Technique for measurement of photoacoustic waves *in situ* with ultrasound probe beam

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A method of measuring photoacoustic (PA) waves *in situ* is proposed and experimentally demonstrated. A focused probe ultrasonic beam passes through a sample and tags the position of the interested PA signal. The probe beam interacts with PA wave. The PA signal modulated probe beam is recorded outside the sample. Reconstruction of the original *in situ* PA signal is accomplished by demodulating the probe beam. The method, thus, provides a measurement system with a high signal-to-noise ratio and reduced background noise for PA wave form recording. © *2003 American Institute of Physics.* [DOI: 10.1063/1.1588361]

I. INTRODUCTION

It is known that the absorption of radiation can lead to changes in physical properties, such as the temperature and volume, of an absorber. The phenomenon is the basis of noninvasive characterization of optical properties in turbid media. The investigation is based on time-resolved measurements of profiles of laser-induced pressure transients, or photoacoustics (PA) waves.[1–5] PA waves can be used to estimate conditions inside a sample, such as finding or determining damaged or pathologic changes of tissue. There are numerous investigations utilizing PA, or, thermoacoustic tomography.[6–7] The technology has great potential in medical applications, for it can distinguish objects that have similar acoustic properties, but can be differentiated optically. A practical example is the metabolically different morbid and normal tissues. Up until now, all of these functions cannot be realized with traditional ultrasonography.

Biotissues are complicated and diversified in structure. An analysis of their PA characteristic signals is a precondition for PA diagnosis and imaging.[6–9] Typically, a detected PA signal is a superposition of acoustic waves radiated from a large source area/volume. The detection is complicated by the scatterings, absorptions, and reflections during the propagations of the incident laser and the PA wave. It is desirable that PA waves, from originating positions, can be distinguished, so image reconstruction can be performed. To achieve the goal, multielement phase-control detection technology or multiposition measurement is necessary.[6,7]

In this article, we propose a technique to measure PA waves with high signal-to-noise ratio (SNR) and spatial resolution. A focused ultrasonic probe beam is introduced into a sample. The probe-beam wave form is effectively modulated by the PA wave that is only within its focal region. The probe beam serves as a PA wave signal carrier and, once recorded, can be demodulated later for PA signal reconstruction. There are several advantages of using a probe beam to facilitate the PA signal measurement, compared to a direct PA measurement. First, the probe-beam technique provides a better signal evaluation from thick samples, due to the difference in the signal attenuation of the two waves. Contrary to a conventional spherical wave-attenuation factor of $(1/r^2)e^{-\alpha \cdot r}$ which governs the PA signal transmission, the signal attenuation of an ultrasonic probe beam is determined by a factor $e^{-\alpha \cdot r}$, where r is the transmission distance and α is the attenuation coefficient. The lack of $1/r^2$ factor in the probe-beam transmission is critically important for thick tissue samples, where large r values often prevent direct measurements of the PA signal. Second, a direct PA measurement records a superimposed signal from a large source volume. With our proposed technique, the probe beam is only modulated by the PA wave within its focal region, due to the narrow probe-beam profile and limited effective range of the PA wave. The spatial resolution, thus, is significantly improved. With proper signal demodulation and reconstruction, this method may provide an *in situ* PA wave imaging technique for thick tissue applications.

II. THEORY

When studying a tissue sample with the PA technique, the excitation light should insert no damages, i.e., vaporization, to the sample, so the PA effect of tissue can be modeled with the thermoelastical theory.[10] Consider a semi-infinite sample, the wave equation of acoustical pressure $p_a(\mathbf{r},t)$ is

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$$\frac{\partial^2 p_a(\mathbf{r},t)}{\partial t^2} - \nu_s^2 \nabla^2 p_a(\mathbf{r},t) = \frac{\beta}{K} \frac{\partial^2 T(\mathbf{r},t)}{\partial t^2}, \tag{1}$$

where ν_s is sound speed, β is the thermal expansion coefficient of tissue, and K is compression coefficient. When the effect of heat conduction can be ignored, i.e., laser pulse interacting with tissue is an adiabatic process, Eq. (1) can be expressed as

$$\frac{\partial^2 p_a(\mathbf{r},t)}{\partial t^2} - \nu_s^2 \nabla^2 p_a(\mathbf{r},t) = \frac{\beta \cdot \nu_s^2}{C} \frac{\partial S(\mathbf{r},t)}{\partial r}, \tag{2}$$

where, C is the heat capacity, $S(\mathbf{r}',t')$ is a generalized heat source, including heat generated by metabolism, eliminated by blood flow, and transferred from absorbed incident light. It is determined by the absorbed energy density distribution and heat diffusion in the course of transient release.

The Green's function solution of Eq. (2) is

$$p_a(\mathbf{r},t) = \frac{\beta}{4\pi C} \int\int\int \frac{\partial S(\mathbf{r}',t')}{\partial t'} \frac{d\mathbf{r}'}{|\mathbf{r}-\mathbf{r}'|}, \tag{3}$$

where $t' = t - |\mathbf{r}-\mathbf{r}'|/\nu_s$. From Eq. (3), we find that the pressure wave or sound wave is generated from temperature fluctuation and volume change of the sample, when a pulse or a modulated light source is used. Because a heat source is related to the absorption and scattering coefficients of a sample tissue, a recorded PA wave, thus, carries the information of both the tissue characterization and the light source.

Consider a probe ultrasound with an acoustic pressure $p_s = A \cdot \sin(\omega t - \mathbf{k}\cdot\mathbf{r})$, where $\mathbf{k}$ is the wave vector and $\omega = k \cdot \nu_s$. Its propagation wave function can be expressed as

$$\frac{\partial^2 p_s(\mathbf{r},t)}{\partial t^2} - \nu_s^2 \nabla^2 p_s(\mathbf{r},t) = 0. \tag{4}$$

In a tissue sample, the acoustic pressure is $p(\mathbf{r},t) = p_a + p_s$. Combining Eqs. (2) and (4), the wave equation of $p(\mathbf{r},t)$ is

$$\frac{\partial^2 p(\mathbf{r},t)}{\partial t^2} - \nu_s^2 \nabla^2 p(\mathbf{r},t) = \frac{\beta \cdot \nu_s^2}{C} \frac{\partial S(\mathbf{r},t)}{\partial r}. \tag{5}$$

Its solution of the equation is in the form of

$$p(\mathbf{r},t) = \frac{\beta}{4\pi C} \int\int\int \frac{\partial S(\mathbf{r}',t')}{\partial t'} \frac{d\mathbf{r}'}{|\mathbf{r}-\mathbf{r}'|} + A \cdot \sin(\omega t - \mathbf{k}\cdot\mathbf{r}). \tag{6}$$

The sound pressure is a function of position and time. The position of the sound source can be derived by calculating the time delay of when an acoustic pressure was recorded by the detector. In general, it would be difficult to obtain an analytical solution of Eqs. (3) or (6).

In the special case of a uniform absorption in the sample and with short laser pulses, the PA pressure on the beam axis can be expressed in the following terms:[11]

$$p_a(t) = \frac{\mu_a \beta F_0 \nu_s^2}{2C} \cdot \frac{\exp(\omega_{ac} t)}{1+D}, \quad t<0,$$

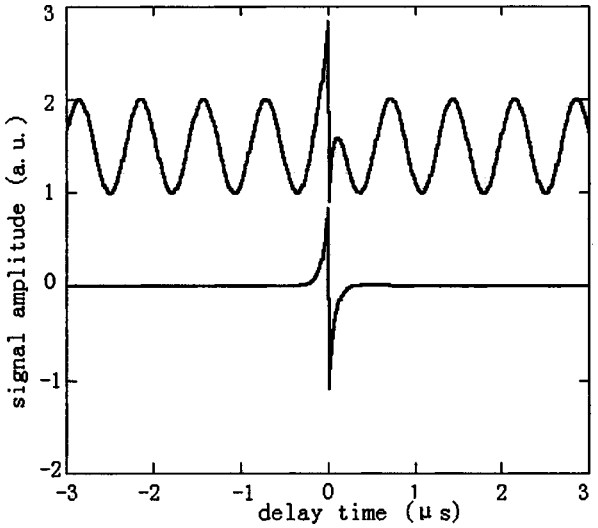

FIG. 1. Computed PA signals and their modulated signals for a short pulse laser incident to dye solution. $\omega_{ac} = 15$ MHz, $\omega_D = 1.5$ MHz, $D = 0.1$, and $\omega = 2\pi \times 1.4$ MHz.

$$p_a(t) = \frac{\mu_a \beta F_0 \nu_s^2}{2C} \left(\frac{\exp(-\omega_{ac} t)}{D-1} - \frac{2D^2 \exp(-\omega_D t)}{D^2-1} \right), \quad t>0. \tag{7}$$

When $t=0$, $p_a(0_-) = \mu_a \beta F_0 \nu_s^2/2C \cdot 1/1+D$, $p_a(0_+) = \mu_a \beta F_0 \nu_s^2/2C\,[1/(D-1) - 2D^2/(D^2-1)]$, it is the onset of a delta-shaped laser pulse, where $\omega_{ac} = \mu_a \cdot \nu_s$ is the characteristic frequency of the PA signal spectrum for the short laser pulse, μ_a is the light absorption coefficient of media, $\omega_D = 2\nu_s z/a_0^2$ is the characteristic diffraction frequency, a_0 is the laser beam radius, z is the distance from laser incident plane to measuring point along incident laser direction, $D = \omega_D/\omega_{ac} = 2z/\mu_a \cdot a_0^2$, F_0 is the incident fluence of the laser pulse, and t is the delay time. Formula (7) is obtained under an assumption of a free boundary, $z=0$, of the light-absorbing medium. So, the modulated wave can be expressed as

$$p(z,t) = p_a(t) + A \cdot \sin(\omega t - k \cdot z). \tag{8}$$

Both PA and modulated signals of a dye solution have been computed with formulas (7) and (8). The theoretically projected wave forms are shown as Fig. 1.

III. MATERIALS AND METHODS

To confirm our theory, the calculated wave forms are tested with an experimental setup for both water-dye solution and biological tissue samples. In the experiments, probe ultrasound waves were measured with and without the excitation laser, therefore, resulting in a corresponding modulated wave and its control wave form. The fast Fourier transform spectra of the two waves were compared and the PA waves restored by inverse transformation of the difference. Because the two waves were recorded under the same condition, except for the laser, the random system noise was reduced after the signals were processed. The process not only demodu-

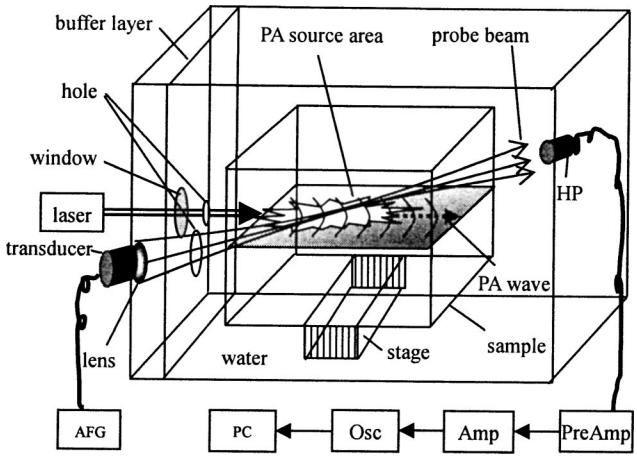

FIG. 2. A schematic diagram of experimental setup (oscilloscope, broadband amplifier, preamplifier, arbitrary function generator and HP).

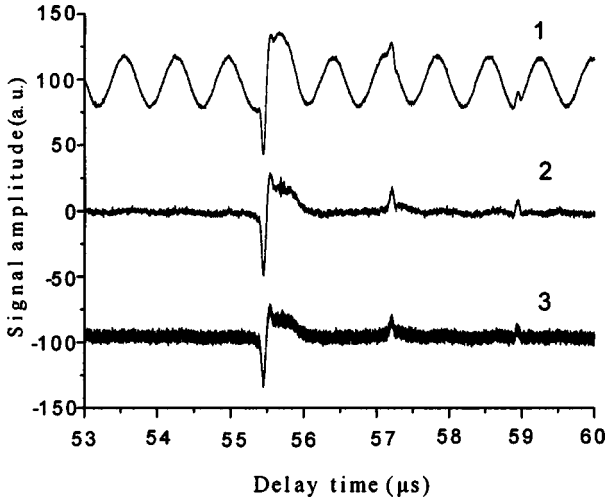

FIG. 3. Wave forms recorded in a sample solution (water with 1% Trypan blue dye): 1—modulated probe wave, 2—discriminated PA wave, and 3—directly measured PA wave.

lates the PA signal from the probe ultrasound wave, but also provides the information of transmission attenuation of the PA waves. The latter could be estimated from the changes in the amplitude of the probe wave.

The experimental setup is shown in Fig. 2. A chamber was custom built with methyl-methacrylate plates with ultrasound and light absorption coating. A quartz window, on one side of the container, allowed the excitation laser beam to enter and project on the sample cell. To reduce the PA signal produced by the interaction between the laser beam and the quartz window, which was interference to the experiment, there was a 50 mm water-filled buffer zone between the optical window and the sample. The entire chamber was filled with water. To simplify the experimental setup in the preliminary investigation, our apparatus had position-fixed laser and ultrasound sources. A computer-controlled three-dimensional position translation stage was used to for tissue sample scanning.

A. Ultrasound source

A signal generator (AFG320, Tektronix) was used to produce a 1.4 MHz sinusoidal wave to drive an ultrasonic transducer at its resonance frequency. To focus the ultrasonic wave onto the sample, an ultrasonic lens was positioned at the output of the transducer. The focal zone of the ultrasonic wave was approximately 20 mm in length and 1.5 mm in diameter, as measured with a sonoluminescence method described earlier.[12]

B. Excitation laser source

A *Q*-modulated, frequency-doubling YAG laser was used as the radiation source. The system outputs a 532 nm laser with 7 ns pulse width. The choice of the 532 nm wavelength was that it had less attenuation due to water absorption, compared to that at 1064 nm. There was a 15° angle between the axes of the laser beam and the ultrasonic probe beam, which allowed the two to effectively interact as described next.

C. Signal detection

The PA signal generated by the incident laser superposed with the probe ultrasonic beam within its focal zone. This resulted in a modulated wave that could be received by a hydrophone [(HP) Precision Acoustics Ltd.]. The HP, with 1 mm diameter detector size, had 950 nV/Pa resolution. The output signal of the HP was amplified with a broadband amplifier and transmitted to an oscilloscope (TDS3032, Tektronix). The signal was then digitized and processed with a personal computer for data analysis. Due to the nature of the HP, it was very sensitive to the direction of the probe wave. Thus, the apparatus could discriminate the wave signals propagating at other directions.

IV. RESULTS AND DISCUSSIONS

Two types of samples, a water mixed with Trypan blue dye (1%, Sigma, T-6146) and a porcine muscle ($50\times50\times40\ \mathrm{mm}^3$), were studied to test the feasibility of the setup. Figure 3 is a representative result from the water-Trypan blue sample. Three recordings are shown in Fig. 3 (top: modulated wave, which is the probe beam profile modulated by the laser generated PA wave; middle: discriminated PA wave, which is obtained after demodulating the probe beam from the signal; and bottom: direct recording of PA wave without using the probe beam, which resulted in a signal identical to that utilizing an ultrasonic probe beam in profile, but a much less SNR ratio. By analyzing the data, we found that the SNR of the discriminated PA waves from the probe beam is 24 dB, compared to 16 dB from the direct PA measurement.

Figure 4 shows the wave forms collected from the porcine muscular sample. The discriminated, original modulated, and directly measured PA waves are shown for comparison to the wave forms. As predicted, by using a probe ultrasonic beam, we obtained a much improved SNR of 20 dB from the discriminated PA wave, compared to 8 dB from the direct PA measurement. It was found that the PA waves produced with a short laser pulse have a bipolar profile. One possible explanation for the phenomena was the thermal ex-

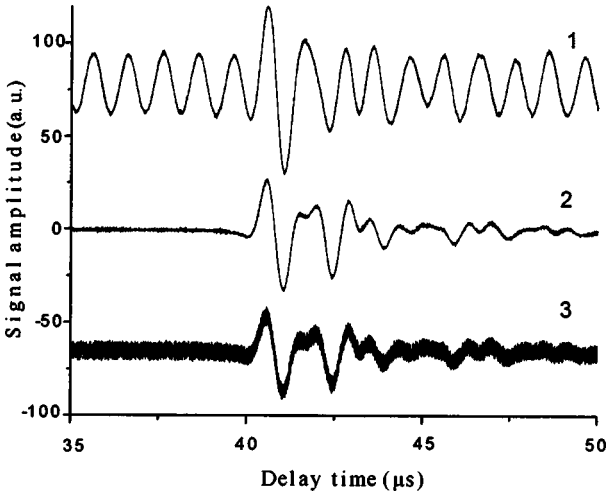

FIG. 4. Wave forms recorded from a porcine muscular sample: 1—modulated wave, 2—discriminated PA wave, and 3—direct measured PA wave.

pansion and contraction of the sample during and after, absorption of the optical energy.[13] The speculation was supported by the observation that, the width of the PA signals depended on the laser pulse width, the optical absorption coefficient of the sample, and the time it took for the sound wave to pass through the sample bulk. In comparison to that from the water-Trypan blue sample, the wave form detected from the porcine sample was more complicated due to the multilayer structure of the sample. The PA signals from different layers were easily distinguished.

Consider the frequency of the ultrasonic probe beam, which is within the range of typical medical applications, the conventional ultrasonic data could be easily incorporated into this method. For example, in the scanning measurement of the PA image, the signal processing must include corrections for PA wave attenuation in the tissue. Attenuation of the detecting wave can be used as a reference. The process can be realized by comparing the amplitude difference of the probe ultrasound before entering and upon exiting the sample.

V. CONCLUSION

We have theoretically proposed and experimentally tested a method for measuring PA waves produced by a 532 nm pulse laser. A focused probe ultrasonic beam passes through a sample and tags the position of the interested PA signal. The PA signal interacts with the probe beam within its focal zone, and results in a modulated wave carrying the PA effect information. By discriminating the modulated wave, we can effectively separate the PA signal originated from the probe-beam focal zone. The attenuation of the PA signal in transmission can be decided by measuring the amplitude difference of the probe ultrasound in front of and behind the sample. The approach, as predicted theoretically and confirmed experimentally in both liquid and biological tissue samples, can simplify the process of tomographic image reconstruction, and at the same time, improve the SNR compared to that of a direct PA measurement. If a high-frequency ultrasonic fine beam is used as the detecting wave, then the spatial resolution can be further improved. We project that, with this method, the vascular or tumor image can be obtained with the appropriate laser wavelength.

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