

Application of transcutaneous diffuse reflectance spectroscopy in the measurement of blood glucose concentration

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Received March 26, 2004

In this paper, the propagation characteristics of near-infrared (NIR) light in the palm tissue are analyzed, and the principle and feasibility of using transcutaneous diffuse reflectance spectroscopy for non-invasive blood glucose detection are presented. An optical probe suitable for measuring the diffuse reflectance spectrum of human palm and a non-invasive blood glucose detection system using NIR spectroscopy are designed. Based on this system, oral glucose tolerance tests are performed to measure the blood glucose concentrations of two young healthy volunteers. The partial least square calibration model is then constructed by all individual experimental data. The final result shows that correlation coefficients of the two experiments between the predicted blood glucose concentrations and the reference blood glucose concentrations are 0.9870 and 0.9854, respectively. The root mean square errors of prediction of full cross validation are 0.54 and 0.52 mmol/l, respectively.

OCIS codes: 250.0250, 300.0300.

Near-infrared (NIR) spectroscopy is considered as the best way to monitor the blood glucose concentrations of the diabetic patients in real time due to its advantages such as high speed, non-invasive, non-infectious, and pollution-free, etc.^[1]. In 1987, Dahne^[2] proposed NIR spectroscopy for non-invasive glucose sensing. In 1999, Stephen *et al.*^[3] applied diffuse reflectance method at NIR range (1050 – 2450 nm) to research non-invasive glucose sensing, demonstrating preliminarily that at this wavelength range diffuse reflectance spectra can be used for predicting glucose concentrations. At present, many groups around the world are expanding their research on this specific field^[4–7]. However, the study of this technique is very challenging as human body is the target object of detection and it requires deep understanding of many various basic disciplines. So far, there is no report about any successful techniques on non-invasive blood glucose concentration detection that can satisfy the requirements of clinic application.

In this paper, an analysis of propagation characteristics of NIR light travelling through human palm skin tissue and a principle of non-invasive blood glucose concentration detection by measuring transcutaneous diffuse reflectance spectrum of the skin tissue are presented. Human palm is chosen as the detection position and a diffuse reflectance spectrum measurement system suitable for the palm is designed to measure the glucose concentrations in the dermis tissue. By this system, oral glucose tolerance test (OGTT) experiments have been performed and good results were obtained.

The palm tissue is made up of four layers: epidermis layer, dermis layer, subcutaneous tissue layer, and muscle layer. The skin tissue composed of epidermis layer and dermis layer is about 4 mm thick and the epidermis layer is about 0.5 mm thick. The probability for the photons of NIR light entering into the subcutaneous tissue and muscle layer is very little due to their thickness. The propagation characteristics of NIR light in the palm tis-

sue are shown in Fig. 1. When incident light I_0 enters into the palm tissue, the reflected light is composed of three different parts if the light reflected from the subcutaneous tissue is ignored. They are: 1) the mirror reflected light I_1 from the palm surface, 2) the diffusely reflected light I_2 from the epidermis layer, and 3) the diffusely reflected light I_3 from the dermis layer. Because there are no blood vessels in the epidermis layer, only I_3 is useful when the blood glucose concentration is measured by transcutaneous diffuse reflectance spectroscopy. Provided that the light path length in the palm tissue is l_λ , the diffusely reflected light is given by

$$I_3(\lambda) = I_0(\lambda)e^{-\mu_{\text{eff}}(\lambda)l_\lambda}, \quad (1)$$

where $\mu_{\text{eff}}(\lambda)$ is the effective attenuation coefficient (in mm^{-1}),

$$\mu_{\text{eff}} = \mu_{\text{eff_epi}} + \mu_{\text{eff_derm}}, \quad (2)$$

$$\mu_{\text{eff_epi}} = \sqrt{3\mu_{\text{s_epi}}[\mu_{\text{a_epi}} + \mu_{\text{s_epi}}(1 - g_{\text{epi}})]}, \quad (3)$$

$$\mu_{\text{eff_derm}} = \sqrt{3\mu_{\text{s_derm}}[\mu_{\text{a_derm}} + \mu_{\text{s_derm}}(1 - g_{\text{derm}})]}, \quad (4)$$

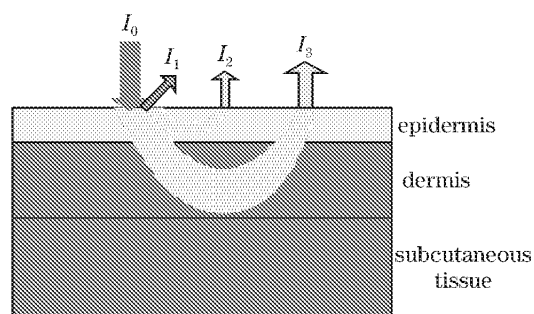


Fig. 1. Propagation characteristics of NIR light in the palm tissue.

where $\mu_{\text{eff_epi}}$ and $\mu_{\text{eff_derm}}$ are attenuation coefficients in the epidermis layer and dermis layer, respectively; $\mu_{\text{a_epi}}$ is the absorption coefficient of epidermis and $\mu_{\text{a_derm}}$ is of dermis; $\mu_{\text{s_epi}}$ is the scattering coefficient of epidermis and $\mu_{\text{s_derm}}$ is of dermis; g_{epi} is the anisotropy factor of epidermis and g_{derm} is of dermis.

In the dermis layer, blood is the main factor that influences the absorption rate and scattering rate of photon. The main carbohydrate in the blood is glucose, which is also called blood glucose. The molecular formula for glucose is $\text{C}_6\text{H}_{12}\text{O}_6$, suggesting a molecular structure involves several bonds of C–H, O–H, which can cause absorption of NIR photon. Thus the blood glucose concentration affects $\mu_{\text{a_derm}}$ directly. According to Eqs. (1), (2), and (4), the transcutaneous diffusely reflected light intensity changes with the blood glucose concentration, which is the theoretical basis of blood glucose detection by NIR spectroscopy. In particular the presence of an abundance of vascular tufts in the papillary layer of dermis layer justifies this blood glucose detection technique being considered as an advisable method^[8]. The diffused spectral energy characteristics from the left palm of the same measured object with different blood glucose concentrations are shown in Fig. 2, which prove that it is practicable to detect the blood glucose concentrations by measuring transcutaneous diffuse reflectance spectrum. However it must be considered that water is a strong absorber composed of O–H and thus interferes with the spectral analysis. As a consequence, multivariate calibration methods have to be used to evaluate the spectra.

This system consists of a tungsten-halogen lamp (PG64623, OSRAM, German), a non-collinear TeO_2 acousto-optic tunable filter (TEAF10-1.0-1.8-S, and the RF driver is VFI-80-50-DDS-B1-C2-E, Brimrose Company, USA), two InGaAs PIN photodiodes (G5851-21, Hamamatsu Photonics K. K., Japan) and a 16-bit data acquisition card (PCI-MIO-16XE-50, National Instrument Inc., USA). This system adopts the comparative measurement method of double beams to reduce the influence of variation of light intensity along time. The wavelengths range from 1100 to 1700 nm.

For each measurement, the spectrum is affected by the variations of measured position and the contact pressure between the optical fiber probe and the measured position^[9]. Thus a charge-coupled device (CCD) camera

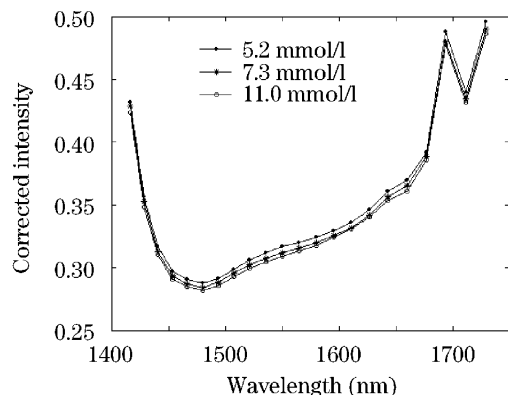


Fig. 2. Diffuse reflectance spectral intensity of the same palm with different blood glucose concentrations.

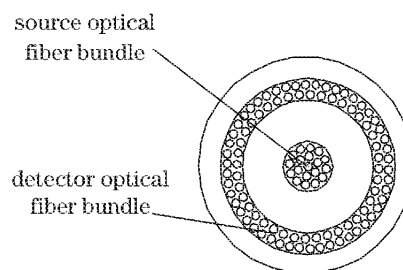


Fig. 3. The fiber optical probe.

and a pressure sensor are used to ensure the position of the optical probe can be reproduced, along with a three-dimensional (3D) servo device that drives the fiber probe to the measuring positions along X , Y , and Z axes.

As shown in Fig. 3, the fiber optical probe is designed so that the optical fiber bundle in the center is used for incident light beam and the optical fiber bundle in the peripheral zone at an annular shape is used for receiving light beam. Such a design enables the light signals to be detected more usefully by an enlargement of the reception area instead of by increasing number of detectors. According to the transmission characteristics shown in Fig. 1, the radial distance between the two fibers is 2.5 mm, which is calculated by the Monte Carlo method. When optical parameters at 1600 nm ($\mu_{\text{a}} = 0.511 \text{ mm}^{-1}$, $\mu_{\text{s}} = 10.43 \text{ mm}^{-1}$, $g = 0.4$)^[10] are used for simulation, the average photon penetration depth at measuring position of optical fiber probe is 0.975 mm. Thus, this optical probe can be used to measure diffuse reflectance spectrum from the dermis layer.

Experiments are performed to assay the blood glucose concentrations of two young healthy volunteers with the measurement system described above. The OGTT method is used to induce the fluctuation of blood glucose concentrations in the body. During each OGTT experiment, vein blood concentrations of the volunteer's right arm measured by a Blood Glucose Test Meter (GT-1640, Arkray Factory Inc., Japan) once per five minutes are used as reference data. For each reference datum, our designed spectrum measuring system is applied to measure diffuse reflectance spectra of the volunteer's left palm. To improve the signal-to-noise ratio (SNR) further, we take the average of 8 diffuse reflectance measurements for each spectral datum.

The SNR of the reference signal in individual OGTT experiment is above 4000:1. For each OGTT experiment, we got about 40 data for constructing model. Then a partial least square (PLS) calibration model was established according to the spectral data and the blood glucose concentration values. And a full cross validation method was adopted to evaluate the prediction ability of the model. The predicted results are shown in Fig. 4. The correlation coefficients between the predicted concentrations and the reference concentrations are 0.9870 and 0.9854, respectively, and the root mean square errors of prediction (RMSEPs) are 0.54 and 0.52 mmol/l, respectively.

In this paper, the propagation characteristics of NIR light in the palm tissue are analyzed, the underlying theory of non-invasive blood glucose detection by

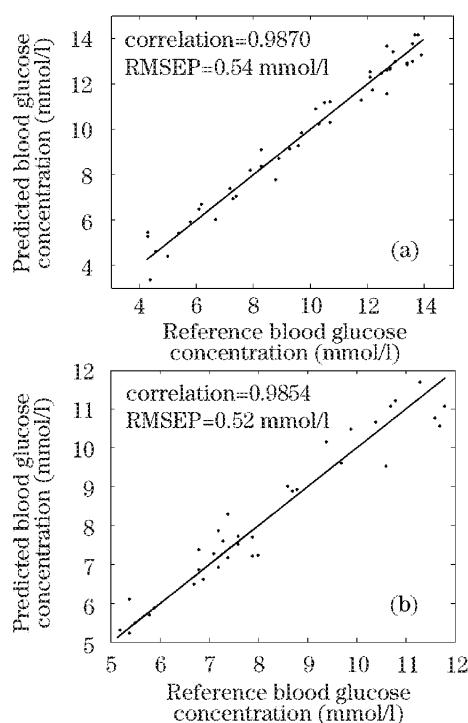


Fig. 4. Correlation plot of the reference values and the predicted values of the blood glucose concentration. (a): volunteer 1; (b): volunteer 2.

transcutaneous diffuse reflectance spectroscopy is presented and its feasibility is discussed. An optical probe suitable for the diffuse reflectance spectrum measurement of the palm is designed, and the NIR spectrum measurement system used for non-invasive blood glucose concentration assay is constructed. Experiments have been performed using this system to measure the blood glucose concentrations of two young healthy volunteers. The OGTT method is used to induce the fluctuation of blood glucose concentrations in the body, and for each experiment a PLS calibration model is constructed by all experimental data. The RMSEPs of full cross validation

are 0.54 and 0.52 mmol/l, respectively, and the correlation coefficients between the predicted concentrations and the reference concentrations are 0.9870 and 0.9854, respectively.

So far, the investigation of our non-invasive blood glucose detection system is carried out in lab. However, the experimental results show that the system and the method are excellent in this field. In the future work, we will try to improve its performance by increasing instrument precision and modifying data processing method.

This work was supported by the National Natural Science Foundation of China (No. 30170261), and the Natural Science Foundation of Tianjin (No. 023800411). K. Xu is the author to whom the correspondence should be addressed, his e-mail address is kexin@tju.edu.cn.

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