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Finger-Photoplethysmography: Intensive Development and Validation for Noninvasive Measurement of Blood Glucose

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Abstract

This paper presents a specialized design and intensive validations for measuring blood glucose using photoplethysmography with pulsed light. Glucose level is an important index because whose excess can cause serious complications. Photoplethysmography had been introduced as a potential method for daily monitoring glucose level. Following the trend, most of the published studies focused on identifying the correlation between the glycemic index and infrared light absorption. However, the simple measurement system limits the development of the potential technique. This paper presents a specialized design and intensive validations to apply and verify the use of pulsed light sources for developing more feasible measurement devices. Experimental results not only confirmed applicabilities of the new design with modulated light, but also exhibited remarkable phenomena and notable parameters for error prevention. Hence, this research could contribute useful reference for further studies.

Keywords: Blood glucose, Glycemic index, Photoplethysmography, PPG

1. Introduction

In recent years, hundreds of millions of people around the world have been affected by diabetes mellitus (DM), one of the chronic diseases tending to spread widely in an uncontrolled manner [1, 2]. In 2011, 336 million people had DM and it is predicted to rise to 552 million in 2030 [3]. DM is a common manifestation of metabolic disorder, the modern lifestyle with unhealthy diets increases the morbidity of this disease, particularly in adults. The glucose concentration in human blood should be 3.9–7.8 mmol/l (70–140 mg/dl). Getting above or below this threshold, the patient is in hyperglycemic or hypoglycemic condition, respectively [4]. It is considered that DM patients have a higher risk of the amputation, loss of vision, renal dialysis, mortality, and coronary artery disease [5]. However, the current technologies cannot comprehensively cure the diabetic patients [6]. Therefore, the need for monitoring glycemic index in the body is increasingly more concerned than ever. Indeed, it is essential to frequently monitor the glycemic condition for early treatment or adjust the diet to achieve normoglycemia level. Hence, effective methods for self-monitoring glucose concentration at home are urgently required.

Over the past decades, in order to estimate the blood glucose level, many approaches have been developed. They can be classified into three categories: invasive, minimally invasive, and non-invasive [4, 7]. The most common invasive technique is blood analysis. The others could be using implantable sensors [8] or accompanying with micro-dialysis [4]. Generally, these methods give accurate results, however, have the potential risk of infection, require complex execution, and cause physical discomfort for patients. Some minimally invasive techniques have been developed such as reverse iontophoresis [9], ultrasonic (sonophoresis) [10], laser-induced micropores [11], microneedle technique [12]. These methods share a common drawback of causing fewer injuries on the skin. Noninvasive methods can be mainly divided into: optics-related [13-16], bio-impedance spectroscopy [17], and electrochemical [18-20]. Among these techniques, the method of using photoplethysmography (PPG) to detect the glycemic concentration has significantly attracted researchers. The main basis of this method is that the blood glucose strongly absorbs near infrared (NIR) light with the wavelength of 750–1500 nm [21]. PPG has many outstanding features such as paint-less, low-cost, easy to use, risk-free, and has ability to monitor glucose level continuously.

In PPG technique, designing a good sensing portion is one of the most important issues. In the transmitter unit, the light source can be controlled in two modes: continuous or pulse emission. The advantage of using continuous emission is simplicity of designing LED drivers and acquisition circuits [22-24]. However, this method leads to inevitable drawbacks such as limited light intensity and the

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strong influence of the ambient light. This causes a serious trouble when measuring thick tissues [25]. Another limitation could be the lack of ability to conduct measurement with multiple wavelengths. The approach of generating interleaved pulses of the light at different wavelengths can address the above drawbacks [8, 25-27]. However, the correlation between signals obtained with the two modes of emission is not considered and validated. There is also no research revealing impossibility of occurring cross-influence when generating interleaved pulses of two different wavelength lights. In addition, although blood glucose gains the peak of light absorption at the wavelength of 1550 nm, water also absorbs strongly this spectrum. This makes the magnitude of the received signal completely unpredictable. A high gain amplifier may necessary for the thick human fingers; however, this can be saturated when measuring thinner ones. Thus, there is a need for studies to develop an intensive design and validate the method of using pulsed light in blood glucose measurement.

In this work, the author proposed a specialized design and an experimental system to validate the use of photoplethysmography with pulsed light for noninvasive measurement of blood glucose. First, a complete measurement hardware and a so-called auto-adjustment process were proposed. This can capture the PPG signal and adapt any thickness of the fingers by regulating the average magnitude of the received signal. The system uses two typical wavelengths of 940 nm and 1550 nm in three modes: continuous emission, pulse emission with single LED, and pulse emission with two LEDs. The pulse width and pulse frequency can be adjusted in flexibility when testing. Second, a dedicated experimental system and intensive validations were proposed to identify any potential problem when using pulsed light. All tests were conducted with a phantom instead of real human fingers to ensure the uniformity of the sample under test.

The experimental results not only confirmed the desired operation of the proposed system, but also exhibited notable facts for future designs. First, the auto-adjustment process allows the system to work fairly well with different thickness of the samples. The pulse mode has a good ambient light noise immunity if there is no abrupt change of background light. Second, the validations showed that at low switching frequencies, there is no difference between the effect of continuous and pulse emission; nonetheless, at higher frequency, there may be differences because of signal distortion. The cross-influence could occur when altering the two LEDs without any idle state. However, this can be solved by a short delay between them. Although the experiments were conducted with phantom only, the achieved results could contribute to developing a highly applicable device.

It should be noted that the aim of this work is to develop a specialized design and validate the use of pulsed light in measuring blood glucose. Methods of estimating the glycemic concentration from the PPG signal could be found in [23, 24, 28].

2. Method

2.1 Measurement hardware

A complete system hardware is shown in Fig. 1. On the transmitter side, the microcontroller unit (MCU), digital-to-analog converter (DAC), and LED drivers control the power, switching frequency, and the pulse width of signals provide for two LEDs. On the receiver side, the analog processing unit amplifies and filters the signal before feed into an analog-to-digital converter (ADC). Digital data are processed by the MCU and transferred to displaying devices.

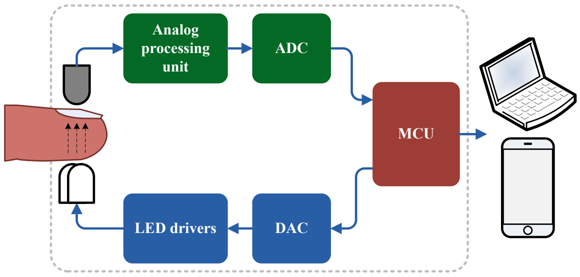

Fig. 1. System hardware with key blocks

The two LED drivers were designed carefully using the schematic shown in Fig. 2. Each of them contains two MOSFETs: T_1 controls the duty cycle while T_2 controls the LED current. Here, the operational amplifier (Op-amp) A_2, transistor T_2, and resistor R_{sens} allow exactly setting the current flow through the LED in a wide range of about 10–600 mA. Thus, the MCU can easily adjust the light intensities of the LEDs by controlling output voltages of the DACs.

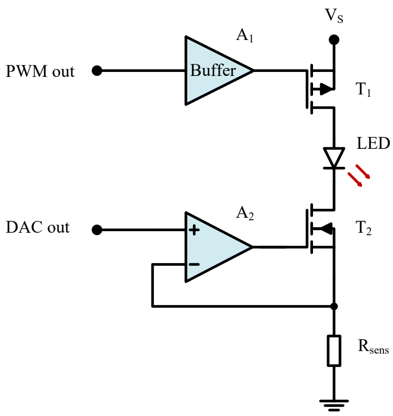

Fig. 2. Simplified schematic of the LED driver

The analog processing unit consists of three major portions. The first stage is a current-to-voltage converter (I-V converter) that converts and amplifies the signal from a PIN photodiode, as shown in Fig. 3. After being high-pass filtered with a cutoff frequency of about 100 Hz at the second stage, the signal is amplified again by an instrumentation amplifier in the third stage. Finally, the output signal pass through a low-pass filter for anti-aliasing. In order to regulate the strength of the received signal, the system has an auxiliary path to measure the output voltage of the I-V converter without high-pass filtering.

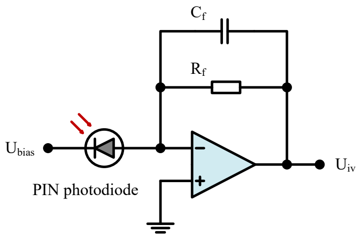

Fig. 3. Simplified schematic of the I-V converter

In some experiments, the author only measured the signal at the output of the I-V converter (U_{iv}) and signal at the output of the high-pass filter (U_{hp}) by a high performance digital oscilloscope. This is to obtain the best evaluation, without the influences of skippable processing steps.

Regarding the component selection, the author chose following configuration for the hardware system:

- Main NIR LED: MTE5015-525 (Marktech Optoelectronics), with the wavelength of 1550 nm.
- Auxiliary NIR LED: IR333-A (Everlight Electronics), with the wavelength of 940 nm.
- Photodiode: C30641GH (Excelitas Technologies) with a large area InGaAs PIN junction.
- I-V converter: using OPA2727 (Texas Instruments), a high precision CMOS Op-amp.
- LED driver: using MAX44246 (Maxim Integrated), a rail-to-rail output Op-amp.
- Microcontroller: Tiva TM4C123GH6PM (Texas Instruments) with integrated 16-bit PWM unit.

2.2 Auto-adjustment process

The auto-adjustment process is an important contribution of this study. The process is performed at the beginning of each measurement to find out the optimal luminous intensities for the LEDs. This takes a few second before each test by using a proportional controller. The MCU compares the average magnitude (process value) of the received signal with a desired value (set point) and adjusts the LED current. Here, the average magnitude of the received signal is obtained by filtering and digitizing the signal from the auxiliary path. The set point is chosen of about half the source voltage to maximize the dynamic range of the signal. Because the process value is nearly unchanged in each measurement, the proportional gain can be easily adjusted, by using manual tuning method. After auto-adjustment, the luminous intensities of the LEDs are fixed and the major measurement process is started.

2.3 Validation with Phantom

In order to validate the applicability of the pulsed light in measuring the glycemic index, the author used a simple phantom instead of real human fingers. The main reason is that the human body always changes by the time. This makes the comparison between signals captured in different period of time become meaningless. In contrast, an artificial phantom allows performing many different tests under almost same condition.

On the basis of the PPG mechanism, the author created the phantom by using a small transparent glove with blood inside. Theoretically, PPG is an optical method to detect blood and its substances volume changes. Blood parameters could be estimated, if any, based on processing these variations. Hence, liquid blood in a soft container can be used to verify the behavior of the PPG in blood glucose measurement.

The structure of the phantom is illustrated in Fig. 4. One finger of the glove was filled up with blood and surrounded by a hard shell. The glove material is chosen to be almost transparent to the measurement wavelengths. A motor and a cam were used to change the pressure inside the finger periodically. This makes the volume of blood and glucose solution in the glove fingertip rises and falls continuously. The periodical changes in glucose volume at fingertip make sure the uniformity of the tests during a short period of time. This experimental setup is a novelty of this study.

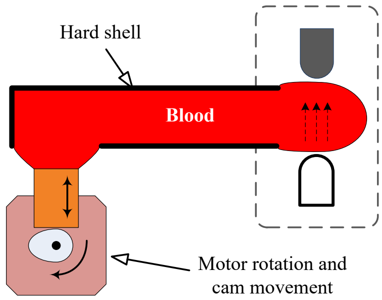

Fig. 4. Simple phantom and experimental setup

3. Experiments and Results

3.1 Experimental Steps

Using the proposed design, the author performed four separated experiments to evaluate and validate the use of pulsed light. In the first test, the size of the artificial finger is changed before each measurement to evaluate the effectiveness of the LED auto-adjustment process. In the second test, the motor is stopped. The main NIR LED is turned on by a continuous current in five second, then by a pulse of 10% duty cycle in the next five seconds. A strong and controllable lamp is used to change the ambient light. The values of both U_{iv} and U_{hp} were recorded for comparison. In the third test, the motor rotates at a speed of 70 revolutions per minute for simulating the change in blood pressure. The main NIR LED is turned on by a continuous current in five second; then by a pulse of 1 kHz, 10% duty cycle, in the next five seconds. The values of U_{iv} were fully recorded for comparison. In the final test, each LED is powered by a pulse of 10% duty cycle, alternatingly. The motor runs in five seconds and stops during the next five seconds. The values of U_{iv} were also fully recorded by the digital oscilloscope for evaluation.

3.2 Results

The first test confirmed a fairly good ability of the proposed design to regulate the strength of the received signal. The author also verified the ability of the LED to flash a high intensity of light. When working with a pulse of 10% duty cycle, the LED can be powered up to 600 mA, six times greater than the maximum acceptable average current, without any problem. At this intensity, the experiment confirmed that the light can pass through a thick layer of water. However, if the artificial finger is too big, the received signal could be very weak because of the limited ability to penetrate.

In the second test, the pulse emission mode showed an excellent ambient light noise immunity, whereas the signal in the continuous emission mode was strongly affected by the background light. Fig. 5 shows the signals at the output of the I-V converter and the output of the high-pass filter when the ambient light is changed. The slow variation of the whole wave totally disappears after passing the filter. In fact, when the ambient light changes fast (e.g., abruptly turn on or turn off the lamp) the output of the high-pass filter has transient voltage. However, the influence is very small and negligible. On the other hand, if the ambient light is much stronger than the LED light, the sensing circuit can be partially or fully saturated. In this case, there is neither noise immunity nor accurate data.

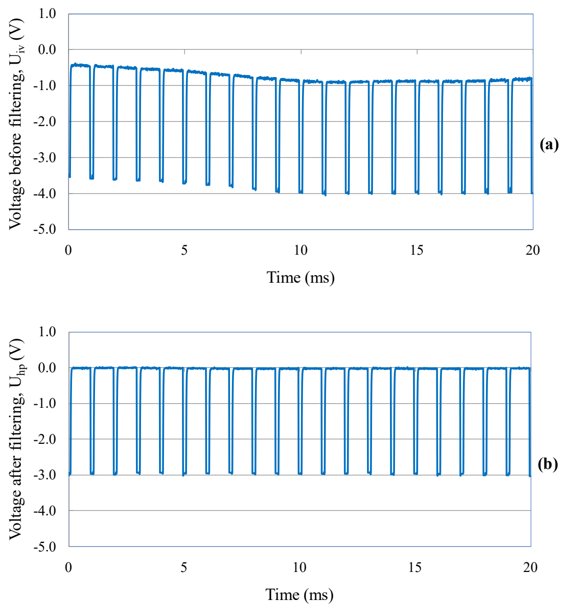

Fig. 5. Measured signals when the ambient light is changed: (a) before filtering, and (b) after filtering

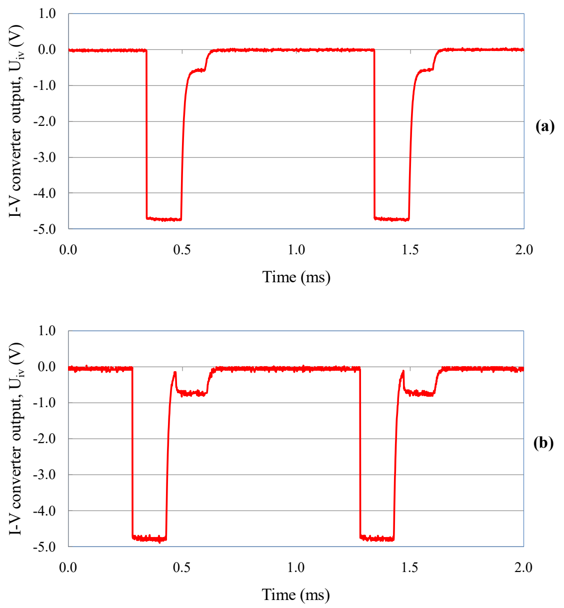

Fig. 6. Cross-influence between two pulses of the lights when: (a) there is no idle time, and (b) there is a delay of 80 µs

In the next test, when the switching frequency of the LED is 1 kHz or lower, there is no difference between the shapes and amplitudes of the captured signals in the two emission modes. However, when both the switching frequency of the pulse and the gain of the I-V converter are high, the captured signal of the pulse emission mode has significant distortion. This can cause serious measurement error.

In the final test, cross-influence occurred when altering the two LEDs without any idle state. The light from the auxiliary LED strongly affects the signal induced by the main LED, as shown in Fig. 6(a). Even, the signal from the main LED could be overridden if the pulse of the lights is short. Nevertheless, when there is a delay of about 80 µs between the two pulses, the cross-influence is no longer significant, as shown in Fig. 6(b).

4. Discussion

The auto-adjustment process has notable advantages. This allows the proposed system to be able to measure the PPG signal at the desired and optimal set point. There is no influence of the control loop to the measurement signal because this process is only activated at the beginning and disabled during the test.

At high frequency of pulsed light, the distortion in the captured signal could be the effect of the combination among the photodiode parasitic capacitance, C_F, R_F (see Fig. 3), and the limited bandwidth of the Op-amp. This could be reduced by using higher quality components. In fact, high frequency may not really necessary for measuring the slow changes in the glucose level.

The ambient light noise immunity and cross-influence effect of the whole system could depend on the DC operating points (DC bias) of both the transmitter and the receiver. Higher transmitting light power may have a better ambient light noise immunity; however, have greater potential of cross-influence.

5. Conclusion

In this work, the author has been successfully proposed a new measurement system and carefully validated the method of using photoplethysmography with pulsed light for measuring glycemic index. In the proposed system, the dedicated measurement hardware and the special auto-adjustment process allow capturing the PPG signal from different finger thicknesses under the optimal conditions. Although experiments were conducted with phantom only, the achieved results exhibited some remarkable phenomena and notable parameters when using pulsed light. First, the intensive tests confirmed a good immunity of the pulsed light from the background light if the set point is well established. This advantage is very meaningful for developing wearable devices. Second, the recorded data confirmed the applicabilities of the pulse emission mode at low frequencies, whereas the higher ones could cause serious errors. Finally, the author discovered and addressed the cross-influence problem when using the two typical wavelengths for measurement of blood glucose. The whole proposed system and validation results could contribute to developing a highly applicable device.

Acknowledgments

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