High Performance Non-Invasive Glucose Monitoring System

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***Abstract* — A low cost, portable, high performance noninvasive glucose meter system is proposed using 3 wavelengths near infrared spectroscopy (NIRS) and bioimpedance spectroscopy (BIS). The glucose level can be calculated by using the measured parameter of the two systems as features to linear regression model. The BIS system performs a two frequency sweeps to record the lowest impedance point. The NIRS system uses 3 different LEDs with three different wavelengths to which the glucose molecules have peak absorption and less sensitive to other blood components. After measurement is done, the results are sent via Bluetooth to a mobile application to be displayed for the user. The results are saved to a cloud database using the 3G mobile connection to be integrated with Internet of Things (IoT) applications in healthcare. The system achieved 95.6% of the results in Region A of Clarke grid analysis. The proposed system does not require any pre-calibration and can be generally used by different users.**

***Keywords*— Non-invasive Glucose Monitoring, Bioimpedance spectroscopy (BIS), Near Infrared Spectroscopy (NIRS), optical and electrical integration, IoT.**

I. INTRODUCTION

According to World Health Organization, Diabetes is a chronic disease in which the human body is incapable of making adequate use of the induced insulin from the pancreas or incapable of producing it in the first place. Diabetes can cause serious damage to the cardiovascular system, nerves, kidneys and eyesight [1].

The key to a healthy living style with diabetes is regular self-monitoring. The traditional monitoring devices in the market like OneTouch® use invasive methods to determine the blood glucose level. The blood glucose meters consist of a test strip and a detector, the user is required to obtain a blood drop to be placed on the test strip by pricking the fingertip which causes pain and discomfort specially by repeating the process 3-4 times daily at the same pricking area.

Many researchers in non-invasive glucose monitoring has been growing over the last few decades in order to address the pain and discomfort problem [2]. Several methods were proposed for non-invasive glucose monitoring systems; Optical, thermal, electrical and nanotechnology methods [3].

Near Infrared Spectroscopy [4], Mid Infrared Spectroscopy [5], Raman Spectroscopy [6] and Optical Coherence Tomography [7] are examples of the optical methods recently. Bio-Impedance Spectroscopy [8],[9], Electromagnetic Sensing [10] are examples of the recent electrical methods. An example to thermal method is Photothermal deflectometry [11]. Nanotechnology aims to develop Nano-biosensors that can measure the glucose level of the saliva or sweat [12, 13]. However, the research in the nanotechnology method is still at its early stages.

In this paper, a non-invasive glucose measurement system is proposed, in which an electrical method: BioImpedance spectroscopy (BIS) and an optical method: Near Infrared Spectroscopy (NIRS) are integrated in one device. The glucose level is provided using a linear regression model that uses the parameters measured by the two systems as features. The result of the measurement is displayed on a mobile application which stores the results on a cloud database using 4G to allow the user to check the measurement history at any time. The overview of the system is shown in Fig. 1.

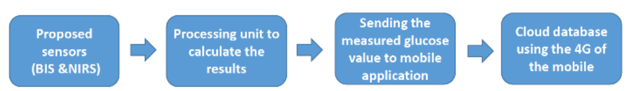

Fig. 1 Overview of the proposed system

The paper is organized as follows: In Section II the proposed system design and system blocks functions are presented. In section III, glucose level calculation is explained. The testing and the results of the integrated system are demonstrated. Finally, conclusions are provided in section IV.

II. PROPOSED SYSTEM DESIGN

As shown in Fig 2, the system consists of three main blocks; Measurement circuit which includes two subsystems (BIS and NIRS), Control unit which analyzes the measured data from the sensors and estimates the blood glucose level and finally sends the results to the third block in order to display the results on a mobile application and save the measurements on a cloud database. All the three blocks are integrated on a double layer PCB with dimensions of 5 cm x 4.8 cm. The PCB was designed using Autodesk® EAGLE software. The bottom of the system is placed on the forearm while the two AgCl electrodes are placed on the wrist with distance 4 cm between the centers of the two electrodes.

The connection between the device and the mobile application is established using Bluetooth connection. After a confirmation that the connection is successful, the user is asked to enter the age and gender information through the mobile application. The system setup is provided as shown in Fig. 3. The bottom of the system is placed on the forearm while the two AgCl electrodes are placed on the wrist with distance 4 cm between the centers of the two electrodes. The measurement is started by pressing the "start" button in the mobile application. The measurement process takes 60-70 seconds and then the results are sent to the mobile to be displayed on the application. Using the internet connection exists on the 3G mobile, the measurement data is transmitted to the cloud database.

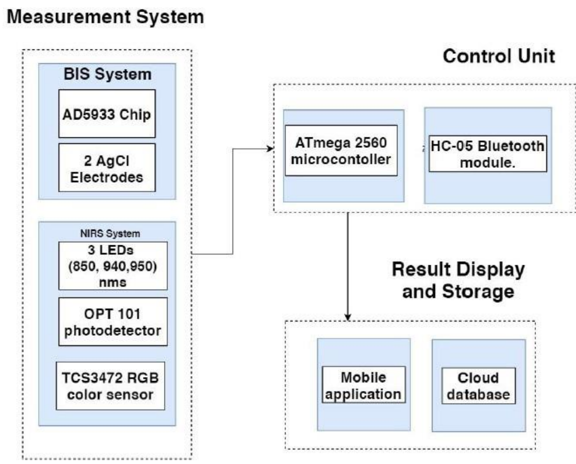

Fig. 2 Block Diagram of the System

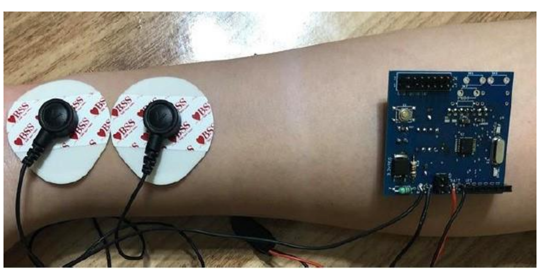

Fig. 3 System setup

A. Measurement System

1) Bio-Impedance Spectroscopy System: The human body cells consist of three parts: Extra-cellular fluid (ECF), Intracellular fluid (ICF) and Cell membrane. ECF is mostly made of interstitial fluid (ISF). Studies proved that the glucose level in ISF is equal to the blood glucose level [14]. The change in glucose level leads to change in the ECF resistance (RE) due to the change in the glucose carrier in plasma. Additionally, glucose level increase in plasma causes transferring of water from ICF to ECF which leads to change in the ICF resistance (RI) and capacitance of the cell membrane (Cm) [15]. When passing mid-range frequency current through the body cells, the lowest impedance value at resonance frequency is directly proportional to the glucose level because of the change of the cell components resistances (RI and RE) and capacitance (Cm).

In the proposed BIS system, The core of the converter circuit is the AD5933; an impedance converter integrated circuit. Two disposable Ag/AgCl electrodes used for ECG purposes are used for each impedance measurement. They are placed on the wrist with distance 4cm between them. AD5933 registers needs to be programmed in order to start a frequency sweep. The starting frequency, number of the steps and the value of each increment are programmed into start frequency register, number of increments register and frequency increment register respectively. The program is initialized using start frequency command in the control register. Then the sweep starts by setting the control register to frequency sweep command. After the sweep is done, the measured real and imaginary values are saved in the real and imaginary registers.

The BIS measurement is provided using two frequency sweeps. The first sweep is achieved from 10 KHz to 100 KHz with a step of 10 KHz. The range is chosen to ensure that all the cell components contributes to the impedance value. The frequencies corresponding to the least two measured impedance values are recorded. The second frequency sweep is achieved between the two recorded points with a step of 1KHz, the lowest impedance point is saved. The magnitude and phase values of the minimum impedance are estimated and passed as features to linear regression model to determine glucose level.

2) Near Infrared Spectroscopy System:

NIRS is based on applying light at certain wavelengths and study the interaction of light with the sample. Due to the interaction, light can be absorbed or scattered. By choosing certain wavelengths for which the target molecules have absorption peaks, the concentration of the molecules can be estimated. The source of Glucose molecules spectrum has absorption peaks at wavelengths 850nm, 940 nm, 970 nm, 1197 nm, 1408nm, 1536nm, 1688nm, 1925 nm, 2100nm, 2261nm and 2326nm [15]. The higher glucose molecules concentration in blood, the higher is the absorption of the applied light and less light intensity can be sensed as output. The main two components of any NIRS system are: the light source and the photodetector. There are 2 main modes of measurement used in NIRS based on the positioning of system components: Transmission mode and diffuse reflectance mode. For Transmission mode, the tested sample is placed between the light source and photodetector. On the other hand, the photodetector and the light source are placed on the same horizontal level on the sample's surface. For the proposed system, diffuse reflectance mode is used with 3 LEDs of wavelengths of 850nm, 940nm and 950nm as the glucose molecules have absorption peaks at these wavelengths while other blood components like hemoglobin exhibit less absorption towards these wavelengths. OPT101 photodetector was used to sense the output light. The distance between LEDs and detector is 9.5mm for 850nm and 950nm wavelengths while it is 12mm for 940nm, the distance was chosen in order to make sure that the applied light penetrates the skin and reaches the dermis layer where the blood vessels exists. The skin tone can affect the NIRS measurement, because melanin existing in epidermis layer can absorb a portion of the applied light which causes error in measurement. In order to address this issue, TCS34725 RGB color sensor is added to the system in order to measure the skin tone to be used as feature in the linear regression model. The measurement site was chosen to be the forearm. Each LED works separately and sensed using the detector with enough time between the measurement of each LED to make sure that there is no interaction between measurement. After the measurement is done, the average reading of the 3 LEDs is taken and passed as a feature to the linear regression model as well as the RGB color sensor reading.

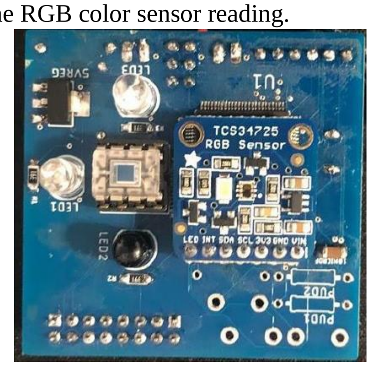

Fig. 4 NIRS system setup

B. CONTROL UNIT

In order to integrate between the components of the system, ATmega2560 microcontroller is used. The communication between ATmega2560 and AD5933 chip was achieved through I2C communication protocol. For NIRS system, OPT101 photodetector is connected to the analog channel of the controller while the RGB color sensor communicates with the controller through I2C communication protocol. After both measurements are finished, the measured magnitude and phase from BIS as well as the photodetector measurement and RGB skin tone from NIRS are substituted in the corresponding linear regression model based on the age and gender of the user in order to calculate the glucose level. After the glucose level is calculated, ATmega2560 sends the results to a mobile application using USART communication protocol through an attached HC-05 Bluetooth module to the system.

C. RESULT DISPLAY AND STORAGE

To display the results after measurement is done, an Android application was designed using MIT app inventor2. As shown in Fig 5, the interface of the application contains an input for selecting the gender and entering the age, an indicator to show whether the Bluetooth connection between the mobile phone and the device is successful or not and finally the result display area. The mobile application saves the results on a cloud database to allow the user to review the measurement history at any time.

Fig. 5 Android application interface

III. GLUCOSE LEVEL CALCULATION AND SYSTEM RESULTS

As mentioned in section II, Linear regression is used to calculate the glucose level. The model has 6 features, the magnitude and phase of the minimum impedance from BIS system, OPT101 sensor measurement and RGB tones of the skin from NIRS system. The model was trained using 161 data samples (116 males and 45 females) aging between 2060 years old with actual glucose levels between 80-140 mg/dL. To train the linear regression model, 3 approaches were followed.

The first approach is to use all the data samples to train one model that can be used to calculate glucose level for all people without regarding the age and gender differences.

The second approach is to divide the data samples into 4 groups according to age. The age groups are 20-29 years old, 30-39 years old, 40-49 years old and 50-59 years old. 4

linear regression models are created corresponding to each age group. The model used to calculate glucose level is selected based on the input age that the user enters through the mobile application.

The third approach is similar to the second approach. However, after dividing the data samples according to age each age group is divided into two groups according to gender. 8 linear regression models are created corresponding to each age and gender group. The model used to calculate glucose level is selected based on the input age and gender that the user enters through the mobile application.

To verify the results and compare between approaches, Clarke Grid Analysis (CGA) was used. CGA is a method proposed in 1987 to verify the clinical accuracy of glucose meters.

TABLE I. COMPARISON BETWEEN THE THREE APPROACHES

Point of comparison	1st approach	2nd approach	3rd approach
Region A	91.9%	93.7%	95.6%
Region B	8.1%	6.3%	4.4%
CC	0.31	0.6	0.74
RMSE	13.7 mg/dL	11.7 mg/dL	9.9 mg/dL

By comparing the results of the three approaches as shown in table 1, the third approach has the highest percentage of results in region A of CGA 95.6% with the highest correlation coefficient 0.91 and least root mean squared error 9.9 mg/dL. The correlation coefficient value

can be improved by collecting more data points which will allow the usage of more advanced algorithms for computation like the neural networks which will yield better results and better correlation coefficient.

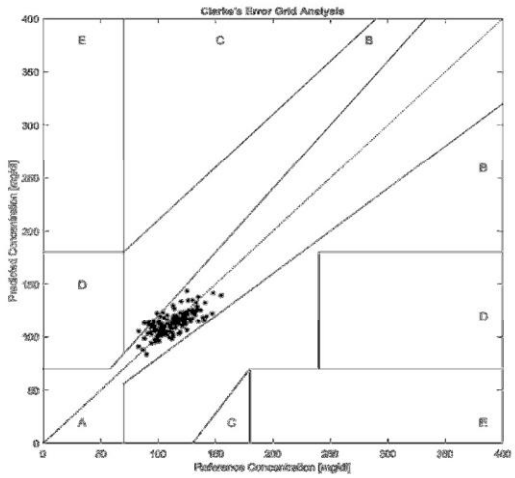

Fig. 6. Actual vs. predicted glucose levels of the proposed system

The first model of the system needed to collect 10 calibration points and can be used only by the user for which the device is calibrated [16]. By applying the new algorithm to calculate glucose level and taking into consideration the age and gender difference, the new proposed model of the system can be generally used by any user without any previous calibration.

Before using the system for measurement the user should follow some steps to avoid error in measurement. Firstly, the user should drink water prior to the measurement from a period of 10-30 minutes and not to consume alcoholic drinks or caffeine to avoid dehydration which leads to increase in the impedance. Secondly, the user should wipe the measurement sites (wrist and forearm) to regulate the skin temperature which causes error in both NIRS and BIS measurement and to remove any dust or sweat that can interact with the light in NIRS measurement. Finally, the user should not use the device while having high heart rate or after doing excessive effort because high heart rate causes error in BIS measurement.

The whole system consumes peak power of 70 mW, weighs less than 30 gm and costs under 18$ which is much cheaper than the non-invasive meters that were in the market (usually costed at least 100$). It has many advantages including low cost, integrated sensors for more accuracy and ease of use.

VI. CONCLUSTION

High performance non-invasive glucose monitoring system is proposed by integrating NIRS and BIS measurement techniques. NIRS system uses 3 LEDs with three different wavelengths placed on the forearm. BIS system achieves two frequency sweeps to measure the lowest impedance point at resonance frequency. The parameters measured by the two systems are passed to the linear regression model as features to estimate the glucose level. 8 linear regression models are trained to calculate glucose level based on the gender and age of the data sample. The system achieves a correlation coefficient of 0.91 and root mean squared error of 9.9 mg/dL. The results are saved to a cloud database using the 3G mobile connection to be integrated with Internet of Things (IoT) applications in healthcare. The system achieved 95.6% of the results in Region A of Clarke grid analysis. The proposed system does not require any pre-calibration and can be generally used by different users.

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