All-Digital 1550 nm Optical Aqueous Glucose Solution Measurement System

Turgul, V. and Kale, I.

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Volkan Turgul and Izzet Kale
Applied DSP and VLSI Research Group (ADVRG), Department of Engineering
Faculty of Science and Technology, University of Westminster
London, W1W 6UW, United Kingdom
E-mail: volkan.turgul@my.westminster.ac.uk, kalei@westminster.ac.uk

***Abstract*—An all-digital 1550 nm optical measurement system is proposed for measuring the concentration of aqueous solutions of glucose to investigate the feasibility of NIR blood glucose measurements. A microcontroller was used to generate the excitation signal for a 1550 nm laser module as well as generate the reference signal to perform the lock-in amplifier function. A sine wave was generated inside the firmware to drive the laser module through a current DAC. The reference signal was generated by reading the monitor diode inside the laser module through the microcontroller's internal ADC. A cooled photodetector was used to measure the light level where its output was digitized by a 24-bit ADC after analog signal conditioning. The glucose concentration result for the measurement was calculated performing DSP functions using the mentioned signals as set out in this paper. A correlation was successfully observed between measured signal level and glucose concentration.**

Keywords—optical; measurement; glucose;concentration; NIR

I. INTRODUCTION

Diabetes Mellitus is affecting over 415 million people worldwide, a well-known disease associated with high blood glucose levels (BGL) [1]. Lower level of insulin hormone is observed in individuals suffering from diabetes due to its lower secretion by pancreas. Insulin may also be less effective in some patients. Both cases lead to uncontrolled levels of glucose in the blood which can be controlled by external means such as medication or insulin injections [2] but BGL must be known before taking appropriate action. BGL measurements can be taken at home using conventional measurement devices requiring a drop of blood obtained by pricking a fingertip. This is an uncomfortable process as some patients may need up to 10 measurements a day. Therefore, there has been a constant interest in the research of non-invasive BGL measurement methods [3]. A popular method is to measure the concentration of molecules utilizing their optical properties such as absorbance, transmittance and reflectance. Molecules exhibit unique optical characteristics at various wavelengths depending on their molecular composition and bonds. Glucose may be measured using its optical properties. However, as biological molecules are mostly composed of carbon, hydrogen and oxygen (C, H, O) atoms, their optical properties are closely related making it harder to distinguish specific molecules [4]. Molecules' optical characteristics are established through spectroscopy by measuring their optical properties over a wide range of wavelengths. Then, specific wavelengths can be utilized for measuring select molecules. For BGL measurements, the most significant constituent in blood is water. Therefore, the wavelength should be chosen such a way that glucose absorbs more light than water. In this study, the suitability of 1550 nm band is investigated for glucose concentration measurements. Aqueous solutions of glucose with various concentrations were measured using a highly sensitive all-digital measurement system that was designed for this purpose. A correlation was observed between measured light level and glucose concentration as detailed in this paper.

II. OPTICAL MEASUREMENT OF GLUCOSE

The measurement principle lies in the optical absorption of the glucose molecules. When light is shone through a sample in a cuvette as shown in Fig. 1, some part of it is reflected, some part of it is absorbed and the rest is transmitted through. When the measured substance is absorptive, that is, only a negligible part is reflected, the relationship between the incident and the transmitted light is governed by the well-known Beer-Lambert law [5]. Beer's law states that the light is attenuated exponentially with the optical path and concentration of the sample, given that the light is monochromatic and collimated and the solution is homogenous.

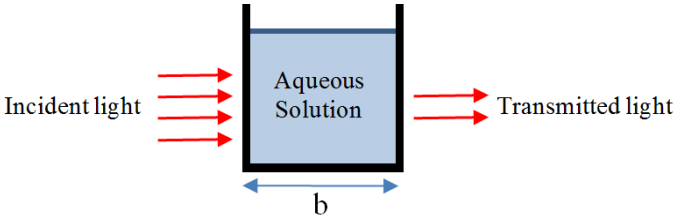

Fig. 1. Light through sample in a cuvette

The relationship between incident and transmitted light is given by:

$$I_{out} = I_{in} e^{-\varepsilon(\lambda)cb} \quad (1)$$

where;

I_{out} and I_{in} are the intensities of the transmitted and incident light, respectively, $\varepsilon(\lambda)$ is the absorptivity at specific wavelength in L/mmol.cm, c is the concentration of the substance in mmol/L and b is the length of the optical path in cm.

The wavelength selection plays an important role for accurate measurement of glucose. Most organic molecules have overlapping absorbance bands due to having similar composition. Hence, the wavelength used to measure the molecule under investigation should be chosen carefully. The factors that need to be considered when selecting the wavelength can be summarised as follows for the blood glucose measurement scenario:

- Penetration depth: The selected wavelength should allow for enough penetration through skin to reach the blood. For example, light cannot penetrate the outer skin below the visible spectrum (UV region) and above the mid-IR region.
- Specificity to the molecule under investigation and other molecules present in the measurement site: The wavelength which the investigated molecule absorbs the most and others absorb the least should be chosen to achieve the best signal to noise ratio (SNR). As 90% of blood is made of water, it is the limiting factor when choosing the operation wavelength. In most bands, water strongly absorbs light that may hinder the detection of glucose.

Considering these points, near-infrared (NIR) region is a good candidate for measuring glucose, since there are some specific absorption bands for glucose in this region [6]. Therefore, a light source in the 1550 nm band was used in this study. Lock-in amplifier principle was realized in digital domain to measure the light transmitted through glucose samples.

III. Phase-Sensitive Detection

Brief background information on phase-sensitive detection and the details of the proposed measurement system are explained in this section.

A. Background Information on Phase-sensitive Detection

Lock-in amplifiers are mostly used to measure low-amplitude signals in noisy environments or when the measured signal's amplitude is below the noise floor of the measurement equipment [7]. For this measurement, the light source is modulated by a reference signal, preferably a sinusoid, and the measured signal is multiplied with the reference. When the phase of both signals is matched, the resulting signal has two components with the sum and difference of the modulating signal's frequency. For the case of matched phase, the component with the difference cancels out resulting in a DC voltage proportional to the amplitude of the measured signal and other component is observed at twice the frequency of the modulating signal. The latter is filtered by passing the signal through a low-pass filter (LPF) and the resulting DC voltage is proportional to the measured light through the glucose sample. The block diagram of the system is shown in Fig. 2.

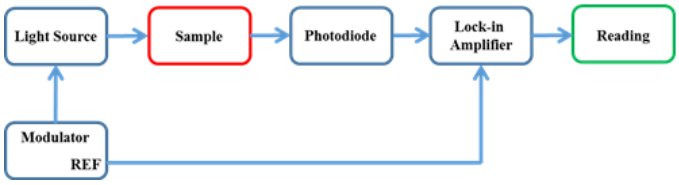

Fig. 2. Block diagram of the phase-sensitive detection system

Ideally, the reference signal frequency should be arbitrary and different from known noise sources such as 50/60 Hz mains frequency to reduce their contribution in the mixing stage and should also be high enough to reduce the effect of flicker $(1/f)$ noise.

Conventionally, light is modulated using mechanical optical choppers. Therefore, modulation performance is limited by the feedback loop controlling the chopper motor and the modulation frequency is limited to the motor's speed as well as the pattern on the chopper disc. Proposed system eliminates the need for mechanical chopper and digitally modulates the light source.

B. Details of the Proposed Measurement System

A 1558.17 nm laser module (Mitsubishi Corp., [8]) with an integrated thermoelectric cooler and monitor diode was used as the light source with 10 mW output power. The laser is driven by a 12-bit current output digital to analog converter (DAC). Laser's output is collimated by a fixed focus collimator (Thorlabs Inc., [9]) and then passed through a cuvette with a 10 mm optical path containing the aqueous solution of glucose. The light is then detected by a low-noise cooled photodetector (Hamamatsu Ltd., [10]) after being focused through a bi-convex lens. The optical setup is shown in Fig. 3.

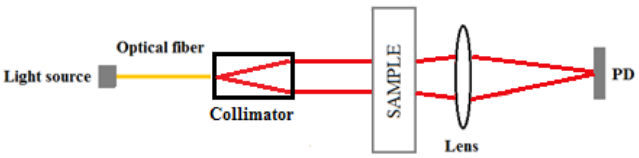

Fig.3. The optical setup (PD=Photodetector)

All digital functions are performed on an STM32F429 microcontroller. A look-up table (LUT) for a sine wave of 100 samples is generated in the firmware. The modulation frequency was arbitrarily selected as 1118 Hz in this experiment. The samples are transferred to the DAC by an interrupt function timed appropriately. The output of the photodetector is amplified by a low-noise instrumentation amplifier with a gain of 1000. The signal is then passed through a LPF to limit its bandwidth. Finally, it is sampled by a 24-bit ADC [11]. The output of the monitor diode inside the laser module is sampled by an ADC input in the microcontroller. This is used as the reference signal for the lock-in function instead of the sine wave generated from the LUT. The reason is that the monitor diode's output mirrors the laser's output, so the phase relationship between the two

signals is as close as possible. Moreover, any jitter in the system does not affect this relationship as both signals are affected the same way by any clocking error. Both ADC conversions for the photodetector and the monitor diode are triggered within the same interrupt routine to minimize phase error between them. The sampled signal is first passed through a band-pass filter (BPF) and then a zero-crossing detector to form the new reference signal as well as a saturation function to limit its amplitude between -1 and 1. This is to create a fixed amplitude reference signal independent of the amplitude of the sampled signal from the monitor diode. It should be noted that the reference signal used in this case is a rectangular signal instead of a sinusoid. Hence, when multiplied with the modulating sine wave, more frequency components are observed other than the fundamental tone. However, these are later filtered through low-pass filters in the firmware.

Photodetector's output is sampled at 90 kHz and 10 averages are taken. Therefore, the effective sampling rate is 9 kHz. A total of 6400 samples are saved into an array for a glucose measurement for further processing. Acquisition time for each measurement is about 710 ms.

The acquired signal is filtered by a 256th order finite impulse response (FIR) band-pass filter whose coefficients were calculated in MATLAB. The passband is $0.2384\pi \leq \omega \leq 0.2583$ rad/sample. At 9 kHz sampling rate the center frequency is 1118 Hz with a bandwidth of 14 Hz. This signal is multiplied with the reference signal generated previously. The result is passed through a 2048th order LPF with a bandwidth of 2 Hz. The reference signal and the filtered signal from the photodetector are shown in Fig. 4 and it can be observed that these signals are phase-locked.

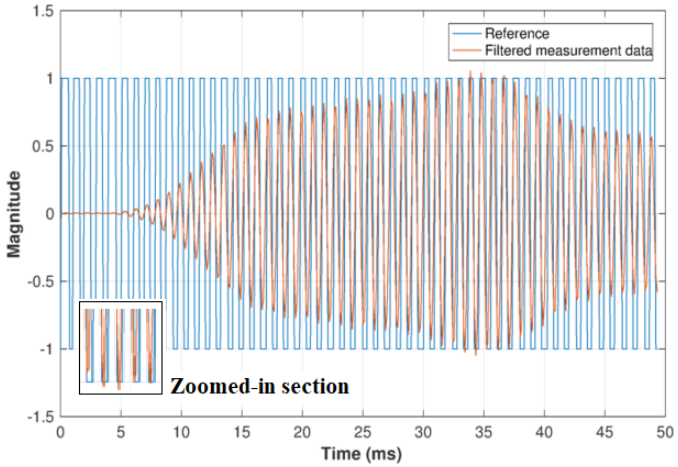

Fig. 4 Phase locked signals

The resulting signal's mean is proportional to the concentration of the glucose sample. To reduce errors, multiple measurements are taken and then averaged. The photograph of the measurement system is shown in Fig. 5. The collimator, cuvette, lens and photodetector are held in place by a 3D printed holder where each component's position can be adjusted for focusing the light onto the photodetector.

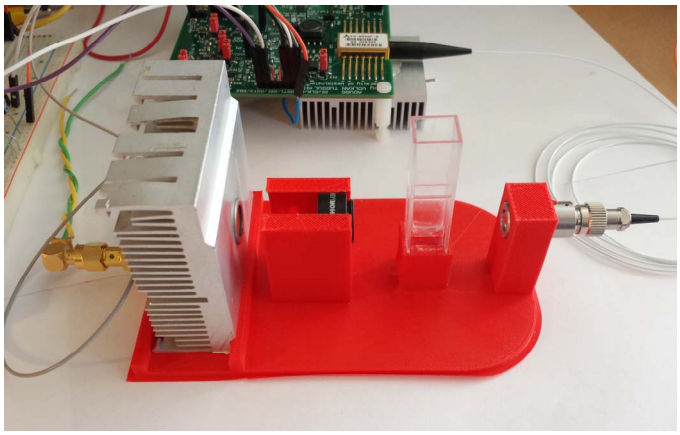

Fig. 5. Photograph of the measurement system

IV. Results

Pure water and aqueous solutions of glucose with concentration values of 100 mg/dl, 250 mg/dl, 500 mg/dl, 750 mg/dl, 1000 mg/dl, 1500 mg/dl and 2000 mg/dl were investigated *in vitro* at 23 °C. A calibration reading was taken with pure water every time before a glucose measurement to check for any instrumentation drift. Each sample was measured 12 times and the results were averaged where the total acquisition time was about 10 seconds for each set of measurements. The amount of light absorbed depends on the length of the optical path according to Beer's law and a linear relationship is expected between the concentration of the sample and the amount of light absorbed. The measurement process was repeated 20 times for each concentration and the mean of the results in arbitrary units as well as the confidence intervals noting the maximum and minimum readings are shown in Fig 6.

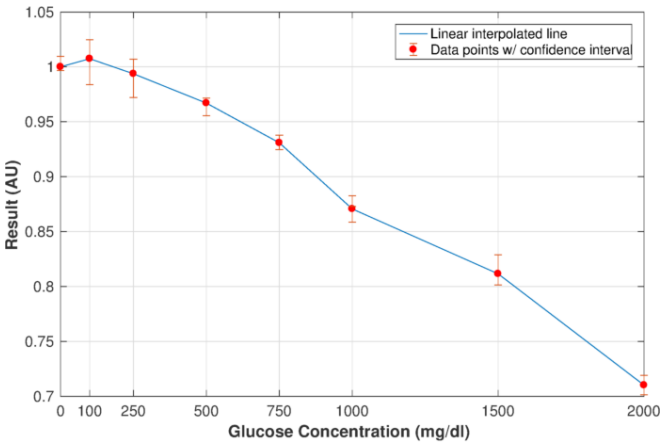

Fig. 6 Measurement results for various concentration values with confidence intervals

It can be seen that the obtained results show almost a linear relationship. However, the confidence interval is quite wide in the low concentration range. This causes prediction errors which should be investigated as the low concentration range is a more realistic representation of actual BGL.

To evaluate the performance of the readings obtained by the optical measurement system, glucose solutions of 50 mg/dl to 400 mg/dl were prepared with 50 mg/dl steps. Each sample was measured *in vitro* 20 times where every measurement is the average of 12 readings as explained previously. Hence, 20 glucose predictions were made by the system for each concentration value and these were plotted on the Clarke's Error Grid chart in Fig. 7 which is a chart commonly used for evaluating the performance of BGL measurement systems. Predicted values are plotted against the real concentration values.

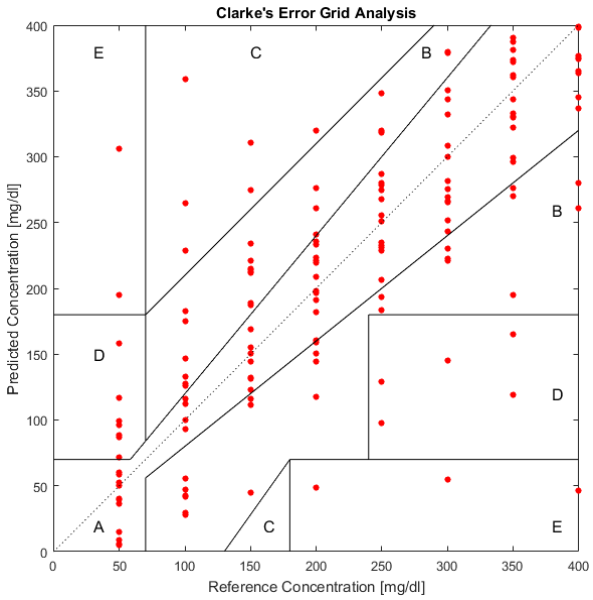

Fig. 7 Predicted data on Clarke's error grid chart

In this chart, results within zone A are acceptable, zone B are outside the acceptable range but error level is not critical. Results in other zones are unacceptable due to high error level. In the case of this experiment the results are categorized as: Zone A: 56.25 %, Zone B: 29.38 %, Zone C: 3.75 %, Zone D: 7.50 % and Zone E: 3.12 %. Most results are in the acceptable range with some room for future improvement. The statistical analysis of the measured results is given in Table I.

TABLE I. STATISTICAL ANALYSIS OF THE MEASURED RESULTS

Concentration	Mean	Standard Deviation	% Error from Mean
50 mg/dl	79.51	72.75	+59.54
100 mg/dl	126.77	84.76	+26.77
150 mg/dl	177.41	62.05	+18.27
200 mg/dl	189.50	59.88	-5.25
250 mg/dl	239.94	63.45	-4.21
300 mg/dl	269.88	76.63	-10.17
350 mg/dl	315.99	78.34	-9.71
400 mg/dl	363.98	89.16	-9.03

V. CONCLUSION

An all-digital 1550 nm optical glucose measurement system was proposed, detailing the optical and hardware setup. Conventionally and most commonly, frequency modulation of the light source is achieved by using a mechanical chopper. These are large in size, limited in maximum frequency that can be used and limited in stability due to mechanical limitations. On the contrary, the designed system digitally modulates the light sources and generates a phase-locked reference signal to be used in phase sensitive detection. The DSP algorithm was realized on a microcontroller. It was demonstrated that the system can measure aqueous solutions of glucose up to a certain accuracy. However, the system was not tested with blood glucose on human subjects. The system proves the concept of using a digitally modulated 1550 nm light source and DSP algorithms such as averaging, filtering and correlation to measure glucose concentration. However, the research needs to be extended to investigate the effects of human tissues for real life application as tissues will introduce measurement errors due to different light absorption and scattering properties. Unfortunately, the authors were unable to find reliable publications to compare the acquired results with. To the author's best knowledge there appears to be a lack of measurement data for glucose in the NIR region. Hence, this study provides a measurement system as well as results for the open literature.

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