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GLUCOSE SIGNAL ESTIMATION USING HIGH PERFORMANCE ADC AND LIGHT PROBES

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Abstract:
A need is felt in recent times to depart from invasive methods of glucose estimation and to adopt non-invasive approaches which are basically harmless in nature. These techniques are more attractive as they surpass the primary fear of the patient i.e. pricking of the body for blood extraction, etc. One of the methods of Glucose estimation is by using a light probe which utilizes the NIR region of electromagnetic radiation. Glucose presents unique absorbance spectra in the NIR region. The authors propose to design an electronic system using LED sources and photodiode detectors as sensors. After the light has passed through the sample, the signal falling on the detector will be used to calculate the absorbance. A trans impedance amplifier will amplify the weak current signal and pass it to a ADC. The system will be equipped with a high precision 32-bit ADC viz.ADS1262.This sigma delta ADC works at 38kSPS and has 10 input channels. These input channels can be used in either in differential mode or single-ended mode. This ADC is interfaced using SPI interface and includes additional features such as 50/60 Hz Rejection, GPIO, Oscillator, Programmable gain control and Temperature Sensor. The digitized signal will be processed using multivariate techniques such as PLSR and the model for prediction will be built using the calibration data. Once the model is ready the glucose concentration can be predicted from unknown sample using the prediction model. The accuracy of the glucose estimation depends heavily upon the resolution of the ADC. Therefore the choice of an ADC is of outmost importance in the design and development of instrumentation for glucose estimation.
Keywords: NIR spectroscopy, Glucose Estimation, ADS1262, Light Probe, PLSR,PGA ADC.

Introduction

The prevalence of diabetes is increasing on the global scale and Asian countries contribute to more than 60 percent of the world diabetes population [1].Diabetes is a disease which is characterized by high levels of glucose in blood. Pancreas plays the role of monitoring the blood glucose level in human blood. Glucose levels in the blood can be stabilized by release of glucagon or insulin for increase or decrease of the glucose levels respectively within the physiological range [2]. Dysfunctional pancreas and reduced insulin sensitivity are the main characteristic of Diabetes mellitus[2]. These metabolic disturbances are generally caused by reduced insulin sensitivity of the glucose consuming cells or deteriorated glucose sensing of the pancreas [2]. Long term diabetes is dangerous as it can cause blindness, damage nerves and kidneys. It also increases the risk of heart stroke and other heart diseases [3].

Glucose level in the blood changes and if this change is not monitored may cause health problems to the patient. Physiological glucose levels are 70 mg/dL to 110 mg/dL or 3.9 to 6.0 mM/L[4]. Glucose levels in a person rise after consumption of food and may reach 140mg/dl.

Enzymatic or biochemical reagent methods are the traditional methods used to determine the blood glucose concentration. These above methods are very accurate methods but are less attractive because of pain associated in these methods, wastage of reagent, long measuring period and possible infection. If only we could manage to develop noninvasive methods which has characteristic such as sample-free operation, pain-free and good accuracy, a diabetic patient will readily embrace it. Many noninvasive methods using optical radiation are suitable choices to avoid the above drawbacks of invasive methods. Different optical approaches are investigated to get desired goal namely polarimetry[5], Raman spectroscopy[6], near infrared (NIR) absorption and scattering[7], and photo acoustics [8].

As NIR radiation exhibits relative deep penetration in biological tissue NIR spectroscopy is a very suitable choice for estimation of glucose levels in blood. This spectral region is known as a “tissue optical window” or “therapeutic window”[9].The continuous spectral data generated by NIR Spectroscopy is used in conjunction with multivariate techniques to predict the concentration of glucose. A calibration model build using PLSR on the continuous spectra of normally present 5 blood constituent was build, which was then used to predict the glucose concentration [10]. In another study Lorentz oscillator was used to model the NIR spectra of blood constituents and chemometrics studies using PLSR algorithm was undertaken [11].

To make the above system portable we can take advantage of the advancement in the optoelectronics devices. The proposed system will employ LEDs of fixed wavelengths and the wavelengths will be choosen to maximize the

signatures of the component which we are targeting that is glucose.

Methods and materials

According to Beer-lambert's law the absorbance of light by a liquid is related to
the concentration of the material by

$$A = \epsilon.c.L \qquad (1)$$

Where ∈ the molar absorptivity of solute at a particular wavelength, c is the
Concentration of the solute and L is the optical path length[2]. Hence for a specific wavelength i, equation (1) may be written as

$A_i = \epsilon_i.c_i.L_i$ (2)

The below graph shows the glucose absorbance in the wavelength range of 2.0µm-2.5µm [10].

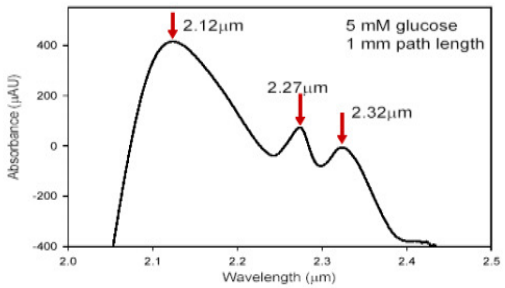

Figure 1. Absorbance spectra of glucose

We can isolate three peaks at 2.12 µm, 2.27 µm and 2.32 µm. We are going to use LEDs at these fixed wavelengths to detect the glucose absorbance signal.

The System consist of the blocks enlisted below

- LIGHT PROBE
- DETECTOR
- AMPLIFIER
- ADC
- MICROCONTROLLER
- DISPLAY

The above block diagram describes the components of the system in the NIR region. Each block is explained in detail below

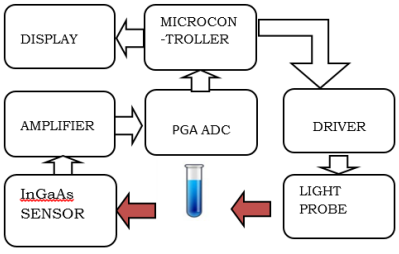

Figure 2. The Block Diagram.

NIR LEDs having a peak emission at the above specified wavelengths are used. These LEDs operate in quasi-continuous wave, pulsed mode operation and continuous wave mode. The usage in the quasi-continuous wave give added immunity to noise as each of three LEDs will be operating at different frequencies. The signal for the specific wavelength can be separated out after digitization using digital filters. The LEDs are driven at three different frequencies by the driver block which is in turn controlled by the microcontroller. The frequency and duty cycle of the LEDs can be controlled using microcontroller.

The sample will be probed using the NIR light from these LEDs. The signal reaching the detector is dependent on the glucose concentration in the sample. Standard 'Si' detectors have a spectral range between 0.35µm to 1.1 µm, and a UV enhanced type extends the range down to 0.2 µm in the ultraviolet. The Photomultiplier detectors are the most sensitive detectors for UV & Visible radiation. InGaAs detectors are sensitive in 0.9µm to 3 µm range.

The photo current generated by the light falling on the detector is given to the Trans impedance amplifier of the amplifier block. The trans-impedance amplifier (TIA) is used to convert the photo current to voltage. A suitable gain is given to the TIA. The op-amp is configured in the TIA mode and for our purpose we will be using a FET input op-amps. The LEDs which are proposed to be used have a considerable linewidth and therefore resolution the measurement decreases. Also if the LEDs are quasi continuous wave operated then there is a slight change in the band gap which leads to spread in the emission wavelength of the LEDs thus increasing the linewidth further. Therefore narrowband filters tuned to the specific frequencies of each LEDs are used to increase the resolution thereby improving the prediction percentage of the components.

The TIA amplified output is given to the Analog to digital converter (ADC) which then digitizes the data. For our application we require a low noise ADC so we have selected ADS1262. It has 11 analog input channels. Being 32-bit the ADC gives high precision and can operate at 38.5 kSPS speed [12]. This sigma delta ADC can give 130-dB of rejection of 50Hz and has a 2.5V internal reference voltage with a temperature drift of 2ppm/°C. The ADC comprised with a low noise, CMOS PGA (gain of 1 to 32), ΔΣ modulator, followed by a programmable digital filter. We can use the 8 GPIOs present on the ADC for other purposes. The interfacing is done to the microcontroller using SPI interface.

To estimate the glucose concentration from the glucose absorbance signal the signal has to be processed using multivariate techniques. The PLSR multivariate technique extracts a given number of factors from the predictor data that takes into account the

variance existing in both predictors and responses. Two datasets one for calibration and one for prediction are prepared. A multivariate technique is used to develop a calibration model for the above calibration dataset. PLSR technique builds a linear relationship between the set of predictors and set of responses. This is called the calibration model. The concentration of the unknown samples is predicted by using the above model. PLSR work in a way to extract the latent factors 'T' and 'U' to account for most of the variation in the response variables which are used for modeling of the responses . T called as X scores are used to predict the Y scores U and these Y scores are used to construct prediction for the responses [13].

$Y = XB + E$

Here Y is n x m response matrix, m is the number of variables and n is the number of observations. X is n x p predictor matrix with p as the number of predictor variables. E is a noise term or residual matrix which has the same dimensions as Y and B is a p x m regression coefficient matrix. A p x c weight matrix W for X is produced in PLSR such that

$T = XW$

Where the columns of W are weight vectors for the X columns, thus producing n x c factor score matrix T. The weights are computed in such a way that maximum covariance exists between the responses and the corresponding factor scores. The loadings for Y denoted as Q are then generated using least squares methods for regression of Y on T such that

$Y = TQ + E.$

Once Q is computed the prediction model is complete and $Y = XB + E$ where $B = WQ$. For the complete description of PLSR procedure an additional matrix p x c factor loading matrix is required which gives factor model where F represents the residual or the unexplained part of the X score [14, 15].After processing using PLSR algorithm the predicted glucose value is displayed on the display device which is interfaced to the microcontroller. Most commonly used Display is a 16 x 2 LCD alphanumeric display.

Results and Conclusion

The laboratory samples will be prepared to perform the experiments. Double distilled water is used to prepare glucose-solution samples with glucose concentrations spanning from half to normal concentration and also double and triple concentration, (i.e. 45 mg/dL, 90 mg/dL, 180 mg/dL and 270 mg/dL). Each sample consists of 20 ml of water, and glucose is added to water to reach the indicated concentrations. The absorbance data of the above samples will be processed using PLSR algorithm. The working of ADC was tested with a low signal input of 20uV.The data generated is free from noise. The programmability was tested for the different gains. A hamamatsu S5971 was used as a sensor for verifying the signal receiving sensitivity and visible light probes were used which are compatible with silicon detector.The whole instrumentation worked in accordance with the design parameters .The further studies using InGaAs sensor for NIR light probe is now be carried out.

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