Time-resolved photoacoustics for glucose concentration measurement: theory and experiment

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ABSTRACT:
The capability of the time-resolved photoacoustic (PA) technique for glucose concentration measurement in the near-infrared range was demonstrated. Both experimental and theoretical studies shown that the concentration dependence of the sound velocity, optical absorption coefficient and thermal property of glucose solution can be simultaneously determined by the time-resolved PA techniques. Good agreement between theory and experiment has been obtained.

Keywords: Photoacoustic technique, time-resolved, glucose

1. INTRODUCTION

Recently there has been great interest in applying infrared optical spectroscopic techniques in the non-invasive blood glucose monitoring. The development of a non-invasive optical monitoring technique for diabetes has important medical implications for the treatment of diabetic patient, whose body cannot maintain normal levels of the glucose present in the blood stream. Various optical spectroscopic techniques such as attenuated total reflection, transmission and diffuse reflection spectroscopy have been studied to determine glucose concentrations. These optical techniques are very sensitive but suffer from light scattering as well as wavelength-dependent penetration depth.

The photoacoustic (PA) technique is quite different from optical method in that it does not rely on the direct detection of the reflected, scattered or transmitted light. The absorption of a laser pulse gives rise to a thermal expansion leading to an accompanying PA pressure wave. In previous studies, a focused laser beam and a piezoelectric transducer were used for acoustic generation and detection, respectively. The response feature of the acoustic detector dominates the shape of the measured PA signal. Therefore only the amplitude of the measured PA signal contains useful information for glucose concentration measurement. In this paper, we will report a new method based on time-resolved PA technique. Theoretical and experimental results show that both the amplitude and the shape of the PA signal measured with time-resolved PA technique contain useful information for glucose concentration measurement. The concentration dependence of the elastic, optical and thermal properties of glucose solution was simultaneously determined by fitting theoretical curve with experimental results.

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2. OUTLINE OF THE THEORY

For simplicity we assume that the laser beam has a uniform spatial distribution in lateral direction. Therefore one-dimension wave equation can be used to describe the PA pressure waves generated in solution by a plan laser beam.

\[
\frac{\partial^2 p}{\partial z^2} - \frac{1}{v^2} \frac{\partial^2 p}{\partial t^2} = -\frac{\beta}{C_p} \frac{\partial H(z,t)}{\partial t}
\]

where \( p \) is the acoustic pressure, \( v \) is the sound speed, \( \beta \) is the isobaric volume expansion coefficient, \( C_p \) is the heat capacity per unit mass, \( t \) is the time and \( H(z,t) \) is the heating function defined as the heat deposited in the fluid per unit time and volume.

\[
H(z,t) = I_0 \alpha \cdot e^{-\alpha z} \cdot f(t)
\]

where \( \alpha \) is the optical absorption coefficient and \( I_0 \) is energy fluence (i.e. the energy per unit area and time in the laser beam), \( f(t) \) is the temporal profile of the laser pulse. Using Green's function method the solution of above wave equation can be written as,

\[
p(z,t) = \frac{\nu \alpha \beta}{2C_p} I_0 \int dz' e^{-\alpha z'} f(t - \frac{z - z'}{v})
\]

If \( p_n \) is the stress generated in a volume adjacent to a material with different acoustic impedance, a reflection occurs at the boundary. This can be taken into account by assuming an image stress distribution \( p_n' \) at \( z<0 \),

\[
p_n'(z,t) = R_p p_n(z,t)
\]

where \( R_p = \frac{(\rho_1 v_1 - \rho_2 v_2)^2}{(\rho_1 v_1 + \rho_2 v_2)^2} \) is the acoustic reflectivity of the boundary, depending on the values of the density \( \rho \) and velocity \( v \) of both media. Index 1 belongs to the absorber and index 2 to the adjacent medium. To calculate \( p(z,t) \) for given absorption coefficient and temporal distribution, the integral in Eq. (3) is calculated numerically.

3. EXPERIMENT

Figure 1 shows the schematic representation of the experimental set-up for time-resolved PA spectroscopy. In the experiment, the optical source was a MOPO laser system (MOPO-710 Spectra-Physics), which can provide laser pulse in the wavelength range from 440-1800 nm with a pulse duration of 7 ns at a repetition rate of 10 Hz. A digitizing oscilloscope (Tektronix TDS 460) was used to capture single-shot PA signals from a wide-band hydrophone measuring the PA pressure waves. The digitized signals were then transferred to a computer for further processing. Usually the signal was averaged over 100 laser pulses in order to improve the signal-to-noise ratio.

Glucose solutions of the concentration range from 1 g/dl to 15 g/dl were prepared by diluting a pre-prepared 30g/dl D-glucose solution with distilled water. In all experiments, the sample temperature was controlled at 23 °C with an accuracy of 0.1 °C in order to minimise the effect of temperature change.
4. RESULTS AND DISCUSSIONS

4.1 PA signal

Figure 2 shows a typical PA signal obtained by irradiating water with a laser pulse (wavelength 1450 nm, energy 1 mJ/cm²) through the glass window. Superimposed on the measured signal is a curve calculated with the experimental values of α and d. The bandwidth of the hydrophone detector (10MHz) was taken into account in the calculation. The PA signal consists of two parts. The first exponential rising part is corresponding to the depth distribution of the absorbed laser energy in the sample. The second part, a fast falling part and an exponential rising slope, is the reflection of the first part at the water-glass interface. Due to the finite thickness of the glass window (6mm), multi-reflection occurs and this causes the discrepancy between the measured and calculated PA signals at the second part.

The sound velocity of the sample can be determined from the peak position if we know the distance between the hydrophone detector and the glass window. Furthermore the optical absorption coefficient of the sample can also be determined by fitting theoretical curves with experimental results. Note that this can be easily done by fitting the logarithm of the PA signal which changes linearly with time, as shown in the inset of Fig.2. The slope of the best-fit line is given by the product of the sound velocity v and the optical absorption coefficient α of the sample. Once the optical absorption coefficient and sound velocity were determined, the thermal property (β/Cₚ) could be easily calculated from the amplitude of the PA signal.

4.2 Effect of the rise time of the detector on the measured PA signal

For PA signal generated by a rapid deposition of heat from a pulsed light source, i.e., f(t)=δ(t), the integration in Eq (3) can be carried out to give the pressure for t>0 as

\[ p(z,t) = \frac{\nu^2 \alpha \beta}{2C_p} \int_0^t \lambda e^{-\alpha(z-\nu \tau)} d\tau \]

Thus the eq.(5) states that in one-dimension, the spatial distribution of heat from a short laser pulse is mapped directly into the time profile of the PA signal. Therefore, three different parameters can then be determined from the measured PA signal: (1) the sound velocity v of the sample can be determined from the peak position of the PA signal. (2) the logarithm of the PA signal is proportional to time t with a slope of αv, therefore the optical absorption coefficient can be calculated from the slope. (3) the amplitude of PA signal is proportional to αv²β/Cₚ, thermal properties can be determined from the amplitude of the PA signal. Adding glucose to water will cause changes of sound velocity, thermal properties and optical absorption coefficient of the glucose solution. However, only the change of optical absorption coefficient is wavelength dependent. Therefore it is of particular importance to know whether the time response of the detector has any effect on the shape of the
Figure 3 The shape of the PA signal changes with the rise time of the detector. The rise time of the detector is 500 (1), 200 (2), 100 (3), 50 (4), 10 ns (5), respectively.

PA signal, especially the slope of the curve of LOG(PA) against time t. Figure 3 shows the simulated PA signals calculated with different rise time of the detectors. It is clear that the peak position and the shape of the PA signal change greatly with the rise time of the detector. However, the slope of LOG(PA) against time t, as shown in the inset of Fig.3, remains constant. This indicates that the PA signal measured with time-resolved PA technique can be used to determine the optical absorption coefficient, provided that the signal-to-noise ratio is high enough. The time response of the detector changes the peak position but has little influence on the slope of the PA signal. This is very important for the development of a glucose monitor based on time-resolved PA techniques.

4.3 Concentration measurements
Glucose solutions with various concentrations were studied by time-resolved PA technique. The amplitude and peak position of PA signals for different glucose concentration at wavelength 1450 nm is plotted in Fig.4 to show their concentration dependence. A linear response is evident in the whole concentration range investigated. In addition, it can also be seen from Fig.4 that the peak position of the PA signal changes linearly with glucose concentration, indicating that the sound velocity of the solution increases with glucose concentration at a fixed slope of 0.15%(g/dl)^-1. Compared with conventional optical technique, the time-resolved PA technique has several advantages. The application of conventional optical techniques is usually limited by the light scattering and the wavelength-dependent penetration depth. It relies on direct detection of transmitted light and therefore is not applicable to samples with high optical absorption coefficient. The time-resolved PA technique, however, has no such limitation. As demonstrated here, the time-resolved PA technique has been successfully applied for studying glucose solutions under the condition of very strong background absorption, i.e., water absorption band around 1450 nm. Furthermore, the glucose solution studied here has a uniform optical absorption coefficient. It should be pointed out that the time-resolved PA technique is mostly suitable to study samples with layered structures. We believe that by using an optical PA detection scheme to increase the time-resolution of pulsed PA technique, the PA contributions from skin and tissue could be easily distinguished by time-resolved PA technique. This is particularly helpful in the development of an

Figure 4 Glucose concentration dependence of the amplitude and peak position changes of the PA signals at 1450nm. The solid line represents the best-fit to these data.
instrument for non-invasive monitoring of glucose concentration in human blood, since skin and tissue have different optical properties.

5. CONCLUSIONS:

In conclusion, time-resolved PA technique has been successively applied to the study of the glucose solutions. The PA signal generated in glucose solution by a plan laser beam was measured by a wide-band hydrophone. Both experimental and theoretical results show that: (1) the sound velocity of the sample can be determined by the peak position of the PA signal. (2) the logarithm of the PA signal changes linearly with time delay at a slope of αv, (3) the amplitude of PA signal is proportional to αvβ/Cp. Therefore, three parameters, i.e., sound velocity v, optical absorption coefficient α and thermal property (β/Cp) can be simultaneously determined in a single experiment. This makes the time-resolved PA technique a powerful tool for studying glucose solution.

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