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Measurement of the surface effect of a small scattering object in a highly scattering medium by use of diffuse photon-pairs density wave

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Abstract. The surface effect close to the boundary of a small light-scattering object in a highly scattering medium is experimentally demonstrated. This is the first attempt to measure the surface effect of a small spherical scattering object in 1% intralipid solution by use of developed diffuse photon-pairs density wave (DPPDW) in terms of the amplitude and phase detection. Theoretically, the surface effect of a small scattering object in turbid media is localized close to the boundary according to the perturbation theory, concerning an inhomogeneous distribution of the diffusion coefficient in the frequency-domain diffusion equation. Hence, an improvement of the spatial resolution of the image via an inverse algorithm, which relates to detection sensitivity of localization to the boundary of the image object in a multiple scattering medium, is anticipated. In this study, we demonstrate that DPPDW is able to sense the surface effect of a 2-mm spherical scattering object in 1% intralipid solution, with high sensitivity. Subsequently, an improvement of spatial resolution of imaging in turbid media by using DPPDW in comparison with conventional diffuse photon density wave (DPDW) using inverse algorithm is discussed. © 2016 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JBO.21.6.060504]

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In past decades, diffuse optical imaging (DOI) has been an emerging imaging modality, probing biological tissue by using near-infrared spectroscopy (NIRS), which shows the abilities of noninvasive detection at high temporal resolution as well as molecular function imaging with high specificity and sensitivity in human tissue.^{1–3} However, to focus on imaging, most biological tissues are highly scattering and, therefore, the

incident photons are quickly diffused before being absorbed or detected. Therefore, imaging by using NIR light becomes necessary because of its greater transparency in human tissue compared with the visible light.¹ Experimentally, measuring amplitude and phase of diffuse photon density wave (DPDW) can recover the image object in a multiple scattering medium via the distribution of position-dependent absorption and reduced scattering coefficients. However, this is based on the simplified diffusion equation, where a position-independent diffusion coefficient is assumed.^{4–6} The constant diffusion coefficient in the diffusion equation enables smoothing out the boundary or surface effect of a small object via an inverse algorithm in the recovery image. In addition, DPDW is generated in the scattering media by using a high-frequency intensity-modulation light source that produces high-level radio frequency (RF) intensity noise in the detected intensity-modulation signal. Then, lower spatial resolution in the recovery image results apparently.^{4–7} In order to improve the spatial resolution of the image, the boundary or surface effect of a small scattering object in a multiple scattering medium becomes critical according to the perturbation theory derived by Ostermeyer and Jacques.^{4,5} Consequently, the properties of the signal induced by the boundaries of scattering objects in multiple scattering media are examined in this study.

Boas et al.⁶ derived the perturbation theory of scattered DPDW by a spherical inhomogeneity in turbid media, where a time-dependent solution of the Helmholtz equation was achieved by using a sinusoidally intensity-modulated point source in a multiple scattering medium under the condition of uniform distribution of diffusion coefficient.^{6–8} The amplitude and phase of the scattered DPDW induced by a spherical inhomogeneity were analytically calculated and experimentally verified.^{6–9} In contrast, Ostermeyer and Jacques⁴ derived an analytical model of solving the diffusion equation of inhomogeneous diffusion coefficient using perturbation theory. When only sharply bounded inhomogeneity with constant optical properties inside is considered, the fluence perturbation ϕ^{Pert} induced by an object in scattering media can be divided into two parts: (1) the surface effect and (2) the volume effect. For the absorber, the contribution from the surface effect is less important than for the scattering effect and vice versa for the scatter in scattering media.⁴ Meanwhile, in the case of a small object by the surface-to-volume ratio, $\text{SVR} > 1 \text{ mm}^{-1}$, the surface effect becomes dominant in perturbation theory, and then ϕ^{Pert} approaches a dipole field. Clinically, the tumor as an image object in tissue generally presents a sharper boundary than a normal cell at early stage.^{1,10,11} Meanwhile, the refractive index mismatch introduces scattering effect at the boundary, which enhances the surface effect. The surface effect relating to the boundary of the small object dominates the spatial resolution of the recovered image, whereas the volume effect smoothes out of the structure image by volume integration.⁴ As a result, the capability of detecting the surface effect from a small object via the amplitude and phase change detection of diffuse photon-pair density wave (DPPDW) has the potential to increase the resolution of the inverse problem not only by direct detection of the surface effect by a small object but also the higher detection sensitivity of the heterodyne signal versus the polarization gating and coherence gating of scattered linear-polarized photon pairs (LPPP).^{12–14}

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However, there has been no experimental demonstration of the surface effect of a small object in a multiple scattering medium, being made possible by means of the conventional DPDW method. One of the reasons is due to the large amount of RF noise generated by a high-frequency intensity modulation of the light source being required in the DPDW setup. As a result, the sensitivities as well as the spatial resolution of the amplitude and phase measurements of the scattered DPDW close to the boundary of the object are limited in the experiment. In our previous studies, the properties of DPPDW in turbid media have been studied.^{12–17} This is based on the features of two-frequency linear-polarized highly correlated photon-pairs laser beam propagating in turbid media via the coherence and polarization gatings, simultaneously, and the heterodyne synchronized detection.^{12–17} Theoretically, the surface effect, which is induced by the boundary of a small scattering object following a dipole-like perturbation,⁴ is anticipated both in amplitude and phase of scattered DPPDW. They are localized close to the boundaries of the image object because DPPDW satisfies the diffusion equation.^{12–14} In this experiment, we measured the surface effect of a 2-mm (in diameter) spherical scatterer in 1% intralipid solution. The experimental result agrees well with the theoretical calculations following the perturbation theory derived by Ostermeyer and Jacques. According to our developed theory, DPPDW provides a coherent detection of photon density wave, which is produced by the collection of the scattered LPPP in a highly scattering medium. LPPP comprises a pair of linearly parallel-polarized light waves with high-spatial and -temporal coherence. The pair of photons also presents a slight difference in temporal frequency derived from a two-frequency laser. Generally, LPPP can be detected via the heterodyne interference signal between the pair of linear-polarized waves and is expressed as

$$I_{AC} = |A_1 e^{-i\omega_1 t} + A_2 e^{-i\omega_2 t + \phi}|_{AC}^2 \cong 2\gamma A_1 A_2 \cos(\Delta\omega t + \phi), \quad (1)$$

where A_1 and A_2 are the amplitudes of the paired linear-polarized photons with the corresponding frequencies ω_1 and ω_2 , respectively. $\Delta\omega = \omega_1 - \omega_2$ is the beat frequency of the two waves, and $\phi = \Delta\omega l/v$ is the path-dependence phase difference between the pair of linear-polarized photons, where l is the optical path length and v is the light speed in the medium. The term γ represents the heterodyne efficiency. As the detection signal of LPPP depends on the amplitude modulation, this ensures the features of high signal-to-noise ratio (SNR), narrower detection bandwidth, and wider dynamic range compared to the intensity modulation adapted by DPDW in the conventional frequency-domain diffusion method. According to the theory of DPPDW, the propagation of LPPP in a highly scattering medium satisfies the diffusion equation. Thus, in a homogeneous and infinite highly scattering medium, DPPDW is written as^{12–14}

$$\Phi_{AC}^{homo} = \gamma A_1 A_2 \frac{v e^{-k_{2r} r}}{2\pi r D} \cos(\Delta\omega t - k_{2i} r), \quad (2)$$

where r is the distance between the emitter and the receiver. k_{2r} and k_{2i} are the real part and the imaginary part of the wave number of DPPDW, respectively, and are expressed by

$$k_{2r} = [3\mu_{2a}(\mu'_{2s} + \mu_{2a})]^{1/2} \quad (3)$$

and

$$k_{2i} = \frac{\Delta\omega}{c} \left(\frac{3\mu'_{2s}}{4\mu_{2a}} \right)^{1/2}, \quad (4)$$

where μ_{2a} and μ'_{2s} are the absorption coefficient and the reduced scattering coefficient of the scattering medium, respectively. The phase velocity of the DPPDW is expressed by

$$V_{2p} = \frac{\Delta\omega}{k_{2i}} = \frac{c}{n} \left(\frac{4\mu_{2a}}{3\mu'_{2s}} \right)^{1/2}. \quad (5)$$

Equations (2)–(5) represent the optical properties of DPPDW with paired highly correlated and polarized photons. Compared with the DPDW, the imaginary part of the complex wavenumber of the DPPDW (k_{2i}) is linearly proportional to the beat frequency $\Delta\omega$ and the real part of the complex wavenumber (k_{2r}) is independent of $\Delta\omega$. However, the real part and the imaginary part of the wavenumber of the DPDW, k_r and k_i are both proportional to the square root of the intensity-modulated frequency ($\sqrt{\omega}$) in the high-frequency regime.⁸ The phase velocity of the DPPDW is similar to that of a DPDW at a lower modulation frequency, whereas the phase velocity of the DPPDW is different from that of a DPDW at a higher modulation frequency (ω), where the phase velocity of DPDW depends on $\sqrt{\omega}$.

In a highly scattering medium, however, the image quality depends on the degree of coherence and degree of polarization of scattered LPPP. This means that the detection of scattered LPPPs in the scattering medium is filtered by the coherence gating, the polarization gating, and, finally, the electronic filter gating via a lock-in amplifier.^{12–17} Those features are introduced by the coherence and polarization properties of DPPDW via heterodyning. In order to verify the ability to detect the surface effect of a small object, the amplitude and phase responses of DPPDW close to the boundary of the scatterer were measured. Meanwhile, to validate the experimental results, the amplitude and phase responses of the surface effect by DPPDW are calculated by adapting the complex Green's function of DPPDW into the perturbation theory.⁴

Figure 1 shows the experimental setup wherein a two-frequency laser (ZMI 7702 laser head, Zygo) was used, which provides the LPPP laser beam by use of an analyzer at azimuth angle of 45 deg to the x -axis located in front of the laser. LPPP requires a pair of parallel linearly polarized light waves with a slight difference (20 MHz) in temporal frequency.

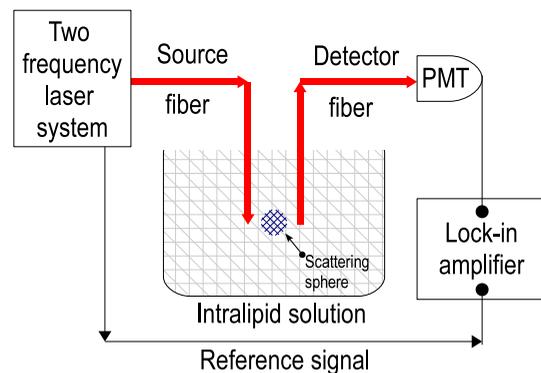


Fig. 1 The experimental setup of amplitude and phase detection of DPPDW for the measurement of the surface effect of a scattering sphere in a highly scattering medium.

The output power and center wavelength of this laser beam are 0.6 mW and 632.8 nm, respectively. A 30-cm × 30-cm × 20-cm water tank filled with 1% intralipid solution was taken as an infinite and homogeneous multiple scattering medium. This gave a reduced scattering coefficient $\mu'_{2s} \sim 14 \text{ cm}^{-1}$ and an absorption coefficient $\mu_{2a} \sim 0.01 \text{ cm}^{-1}$. The laser beam is delivered into the scattering medium through a source fiber, whereas the fluence of scattered LPPs is collected by a movable detector fiber and detected by a photomultiplier tube. Finally, the amplitude and phase signals of DPPDW are measured simultaneously by use of a lock-in amplifier. In this experiment, a scattering sphere with a 2-mm diameter was made with optical properties $\mu'_{2s} \sim 28 \text{ cm}^{-1}$ and $\mu_{2a} \sim 0.01 \text{ cm}^{-1}$ from a polyester resin mixture containing 3.5-mg TiO_2 powder (scatters) for every 1 ml of polyester resin.¹⁸ There is no extra absorption dye in the resin mixture. The scattering order of the scatterer to the background medium by $\log(\mu'_{2s,\text{sphere}}/\mu'_{2s,\text{medium}})$ was 0.3. The geometry of measurement is shown in Fig. 2, where the source fiber was fixed at $x = -32 \text{ mm}$, and the sphere was fixed at $x = 0 \text{ mm}$ in the tank. For the detection of surface effect, the total complex fluence (i.e., amplitude and phase) of DPPDW (Φ) was measured as a function of the position of the detector fiber, which was scanned from $x = -12$ to $x = 6 \text{ mm}$ at 1-mm intervals. The moving step was adjusted to 0.5 mm when the detector fiber was moving close to the scattered sphere to ensure that the surface effect was measured properly. In addition, the homogeneous complex fluence (Φ^{homo}) was also measured under the same arrangement without the scattering sphere. Thus, the perturbation complex fluence Φ^{pert} or the surface effect can be obtained by subtracting Φ^{homo} from Φ . Note that the size of the sphere is small enough that it satisfies the condition of surface-to-volume ratio $> 1 \text{ mm}^{-1}$. Then, Φ^{pert} is dominated by the surface effect and the volume effect is ignored.

Figure 3 shows the experimental results (dots) of (a) the amplitude and (b) the phase response of the surface effect measured by DPPDW. Both results are compared to the theoretical calculation (solid curves) according to the perturbation theory.⁴ In this theoretical calculation, μ'_{2s} and μ_{2a} of this scattering sphere (2 mm in diameter) are 28 and 0.01 cm^{-1} , respectively; μ'_{2s} and μ_{2a} of the turbid medium are 14 and 0.01 cm^{-1} , respectively. In Fig. 3(a), the amplitude response was normalized by

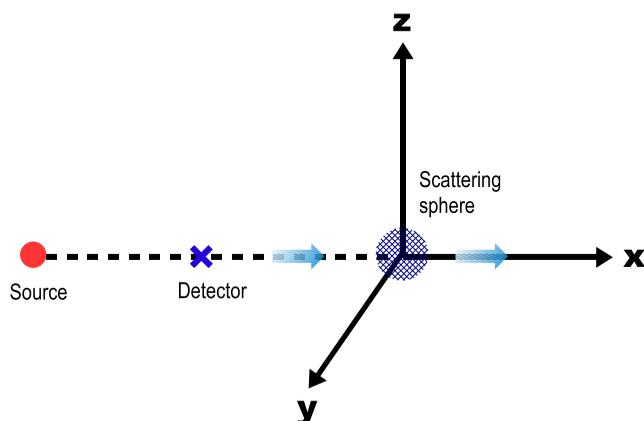


Fig. 2 Schematic geometry of surface effect measurement for a scattering sphere in a multiple scattering medium. The source fiber was fixed at $x = -32 \text{ mm}$ and the sphere was fixed at $x = 0 \text{ mm}$ in the tank. The detector fiber was scanned along x -axis to collect the total complex fluence of DPPDW.

Φ^{homo} and the surface effect, which produces a rapid change close to the boundary of the scattering object, is seen clearly. This result shows a dipole-like perturbation whereas the magnitude is positive at the front surface ($x < 0$) and then becomes negative at the rear surface ($x > 0$) of the scattered sphere. Note that the dipole-like perturbation is asymmetric and the magnitude of the positive peak is larger than that of the negative one. These results agree well with prediction from perturbation theory ($R^2 = 0.958$), where the volume effect is ignored. The phase signal of DPPDW is also shown in Fig. 3(b) and the result is similar to the amplitude response ($R^2 = 0.969$). These results not only show high sensitivity to surface effect detection but also

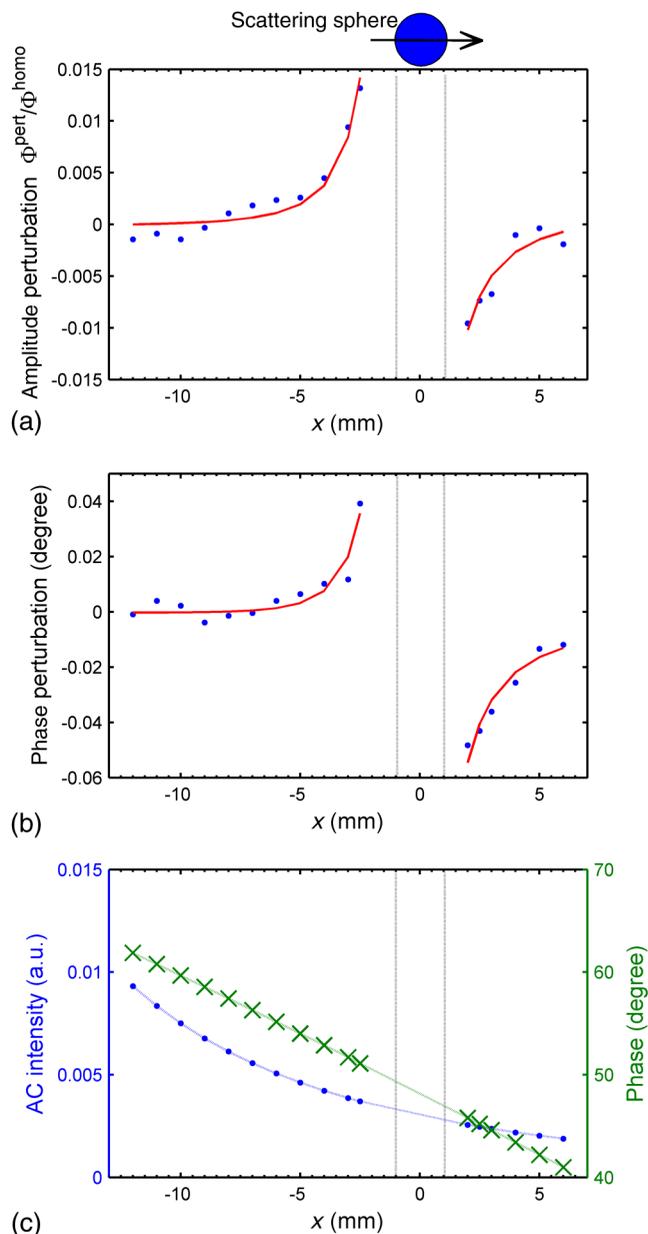


Fig. 3 The surface effect of a 2-mm-in-diameter scattering sphere in (a) amplitude response and (b) phase response measured by the DPPDW method. Both present the dipole-like perturbation with a rapid change close to the scatter boundary. The correlation between measured data with prediction are $R^2 = 0.958$ in (a) and $R^2 = 0.969$ in (b). In homogeneous multiple scattering media, the amplitude and phase responses of DPPDW in setup without scattering object in 1% intralipid solution is shown in (c).

no surface effect mismatch following the prediction of perturbation theory⁴ under a strong surface effect by a small scattering object in turbid media. This also implies a significant improvement on spatial resolution of the image of a small object in turbid media.

From these experimental results, we also validate that the propagation of DPPDW satisfies the diffusion equation in terms of perturbation theory of position-dependent diffusion coefficient near image object in a multiple scattering medium. Meanwhile, using DPPDW, high-detection sensitivity at a relatively low beat frequency (20 MHz) is applicable as well. In this experiment, the surface effect of the 2-mm scatter in 1% intralipid solution are $\sim 1.4\%$ in amplitude perturbation and ~ 0.04 deg in phase perturbation close to the boundary of the scatter.

This, for the first time, shows the surface effect of a small scatter (2 mm in diameter), which leads to rapid changes of polarized photon-pairs fluence both in amplitude and phase at the boundary of the scatter. The perturbation theory of diffusion equation with position-dependent diffusion coefficient in frequency domain has also been verified. It is in contrast to the conventional DPDW method wherein the surface effect is not available due to high levels of RF noise inherent with high-frequency modulation. From this result, DPPDW potentially becomes an approach to improve the spatial resolution of the recovery image in multiple scattering media in comparison with DPDW. These results not only enhance the boundary detection sensitivity of a scatter but also provide the possibility of enhancing the boundary detection sensitivity of an absorber via its phase response. This is because the phase difference of DPPDW close to the boundary of an absorber is $\mu_{2a}^{-3/2}$ dependent. (The phase of DPPDW is proportional to k_{2i} which is $\mu_{2a}^{-1/2}$ dependent, so the sensitivity of phase change across the boundary of an absorber in a multiple scattering medium becomes $\mu_{2a}^{-3/2}$ dependent.) As a result, the localization of surface boundary of an absorber in multiple scattering media can be enhanced at lower μ_{2a} via DPPDW accordingly.

In contrast, the features of coherence and polarization gatings of LPPPs in DPPDW method mean that the common background phase noise is reduced significantly due to the common-path propagation of LPPP in turbid media.^{12–17} This also introduces less dephasing or higher SNR in the detected beat signal that is beneficial to surface effect detection sensitivity. Additionally, the amplitude response via heterodyne interference in DPPDW also increases the dynamic range of detection in contrast to the high-frequency intensity-modulated signal in a conventional DPDW setup. Clinically, these advantages for surface effect detection can become very critical, e.g., to differentiate a benign tumor from a malignant one due to the surface scattering effect being dominant in a malignant tumor.¹⁰ In addition, a nonpolarized photon-pair laser beam can be used in the DPPDW method, in which highly spatial and temporal correlated but nonpolarized photon pairs propagate in a scattering medium. The advantage of using nonpolarized photon pairs is that DPPDW becomes insensitive to birefringent properties of the scattering medium. However, using a linear-polarized photon-pairs laser beam could introduce polarized image contrast and maybe further improve the quality of recovered images.

In conclusion, the capability of measuring the surface effect of a small scattering object in a multiple scattering medium via DPPDW has been experimentally verified. As the surface effect presents a sharply dipole-like amplitude and phase change of

DPPDW near the boundary of a small scattering object in turbid media, it becomes highly sensitive to the shape and orientation of the image object. Therefore, we can anticipate the ability to localize the boundary of scattering objects in turbid media via the surface effect that is potentially able to improve the spatial resolution in the recovered image. With regards to an absorber in turbid media, the phase response of DPPDW can also be used to enhance the boundary detection sensitivity of an absorber due to $\mu_{2a}^{-3/2}$ dependence in the phase response, particularly for the image object with lower μ_{2a} . Furthermore, polarized or nonpolarized photon pairs can be used as a light source in the DPPDW method.

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