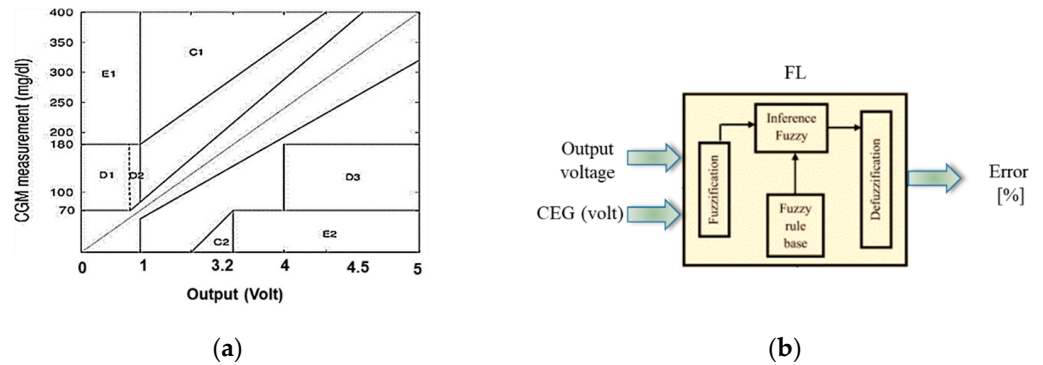
Figure 2. Proposed methodology of mapping the voltage-from-Arduino-to-glucose concentration and estimating the error tolerance using FL: (**a**) Clarke grid using voltage output on horizontal axis; (**b**) proposed fuzzy logic with two inputs of voltage and CGM and error output.

Fuzzy logic goes through several stages to reach a complete solution as follows:

1. Fuzzification: includes defining the membership functions (MF) for the input variables to determine the degree of truth in each rule. The input contains two variables: Arduino output and voltage accuracy based on the areas of CEG. The MFs of voltage output are shown in (Figure 3a), where the MFs of output voltage are represented with two triangle functions labelled as low glucose (LoGl) and high glucose (HiGl), and two triangle functions named mild (MiGl) and moderate (MoGl) glucose. The second input contains MFs with (A–E) labels that represent the areas of CEG. The MFs of the output are identical to the second input but the real values, range between 0 and 100 as a percentage of error.

2. Inference: contains the fuzzy if–then rules. In this study, the fuzzy rules were built based on the experimental observations of glucose and its coordinates on the areas of Clarke grid. The used fuzzy rules include:
    If Voltage is LoGl and CEG is A then Error is A.
    If Voltage is LoGl and CEG is B then Error is B.

3. Defuzzification: the "centroid" that depends on the center of gravity is used to obtain the final output, which is the error percentage of glucose concentration.

(**a**)   (**b**)
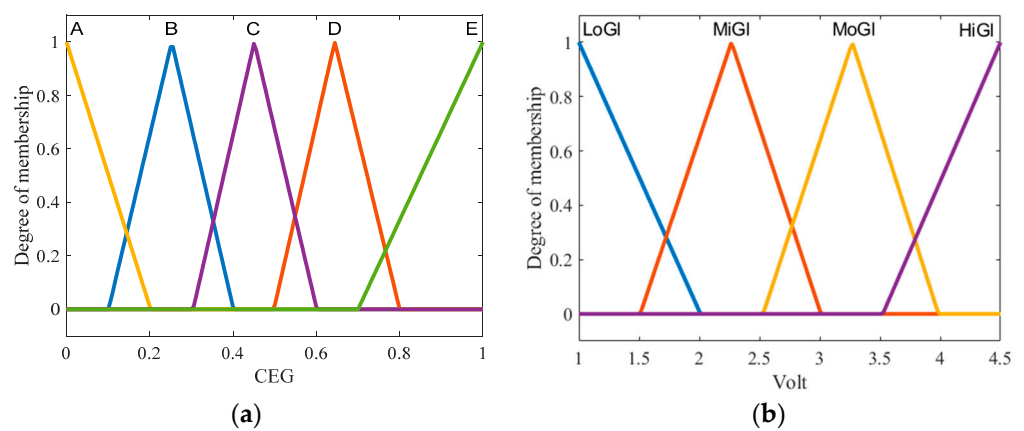
Figure 3. *Cont.*
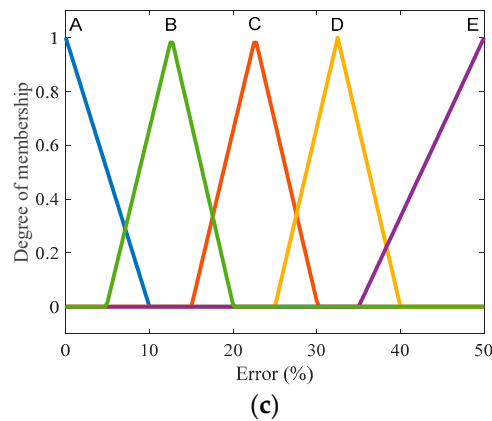
Figure 3. Membership functions of input and output in the proposed FL system: (**a**) MFs of analoge-voltage input; (**b**) MFs of CEG input; (**c**) MFs of the FL output.

4. Results and Discussion

4.1. Hardware Design

Non-invasive blood glucose monitoring using IR light is considered to represent a useful and reliable tool for measuring blood sugar levels during daily activities. The IR-based glucose monitoring principle depends on the variant absorption levels of IR light waves by blood, with high or low levels of glucose solution.

To test our device, we conducted a preliminary study on 30 subjects, including 15 subjects with diabetes and 15 healthy controls. We measured their blood glucose levels using our device and a reference device that uses the standard finger-prick method.

Our suggested system based on 940 nm IR light source seemed to be able to produce detectable signals. As shown in Table 1, we can notice that the recorded signals seem to vary between the subjects, and especially between normal (1.22–2.25 volts) and diabetic (2.9–3.5 volts) subjects. These results concord with the study of Yunos et al. which preferred the use of the IR principle to increase the sensitivity of the measurement and highlighted the accuracy of this method in differentiating between different groups of possible patients [12].

Table 1. Glucose levels with the corresponding measured signal values of 15 subjects.

Glucose [1] (mg/dcl)	Output (Volt)	Age	Glucose Using Device [2] (mg/dcl)	Gender	Diabetes (Neg/Pos)	Fasting
110	1.55	16	116	M	Neg	No
115	1.75	24	121	M	Neg	No
104	1.25	24	96	M	Neg	No
167	3.2	65	158	F	Pos	Yes
126	2.15	23	138	M	Neg	No
128	2.25	23	125	M	Neg	No
120	2.05	23	113	F	Neg	No
103	1.22	25	99	M	Neg	Yes
109	1.53	23	102	F	Neg	No
115	1.74	24	109	M	Neg	No
162	3.01	45	175	F	Pos	Yes
170	3.4	50	161	M	Pos	Yes
155	2.9	48	168	M	Pos	Yes
172	3.45	45	166	F	Pos	Yes
175	3.5	58	178	M	Pos	Yes

[1] using reference device. [2] calculated glucose using voltage output.

The final measurements of Table 1 are depicted on CEG as shown in Figure 4. The values show a not fully satisfactory convergence in the "A" and "B" areas which illustrates the error in estimated glucose level, thus making the utilization of FL necessary to compute the expected tolerance.
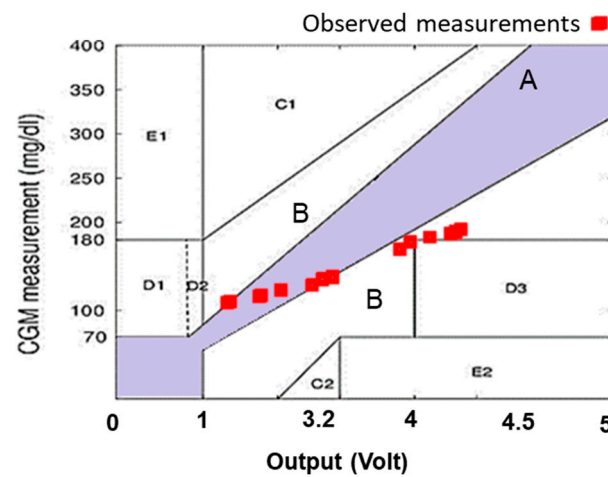
Figure 4. Graphed measurements using Arduino and Reference device on Clarke grid.

4.2. Glucose Measurement Using FL

As shown in Table 2, we notice that FL could be suggested for errors mapping and validation. The calculated tolerance of glucose using FL output gives a more reliable measurement of the monitor system by determining the expected error. The healthy samples show a glucose level between 104 and 115 (mg/dcl) with an error of less than ±10%. The diabetic samples mostly show an error in glucose between ±5% and ±10%.

Table 2. A comparison of the measured glucose levels with the referential device and FL-based error of 15 subjects.

Glucose [1] (mg/dcl)	Output (Volt)	Glucose Using Device [2] (mg/dcl)	Glucose Using FL [3]
110	1.55	116	116 ± 6
115	1.75	121	121 ± 6
104	1.25	96	96 ± 8
167	3.2	158	158 ± 9
126	2.15	138	138 ± 12
128	2.25	125	125 ± 3
120	2.05	113	113 ± 7
103	1.22	99	99 ± 4
109	1.53	102	102 ± 7
115	1.74	109	109 ± 6
162	3.01	175	175 ± 13
170	3.4	161	161 ± 9
155	2.9	168	168 ± 13
172	3.45	166	166 ± 6
175	3.5	178	178 ± 3

[1] using reference device. [2] calculated glucose using voltage output. [3] calculated glucose with possible error using FL.

The results showed that the finger probe can measure glucose in a non-invasive and painless manner with an acceptable accuracy and reliability. This result concords with the finding of Mehmood et al. study which reported promising results with the use of fuzzy logic in artificial pancreas control strategies [13].

In this study, we tried to introduce the principle of FL-based Clarke error grids. The finger probe consisted of an infrared emitter and detector that were attached to the fingertip and connected to an Arduino microcontroller. Many studies preferred the use of fuzzy logic to perform glucose levels measurement [13,14]. The FL algorithm seemed to evaluate with an accepted rate of accuracy and reliability of the glucose measurement using the Clarke error grid. It provided a graphical method with which to compare different methods of

glucose measurements. By dividing the measurement space into five zones, A, B, C, D, and E, we were able to classify the measurements from the most accurate measurements to the most erroneous measurements, leading to dangerous outcomes. Fuzzy logic represented a flexible and realistic representation of the measurement errors. Based on the assignment of membership to each zone of Clarke error grid, the FL algorithm was able to produce more accurate glucose measurements [15].

5. Conclusions

The achievement of on-invasive blood glucose monitoring is a desirable goal for many diabetic patients who need to measure their glucose levels frequently and accurately. However, most of the existing methods are either invasive or require expensive and complex equipment. Fuzzy logic is a mathematical technique that can handle uncertainty and imprecision in data, and has been applied to various biomedical problems, such as artificial pancreas control and glucose measurement using heart rate variability. FL can also be used to design simple and robust measurement devices that can adapt to different physiological conditions and environmental factors.

In this paper, we presented a contribution related to the use of FL measurements to estimate the blood glucose level from the fingertip. To test our device, we conducted a preliminary study on 30 subjects, including 15 subjects with diabetes and 15 healthy controls. We measured their blood glucose levels using our device and a reference device that uses the standard finger-prick method. We performed the measurements before and after a meal, at intervals of 15 min, for a total of 12 measurements per subject. We then compared the FL readings with the reference readings using the Clarke error grid analysis, which is a widely used method to evaluate the accuracy of glucose meters.

The results show that our device has a high accuracy and reliability, with an error rate of less than 3% according to the EGA. Out of 360 readings, 97.5% fell into zone A, 2.2% into zone B, and 0.3% into zone C. No readings fell into zones D or E. This indicates that our device can provide clinically accurate and acceptable estimates of blood glucose level without causing any harm or discomfort to the user.

We conclude that our device is a promising alternative to invasive methods of blood glucose monitoring, especially for diabetic patients who need frequent measurements. Our device uses FL measurements to estimate the blood glucose level from the skin impedance, which is a simple and non-invasive technique that can be implemented in a portable device. Our device has high accuracy and reliability, with an error rate of less than 3% according to the Clarke error grid analysis. This method of using FL with Clarke error grid seems to provide a more confident and precise output for this type of portable device.

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