Noninvasive Glucose Monitoring by Mid-infrared Self-emission Method

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Keywords: Non-invasive Glucose Monitoring, Mid-infrared Self-emission, Skin Glucose, Blood Glucose.

Abstract: In this article we present a non-invasive glucose monitoring technique by measuring human body mid-infrared self-emission. The human body is a black body radiator that provides a stable temperature and infrared radiation; thus the human body is considered a continuous radiation energy source in the mid-infrared range. The fingerprint spectrum of glucose shows strong peaks between 8.5 μm to 10.4 μm, therefore, measuring the self-emission form human body in the mid-infrared range allows estimation of glucose concentration. Using a simple and miniaturizable design with a tunable Fabry-Perot filter (FPF) and a thermal detector, glucose concentration can be measured through the human skin.

1 INTRODUCTION

It has been decades since blood glucose monitoring techniques were introduced for diabetes patients to help them with daily management of diabetes treatments, including diet control, oral medication and insulin injection. The traditional measurement of blood glucose concentration requires the patients to stab themselves in the finger with a needle to extract the blood to the skin surface so that the blood can be collected for enzymatic reaction and analysis. However, in the past decade, the desire to avoid the pain resulting from the puncture and to realize continuous blood glucose monitoring has driven research in a variety of non-invasive glucose sensing techniques. The non-invasive glucose monitoring techniques can be classified into two different types, transdermal (Rao, 1993; Volden, 1980; Gebhardt, 2001) and optical (Shen, 2003; Nelson, 2006; Enejder, 2005). The main idea of transdermal glucose sensing techniques is to extract the glucose from the interstitial fluid to the outer surface of the skin, where the glucose will be collected and analyzed by a traditional glucose sensor. The popular transdermal techniques include reverse iontophoresis, sonophoresis and skin suction blister technique (Kost, 2000.). Essentially, the key point of these methods lies in the different approaches to collect the glucose. The technique used to identify and quantify glucose remains the same, which is based on enzymes. By contrast, the optical methods aim at identifying the unique spectral signature of glucose and exploring the best way to calibrate and quantify optical measurements. Due to the noise coming from the skin, both SNR and sensitivity are affected. A significant advantage of this system is not requiring an enzyme replacement.

Non-invasive optical glucose monitoring methods basically include three different techniques to measure glucose in the infrared region. Of the three methods, near-infrared (NIR) (Nelson, 2006) spectroscopy, mid-infrared (MIR) (Shen, 2003) spectroscopy, Raman spectroscopy (Enejder, 2005), only MIR spectroscopy can measure glucose without a light source. Because the human body is an excellent black body, it will cause heat emission in the MIR wavelength range. Therefore, self-emission from the human body can generate good target glucose spectra, and enable an easy to measure glucose concentration in the human body. In the mid-IR, glucose has a stronger absorption than most other chemicals, and if avoids most of the water signal peaks. Also, using the MIR method can avoid the use of high-energy light sources on the skin, which can cause burns. Furthermore, these advantages facilitate the implementation of the non-invasive system on a single microelectromechanical system (MEMS) chip, which is our long-term goal. Therefore, we chose to use thermal emission spectroscopy as our scheme to realize a non-invasive glucose sensor. The most significant advantage is

Yeh Y., Yang S., Zhao F. and Schmidt D..
Noninvasive Glucose Monitoring by Mid-infrared Self-emission Method.
DOI: 10.5220/0004750101070111
In *Proceedings of the International Conference on Biomedical Electronics and Devices* (BIODEVICES-2014), pages 107-111
ISBN: 978-989-758-013-0

the relative simplicity of the system, which does not require a light and is relative to fabricate.

2 EXPERIMENTAL

The principle of the glucose measurement device is that the human body emits strong mid-infrared (MIR) radiation and some of the chemical molecules in the human body would cause the distinct absorption at their characteristic peaks (Vonach, 1998). The human body is essentially a black body that emits MIR radiation. According to Planck's law (Planck, 1991), we know the relationship between temperature and intensity of radiation. Glucose molecules have strong characteristic peaks in both near-infrared (NIR) and mid-infrared (MIR) spectrum (Carl, 2002). However, the glucose radiation can only be measured by human body self-emission in the MIR region, at least without a strong light source. Also, the glucose IR spectra can avoid the strong water signal from human body in MIR range rather than NIR range.

The main application of the device is a measurement of the glucose MIR radiation from the self-emission of the human body. Due to the vibration of the glucose chemical bond, the molecule would cause absorption or emission of radiant energy. Therefore, a molecule such as glucose would form several distinct peaks in the MIR spectra between 8.5 μm and 10.5 μm. Figure 1 shows that the IR spectra of D-glucose in a potassium bromide (KBr) sample, which was measured by FTIR spectroscopy (Shumadzu FTIR 8900).

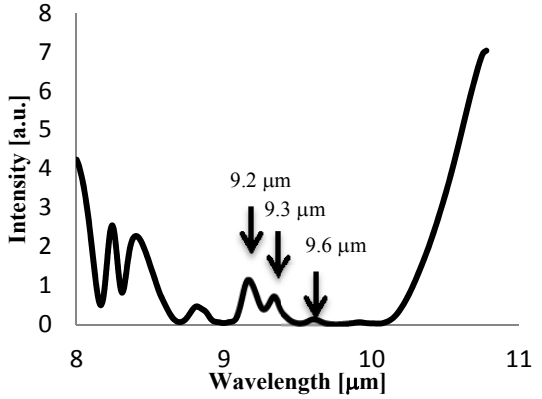

Figure 1: D-glucose spectrum that were measured by FTIR spectroscopy in a KBr sample. The spectra show the characteristic peaks between 8 μm to 10.5 μm.

According to Fig 1, we can recognize the characteristic peaks of glucose at 9.2 μm, 9.3 μm, and 9.6 μm. By measuring the distinct peaks from human body self-emission, the relationship between MIR radiation at the special wavelength and glucose concentration can be obtained.

The targets were the men whose age ranged between 25 to 27 years old and no diabetes history. Blood glucose measurements started before the target had a meal and continued measuring the glucose concentration every 20 minutes. After the target had a meal, the glucose concentration started to increase, and we measured the glucose concentration continuously until the glucose concentration decreased and become stable. Every measurement test was done by both the non-invasive self-emission measurement system (Fabry-Perot filter system) and the invasive blood test. The Bayer's Contour Next meter was used to measure the glucose concentration by stabbing target's finger for getting blood and measuring the glucose on the chemical strip. The results of the blood invasive measurement were taken as the reference blood concentrations.

The self-emission detector system was built up as shown in Fig 2. The detector was a pyro-electric thermal detector combined with a tunable Fabry-

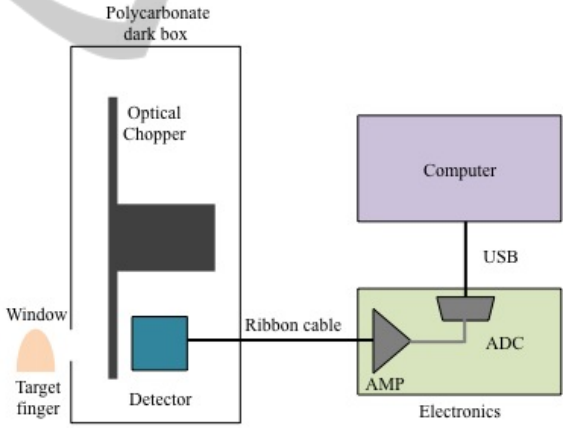

Figure 2: Schematic of the Fabry- Perot filter with system.

Perot filter (FPF), which was made by InfraTec (LFP-80105-337). The tunable Fabry-Perot filter is a microelectromechanical system (MEMS) optical filter, and the scanning range was from 8 μm to 10.1 μm. The detectivity and the noise density of the pyro-electric thermal detector are $3.7x10^8$ cm(sqrt[Hz])/W and 75 μV/(sqrt[Hz]), respectively. The detectivity and the noise density of the whole sensor are $3x10^6$ cm(sqrt[Hz])/W and 75 μV/(sqrt[Hz]), respectively. The electronics are purchased from InfraTec for processing the signal

and transferring to the computer. The schematic is shown in Fig. 3. The aperture diameter size of the sensor was 1.9 mm, and there was a hole on the polycarbonate black box, which is aligned with fitting finger the aperture of the sensor. This hole is used for positioning the target's finger putting target's finger and fixes the position of target.

Since the pyro-electric thermal detector is measuring the temperature difference, the detector can only measure an absolute temperature change. To measure stable IR radiation, an optical chopper (Stanford research system SR 540) was connected with the pyro-electric thermal detector to measure the IR radiation continuously.

The background signal was subtracted from the intensity result before the averaging process. The intensity results were plotted against the real time blood test result to establish a relationship.

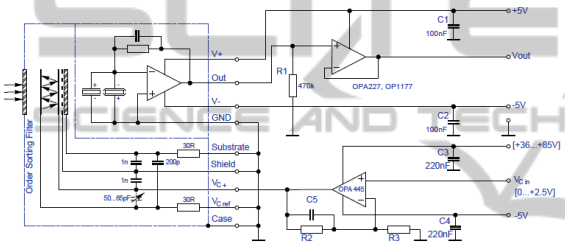

Figure 3: Schematic of the electronics part (InfraTec, 2013).

3 RESULT AND DISCUSSION

The target had their blood glucose concentration measured every 20 minutes in 200 minutes and had a meal during the experiment. After having the meal, the target's blood glucose concentration increased, and then decreased with time as shown in Fig 2. The main band at 9.3 μm was used as the detection characteristic peak from infrared self-emission measurement by FPF system. Figure 4 (a) shows the blood glucose measurement result by detecting the self-emission from target's finger skin. The concentration change had almost the same tendency as the measurement result by blood test meter (Fig 4 (b)).

The highest blood glucose concentration was 143.2 mg/dl that measured by FPF system, and the same point related to 140 mg/dl that was measured by blood glucose meter. The first point and the last point measured by the FPF system were 125.4 mg/dl and 114.3 mg/dl, and related to 124 mg/dl and 108 mg/dl in blood glucose test, respectively.

The relationship between the intensity of the target's infrared radiation and real blood glucose concentration is shown in Fig 5. The measurement took the blood glucose concentration from 108 mg/dl to 187 mg/dl by measuring a target person who was just having a meal. Figure 5 (a) and (b)

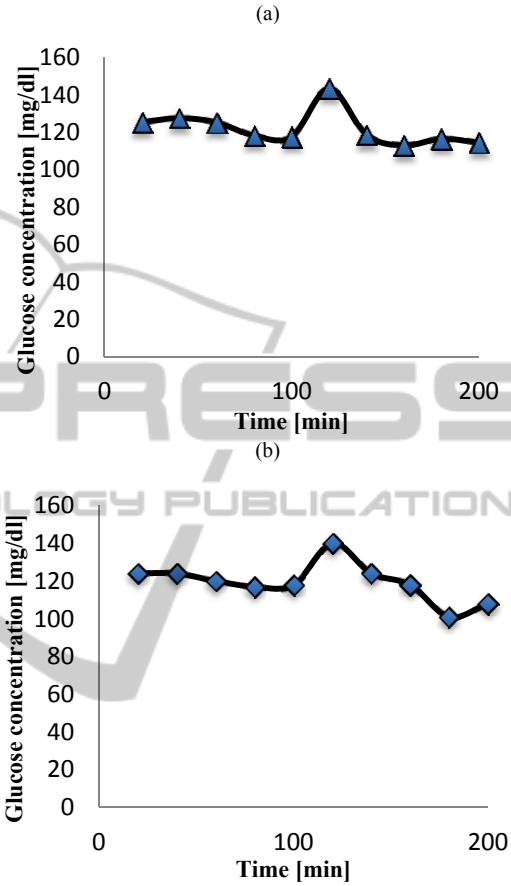

Figure 4: Continuous blood glucose concentration test result by different two methods. (a) Continuous glucose monitoring by FPF system. Measured the glucose concentration by detecting the skin of the target's finger by the FPF system. (b) Continuous glucose monitoring by the blood test meter in 200 minutes. Measured the glucose concentration by stabbing target's finger to get the blood and measuring by Bayer's Contour meter.

shows the measurement of the band at 9.3 μm and 8.9 μm. The equation of the trend lines was y = 0.171x - 3.8144 and y = 0.1759x - 4.1653, and the R^2 value of the trend line was 0.723 and 0.712 individually, thus it showed the correlation between infrared radiation and glucose concentration in human body. However, the accuracy of the FPF system still needs to be improved. The body temperature and the ambient temperature caused a part of the error, and that was because the detected

signal was affected by heat from surrounding materials.

According to Plank's law, the infrared radiation and the temperature are related. One of the conditions that affects the self-emission measurement is the temperature of the target's skin. The more difference between the trend line (trend line of intensity vs. glucose concentration) and each measurement point would be located in a lower temperature region (temperature was measured by a thermopile). The relationship between the temperature and the difference value is shown in Fig. 6, and the R^2 value is 0.664. The next step for improving the relationship between the intensity of the target's infrared radiation and real blood glucose concentration is temperature effect elimination through improved temperature calibration. Also the materials surrounding the target need to have a low thermal mass so they don't affect the target temperature.

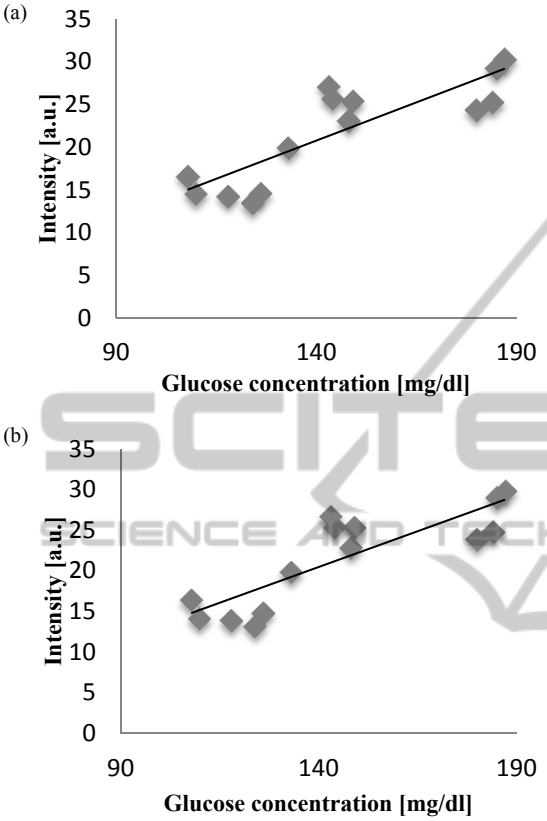

Figure 5: Calibration curve of intensity signal versus blood glucose concentration. (a) Measuring the band at 9.3 μm, and the R^2 value of the trend line is 0.723. (b) Measuring the band at 8.9 μm, and the R^2 value of the trend line is 0.712.

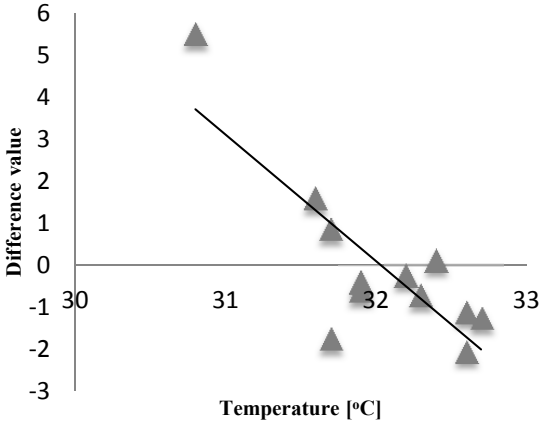

Figure 6: Temperature effect. The relation difference value and the temperature of target's skin.

4 CONCLUSIONS

The Fabry-Perot filter (FPF) system can measure the mid-infrared radiation from the human body without an external light source. By measuring the distinct band from the self-emission of the human body, the blood glucose concentration can be monitored. This non-invasive glucose measurement system allows patients to avoid the pain from stabbing their skin when they monitor their blood glucose concentration. However, the system still needs to calibrate several effects, such as the body temperature and ambient temperature. All the components in our setup can be fabricated on a little chip with a microelectromechanical system (MEMS). Our final goal is to use this concept to build a complete non-invasive glucose monitor on a 1 x 1 cm chip.

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