

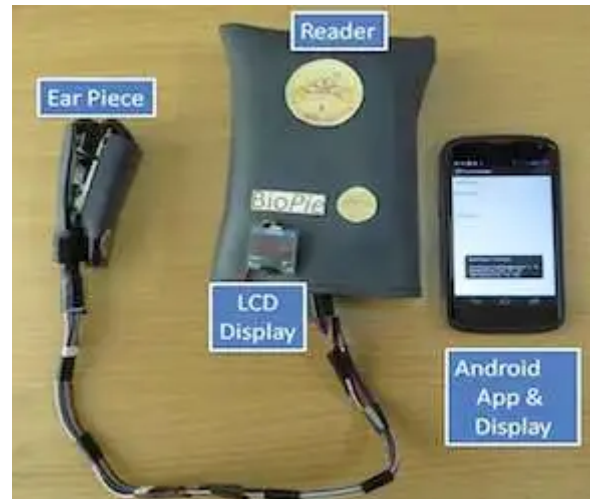
Non-invasive blood glucose monitoring using near-infrared spectroscopy

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Blood glucose monitors are used to measure the amount of glucose in blood, especially of patients with symptoms or a history of abnormally high or low blood glucose levels. Most commonly, they enable diabetic patients to administer appropriate insulin doses. The availability of home-use glucometers, as opposed to clinical-use equipment, has greatly improved the quality of life of such individuals. However, such monitors require a blood draw through finger pricks for each test, which causes pain and inconvenience. Each test also requires a new test-strip, contributing to the recurring cost of such a device.



Optimum insulin dosage, however, requires frequent/continuous monitoring of blood glucose, and currently available glucometers do not address this requirement. Continuous monitors do exist, but they need to be implanted under the skin, causing trauma while being implanted, and they need to be replaced every week. An alternative exists in non-invasive blood glucose monitors. This article introduces an architecture that uses Near Infrared (NIR) spectroscopy to determine blood glucose levels based on transmittance spectroscopy on the ear lobe. Using various body parameters, such as tissue thickness, blood oxygen saturation, and a linear regression-analysis based calibration system, an accurate and real-time architecture is proposed. An example implementation using full analog, digital, and mixed signal capabilities of a programmable system-on-chip, the PSoC-5LP controller from Cypress, is given as well.

Hyperglycemia and Hypoglycemia

Hyperglycemia and Hypoglycemia refer to medical conditions that exhibit abnormally high or low blood glucose/sugar levels. Diabetes is a condition in which the pancreas of the body ceases to produce insulin, which controls blood glucose levels. The causes of diabetes in humans are not yet fully understood, but the widely accepted hypothesis is that it may be genetic and may be caused by a high sugar intake as part of a daily meal serving [1]. Once diabetes is diagnosed, the blood sugar level needs to be continuously monitored in order to facilitate medicinal insulin intake. Patients with hyperglycemia, in which continuously high blood glucose levels are exhibited, may require continuous blood glucose monitoring [1]. This will require a continuous supply of blood from the patient as

current measurement devices invasively monitor sugar levels, which sometimes leads to other complications such as hemorrhaging, blood loss, and other irritable conditions. Non-invasive techniques resolve blood requirement issues. This article explores and implements a non-invasive approach to blood glucose monitoring.

Near-Infrared Spectroscopy is chosen due to its sensitivity, selectivity, low cost, and portability [1]. A wavelength of 1550nm is chosen due to its high signal-to-noise ratio (SNR) for glucose signals.

Operating Principle/System Design

Near Infrared transmittance spectroscopy is used across the ear lobe to measure glucose. Transmittance spectroscopy involves a light source and a light detector positioned on either side of the ear lobe. The amount of near infrared light passing through the ear lobe depends on the amount of blood glucose in that region. The ear lobe was chosen due to the absence of bone tissues and also because of its relatively small thickness [1]. Near Infrared (NIR) light is applied onto one side of the ear lobe, while a receiver on the other side receives the attenuated light. This attenuated signal is then sampled and processed. Two LEDs from Thor Labs (LED 1550E) were used as the light source. Since conventional silicon photodiodes have limited spectral bandwidth, they cannot be used for receiving near infrared light; therefore other types of photodiodes must be considered. An Indium Gallium Arsenide (InGaAs) photodiode from Marktech with a high response around a wavelength of 1550nm was used. An RC low pass filter was also connected to the output of the photodiode to reduce high frequency noise. The light transmitters and receptors around a wavelength of 1550nm are relatively low cost as compared to other wavelengths with equal or higher response to glucose.

Apart from the level of glucose in blood, the transmittance of NIR light also depends on the amount of blood in the path of the light. That is, for the same glucose level, a large amount of blood will result in lower transmittance, whereas less blood will result in a larger transmittance. The glucose value needs to be scaled according to the amount of blood residing inside the ear lobe at a time of measurement. The amount of blood can be estimated by measuring the blood oxygen levels [1]. Pulse Oximetry was used to measure blood oxygen. Pulse Oximetry uses Red and Infrared (IR) light to distinguish between Hemoglobin and Oxy-Hemoglobin in the blood, on which further processing is applied to get the oxygen saturation [2].

Another physical parameter that affects the glucose measurement is the ear lobe tissue thickness. This is an issue when the same device is used by more than one person, in which case the ear lobe thickness could be different for each. Tissue thickness determines the 'path length' of NIR, so a greater path length would result in lower transmittance. Tissue thickness was measured using green light, which has high skin based attenuation.

The same InGaAs photodiode used to sense the NIR signals was also used to sense the other wavelengths (green, red, and IR), as its spectral response also contains these wavelengths.

The block diagram illustrates the system architecture centered around the PSoC 5LP. The main processing unit, PSoC 5LP, contains a Finite State Machine 32-bit ARM. This unit is connected to several peripheral components:

- Output Path:** The Finite State Machine 32-bit ARM sends signals to PWMs, which then drive Drivers connected to Light Sources. It also controls an LCD Controller, which is connected to a Measured Glucose Display.
- Input Path:** Light Sensors are connected to an RC Filter, which then feeds into an Amplifier + ADC. The output of the Amplifier + ADC is sent to the Finite State Machine 32-bit ARM.
- Communication:** The Finite State Machine 32-bit ARM is connected to a UART, which interfaces with a Bluetooth Serial Module.
- Power Supply:** A Cell Phone Battery provides power to a Rectifier, which then supplies the PSoC 5LP.

Additional components shown include an Ear Lobe sensor and a dashed box indicating the internal components of the PSoC 5LP.

Sensing and Pre-Processing

Figure 2 PSoC Peripherals and Schematics

The transmitted power of LEDs can be controlled with the use of pulse width modulation (PWM). As five LEDs were being used (2 NIR, 1 IR, 1 red, and 1 green), five 8-bit PWM modules were implemented. In the case of the NIR LEDs, the transmitted wavelength also changes based on the average DC voltage across it. The NIR LEDs were run at 3 different duty cycles to vary the optical wavelength around 1550nm. This was used to reduce noise between raw glucose values.

Heart beat- and heart rate-based blood variations in the ear-lobe can become a major noise source if not accounted for correctly. To remove heart rate variations, the red, IR, and NIR LEDs were turned on, and their attenuated signals were sampled within 100ms. 20 samples were collected for each LED output; thus, a total of 120 samples were captured (60 for the three NIR wavelengths, and 20 each for IR, red, and green). Ambient light sources also generate a lot of noise that is captured by the optical sensors. To nullify this noise, several samples are stored before the LEDs are turned on. These ambience measurements are later subtracted from the actual signals. All samples were stored in 32-bit integer variables to account for multiplications and addition overflows.

[To learn more about implementing vital signs monitoring technologies into products that support wearables, register for [this free webcast](#) “Technologies for Wearable and VSM” sponsored by Analog Devices]

Signal processing

Once all the variables have been stored, the processing begins. The algorithm flow is given in **Figure 3**.

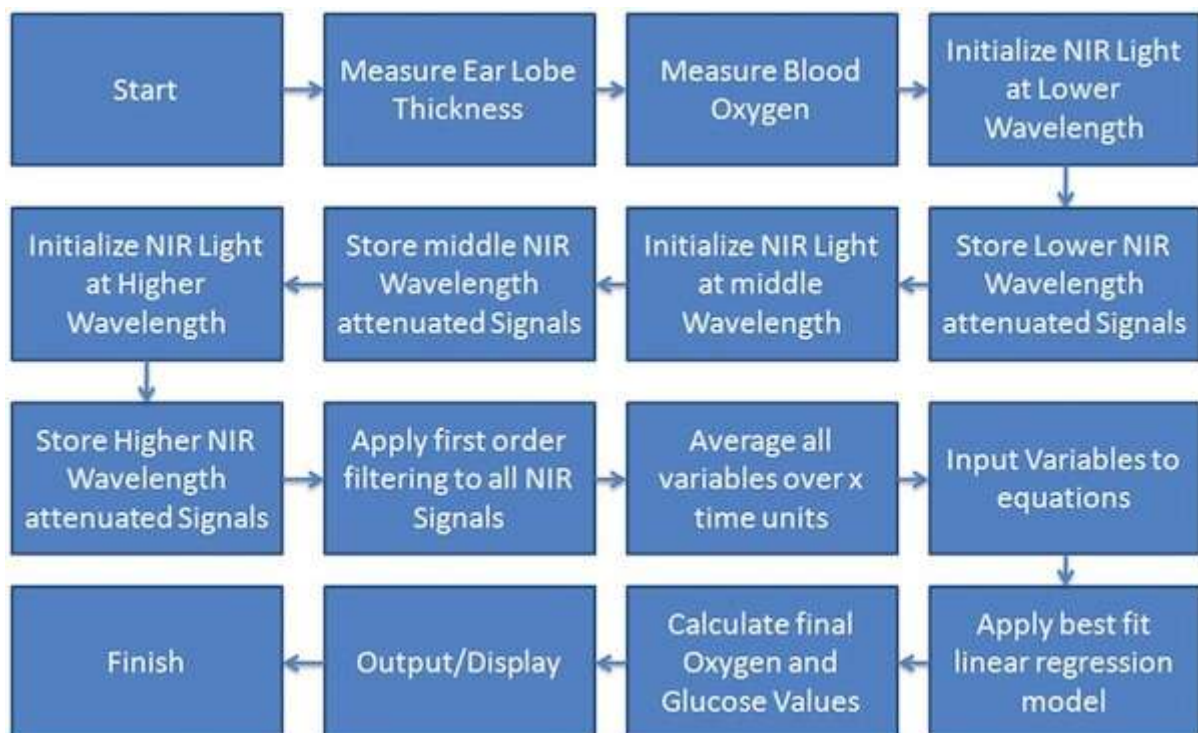


Figure 3 Non-Invasive Glucometer Algorithm Flow

Firstly, the tissue thickness is computed by approximating the exponential Beer-Lambert Law by a linear small signal model (similar to the one used in IV curves in electronics), as given by (1). According to (1), the light penetration into the skin decreases exponentially. However, as the ear lobe thickness varies by very small amounts, typically around 2mm to 4mm, a linear equation can be used to fit this model, where 'y' is the penetration depth, 'x' is the optical power, and 'A', 'b', 'C', 'D', and 'E' are absorption constants.

(1)

Secondly, blood oxygen saturation levels are computed using red lights to determine the amount of blood present. Both these variables, skin thickness

$$y = Ae^{-bx} + C \cong -Dx + E$$

and amount of blood, determine whether the blood is at the required level inside the ear lobe. Non-invasive meters may not work reliably on infants because of very small thickness of the ear lobe (<2mm). Similarly, any medical condition that inhibits blood flow to the ear lobe will result in erroneous readings. The blood oxygen is computed through pulse Oximetry, given in (2), while blood detection is simply measured using trough voltage spike reductions due to absorbance. The AC components of both variables are filtered out from the raw signals by using a high pass filter with a cut off of 5Hz, whereas the DC components are computed by its low pass counterpart. The unscaled O₂ level from (2) is then scaled from 0-100 to determine the percentage oxygen saturation.

(2)

Finally, the glucose levels are computed. We have three different wavelengths in the NIR region comprised of 20 samples each, so we have a 3×20 matrix. According to [1], applying a single register first order filter on different wavelengths reduces noise levels, and brings

$$R(\text{unscaled } O_2 \text{ Level}) = \frac{\frac{AC_{Red}}{DC_{Red}}}{\frac{AC_{IR}}{DC_{IR}}}$$

the three wavelengths onto the same level so the same processing can be applied onto them. This Finite Impulse Response (FIR) filter was constructed in the C code for the PSoC. The filtered samples were interpolated to form a linear best fit line through linear regression. Central value of this line represents the biased glucose value. It is then mapped onto a scale of 55-355 mg/dl. The result is then linearly compensated for the tissue thickness and the oxygen level. A higher thickness would require an increase in the glucose level, by 10 times the thickness in mm. This signal processing takes a few milliseconds for computation of the required high accuracy.

Blood Sugar Level

Low Blood Sugar (Hypoglycemia)	= 0-70 mg/dl
Normal Blood Sugar	= 70-135 mg/dl
High Blood Sugar (Hyperglycemia)	= 135-450 mg/dl

Blood Oxygen Level

Low Oxygen Saturation = 0-90%

Normal Oxygen Saturation =90-99%

Carbon Monoxide Poisoning =100%

The lower limit of detection using NIR in this setup is 55mg/dl. A sugar level below this cannot be accurately measured. However, this can be improved by increasing the power output of the LEDs. The upper limit is set to 355mg/dl, although higher levels can be measured easily.

Display

Although the final glucose value can be displayed on a simple LCD, in this design it is also displayed on an android phone using Bluetooth connectivity. The Universal Asynchronous Receiver Transmitter (UART) of the PSoC is connected to the Bluetooth device. A simple communication protocol was implemented inside the PSoC and the mobile device. When a user asks for a glucose value, the Android platform sends a 'get' to the PSoC, which waits for glucose computation after which it sends the glucose value and an acknowledgement. The Android device displays the glucose value upon receiving it. The whole process takes about 2s.

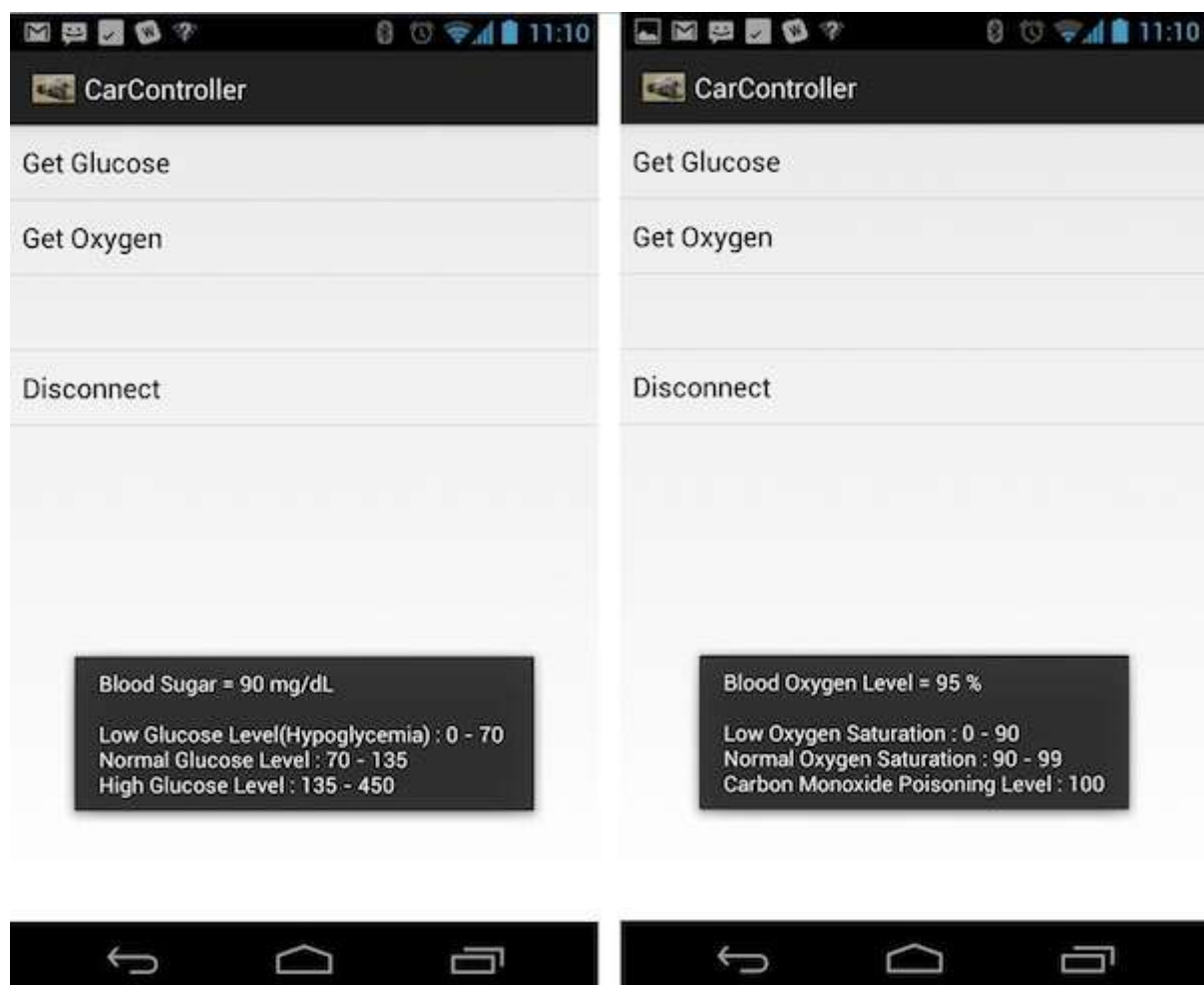


Figure 4 Snap-shots of the Android Device



Figure 5 Complete Setup

Results

To determine the accuracy of the device described above, its readings were compared against an off-the-shelf handheld home-use invasive glucometer available in the market. A Clarkson Error Grid [1] is a standard specifically used to determine the accuracy of glucose monitoring devices. The y-axis represents the values read by the non-invasive device, and the x-axis represents the values recorded by the invasive off-the-shelf device, for the same patient, at the same time. Over 100 test points were taken on 80 patients. The error grid is shown in **Figure 6**. Around 75% of the data points lie in region A, while all the remaining points lie in region B. No data point lies in the other regions. The correlation coefficient between measurements from non-invasive glucometer and reference glucometer is equal to 0.85, which is very good. This accuracy is better than

most non-invasive glucose meters present in the literature (although the sample size presented in this study may not be large enough and further testing and calibration may be required). This high performance is made possible in part due to the fact that PSoC-5LP provides highly integrated analog and digital capabilities, with a low noise floor, and high-resolution analog-to-digital conversion. Further improvements in accuracy can be made by increasing the LED power, by using more sensitive photodiodes, and by including further parameters like ambient and body temperatures.

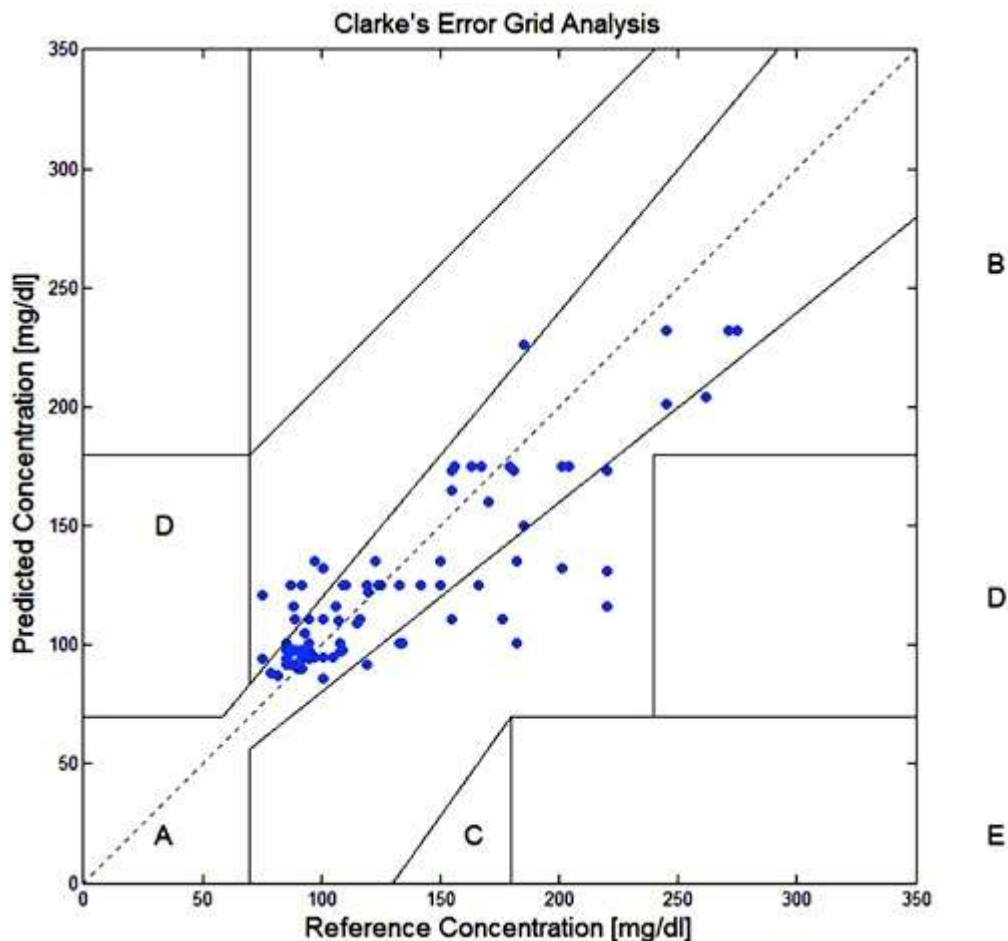


Figure 6 Clarkson Error Grid for the PSoC based Non-Invasive Glucometer

Conclusions

In this article we have presented a non-invasive blood glucose meter that can provide glucose measurements painlessly, without a blood sample or finger pricks, within a few seconds. The device can be easily adapted to provide continuous blood glucose monitoring and blood oxygen level and maintain a history of these measurements. The device algorithm can also be modified to provide other capabilities like heart rate using the same devices and sensors.

Caution

The device presented here is only a proof of concept, showing good correlation between NIR transmittance and blood glucose. However, as such an experimental device is not FDA approved, it should only be used for academic or informative purposes, and should not be used to make any medical decisions including but not limited to administering medicine.

References

[1] V. A. Saptari, "A Spectroscopic system for Near Infrared Glucose Measurement," *PhD Thesis, MIT*, 2004.

[2] A. Tura, A. Maran, and G. Pacini, "Non-invasive glucose monitoring: Assessment of technologies and devices according to quantitative criterion," *Elsevier J. of Diabetes Research and Clinical Practice*, vol. 77, no. 6, pp. 16-40, 2007.

Also see :