Quantifying tissue optical properties with Single Fiber Reflectance spectroscopy

Modeling the short journey of photons

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Publication date
2020

Document Version
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CHAPTER 2

MODELING SUBDIFFUSE SCATTERING BY INCORPORATING THE TISSUE PHASE FUNCTION AND DETECTOR NUMERICAL APERTURE

Abstract. To detect small-scale changes in tissue with optical techniques, small sampling volumes and, therefore, short source-detector separations are required. In this case, reflectance measurements are not adequately described by the diffusion approximation. Previous studies related subdiffuse reflectance to γ or σ, which parameterize the phase function. Recently it was demonstrated that σ predicts subdiffuse reflectance better than γ, but also that σ becomes less predictive for lower numerical apertures (NA). Here, we derive and evaluate the parameter R_{pNA} to model Single Fiber Reflectance (SFR) spectroscopy. R_{pNA} incorporates the NA of the detector and the integral of the phase function over the NA in the backward and forward direction. We performed Monte Carlo simulations for SFR spectroscopy, for a range of phase functions, reduced scattering coefficients, NAs, and fiber diameters and demonstrate that R_{pNA} improves prediction of the measured reflectance compared to γ and σ. It is, therefore, expected that R_{pNA} will improve the derivation of optical properties from SFR measurements.

Based on: A.L. Post, S.L. Jacques, H.J.C.M. Sterenborg, D.J. Faber, T.G. van Leeuwen, "Modeling subdiffusive light scattering by incorporating the tissue phase function and detector numerical aperture," *J. Biomed. Opt*. 22 (5), (2017)

INTRODUCTION

Light that has traveled through tissue carries information about tissue properties, such as its structure and biochemical composition. The distance light travels determines the scale on which tissue is investigated, as the measured spectra are averaged over the sampling volume. Techniques such as Diffuse Reflectance Spectroscopy (DRS) average the measured spectra over a volume in the order of several mm^3. Single Fiber Reflectance (SFR) spectroscopy, in contrast, has a sampling volume in the order of the fiber diameter $\sim d_f^3$ [11], where d_f is generally a few hundred micrometers. This small sampling volume makes SFR spectroscopy more suitable to detect small-scale and superficial changes in tissue. In SFR spectroscopy, light is emitted and collected through the same fiber, which is connected to a broadband light source and a spectrometer. Since a single fiber is both the source and detector, the distance between the location where photons enter the tissue and where they are detected is generally less than the transport mean free path $1/\mu_s'$, where μ_s' is the reduced scattering coefficient. Therefore, diffusion theory alone is not appropriate to model the reflectance as a function of tissue optical properties for SFR spectroscopy; SFR measurements are in the so-called subdiffuse regime.

In the diffuse regime, photon direction is randomized and reflectance does not depend on the exact shape of the phase function ($p(\theta)$, the probability distribution of scattering angles), but only on the scattering anisotropy, g_1. In the subdiffuse regime, in contrast, the photon direction is not fully randomized and, therefore, measurements are sensitive to the tissue phase function [8], [21]. To model light transport, solutions to the radiative transport equation (RTE) involve expanding the radiance into a series of i spherical harmonics, and the phase function into i Legendre polynomials. The latter are weighted with their moments g_i, where g_1 is commonly referred to as the scattering anisotropy. For $i = 1$, the diffusion approximation to the RTE is obtained, with the similarity relation $\mu_s(1\text{-}g_1) = \mu_s^*(1\text{-}g_1^*)$, which expresses that tissues with different scattering coefficient μ_s and g_1 but equal μ_s' yield the same reflectance. However, reflectance at short source-detector separations is inadequately described for $i = 1$. Improvement is possible by increasing i, giving additional similarity relations. For $i = 2$, Bevilacqua and Depeursinge suggested an alternative form of these similarity relations using the parameter γ [9]:

$$\gamma = \frac{1 - g_2}{1 - g_1} \tag{1}$$

Various studies have investigated describing subdiffuse reflectance using γ in combination with μ_s', μ_a and the fiber diameter d_f [22]–[24]. However, recent work showed that a range of γ values (for the same μ_s', μ_a and d_f) can result in the same subdiffuse reflectance [25], [26]. Therefore, Bodenschatz et al. [20] incorporated more similarity relations into the parameter σ, employing all phase function moments:

$$\sigma = \sum_{i=2}^{\infty} (-c)^{i-2} \frac{1-g_i}{1-g_1} \tag{2}$$

where c depends on both the measurement geometry and the scattering regime (empirically, $c = 0.5$ was found to give the best results). Bodenschatz et al. concluded that σ predicts subdiffuse reflectance better than γ, but also that σ becomes less predictive for lower numerical apertures.

To model the reflectance for SFR spectroscopy, we consider the reflectance as the sum of a diffuse component and a semiballistic component. For the semiballistic component, only photons are considered which have experienced a single backscattering event in combination with an arbitrary number of small-angle forward scattering events. To model the semiballistic contribution, not all details of the phase function are needed. Rather, we consider the phase function within the acceptance angle, θ_{acc}, of the fiber. The acceptance angle is characterized by the fiber numerical aperture (NA) and the refractive index of the medium (n) as $\theta_{acc} = \mathrm{asin}(\mathrm{NA}/\mathrm{n})$. We propose a new theoretically derived parameter, R_{pNA}, for the semiballistic contribution to the reflectance. R_{pNA} is related to the acceptance angle of the fiber and the integral of the phase function over the corresponding angular interval in the backward ($p_{NA,b}$) and forward ($p_{NA,f}$) direction as:

$$R_{pNA} = \frac{p_{NA,b}}{1-p_{NA,f}} \tag{3}$$

We show the theoretical derivation of R_{pNA} and the improved prediction of the reflectance measured with SFR spectroscopy by R_{pNA} compared to σ and γ. R_{pNA}, therefore, has the potential to improve models used for SFR spectroscopy to extract optical properties.

THEORETICAL DERIVATION OF R_{PNA}

We consider photons semiballistic if they are backscattered once in combination with an arbitrary number of forward scattering events and assume that these photons will only be detected if subsequent scattering events occur at angles smaller than or equal to the acceptance angle, θ_{acc}, of the fiber. We introduce the probabilities $p_{NA,b}$ and $p_{NA,f}$ as:

$$p_{NA,b} = 2\pi \int_{\pi-\theta_{acc}}^{\pi} p(\theta)\, sin(\theta)\, d\theta \tag{4}$$

$$p_{NA,f} = 2\pi \int_{0}^{\theta_{acc}} p(\theta)\, sin(\theta)\, d\theta \tag{5}$$

The contribution of semiballistic photons to the reflectance scales with the probability of a single backscattering event in the path length interval dl as $\mu_s \cdot p_{NA,b} \cdot dl$. To determine the effect of forward semiballistic scattering, we use the result obtained by Wang et al. [27],

which is the probability of photons traveling a pathlength l while experiencing N forward scattering events:

$$prob_{NA,f}(l,N) = \frac{\left(p_{NA,f} \cdot \mu_s \cdot l\right)^N}{N!} e^{-\mu_s l} \tag{6}$$

Summing Eq. 6 over all possible number of forward scattering events, N from 0 to ∞, we obtain:

$$prob_{NA,f}(l) = e^{p_{NA,f} \cdot \mu_s l} e^{-\mu_s l} = e^{-\mu_s l(1-p_{NA,f})} \tag{7}$$

The combined probability of one backscatter event and an arbitrary number of forward scattering events, each occurring at scattering angles within θ_{acc}, is given by integration over all possible pathlengths, 0 to ∞:

$$prob_{NA} = \int_0^\infty p_{NA,b}\mu_s \cdot e^{-\mu_s l(1-p_{NA,f})}\, dl = \frac{p_{NA,b}}{1-p_{NA,f}} \equiv R_{pNA} \tag{8}$$

METHODS

For our Monte Carlo simulations, we modified the software of Prahl et al. [28] (which was the core programming later used in MCML software [29]), to allow the use of arbitrary phase functions using the method of Zijp and ten Bosch [30]. The modified code was benchmarked against standard MCML using the Henyey Greenstein phase function. Photons were launched from a location based on a uniform distribution across the fiber face with an angle from a uniform angular distribution within the NA. Photons were detected if they arrived at the fiber face with an angle within the acceptance angle of the fiber. We performed simulations using 15 modified Henyey Greenstein (MHG) [31], 144 Two-Term Henyey-Greenstein (TTHG) [13], 8 modified power of cosines (MPC) [9] and 46 Reynolds McCormick [17] phase functions (RMC, which is equivalent to the Gegenbauer Kernel phase function) employing the parameters specified in Table 2.1 and applying the restrictions $g_1 \geq 0.5$ and $g_2 < 0.9$ to exclude biologically unreasonable phase functions. For each set of phase functions, we performed simulations for three values of $\mu_s' d_f$: 0.1 ($\mu_s' = 10$ cm^{-1}, $d_f = 100$ μm), 1.0 ($\mu_s' = 100$ cm^{-1}, $d_f = 100$ μm) and 9.0 ($\mu_s' = 100$ cm^{-1}, $d_f = 900$ μm) in combination with an NA of 0.22 or 0.5. We used an absorption coefficient of 0.1 cm^{-1} and refractive indices inside and outside of the sample of 1.35 and 1, respectively.

Table 2.1 Parameters employed in the selection of phase functions

Phase function	Parameters
Modified Henyey Greenstein	$0.01 \leq g_{HG} \leq 0.95$, 10 linear steps $0.01 \leq \alpha \leq 0.99$, 10 linear steps
Two-term Henyey Greenstein	$0.5 \leq \alpha \leq 0.9$, 3 linear steps $0.91 \leq \alpha \leq 0.99$, 5 linear steps $0.05 \leq g_f \leq 0.95$, 10 linear steps $-0.50 \leq g_b \leq -0.05$, 5 linear steps
modified power of cosines	$0.01 \leq \alpha \leq 0.99$, 10 linear steps $0.01 \leq N \leq 10$, 10 logarithmic steps
Reynolds McCormick	$0.01 \leq \alpha \leq 2.5$, 10 linear steps $0.01 \leq g_R \leq 0.95 - 0.2 \cdot \alpha$, 10 linear steps

RESULTS

Fig. 2.1 shows the simulated reflectance versus R_{pNA}, σ and γ for an NA of 0.22 and 0.5 and three different values of $\mu_s' d_f$ (0.1, 1.0 and 9.0). Reflectance correlates with all three parameters for $\mu_s' d_f$ of 0.1 and 1.0. This correlation is far less pronounced for $\mu_s' d_f = 9.0$. To compare R_{pNA}, σ, and γ, we determined the dispersion in each of these three parameters for a chosen reflectance (+/- 10%) relative to the total range of the parameter (Table 2.2). For example, for $\mu_s' d_f = 0.1$, $NA = 0.22$ and a reflectance of 0.001 (+/- 10%), γ ranges from 1.43 to 1.66. The total range of γ is 0.68 to 2.43; so the relative dispersion was calculated as 0.23/1.75 = 0.13. For all combinations of NA (0.22 and 0.5) and $\mu_s' d_f$ (0.1 and 1.0), we determined the relative dispersion for three reflectance values and found the relative dispersion to be lowest for R_{pNA} compared to σ and γ.

DISCUSSION

We have theoretically derived the parameter R_{pNA} to model subdiffuse light scattering for SFR spectroscopy and we have shown with Monte Carlo simulations that the reflectance depends on R_{pNA}. In comparison to σ and γ, R_{pNA} improves the prediction of the reflectance. Our findings indicate that for SFR spectroscopy the reflectance does not depend on the details of the phase function - knowledge of all Legendre moments is not required - but only on the magnitude of the phase function within the acceptance angle of the fiber (in the backward and forward direction). Currently, the parameter γ is widely used to model subdiffuse reflectance. Since R_{pNA} improves prediction of the measured reflectance, incorporating R_{pNA} into subdiffuse models is expected to improve their reliability and thereby also the estimation of other optical properties, such as μ_s'. For higher values of $\mu_s' d_f$ the reflectance becomes more diffuse and therefore depends less on R_{pNA}, σ or γ. The contribution of diffuse photons is a remaining challenge to describe subdiffuse scattering. Furthermore, in our simulations, we kept the absorption coefficient constant. While the absorption affects the diffuse contribution to the reflectance, it has a minor effect on semiballistic photons since these have short path lengths. The next step is to develop a model to relate the measured reflectance to tissue optical properties for SFR spectroscopy, incorporating R_{pNA}, the diffuse reflectance, and absorption.

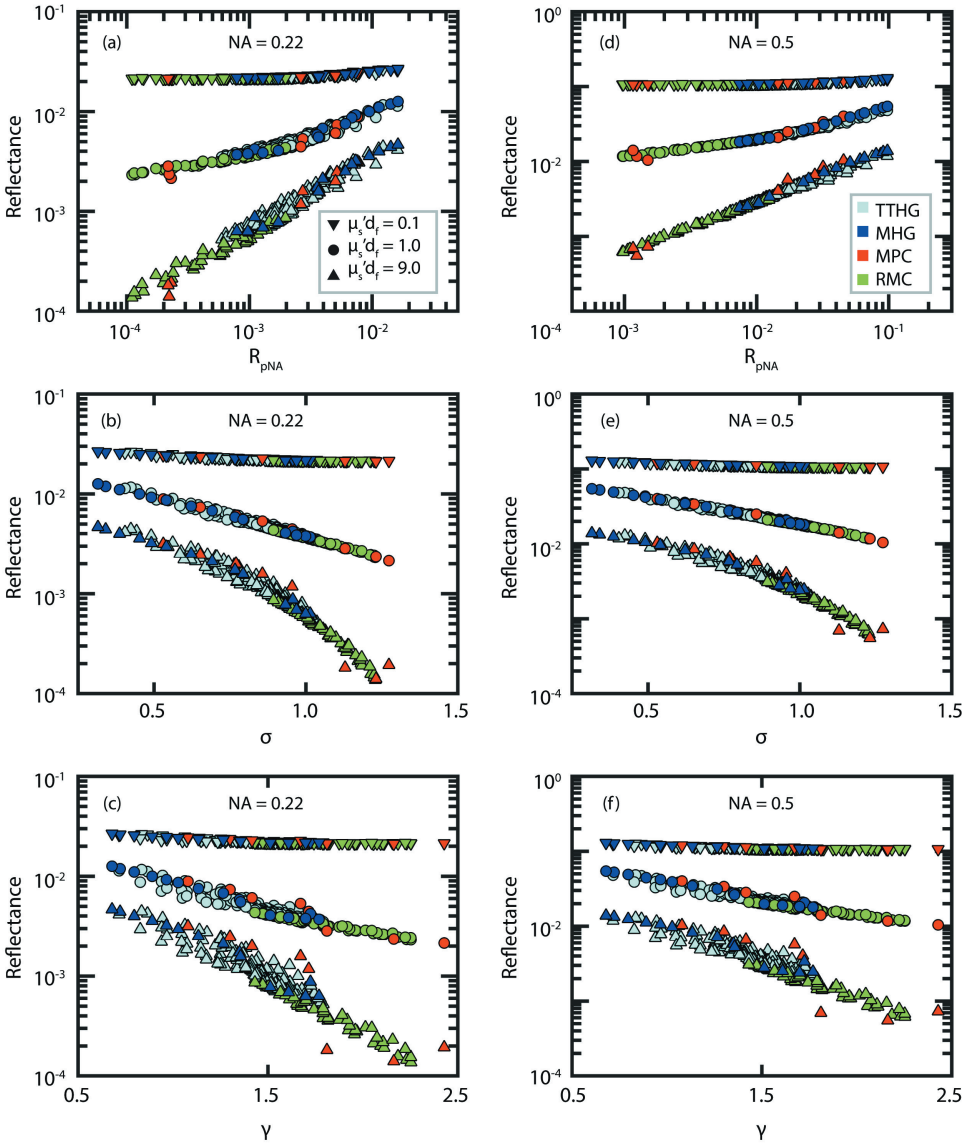

Fig. 2.1 Simulated reflectance versus R_{pNA}, σ and γ. NA = 0.22 (left) and NA = 0.5 (right). Symbols indicate $\mu_s'd_f$ values, colors indicate phase function types. Note the log scales for both the reflectance and R_{pNA}.

Table 2.2 Relative dispersion of R_{pNA}, σ, and γ. Relative dispersion was defined as the dispersion in R_{pNA}, σ and γ values for a chosen reflectance (+/- 10%) relative to the total range of each parameter.

			Relative dispersion		
$\mu_s' d_f$	NA	Reflectance	R_{pNA}	σ	γ
0.1	0.22	0.0005	0.01	0.04	0.08
		0.001	0.05	0.08	0.13
		0.003	0.24	0.16	0.20
	0.5	0.001	0.01	0.05	0.11
		0.003	0.04	0.10	0.17
		0.005	0.08	0.13	0.20
1	0.22	0.003	0.04	0.11	0.16
		0.004	0.07	0.13	0.20
		0.006	0.15	0.18	0.23
	0.5	0.015	0.04	0.09	0.15
		0.020	0.08	0.14	0.20
		0.030	0.24	0.19	0.27

CONCLUSION

In conclusion, the theoretically derived parameter R_{pNA} predicts subdiffuse light scattering for SFR spectroscopy better than the subdiffuse parameters σ and γ. Consequently, the reflectance does not depend on the details of the entire phase function, but on the phase function within the acceptance angles of the detector. R_{pNA} improves prediction of the measured reflectance compared to σ and γ for SFR spectroscopy. Therefore, incorporation of R_{pNA} in a model to relate the measured reflectance to tissue optical properties is expected to improve the accuracy of optical properties derived from SFR measurements.

ACKNOWLEDGMENTS

We would like to thank the Organization Committee of the Spinoza Chair from the Academic Medical Center of the University of Amsterdam for funding a Spinoza lectureship for Steven L. Jacques.