We present measurements of photon time-of-flight distributions for a 9-ps, 532-nm laser pulse traveling through Intralipid suspensions and compare the measurements with the results of Monte Carlo simulations that yield the corresponding temporal point-spread function. We show that to obtain satisfactory agreement of experiments and simulation results, one must assume a quadratic dependence of the scattering coefficient on the Intralipid concentration. © 2003 Optical Society of America

1. INTRODUCTION

Knowledge of the optical behavior of highly scattering media is important for many applications, with a special role played by imaging of opaque and translucent objects immersed in these media. Within this framework, although many experimental techniques have been used to detect the light emerging from a turbid sample containing an object,1 not all of them are suitable to provide information on the object and its surrounding medium. This is particularly true when the medium is highly turbid and the wave properties of the impinging light are almost completely lost. In principle, measurements of time-of-flight (TOF) distributions of photons emerging from a diffusing sample, if they are made with suitably high temporal resolution, allow the behavior both of the early-arriving photons (which bear the coherent information on the object hidden in the medium) and of the diffuse late-arriving ones, which give information on the scattering medium itself, to be recovered. From a theoretical point of view, Monte Carlo modeling of the light transport in a highly turbid medium is being increasingly used to construct the temporal point-spread function (TPSF), i.e., the response of the medium to a delta-like input. Although Monte Carlo modeling is still time consuming with the present computing technology, it provides the only acceptable choice where other models break down, for instance, when data are required close to the sample boundaries. Moreover, it can deal with arbitrarily complex geometries of the samples and can even take account of the detector geometry (e.g., pixel size and location of the CCD sensor, shape and size of the effective sensitive area of the detector). For these reasons, a reliable Monte Carlo method represents a powerful tool for dealing with nontrivial experimental situations.

In the present study we compare the TPSF for a pulse traveling through different samples of Intralipid suspension in water, obtained with a parallel Monte Carlo code, with the TOF distributions of photons measured with a single-photon avalanche photodiode (SPAD). The aims of the study are to test the reliability of the simulation code and to adjust the experimental parameters such that the code will be applicable to more-difficult and -interesting...
2. MATERIALS AND METHODS

A. Experimental Setup

We made TOF measurements of the photons emerging from a glass cuvette (1-cm optical path; 5 cm × 5 cm transverse area; 2.5-mm window thickness; from Hellma GmbH, Müllheim, Germany) filled with mixtures of Intralipid 10% (Fresenius Kabi AB, Stockholm, Sweden) at several dilutions in doubly distilled water, on irradiation at 532 nm. In our setup, sketched in Fig. 1, the light source was a semiconductor saturable-absorber mirror mode-locked diode-pumped Nd:vanadate laser (Model GE-100-1064-VAN, Time-Bandwidth Products GmbH, Zürich, Switzerland), emitting 9-ps pulses at the fundamental wavelength (1064 nm) at a repetition rate of ~100 MHz. The laser has a built-in module for second-harmonic generation composed of a 5-mm-long KDP crystal followed by a filter to cut most of the residual fundamental in the frequency-doubled output. To further select the photons at 532 nm we inserted a prism in the beam path, followed by an iris to eliminate stray light. When needed, neutral-density filters were inserted between the iris and the sample. During all the measurements, the beam, with a TEM$_{00}$ profile, was directed at the sample. In our procedure, several batches of intralipid 10% (Fresenius Kabi AB, Stockholm, Sweden) at various dilutions in doubly distilled water, on irradiation at 532 nm.

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B. Monte Carlo Simulations

The computation of photon transport inside the scattering medium was performed by means of a parallel Monte Carlo code developed by some of us. The parallel structure was adopted to decrease the long computation time necessary for obtaining statistically significant simulations of our measured TOF distributions, which were recorded with high time and angular resolution and for highly turbid samples. This code, originally written to run on the parallel computer Cray T3E at the Centro di Calcolo Interuniversitario dell’Italia Nord-Orientale, was adapted to the Cluster Beowulf computer operating at the same location. Details of the parallel structure as well as of the operation of the Cray T3E version of the code can be found in Ref. 6. Hereafter we only briefly recall its main features: the photons impinge, at normal incidence, at the same point and at the same time on the sample, which consists of an infinite plane-parallel slab (of thickness z) characterized by known optical parameters (i.e., refractive index, $n$; absorption coefficient, $\mu_a$; scattering coefficient, $\mu_s$; and anisotropy coefficient, g). Then the photons are allowed to propagate stochastically inside the medium and according to the Henyey–Greenstein formula for the average scattering cosine. We score reflected and transmitted photons to compute the reflectance and the transmittance of the sample as a function of the transverse positions on the slab boundaries and of the angle and of the time of emergence from the entrance–output surfaces. Similarly, we score absorbed photons to compute the fractional energy absorbed at each point inside the sample. In our procedure, several batches of  even a single photon can trigger a macroscopic avalanche current pulse, which can be easily detected by the following electronics, precisely marking the photon’s arrival time. The reference laser signal was instead provided by a p–i–n photodiode. These signals were then sent into a time-to-amplitude converter (Model 2145, Canberra, Inc., Meriden, Conn.) operated in reverse mode and into a PC-based multichannel analyzer. The SPAD used in the experiments, described by Lacaita et al.,3 has an epitaxial device structure with a shallow p–n junction, and it basically determines the achievable time resolution of our setup. The pulse response exhibits a fast peak with ~47 ps FWHM (owing to photons absorbed in the junction) and a much lower exponential tail with a time constant of 270 ps (owing to diffusion of photogenerated carriers in the quasi-neutral p layer that underlies the junction). It must be pointed out that neither the device’s design nor the operating bias conditions were optimized for minimum time resolution. Rather, we used the minimum bias that provided sufficient resolution to minimize the dark-count rate, which in our case was reduced to ~100 counts/s. In fact, a low dark-count rate is a primary requirement produce a reliable result for the highest concentration samples, for which only a few thousand photons per second reach the SPAD. The SPAD’s timing performance is more than sufficient for this application, as we shall see in what follows. If needed, SPADs with improved performance, with respect to both the FWHM and the diffusion tail, are readily available.5,5 The active area of our device was ~10 $\mu$m in diameter.
photons were launched and an estimate of the variance of the results was built after each of them by use of the cumulative computed space profile of the transmittance. When this quantity achieved a value lower than a predetermined one, the program stopped, and no further photon batch was launched. The outputs for all batches were averaged in multidimensional matrices that were downloaded to a PC, where they were elaborated off line by software developed for this purpose. For the simulations in the present paper, which require high time and angular resolution, we launched batches of $5 \times 10^7$ photons. The elaboration stops as soon the relative variance falls below $10^{-2}$. We chose the simulation parameters to mimic the experimental situation, and thus we set the thickness of the sample to $z = 1\, \text{cm}$. As for scattering coefficient $\mu_s$, anisotropy factor $g$, and the refractive index of our commercial sample of Intralipid 10% we took the values quoted in the literature, namely, $g = 0.85$, $\mu_s = 521\, \text{cm}^{-1}$, and $n = 1.40$. As for absorption coefficient $\mu_a$, based on the determinations reported by Jacques, we decided to adopt a value of 0.01 cm$^{-1}$ for Intralipid 10% rather than to assume that $\mu_a = 0$, as has been done in most papers in which TOF measurements or simulations were reported at Intralipid concentration values lower than given here (see, for instance, Nishimura and Kuga). The $\mu_s$ and $\mu_a$ values to be used for the simulations were then simply scaled for the concentration values, whereas both $g$ and $n$ were considered independent of the concentration.

3. RESULTS

We measured TOF distributions for samples with Intralipid weight-to-volume concentrations that varied from 1% to 10% (namely, 1%, 1.5%, 2%, 2.5%, 3.3%, 5%, 8%, and 10%). Figure 2 shows the experimental results for some of the measured concentrations as well as the TOF distribution of the laser pulse through the air. We performed simulations for reduced scattering coefficient val-

\begin{align}
  y = y_0 + A \exp \left( \frac{\ln^2(t/t_c)}{2w^2} \right),
\end{align}

where $A$ represents the peak value, $t_c$ is the abcissa of the peak, and $w$ is a width parameter of the curve. The curves obtained from Eq. (1) do not pretend to be optimal fittings for the two classes of data but provide a neutral means for evaluating features such as peak positions and widths of the TOF and TPSF distributions.

Whereas the TPSF is the transmittance time profile computed for an infinitely short (deltalike) incident-light pulse, the experimentally measured profile depends also on the finite-width instrumental response function that is due to the SPAD resolution (main contribution) and to the laser pulse width (minor contribution). These terms can easily be obtained by direct measurement of the laser pulse, without any turbid medium. A deconvolution operation should then be carried out to correct the experimental data. However, it is simpler and equally correct instead to follow a convolution approach: The computed TPSF profiles can be convoluted with the instrumental response and the result directly compared with the experimental TOF data. Figure 4 shows the TPSFs, normalized to their peaks, after the convolution operation with the laser time profile (the solid, leftmost curve in Fig. 2). Also, these profiles can be well fitted by log normal func-

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig2.png}
\caption{TOF distributions measured for photons at 532 nm (9-ps incident pulses) emerging from a 1-cm optical path cell containing Intralipid suspensions at the indicated concentration values. The solid curve at the extreme left is the instrumental response function directly measured with the laser pulse in free air.}
\end{figure}
tions. Note that, although the convolution operation permits a partial recovery of the time delay between experimental data and simulation results (see Fig. 3), the computed profiles show in any case a shorter decay time than those experimentally observed. We tried to account for this discrepancy by increasing the refractive index of Intralipid in the simulations to the value $n = 1.5$ (Ref. 8) and found both a shift and a broadening of the peak. Nevertheless, this effect was not large enough to explain the decay of the experimental curves. Inasmuch as it seems unrealistic to assume values for $n$ much greater than 1.5, we formulate the hypothesis that the discrepancy can be imputed to an underestimation of the reduced scattering coefficient that we used. We thus decided to collect more data by repeating the experimental measurement for other Intralipid concentrations as well as by running other simulations for other values of $\mu_s'$. To obtain the value of $\mu_s'$ that shows a better fit with experimental data we proceeded as follows:

(a) We fitted the experimental data to log normal curves according to Eq. (1), and we obtained the peak position $t_{\text{exp}}$ and width $w_{\text{exp}}$ for each value of the concentration of Intralipid solutions.

(b) We plotted and then fitted the values of $t_{\text{exp}}$ to the values of experimental Intralipid concentration $C$ (Fig. 5).

(c) We fitted the Monte Carlo transmission profiles to log normal curves, and we obtain the peak $t_{\text{MC}}$ and the width $w_{\text{MC}}$ for each value of the reduced scattering coefficient $\mu_s'$.

(d) We plotted and then fitted the values of $t_{\text{MC}}$ to the values of the reduced scattering coefficient $\mu_s'$ (Fig. 6).

(e) We assumed that $t_{\text{exp}}(C)$ obtained in step (b) is equal to $t_{\text{MC}}(\mu_s')$ obtained in step (d). This equation gives the analytical relationship between Intralipid concentration $C$ and the reduced scattering coefficient $\mu_s'$, which we henceforth call the effective reduced scattering coefficient, $(\mu_s')_{\text{eff}}$ (Fig. 7).
The relationship between $C$ and $(\mu_s')_{\text{eff}}$ turns out to be nonlinear, as is most commonly assumed in the literature, showing a quadratic trend (see the fitting curve superimposed upon the data in Fig. 7). The nonlinear dependence has already been suggested in some previous publications and was recently demonstrated by experiments performed by Zaccanti et al. Those authors studied the behavior of the optical parameters of Intralipid solutions as a function of concentration at $\lambda = 632.8$ nm. By comparing Fig. 6 of Ref. 17 with our Fig. 7 we see that the results are comparable although they were obtained at different wavelengths. Furthermore, a theoretical interpretation of the results in Ref. 17 has been made by Giusto et al., who recovered the nonlinear behavior of the scattering coefficient from the iterative solution of the Foldy–Twersky equation that takes into account all the multiple scattering processes (neglecting cyclic path). The deviation from linear behavior can thus be imputed to the relevance of multiple scattering events at the concentrations under investigations. As our experimental technique does not permit a direct measurement of $\mu_s'$, to validate our approach we have to verify that the dependence $(\mu_s')_{\text{eff}}$ on $C$ that we found leads to an agreement between experimental and simulation values of the width of the peaks of the curves, which in our case represents the only other parameter of the log normal function (because the height of the peak cannot be considered in this study). As the parameter that describes the log normal, we used the FWHM value whose results depend on both $t_s$ and $\varphi$. We plotted FWHM$^{\exp}$, the FWHM of log normal fitting of the experimental TOF data, as a function of the values of $(\mu_s')_{\text{eff}}$ obtained from the experimental values of Intralipid concentration by means of the function $\mu_s'(C)$. Then we compared this dependence with the dependence of the FWHM values obtained from log normal fitting of simulation data FWHM$^{\text{MC}}$ as a function of the simulation code input values of $\mu_s'$. Figure 8 shows that the agreement of these two curves is quite satisfactory.

4. CONCLUSIONS

The results presented in this paper show that our Monte Carlo code is able to simulate the propagation of photons in a turbid medium. The computed transmission time profiles of water suspensions of Intralipid depend on three parameters: the absorption coefficient, the reduced scattering coefficient, and the refractive index of the sample. Whereas the first quantity affects mostly the height, the other ones affect sensibly the position of the peak and the width of the transmission profile, which can be fitted in an accurate way by a log normal curve. In this study, in which the number of photons impinging upon the sample has been not measured, we consider only experimental transmittance curves normalized to their peak values. By disregarding the height of the peak, one can draw no inference about the dependence of the absorption coefficient on Intralipid concentration. However, we took the minor effect of this quantity on the position and the width of the peak into account by using, for Monte Carlo simulations, an absorption coefficient linearly scaled with the concentration, according to the literature and to the recent measurements of Zaccanti et al.

The influence of the reduced scattering coefficient and of the refractive index of the medium on the two remaining best-fit parameters, the peak position and the width, is the same: Indeed, when either of them is increased, the position of the peak shifts toward longer times and the width increases. From the comparison with experimental transmission time profiles, which also can be fitted with log normal dependence, it is evident that simulation curves have a peak at shorter time and a smaller width than do experimental data. This discrepancy cannot be explained either by the fact that the laser pulse has a finite time width or by a too-low value of the refractive index for the input data of simulations. We suggest that it can be explained only by a too-low value of the reduced scattering coefficient $\mu_s'$ with respect to the value usually quoted in the literature, owing to nonlinear behavior at concentrations of Intralipid in the range 1–10%. We thus conclude that the dependence of $\mu_s'$ on the concentration of the scattering sample must be nonlinear and approximates a quadratic behavior from 1% to 10%, as shown in Fig. 7. This hypothesis is supported by recent results, both experimental and theoretical.

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M. Bondani’s e-mail address is maria.bondani@uninsubria.it.

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