

# Influence of the phase function on determination of the optical properties of biological tissue by spatially resolved reflectance

Alwin Kienle, Florian K. Forster, and Raimund Hibst

*Institut für Lasertechnologien in der Medizin und Messtechnik, Helmholtzstrasse 12, D-89081 Ulm, Germany*

Received May 10, 2001

Spatially resolved reflectance measurements are widely used for determination of the optical properties of biological media. However, the influence of the phase function on these measurements has not been quantified. We show that errors in the derived reduced scattering and absorption coefficients are as great as 100% for both absolute and relative spatially resolved reflectance measurements if a standard solution of the diffusion equation is used in the analysis. In addition, we investigated nonlinear regressions, using Monte Carlo simulations and an additional fitting parameter that characterizes the phase function, and found that the errors in the obtained optical coefficients were  $\leq 20\%$ . © 2001 Optical Society of America

OCIS codes: 170.0170, 170.3660, 170.7050, 250.4210.

Knowledge of the optical properties of biological tissue is a prerequisite for many diagnostic and therapeutic applications of light in medicine. A standard method for determination of the optical properties is the measurement of the relative<sup>1–3</sup> and absolute<sup>4–7</sup> spatially resolved reflectance from tissue,  $R(\rho)$ . In this technique a narrow beam of light is directed onto the tissue, and diffusely reflected light is collected at several distances  $\rho$  from the entry point on the surface. Usually a solution of the diffusion equation  $R_{\text{Diff}}(\rho)$  is used to derive the reduced scattering ( $\mu_s'$ ) and the absorption ( $\mu_a$ ) coefficients. The diffusion equation is an approximation of the transport equation for description of the propagation of light in tissue and does not account for the specific form of the scattering function [phase function  $p(\theta)$ , where  $\theta$  is the scattering angle]. It has been shown that  $R_{\text{Diff}}(\rho)$  is close to  $R(\rho)$  obtained from the transport equation or equivalently with Monte Carlo simulations,  $R_{\text{MC}}(\rho)$ , if the often used Henyey–Greenstein phase function is applied in the simulations.<sup>8</sup> However, for other phase functions and for  $\rho < 10/\mu_s'$  the differences between  $R_{\text{Diff}}(\rho)$  and  $R_{\text{MC}}(\rho)$  may be substantial.<sup>9–11</sup> Recently, Bevilacqua and Depeursinge introduced a parameter  $\gamma = (1 - g_2)/(1 - g_1)$  that depends on the first and second (Legendre) moments of  $p(\theta)$ ,  $g_1$  and  $g_2$ , and showed that  $R(\rho)$  can be approximately described by  $\mu_s'$ ,  $\mu_a$ , and  $\gamma$ .<sup>11</sup>

In this study we applied Monte Carlo simulations to calculate the spatially resolved reflectance by using different phase functions. These reflectance curves served as experimental data; first, we fitted them with  $R_{\text{Diff}}(\rho)$ , using  $\mu_s'$  and  $\mu_a$  as fitting parameters. Second, we applied Monte Carlo simulations to fit the experimental data, using, besides  $\mu_s'$  and  $\mu_a$ , an additional fitting parameter that characterizes the phase function.

Eight different phase functions were employed in the calculation of the experimental reflectance curves, three of which were goniometrically measured on tissue samples. Fried *et al.*<sup>12</sup> and Jacques *et al.*<sup>13</sup> found that  $p(\theta)$  of dental enamel and dermis, respectively, can be described by a combination of the

Henyey–Greenstein function,  $p_{\text{HG}}(\theta, g_{\text{HG}})$ , and an isotropic contribution

$$p_{\text{Fried, Jacq}}(\theta) = \alpha p_{\text{HG}}(\theta, g_{\text{HG}}) + (1 - \alpha)/(4\pi), \quad (1)$$

where  $p_{\text{HG}}(\theta, g_{\text{HG}}) = (1 - g_{\text{HG}}^2)/[1 + g_{\text{HG}}^2 - 2g_{\text{HG}} \cos(\theta)]^{3/2}/(4\pi)$ .  $\alpha = 0.65$  and  $g_{\text{HG}} = 0.96$  were obtained by Fried *et al.*<sup>12</sup>;  $\alpha = 0.9$  and  $g_{\text{HG}} = 0.91$ , by Jacques *et al.*<sup>13</sup> Van der Zee *et al.* measured  $p(\theta)$  of white matter of a neonate brain.<sup>14</sup> We approximated their experimental data by using a double Henyey–Greenstein function:

$$p_{\text{Zee}}(\theta) = \beta p_{\text{HG}}(\theta, g_{\text{HG}1}) + (1 - \beta)p_{\text{HG}}(\theta, g_{\text{HG}2}) \quad (2)$$

and found that  $\beta = 0.995$ ,  $g_{\text{HG}1} = 0.992$ , and  $g_{\text{HG}2} = -0.93$ . We also investigated the phase functions of two widely used phantom media, namely, polystyrene spheres surrounded by water [ $p_{\text{Poly}}(\theta)$ , with a diameter of 806 nm] and Intralipid ( $p_{\text{Int}}$ ). These phase functions were calculated by Mie theory. In the case of Intralipid the size distribution of the scattering particles was taken into account.<sup>15</sup> In addition, a pure Henyey–Greenstein function,  $p_{\text{HG}}(\theta)$ , with  $g_{\text{HG}} = 0.8$ , and a pure isotropic phase function [ $p_{\text{Iso}}(\theta)$ ,  $\alpha = 0$  in Eq. (1)] were applied. Finally, we used the phase function of Rayleigh scatterers for unpolarized incident light:  $p_{\text{Rayl}}(\theta) = 3[1 + \cos^2(\theta)]/(16\pi)$ . The spatially resolved reflectance for these eight phase functions and typical optical parameters of biological tissue,  $\mu_s' = 1 \text{ mm}^{-1}$ ,  $\mu_a = 0.01 \text{ mm}^{-1}$ , and  $n = 1.4$ , were calculated by the Monte Carlo method (experimental data). In Fig. 1 four of the  $R(\rho)$  curves are depicted. Similarly to those reported in Ref. 11, these reflectance curves have considerable differences. The remaining four  $R(\rho)$  curves (not shown in Fig. 1) for the most part lie between  $R_{\text{Rayl}}(\rho)$  and  $R_{\text{HG}}(\rho)$ . We note that all  $R(\rho)$  curves have similar reflectance values at  $\rho \approx 0.7 \text{ mm}$ .

To investigate how these differences in the reflectance curves influence the determination of the optical coefficients, we used a Levenberg–Marquardt

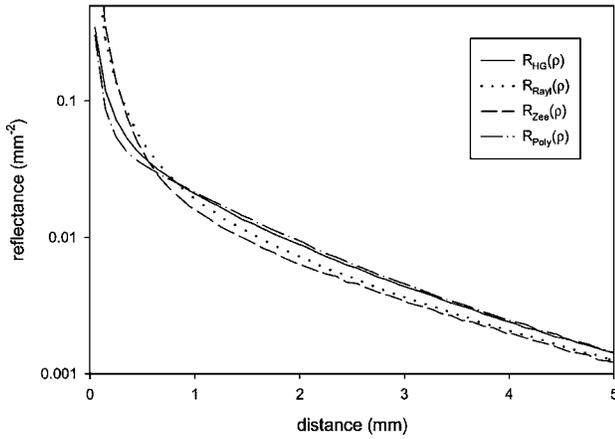


Fig. 1. Spatially resolved reflectance simulations from semi-infinite homogeneous turbid media with several phase functions. The other optical properties are  $\mu_s' = 1 \text{ mm}^{-1}$ ,  $\mu_a = 0.01 \text{ mm}^{-1}$ , and  $n = 1.4$ .

nonlinear regression routine to fit these reflectance curves (minimizing  $\chi^2$ ) with a standard solution of the diffusion theory  $R_{\text{Diff}}$  (the EBC solution in Ref. 8). The weights employed in the nonlinear regression were obtained from the standard deviation,  $\sigma_{\text{MC}}(\rho)$ , of five simulations with 500,000 photons for each simulation. The start and end distances ( $\rho_s$  and  $\rho_e$ ) of the fitting range were varied. Figures 2(a) and 2(b) show the relative errors in the derived absorption coefficient  $[(\mu_{a,\text{fitted}} - 0.01 \text{ mm}^{-1})/0.01 \text{ mm}^{-1}]$  when  $R_{\text{Zee}}(\rho)$  is fitted, assuming absolute and relative measurements, respectively. For absolute reflectance measurements the errors are  $\sim 90\%$  and are weakly dependent on the distance range, whereas for relative reflectance data the errors depend strongly on the distance range. The average errors in the optical properties found for the other reflectance curves are summarized in Table 1. For absolute reflectance measurements the average errors ( $\mu_{a,\text{abs}}$ ,  $\mu_{s,\text{abs}}$ ) obtained from the nonlinear regressions for start distances  $1 < \rho_s < 4 \text{ mm}$  and end distances  $8 < \rho_e < 18 \text{ mm}$  are shown. For relative measurements the errors ( $\mu_{a,\text{rel}}$ ,  $\mu_{s,\text{rel}}$ ) for two different ranges of end distance ( $8 < \rho_e < 13 \text{ mm}$  and  $13 < \rho_e < 18 \text{ mm}$ , with  $1 < \rho_s < 4 \text{ mm}$  for both) were considered, because of the strong dependence of these errors on  $\rho_e$ . As is expected from Fig. 1, for some of the investigated phase functions large errors in the derived values  $\mu_a$  and  $\mu_s'$  were found. We note that, for reflectance curves calculated with other optical parameters, errors similar to those shown in Table 1 were determined.

To investigate whether the errors in the derived optical coefficients listed in Table 1 are considerably smaller than if the form of the phase function were also considered in the nonlinear regression, we used Monte Carlo simulations to fit the eight experimental reflectance curves. The phase function applied for the simulations in the fitting routine was a combination of a Henyey–Greenstein function ( $g_{\text{HG}} = 0.8$ ) and a Rayleigh scattering function for linearly polarized incident light whose polarization direction is parallel to the scattering plane:

$$p(\theta) = \delta p_{\text{HG}}(\theta, g_{\text{HG}1}) + (1 - \delta)3 \cos^2(\theta)/(4\pi). \quad (3)$$

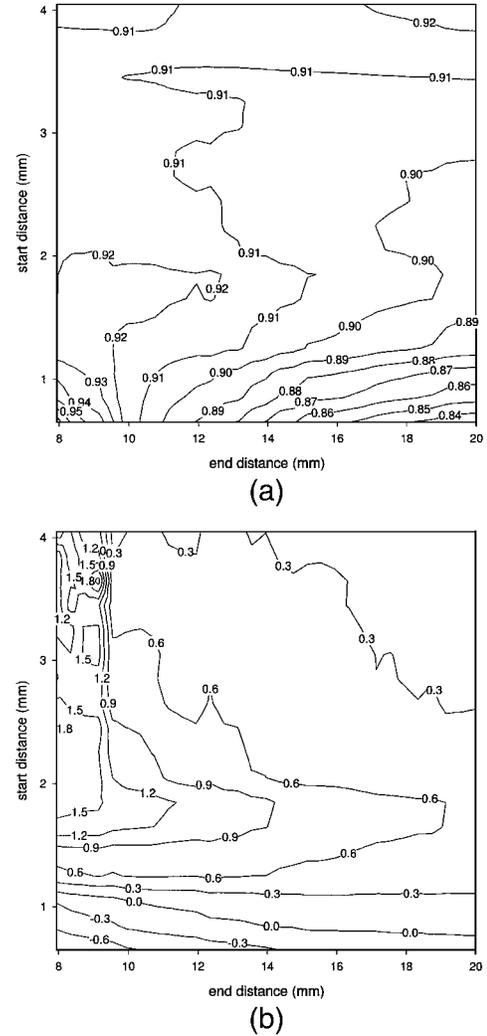


Fig. 2. Relative errors of the absorption coefficients derived by nonlinear regressions of  $R_{\text{Diff}}(\rho)$  to  $R_{\text{Zee}}(\rho)$ . The start and end distances of the fitting range are varied. The optical properties are  $\mu_s' = 1 \text{ mm}^{-1}$ ,  $\mu_a = 0.01 \text{ mm}^{-1}$ , and  $n = 1.4$ . Fitting of (a) absolute reflectance data and (b) relative reflectance data.

**Table 1. Average Absolute Values of Relative Errors in Optical Coefficients Found by Fitting of  $R_{\text{Diff}}(\rho)$  to  $R_{\text{MC}}(\rho)$  Calculated with Various  $p(\theta)$**

Error <sup>a</sup>	Coefficient					
	$\mu_{a,\text{abs}}$ <sup>b</sup>	$\mu_{s,\text{abs}}$ <sup>b</sup>	$\mu_{a,\text{rel}}$ <sup>c</sup>	$\mu_{s,\text{rel}}$ <sup>c</sup>	$\mu_{a,\text{rel}}$ <sup>d</sup>	$\mu_{s,\text{rel}}$ <sup>d</sup>
$p_{\text{Int}}(\theta)$ (%)	20	7	17	5	9	3
$p_{\text{Fried}}(\theta)$ (%)	49	19	10	8	9	9
$p_{\text{Jacq}}(\theta)$ (%)	31	12	13	5	4	4
$p_{\text{Iso}}(\theta)$ (%)	54	21	8	7	7	9
$p_{\text{Poly}}(\theta)$ (%)	3	6	29	16	17	12
$p_{\text{Zee}}(\theta)$ (%)	91	32	80	29	45	24
$p_{\text{Rayl}}(\theta)$ (%)	71	26	11	11	15	14
$p_{\text{HG}}(\theta)$ (%)	11	3	23	9	12	5

<sup>a</sup>The value of  $\rho_s$  for all listed coefficients is 1–4 mm.

<sup>b</sup> $\rho_e$  values are 8–18 mm.

<sup>c</sup> $\rho_e$  values are 8–13 mm.

<sup>d</sup> $\rho_e$  values are 13–18 mm.

**Table 2. Optical Coefficients and Relative Errors ( $e_r$ ) Derived by Fitting of Monte Carlo Simulations to  $R_{MC}(\rho)$  Calculated with Several Values of  $p(\theta)^a$** 

$p(\theta)$	$\mu_a$ (mm) <sup>-1</sup>	$e_r$ (%)	$\mu_s'$ (mm) <sup>-1</sup>	$e_r$ (%)	$\delta$	$\gamma_{fit}$	$\gamma_{th}$
$p_{Int}(\theta)$	0.0090(2)	10	1.05(1)	5	0.93(1)	1.47	1.62
$p_{Fried}(\theta)$	0.0080(3)	20	1.12(2)	12	0.70(3)	0.98	1.07
$p_{Jacq}(\theta)$	0.0084(2)	16	1.08(2)	8	0.86(3)	1.26	1.40
$p_{Iso}(\theta)$	0.0080(2)	20	1.13(2)	13	0.68(2)	0.95	1.00
$p_{Poly}(\theta)$	0.0092(1) <sup>b</sup>	8	1.06(1) <sup>b</sup>	6	1.00(0) <sup>b</sup>	1.80 <sup>b</sup>	2.19
$p_{Zee}(\theta)$	0.0120(3)	20	0.89(1)	11	0.73(3)	1.02	0.94
$p_{Rayl}(\theta)$	0.0080(4)	20	1.14(3)	14	0.55(5)	0.84	0.90
$p_{HG}(\theta)$	0.0093(5)	7	1.04(3)	4	0.98(2)	1.69	1.8

<sup>a</sup>Uncertainty of the last given digit shown in parentheses.

<sup>b</sup>Phase functions used were restricted to  $\delta$  values of  $\leq 1$ .

Polarized light is used to cover a larger range of  $\gamma$  values than is possible with unpolarized light. The fitting parameters were  $\mu_a$ ,  $\mu_s'$ , and  $\delta$ , assuming absolute reflectance measurements. The start and end distances of the fitting range were  $\rho_s = 1$  mm and  $\rho_e = 20$  mm. For the nonlinear regressions four Monte Carlo simulations were run for each iteration, one for the calculation of  $R(\rho)$  with the actual optical parameters and one for the calculation of the derivatives of each fitting parameter. We applied 2.5 million photons (5 times 500,000 photons) for each simulation. We used the standard deviation of the five partial simulations (each run with 500,000 photons),  $\sigma_{MCFit}(\rho)$ , to calculate the weights employed in the nonlinear regressions with  $w(\rho) = 1/[\sigma_{MC}^2(\rho) + \sigma_{MCFit}^2(\rho)]$ .<sup>16</sup> For each experimental  $R(\rho)$  curve we performed several nonlinear regressions that had different starting values of the fitting parameters. The average values and the standard deviations of the optical parameters derived by these fits are listed in Table 2. The table also shows the  $\gamma$  values calculated from the fitted  $\delta$  and Eq. (3) ( $\gamma_{fit}$ ) and those determined directly from the theoretical phase functions ( $\gamma_{th}$ ). The derived errors of  $\mu_a$  and  $\mu_s'$  are  $\leq 20\%$ , and  $\gamma$  could usually be determined with errors of  $\leq 10\%$ . The results for  $p_{Poly}(\theta)$  have to be cautiously regarded, because the phase function used in the Monte Carlo simulations of the fitting routine [Eq. (3)] is restricted to  $\delta$  values that are  $\leq 1$ . Thus the largest  $\gamma$  that can be obtained from the nonlinear regression is 1.8, which is considerably smaller than the  $\gamma_{th} = 2.19$  derived directly from  $p_{Poly}(\theta)$ .

In summary, we have shown that an analysis of spatially resolved reflectance measurements obtained by use of a solution of the diffusion equation may result in prohibitively large errors in the derived optical coefficients, whereas the errors obtained from fitting Monte Carlo simulations are considerably smaller (compared with the corresponding errors obtained by fitting of the diffusion solution to absolute measurements). In

addition, the supplement fitting parameter ( $\delta$  or  $\gamma$ ) can provide further information about the tissue under investigation.

The disadvantage of this inverse Monte Carlo approach is the large computation time required for the nonlinear regressions. One possibility for shortening the time drastically is the use of a neural network that was trained with Monte Carlo simulations. It has to be determined whether this method, which has been described for fitting  $\mu_a$  and  $\mu_s'$ ,<sup>4,17</sup> can be successfully applied for determining  $\mu_a$ ,  $\mu_s'$  and  $\gamma$ .

If the phase function of the tissue under investigation is known, however, a single Monte Carlo simulation can be applied for fast and accurate determination of optical properties by use of scaling principles.<sup>18</sup>

A. Kienle's e-mail address is alwin.kienle@ilm.uni-ulm.de.

## References

1. R. A. J. Groenhuis, H. A. Ferwerda, and J. J. ten Bosch, *Appl. Opt.* **22**, 2456–2462 (1983).
2. T. J. Farrell, M. S. Patterson, and B. C. Wilson, *Med. Phys.* **19**, 879–888 (1992).
3. E. L. Hull, M. G. Nichols, and T. H. Foster, *Phys. Med. Biol.* **43**, 3381–3404 (1998).
4. A. Kienle, L. Lilge, M. S. Patterson, R. Hibst, R. Steiner, and B. C. Wilson, *Appl. Opt.* **35**, 2304–2314 (1996).
5. F. Bevilacqua, D. Piquet, P. Marquet, J. D. Gross, B. J. Tromberg, and C. Depeursinge, *Appl. Opt.* **38**, 4939–4950 (1999).
6. J. S. Dam, C. B. Pedersen, T. Dalgaard, P. E. Fabricius, P. Aruna, and S. Andersson-Engels, *Appl. Opt.* **40**, 1155–1164 (2001).
7. T. H. Pham, F. Bevilacqua, T. Spott, J. S. Dam, B. J. Tromberg, and S. Andersson-Engels, *Appl. Opt.* **39**, 6487–6497 (2000).
8. A. Kienle and M. S. Patterson, *J. Opt. Soc. A* **14**, 246–254 (1997).
9. A. Kienle, "Lichtausbreitung in biologischem Gewebe" (University of Ulm, Ulm, Germany, 1995).
10. J. R. Mourant, J. Boyer, A. H. Hielscher, and I. J. Bigio, *Opt. Lett.* **21**, 546–548 (1996).
11. F. Bevilacqua and C. Depeursinge, *J. Opt. Soc. A* **16**, 2935–2945 (1999).
12. D. Fried, R. E. Glana, J. D. B. Featherstone, and W. Seka, *Appl. Opt.* **7**, 1278–1285 (1995).
13. S. L. Jacques, C. A. Alter, and S. A. Prahl, *Lasers Life Sci.* **1**, 309–333 (1987).
14. P. van der Zee, M. Essenpreis, and D. T. Delpy, *Proc. SPIE* **1888**, 454–465 (1993).
15. H. J. van Staveren, C. J. M. Moes, J. van Marle, S. A. Prahl, and M. J. C. van Gemert, *Appl. Opt.* **30**, 4507–4514 (1991).
16. G. Alexandrakis, D. R. Busch, G. W. Faris, and M. S. Patterson, *Appl. Opt.* **40**, 3810 (2001).
17. T. J. Farrell, B. C. Wilson, and M. S. Patterson, *Phys. Med. Biol.* **37**, 2281–2286 (1992).
18. A. Kienle and M. S. Patterson, *Phys. Med. Biol.* **41**, 2221–2227 (1996).