Non-invasive measurement of human physiological parameters

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Certificate of Approval

This is to certify that the project report entitled “Non-invasive measurement of human physiological parameters” is a record of bonafide work carried out by Shashi Shekhar under my supervision and guidance.

The report has partially fulfilled the requirements towards the degree of Bachelor of Technology in Electronics and Communication Engineering at Indian Institute of Information Technology, Guwahati.

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1. Introduction

Diabetic mellitus (DM) is a very common disease that occurs not only among adults but also among children and infants. It consists of metabolic disorders in which there are high blood sugar levels over a prolonged period. Serious long term complications can lead to cardiovascular disease, stroke, chronic kidney disease, damage nerves and blindness. There is a need for more frequent blood glucose monitoring for diabetic patients as the amount of insulin intake has to be decided in accordance with the continuous monitoring. The commonly used methods to measure blood glucose are invasive which is based mainly on capillary blood obtained by finger-prick. This process cause physical discomfort and also involves risk of spreading infectious diseases, which is not suitable for daily, frequent self-monitoring.

Non-invasive glucose monitoring can overcome the disadvantages of the invasive methods. Non-invasive methods mainly include optics-related methods[1-5], polarimetric method [6] and bio-impedance spectroscopy method[7]. Due to complications related to human body tissues and physiological measurements, there has been no single non-invasive method that can achieve sound clinical results; therefore researchers have conducted their studies on different non-invasive methods. Most effective of them is near-infrared spectroscopy method.

1.1. Near-Infrared Spectroscopy (NIRS)

Infrared light is composed of a range of electromagnetic waves with wavelengths longer than the visible light and shorter than microwaves (750nm-1mm). Infrared light is further classified into near infrared (750nm-1400nm) and far infrared (1400nm-1mm).

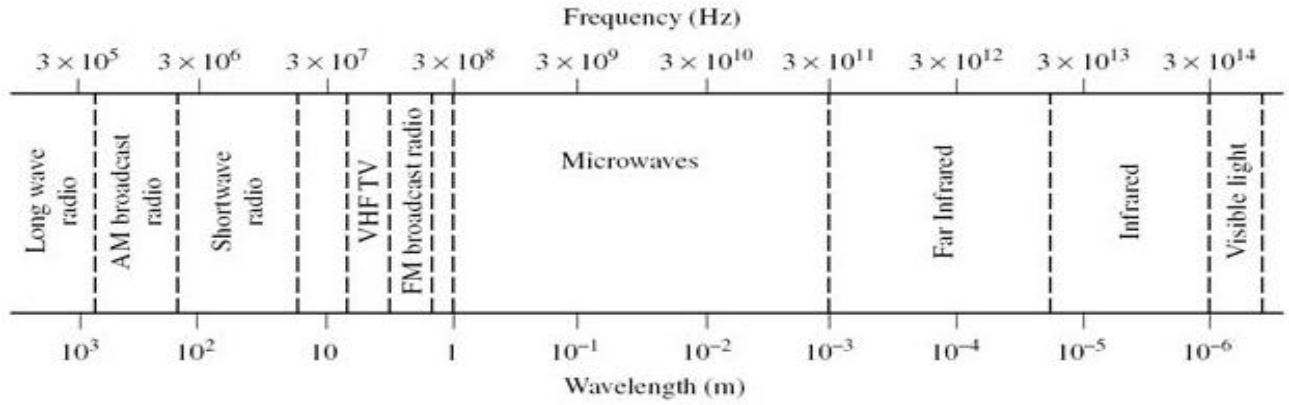

Fig.1.The electromagnetic spectrum [8]

Near-infrared Spectroscopy was introduced by F.F.Jobsis back in 1977 [9]. In early 1980s, more studies were conducted to validate and test the limits of this method. Later in 1990s, time-resolved and frequency-resolved techniques were developed; which were applied in brain-mapping studies and breast cancer diagnosis. From last decade, lot of research work is going on non-invasive measurement of human physiological parameters; of which most explored parameter is blood glucose measurement. NIR spectroscopy is based on Absorbance-Transmittance Photometry.

There exists a number of various non-invasive glucose monitoring techniques:

1. Near-Infrared (NIR) Spectroscopy
2. Mid Infrared (MIR) Spectroscopy
3. Raman Spectroscopy
4. Occlusion Spectroscopy
5. Optical Coherence Tomography
6. Fluorescence technology
7. Optical Polarimetry
8. Photo acoustic Spectroscopy
9. Electromagnetic Sensing
10. Bio-Impedance Spectroscopy

Compared to other spectroscopy techniques, NIR spectroscopy has several advantages:

- The energy of NIR radiation is non-destructive
- NIR spectroscopy is associated with the combinations and overtones of C-H, O-H, and N-H fundamental vibrations[10,11] which means most biomolecules have features in the NIR region
- Fast spectra time-acquisition combined with complex data analysis makes NIR spectroscopy well suited for real time sensing
- Reasonable path length requirements from the Beer-Lambert law makes it possible to analyse a variety of samples with minimal pre-treatment.

However, peak broadening and overlapping spectral signatures make NIR challenging for quantitative analysis in complex biomolecules and mixtures.

1.1.1 Beer-Lambert Law

When a light ray passes through human tissues, it is both absorbed and scattered by the tissues. Concentration of some absorbers do not change with time such as water, melanin and bilirubin but concentrations of some absorbers such as oxygenated haemoglobin (HbO_2) and deoxy haemoglobin (Hb) are related to the tissue metabolism. So the optical window for non-infrared spectroscopy is in the range of 650nm to 1000nm.

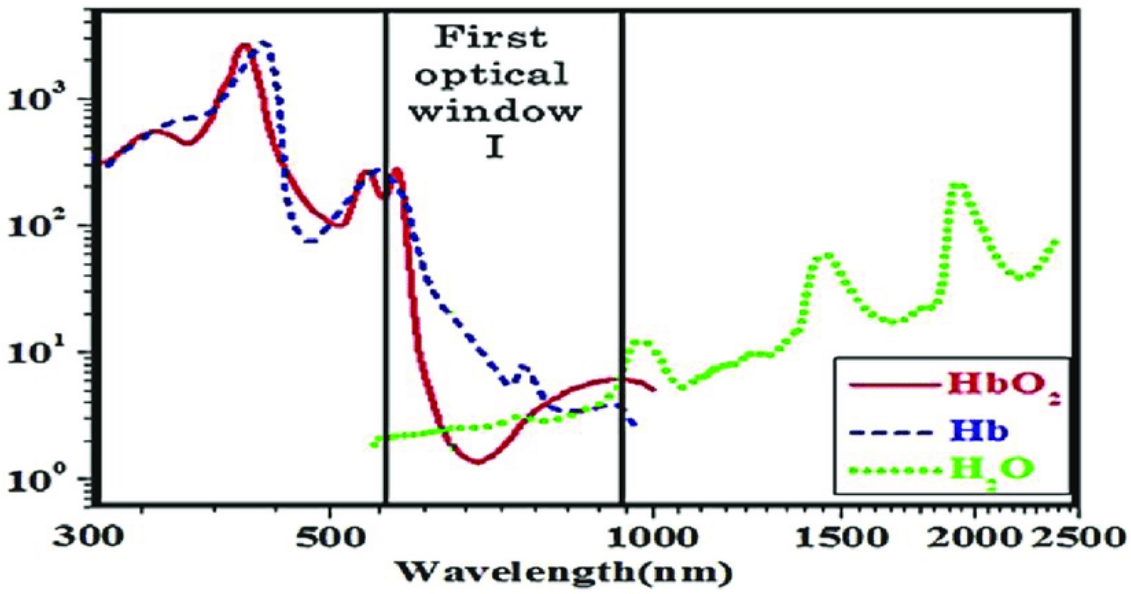

Fig.1.1 Absorption spectra of oxygenated haemoglobin (HbO_2), deoxy haemoglobin (Hb) and water in visible and Near-infrared region [12]

Light scattering occurs in biological tissues due to the mismatch between the refractive index of extracellular fluid and the membranes of the cells. Variation in glucose level in blood affects the intensity of light scattered from the tissue. Beer-Lambert Law plays a major role in absorbance measurement which states that absorbance of light through any solution is in proportion with the concentration of the solution and the length path travelled by the light ray.

$$I = I_o \, e^{-L\mu_{eff}}$$

where
I = Reflected light intensity
I_o = Incident light intensity
L = Optical path length
μ_{eff} = Effective attenuation coefficient

$$\mu_{eff} = [\, 3\, \mu_a\, (\mu_s + \mu_s') \,]^{1/2} \qquad \mu_a = 2.303\varepsilon C \qquad \mu_s' = \mu_s(1-g)$$

where
μ_a =Absorption coefficient
μ_s = Scattering coefficient
μ_s' = Reduced scattering coefficient
ε = Molar extinction coefficient
C = Tissue chromophore concentration
g = Anisotropy
Thus from these equations it can be concluded that μ_a depends on the glucose concentration in blood. Thus the scattering decreases if blood glucose concentration increases.

The Beer-Lambert Law states that for an absorbing compound dissolved in non-absorbing medium, the optical density (OD) is proportional to the concentration of the compound in the solution (C)

and the optical pathlength (d) :

$$OD = \log_{10}[I_o / I] = \varepsilon.C.d$$

The modified Beer-Lambert Law to be applicable for human tissue is given by:

$$OD = \log_{10}[I_o / I] = \varepsilon.C.d.\ DPF + G$$

where G is term added to compensate for scattering losses and DPF is the Differential path length factor. This can also be written as:

$$OD = \log_{10}[I_o / I] = \varepsilon.C.L + G$$

where L= d.DPF = Optical path length

2. Motivation

In light of present lifestyle, where food is available on our fingertips; there is a need for continuous monitoring of our daily intake of glucose. A continuous monitoring of glucose present in blood is important to avoid complications of diabetes and damage to organs. As a global chronic disease, diabetic mellitus (DM) is associated with high morbidity. Even a larger section of people than those of diabetic mellitus are suffering from impaired glucose tolerance (IGT). These people have increased risk of cardiovascular disease (CVD) compared with healthy people. People who are diagnosed with diabetic mellitus (DM), a continuous glucose monitoring can play a role in monitoring the therapeutic effect during the treatment process, so as to regulate the therapeutic strategy in a timely manner. Therefore, it will be of such a great help for IGT and diabetic mellitus patients to self-monitor the glucose concentration in a continuous manner

The techniques present at current for glucose measurement is based on invasive and non-invasive methods. Invasive method consists of blood obtained by finger-prick. This method causes physical discomfort and an increased rate of spreading infectious diseases, whereas non-invasive method consists of near-infrared ray to penetrate the body part and measure the glucose level by the received ray. It is painless, risk-free and a low cost process compared to invasive method.

3. Problem Statement

The main objective of this project is to design a non-invasive method based device to monitor blood glucose measurement which is utilising the near-infrared region. There are some devices that are based on various non-invasive techniques but this project proposed a device based on artificial neural network for regression analysis to predict the blood glucose levels, which is absent from any other such device till date.

4. Work Done

4.1 Photoplethysmogram (PPG)

Photoplethysmography is an optical technique widely used to measure the pulse rate, arterial blood oxygen saturation and blood volume changes. It uses a clip which contains a light source and a detector on the opposite sides to detect the cardio vascular pulse wave that propagates through the body. The PPG waves can be described as containing a DC component due to venous blood and an AC component due to blood volume changes in the arteries [13].

For a specific wavelength i, modified Beer-Lambert law can be written as

$$OD = \varepsilon_i C_i L_i + G_i$$

In our particular case, that wavelength I corresponds to 940nm. As the concentrations and path lengths are same for a person at a particular time,

$$\Delta OD_\lambda = \log\left[1 + \frac{\Delta I_\lambda (t_i)}{I_\lambda (t_{i+1})}\right]$$

where ΔOD_λ is difference between optical densities at time t_i and t_{i+1} , $\Delta I_\lambda(t_i)$ is the pulsatile component at time t_i and I_λ (t_{i+1}) is the intensity of light at time t_{i+1} .

4.2 Hardware Layout

The proposed model for the circuit consists of an infrared LED acting as a light sensor and a photodiode as detector to detect small changes in incident light. The incident light penetrates through the finger-tip.

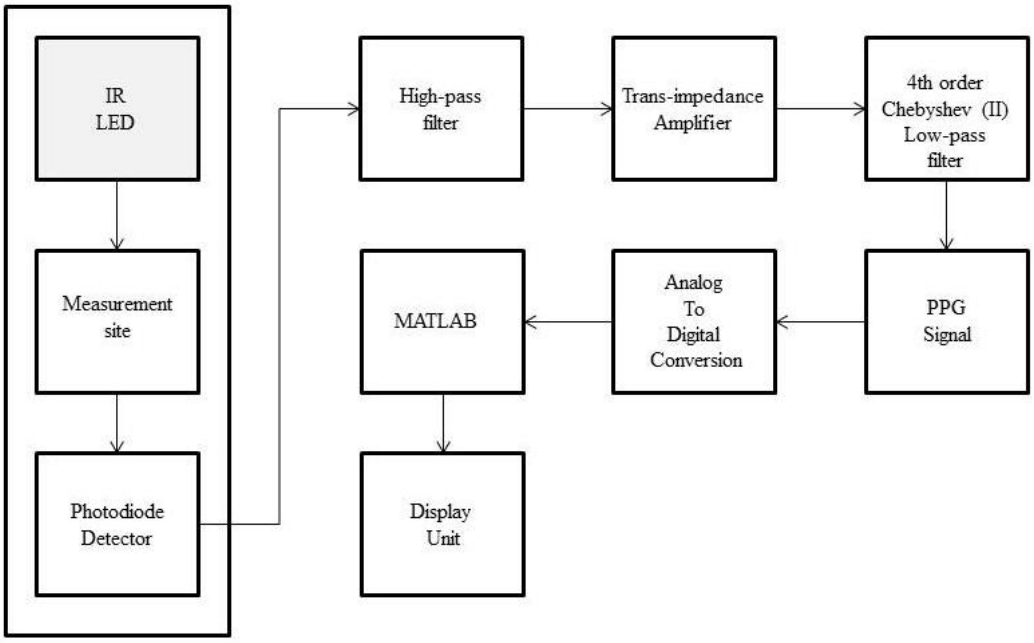

Fig 4.2 Block Diagram of non-invasive glucose measurement system

This light is converted to an equivalent current by the IR detector which is then high pass filtered with cut-off frequency 1.2Hz. Then it is amplified by the trans-impedance amplifier. After the signal amplification is done, it has to go through low pass filter to obtain a PPG signal. A 4^{th} order chebyshev (II) filter, most optimal filter for a PPG wave is used at normalised stopband edge frequency of 200Hz. The AC values obtained from the PPG wave is then send to MATLAB for applying regression analysis to obtain the glucose values. After the analysis obtained from MATLAB, we display the glucose values over a display unit.

4.3 Sensor Biasing Circuit

We are using a reflective optical sensor TCRT1000. The TCRT1000 have a compact construction where the emitting-light source and the detector are arranged in the same direction to sense the presence of an object by using the reflective IR-beam from the object. The operating wavelength is 950 nm. The detector consists of a photo transistor.

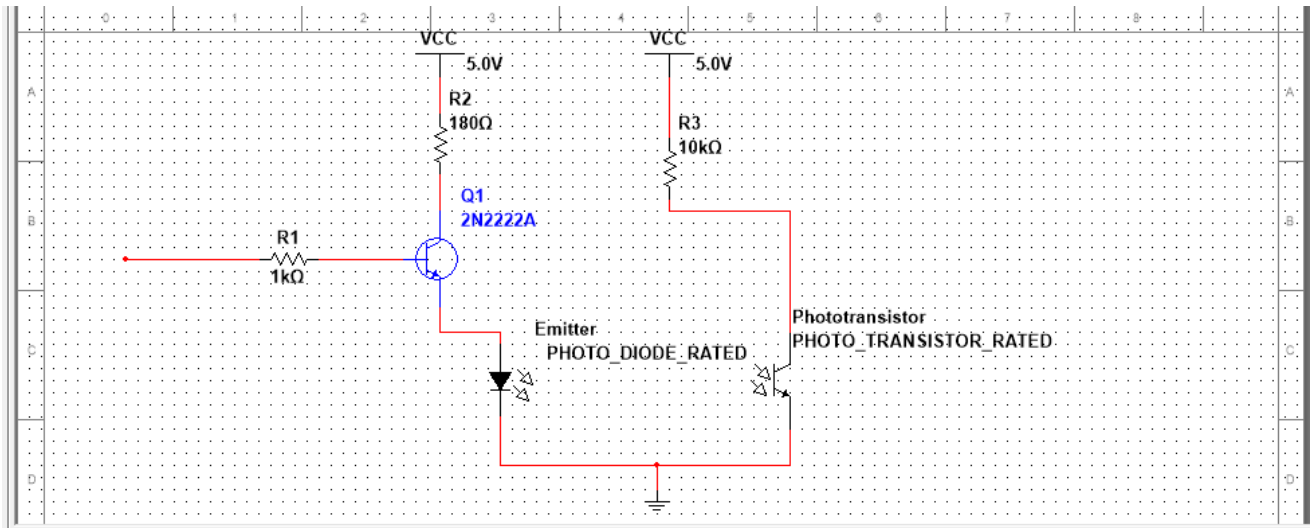

Fig 4.3 Biasing circuit for TCRT1000 sensor

The circuit diagram shown above would be active after pulling the enable pin high. The output from the sensor is a periodic physiological signal attributed to variations in the reflected IR light which is caused by the pulsatile tissue blood volume.

4.4 Signal Conditioning

We designed an alternate approach to our hardware design by using the functionality of TTL signal. There are two stages of signal conditioning for the sensor output. The first stage of the signal conditioning will suppress the large DC component and boost the weak pulsatile AC component, which carry the required information of pulsatile blood volume.

At first, the sensor output is passed through a RC high-pass filter (HPF) to get rid of the DC component. Then this output is passed through active low-pass filter (LPF) with cut-off frequency of 2.34 Hz and a gain factor of 101 using an operational amplifier circuit. Thus the combination of HPF and LPF effectively removes unwanted DC signal and high frequency noise including 50Hz-60Hz mains interference. It also amplifies the low amplitude pulse signal by 101 times.

The output of first signal conditioning stage further uses a similar kind of combination of HPF and LPF to filter and amplify the signal at much better level. The total voltage gain received from these two cascaded stages is 101*101 = 10201. These two stages of cascading converts the distorted PPG wave into a TTL wave whose values go to MATLAB for using the regression model. In case it is required to decrease the gain of 10201, a 5k potentiometer placed between the stages will be used.

Calculation of Cut-off Frequencies:

Passive HPF:

$$Fc = \frac{1}{2\pi * Rf * Cf}$$

$$Fc = \frac{1}{2\pi * 47K * 4.7\mu F}$$

$$Fc = 0.7\ Hz$$

Active LPF:

$$Fc = \frac{1}{2\pi * Rf * Cf}$$

$$Fc = \frac{1}{2\pi * 680K * 100nF}$$

$$Fc = 2.34\ Hz$$

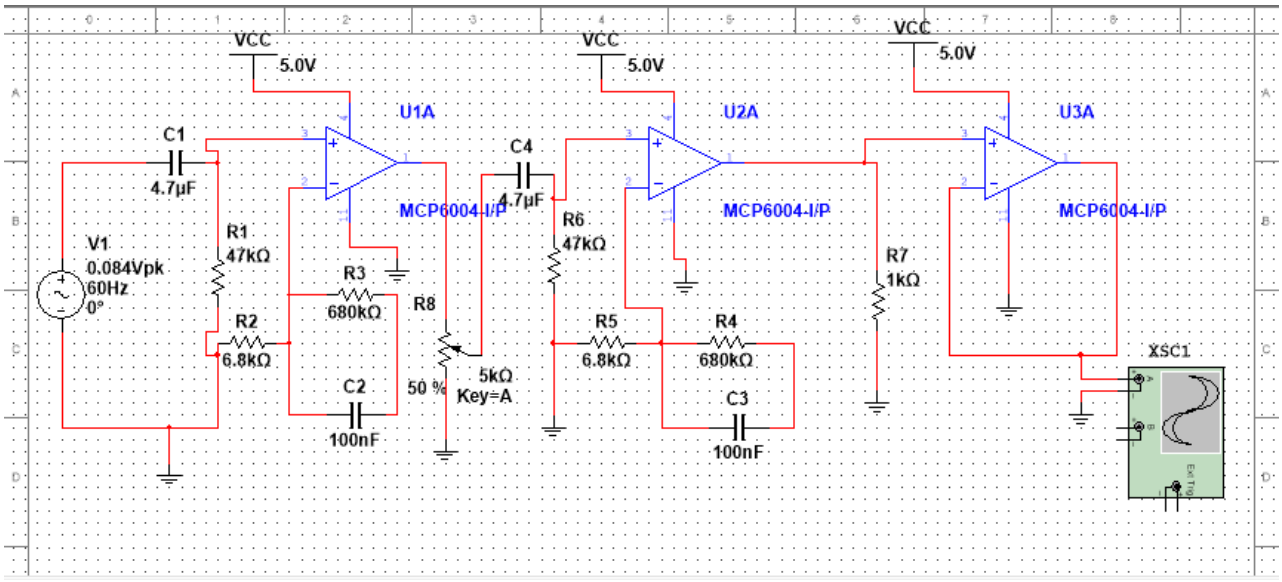

Fig 4.4.1 Simulation Circuit for TCRT1000

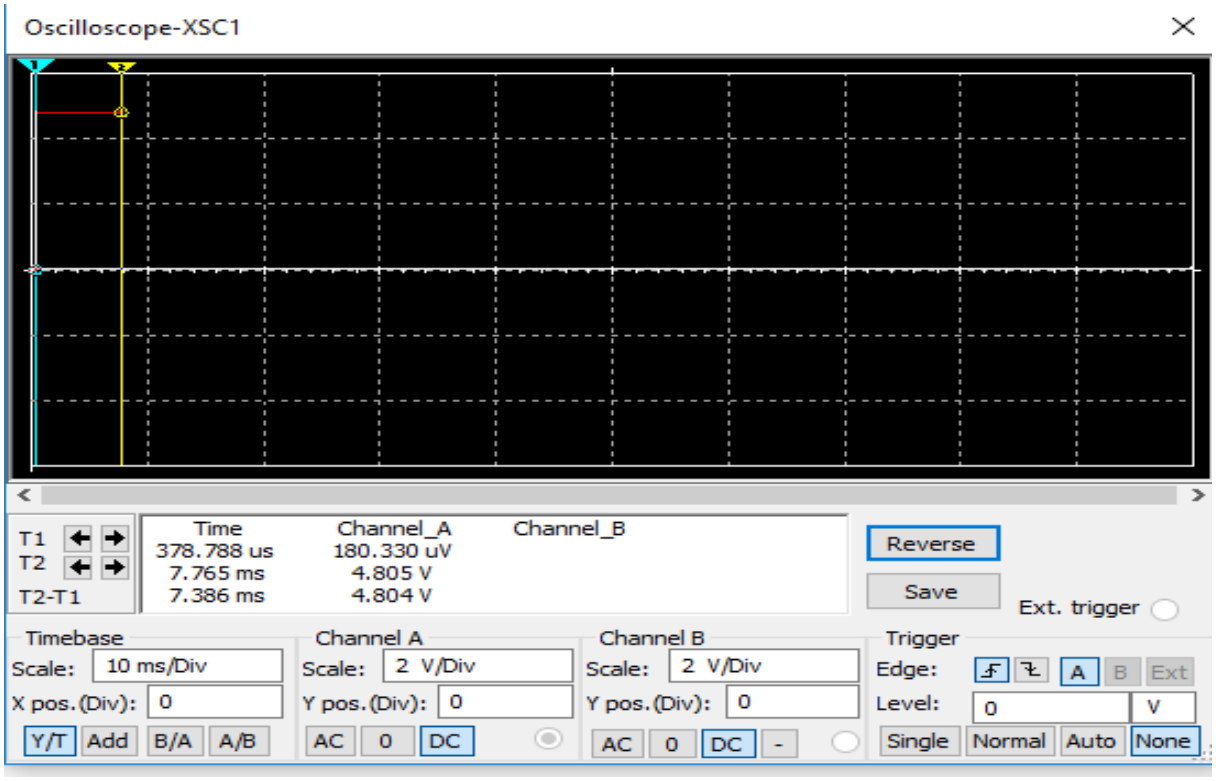

Fig 4.4.2 Simulation output (one period) of TCRT1000 using virtual Oscilloscope-XSC1

4.5 Artificial Neural Network (ANN)

There are many types of calibration models exist for the quantitative spectroscopic analysis. Most commonly used among them are multivariate calibration models due to their ability to overcome the shortcomings of Beer-Lambert law. It does not account the deviations of Beer-Lambert law such as overlapping spectral bands and interactions between components [14].

Partial Least Squares (PLS) and Principal Component Regression (PCR) are the most widely used chemo-metric techniques for quantitative analysis of complex biomolecules. These methods are not optimal when the relationship between the IR absorbance's and the constituent concentration deviates from linearity. A detailed theory and application of artificial neural network (ANN) technique for chemo-metric measurement have been presented in the paper [15].

In this project, ANN is used for function fitting to measure non-invasive glucose data by using PPG waveform. For the neural network, the input consists of two nodes: [ΔOD_i] matrix and A_i where i represents the number of human subjects being considered at a particular wavelength and A being age of i^{th} human subject. The output consists of [C_i] where C being the concentration of glucose in the i^{th} human subject. MATLAB neural network toolbox has been used. A two layer feed forward network with sigmoid hidden neurons and linear output neurons has been considered.

To increase the sensitivity and minimize the error in the results, regression has been used thrice, i.e., triple regression. So we will obtain three sets of coefficients for three different datasets. The first set of regression coefficients are used to estimate glucose levels. But if it falls above 105 mg/dL second set of regression coefficients are being used. Further if it falls above 115 mg/dL finally the third set

of coefficients is being used to determine the result accurately. The performance is evaluated in terms of root mean square error analysis.

5. Results

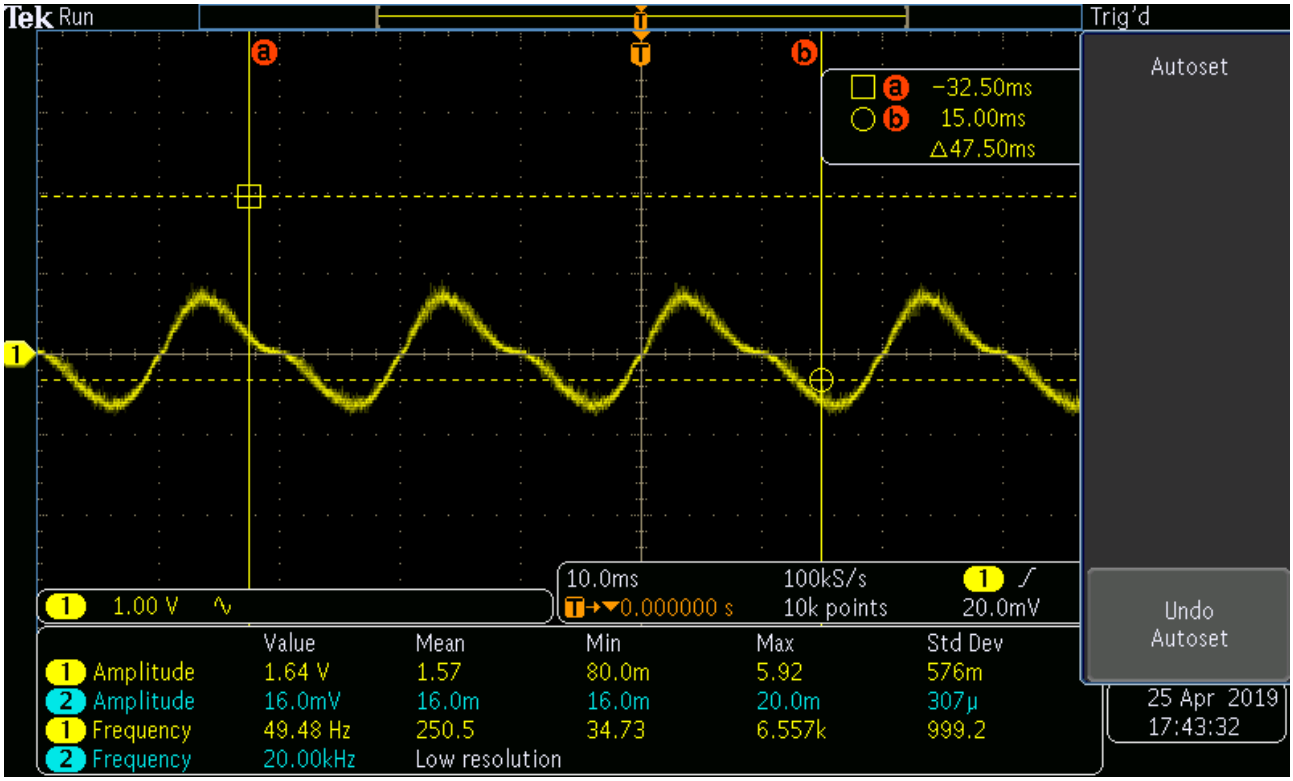

Fig 5.1 Real world output of human subject 1 obtained on MDO3012-Mixed Domain Oscilloscope

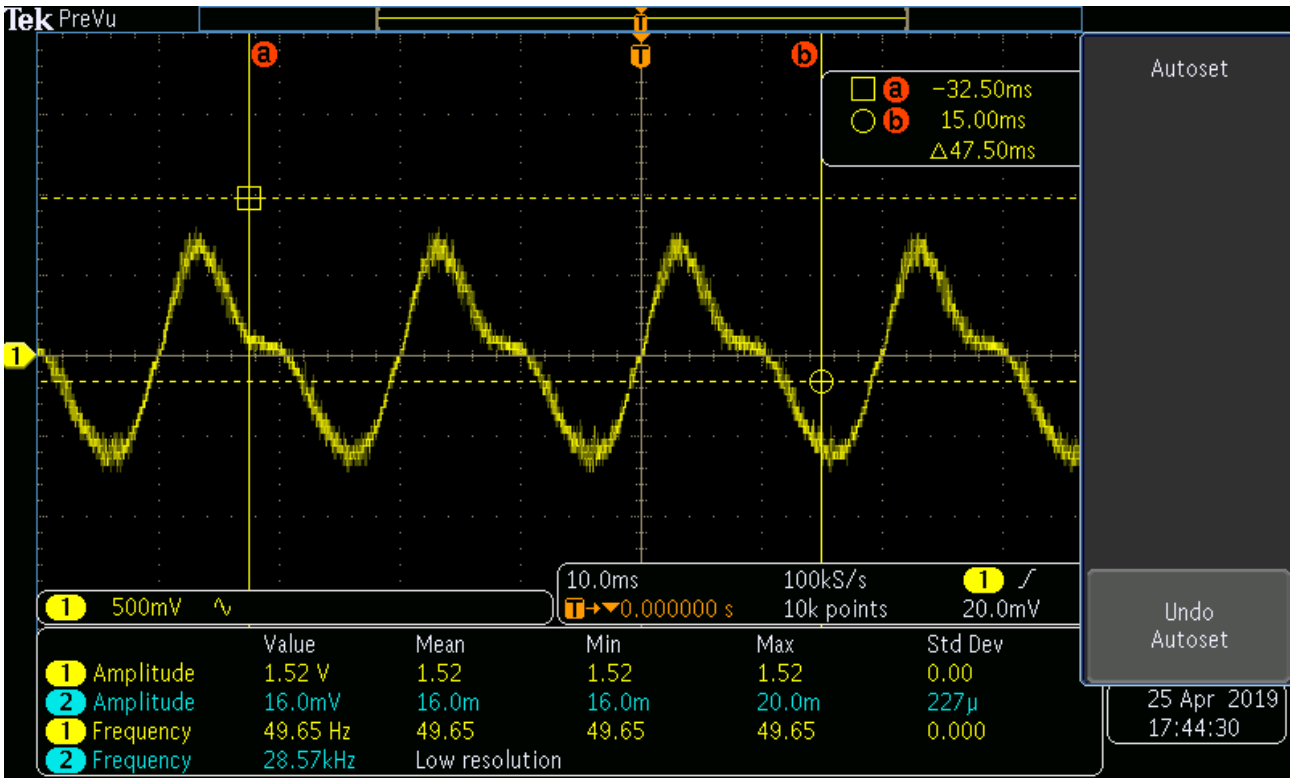

Fig 5.2 Real world output of human subject 2 obtained on MDO3012-Mixed Domain Oscilloscope

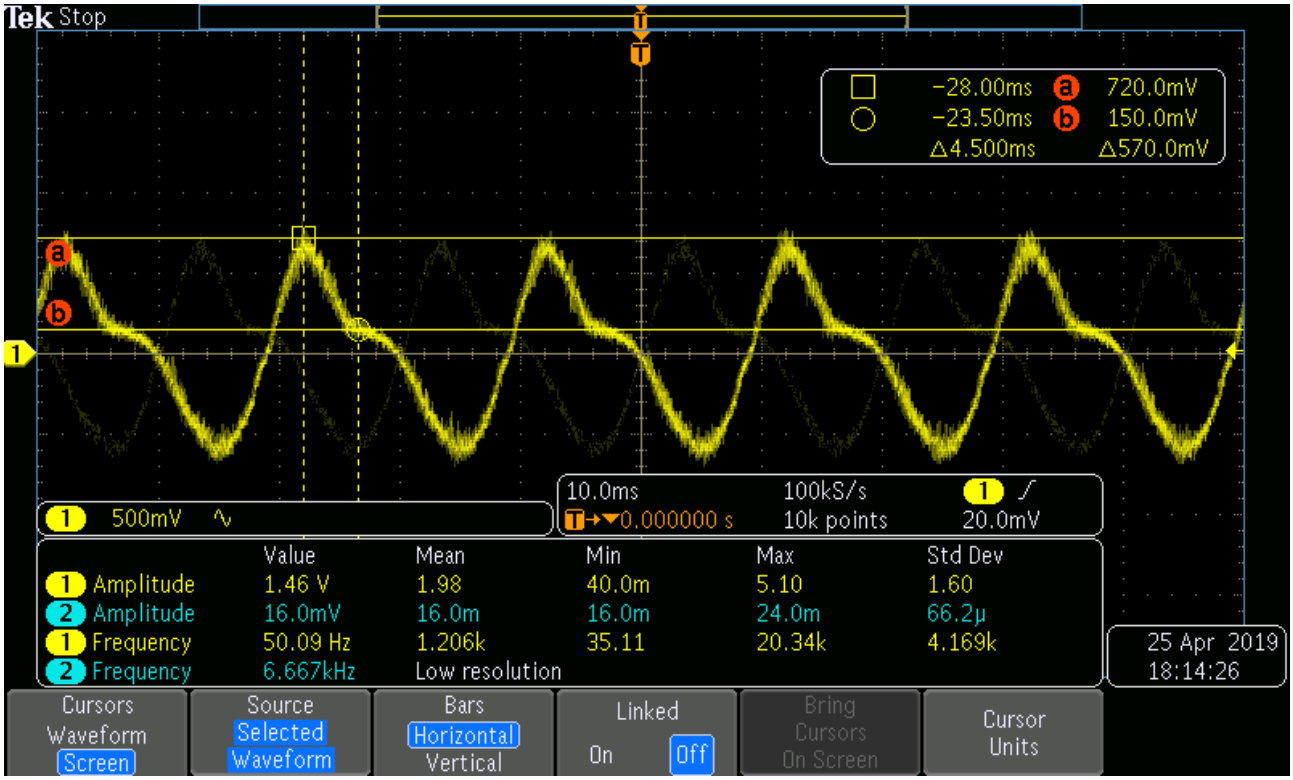

Fig 5.3 Real world output of human subject 3 obtained on MDO3012-Mixed Domain Oscilloscope

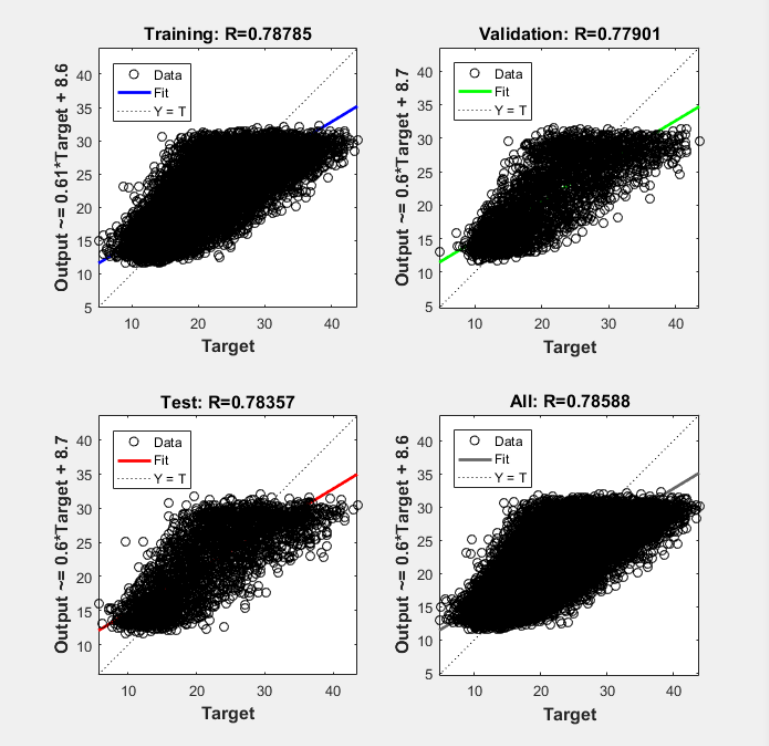

Fig 5.4 Regression Analysis obtained for human subject 1

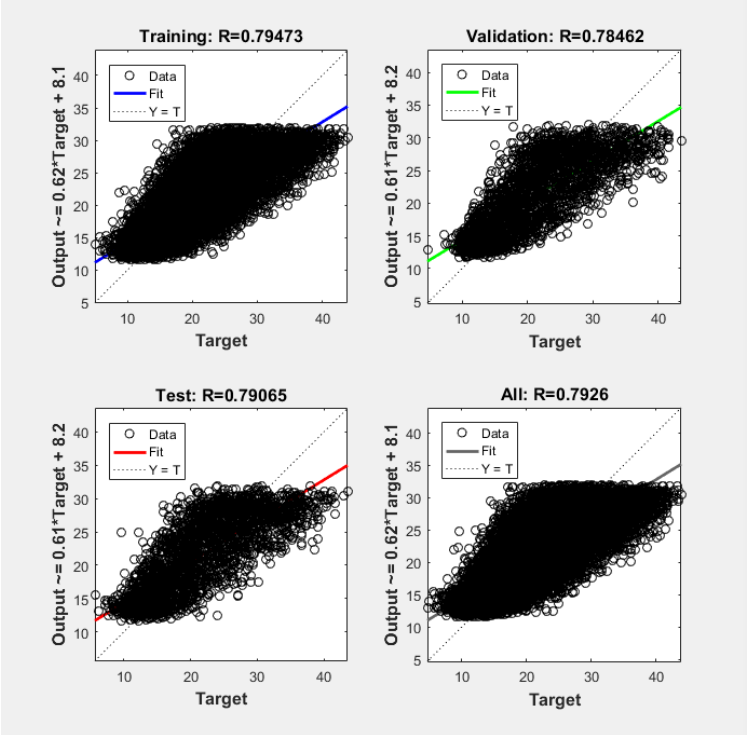

Fig 5.5 Regression Analysis obtained for human subject 2

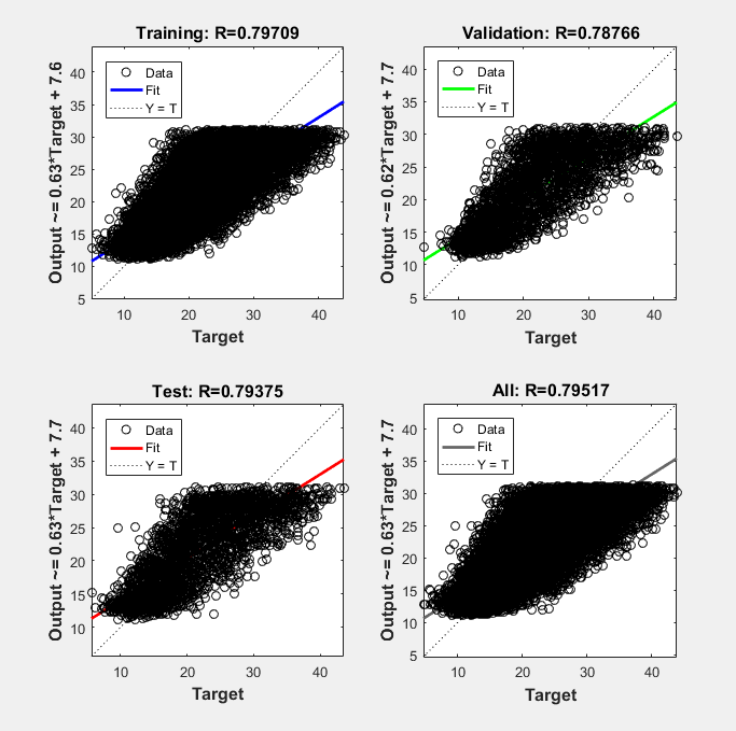

Fig 5.6 Regression Analysis obtained for human subject 3

6. Conclusion and Future Work

The proposed simulation has been verified on a test data samples. The glucose level of human subject 1- 106.7 mg/dL, human subject 2- 121 mg/dL, human subject 3- 120.3 mg/dL are obtained from the analysis. The subjects were tested within 2 hours of taking a meal.
The proposed design is simple, non-invasive, low cost and user friendly device for continuous glucose measurement. There already exists a glucometer based on NIR spectroscopy technique which data deviates from the actual invasive glucometer by a fair margin. So the challenge is to design a low-cost yet an accurate non-invasive glucometer for daily use. This project exploits the limits of artificial neural network to determine glucose levels.

The future work that can be done on this project is through increasing the accuracy in the blood glucose measurement. It can be achieved on two different levels: hardware and software. Hardware based changes can be implemented to use PPG wave more efficiently and use some other physiological parameters for the glucose measurement. This can be achieved by changing the IR source sensor, changes in measurement site (use ear lobe instead of finger-tip), a better signal amplification and noise reduction to obtain PPG wave. Software based changes can be done by using different regression models. Anemia can also be diagnosed by continuous monitoring of haemoglobin in blood. It can be done in a non-invasive method by using the same method with different source wavelength.

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