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A hybrid method for fast Monte Carlo simulation of diffuse reflectance from a multi-layered tissue model with tumor-like heterogeneities

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ABSTRACT

We present a hybrid method to speed up the Monte Carlo simulation of diffuse reflectance from a multi-layered tissue model with finite-size tumor-like heterogeneities. The proposed method consists of two steps. In the first step, a set of photon trajectory information generated from a baseline Monte Carlo simulation is utilized to scale the exit weight and exit distance of survival photons for the multi-layered tissue model by using a multiple scaling method. In the second step, another set of photon trajectory information including the locations of all collision events from the baseline simulation and the scaling result obtained from the first step are employed by the perturbation Monte Carlo method to estimate diffuse reflectance from the multi-layered tissue model with tumor-like heterogeneities. Our method is demonstrated to be able to shorten simulation time by several orders of magnitude. Moreover, this hybrid method works for a larger range of probe configurations and tumor models compared to the scaling method or the perturbation method alone.

Keywords: Perturbation Monte Carlo, Scaling method, diffuse reflectance, tumor-like heterogeneity, epithelial cancer

1. INTRODUCTION

Ultraviolet-visible diffuse reflectance spectroscopy has been explored for the early detection of epithelial cancers for decades [1-3]. In this technique, an accurate model of light transport is essential to quantitatively extract optical properties from measured diffuse reflectance spectra. Diffusion theory and its modified versions have been frequently used to extract optical properties from diffuse reflectance measurements [4, 5]. However, diffusion theory is not valid to describe light transport at small source-detector separations[5] or when absorption and scattering coefficients are comparable, such as in the ultraviolet-visible spectral region. Another limitation of these analytical methods is that the tissue model has to consist of one or more semi-infinite layers. Thus it may not be applicable to early epithelial cancer, in which it is more appropriate to apply a multi-layered tissue model with tumor-like heterogeneities[6]. In this situation, the Monte Carlo (MC) method provides a flexible tool to model light transport. Since the MC method can solve radiative transport equation with any accuracy[7] for a complex tissue model and probe geometry, it is considered as the gold standard method to model light transport in turbid media. However, the main drawback of the MC method is the requirement of intensive computation to achieve results with desirable accuracy which makes it extremely time consuming. Several methods have been proposed to speed up the MC method for modeling light transport in complex tissue models. Liu et al[8] presented a scaling method for fast MC simulation of diffuse reflectance spectra from multi-layered turbid media. Hayakawa et al [9] proposed a perturbation Monte Carlo (pMC) method to solve inverse photon migration problems in a two-layered tissue model based on spatially resolved diffuse reflectance and validated this method experimentally[10]. Sassaroli et al[11] proposed a fast pMC method for photon migration in a tissue model with an arbitrary distribution of optical properties, moreover the method has minimal requirements in terms of hard disk space thus it will be very useful for diffuse optical tomography. However, to our best knowledge, there has been no effort in the literature to speed up the MC method in multi-layered tissue model with finite-size tumor-like heterogeneities. Theoretically, the pMC method may be used in this case, but the applicable range of optical properties in the tissue model and the heterogeneity will be limited. In this paper, we propose a hybrid method that combines a multi-layered scaling method[8] and a pMC method[9] to address this problem.

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2. METHODS

2.1 Principle of hybrid method

Our method consists of two steps as shown in Fig.1. The first step applies the multi-layered scaling method on a set of photon trajectory information including the exit weight, the x and y offsets in each random walk step of all survival photons escaping from the top surface of the tissue model, generated from a single baseline simulation to scale the exit weight and exit distance of photons for the multi-layered tissue model without heterogeneities. In the second step, a convolution scheme is used to determine the probability of a survival photon collected by the fiber-optic probe geometry of interest[12]. Then the second set of photon trajectory information including the locations of all collision events for each collected photon, which is generated from the same baseline MC simulation, will be processed to determine the path length and the number of collisions of photon spent in the tumor. Finally, the scaling result, i.e. the exit weight of collected photons, as well as the path length and the number of collisions spent in the tumor will be utilized by pMC method to compute the diffuse reflectance for the given probe configuration.

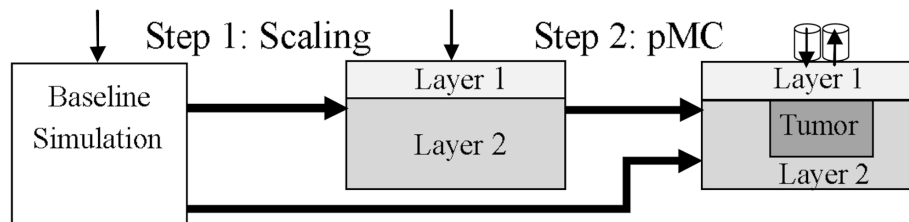


Figure 1. Schematic representation of the hybrid method. The single baseline simulation is run on a homogeneous tissue model as shown in the left block.

2.2 Tissue model and simulation setup

A previous MC code[8] was modified to create a photon trajectory database for scaling and perturbation. A single simulation was run for a homogeneous baseline tissue model, in which $\mu_a = 0 \text{ cm}^{-1}$, $\mu_s = 100 \text{ cm}^{-1}$, and the anisotropy factor $g = 0.8$. The refractive indices of the medium above the tissue model, the tissue model and the medium below the tissue model were set to be 1.47, 1.4 and 1.4, respectively. These two values represent the refractive indices of the fiber material, i.e. glass in this case and the tissue at 500 nm. The thickness of the tissue model was set at 4 cm to mimic a semi-infinite medium. A total of 10^7 photons were launched at the origin of a Cartesian coordinate system to obtain the impulse response of the tissue model in diffuse reflectance. When a photon exits from the top surface of the tissue model, its exit angle relative to the z-axis will be calculated. If the exit angle is smaller than the cut-off angle defined by an NA of 0.22, the relevant trajectory information of this photon will be stored in a numerical array. Approximately 2.4×10^5 photons were detected in this manner and a total memory of 10 gigabytes (GB) was needed for the storage of the trajectory data. Then based on the stored trajectory data, the multi-layered scaling method [8] and the pMC method [9] will be sequentially carried out as described previously to estimate diffuse reflectance from the multi-layered tissue model with finite-size heterogeneities. Both the scaling and pMC methods were coded and run in Matlab 10 (Mathworks, Natick, Massachusetts, US).

A basal cell carcinoma (BCC) skin tissue model was used to evaluate the effectiveness of the hybrid method. The BCC usually originates from the basal layer of the epidermis and frequently grows downward deeply into the dermis [13, 14], thus it is induced into the dermis in our theoretical tissue model as shown by the cross-sectional view in Fig. 2. The thickness of the epidermis was set to be 80 μm and the thickness of the dermis was set to be 4 cm to mimic a thick skin tissue. The epidermal thickness is representative of that on the neck and back[15]. The length, width and thickness of BCC tumor were all set to be 400 μm . The optical properties of the epidermis and dermis were selected from the literature [16] and listed in Table 1. A refractive index of 1.4 and an anisotropy factor of 0.8 were used in the entire tissue model including the BCC tumor. The absorption and scattering coefficients of the tumor were varied sequentially to investigate the valid range of the hybrid method. The source and detector fibers were placed side by side, both of which were perpendicular to the tissue surface. The bisecting line between the two fibers overlaps with the middle line of the tumor in the width dimension, i.e. the x dimension in Fig. 2. The two fibers both had a core diameter of 200 μm and a

NA value of 0.22. The refractive indices of the fibers were set to be 1.47. Totally two sets of tests were performed. In the first set, the absorption coefficient, i.e. μ_a , of the tumor was varied from 1% to 400% of that of the dermis, while the scattering coefficient, i.e. μ_s , of the tumor was kept identical to that of the dermis. In the second set, the scattering coefficient, i.e. μ_s , of the tumor was varied from 25% to 190% of that of the dermis, while the absorption coefficient, i.e. μ_a , of the tumor was kept identical to that of the dermis. Diffuse reflectance values, which refer to the ratio between detected and incident powers in this paper, calculated by the hybrid method were compared to those from independent MC simulations (no scaling or perturbation methods were used) which were run by using a previously validated MC code[17], to evaluate the effectiveness of the hybrid method.

Each independent simulation was run five times and 10 million photons were used. The percent deviation in diffuse reflectance between results calculated by the hybrid method and those simulated independently was calculated by Eq. (1) to quantify the accuracy of the calculated results.

$$\text{Percent Deviation} = \frac{\text{Hybrid} - \text{Simulated}}{\text{Simulated}} \times 100 \quad (1)$$

where “Hybrid” refers to the diffuse reflectance value calculated by the hybrid method and “Simulated” refers to the mean of simulated diffuse reflectance values from five runs of the independent simulation on the same tissue model. The percent deviations of five individually simulated diffuse reflectance values relative to their mean were also calculated in the same manner. The 95% confidence interval (CI) of the percent deviation of simulated diffuse reflectance values relative to their mean was then estimated by Eq. (2).

$$95\% \text{CI} = \left[\text{mean} - 1.96 \times \frac{\text{std}}{\sqrt{m}}, \text{mean} + 1.96 \times \frac{\text{std}}{\sqrt{m}} \right] \quad (2)$$

where m is the number of runs ($m=5$), and “mean” and “std” refer to the mean and standard deviation of the percent deviations for simulated diffuse reflectance values, respectively. It should be noted that the mean of the percent deviations calculated in this manner is always zero as indicated by circle symbols in Fig. 3(b) and 4(b).

Table 1. Optical properties of BCC tissue model at 500 nm [16].

Tissue	$\mu_a(\text{cm}^{-1})$	$\mu_s(\text{cm}^{-1})$	g
Epidermis	7.0	350	0.8
Dermis	3.5	250	0.8

Note: μ_a : absorption coefficient; μ_s : scattering coefficient; g : anisotropy

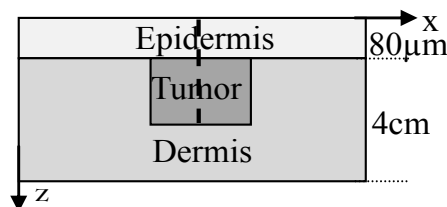


Figure.2. Cross-sectional view of the theoretical BCC model

3. RESULTS

Fig. 3(a) shows the comparison in diffuse reflectance values between the hybrid method and independent MC simulations for μ_a varying from 1% to 400% of the dermal value. The two sets of symbols completely overlap at nearly every point, which indicates the high accuracy of the hybrid method. Fig. 3(b) shows the percent deviations of diffuse reflectance calculated by the hybrid method according to Eq. (1) and the 95% CIs of the percent deviations of simulated diffuse reflectance calculated by Eq. (2) as indicated by the error bars. The percent deviations for the hybrid method are always smaller than 5% when μ_a is varied from 1% to 390% of the dermal value. Moreover, they are all close to or within the 95% CIs of the percent deviations of simulated diffuse reflectance values. Fig. 4 (a) compares diffuse reflectance values between the hybrid method and independent MC simulations for μ_s varying from 25% to 190% of the

dermal value. Fig. 4 (b) compares the percent deviations of diffuse reflectance values obtained by the hybrid method with the 95% CIs of the percent deviations for independently simulated diffuse reflectance values as indicated by the error bars. The percent deviations for the hybrid method are all less than 5% when μ_s is varied from 30% to 180% of the dermal value. Moreover they all fall within or close to or the 95% CIs of the percent deviations of simulated reflectance values. The following interesting trends have been observed in Fig.3 and Fig.4. The hybrid method overestimates the reflectance value when the absorption coefficient of the tumor is larger than that of the dermis and underestimates the reflectance value when the absorption coefficient of the tumor is smaller than that of the dermis. The trend for the scattering coefficient is opposite. The similar trends have been observed for pMC method [9, 10]. Thus the trends are most likely caused by the perturbation part of the hybrid method.

All tests were performed on a laptop computer with an Intel Core i5 CPU and 4GB memory. Ten hours were needed to run the baseline simulation and generate the photon trajectory information. It should be noted that the major portion of the time in the baseline simulation was spent in saving data but not the simulation. It took about 1.5 minutes for the scaling step, 15 seconds for the convolution scheme to calculate the probability of each survival photon being collected and about 6 minutes to determine the path length and the number of collisions spent in the tumor. The pMC step took about 90 milliseconds for each set of optical properties to yield the final diffuse reflectance. In contrast, it took about 30 minutes to run one independent MC simulation to get the same value.

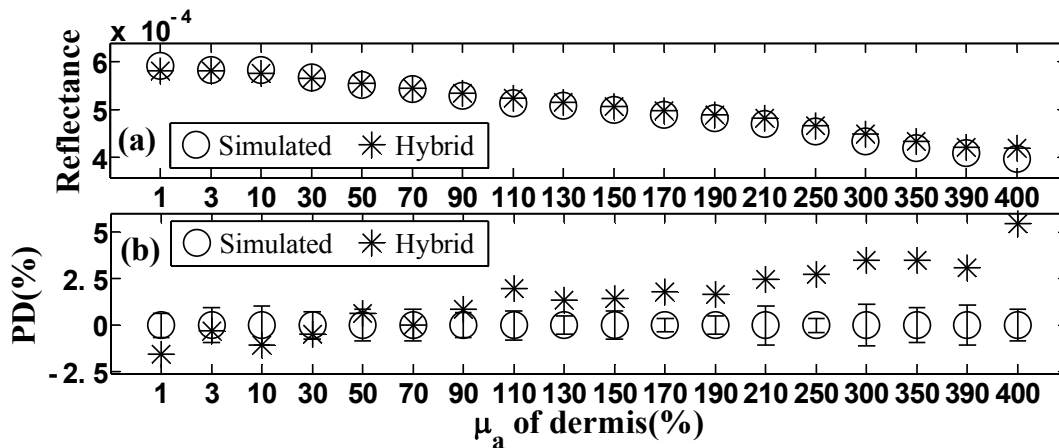


Fig.3. Comparison in (a) diffuse reflectance and (b) percent deviation, between the hybrid method, i.e. “Hybrid”, and independent MC simulations, i.e. “Simulated”, with varying μ_a in the tumor. “PD” refers to percent deviation. The error bars in (b) indicates the 95% CI of the percent deviations for diffuse reflectance values from independent MC simulations as calculated by Eq. (2)

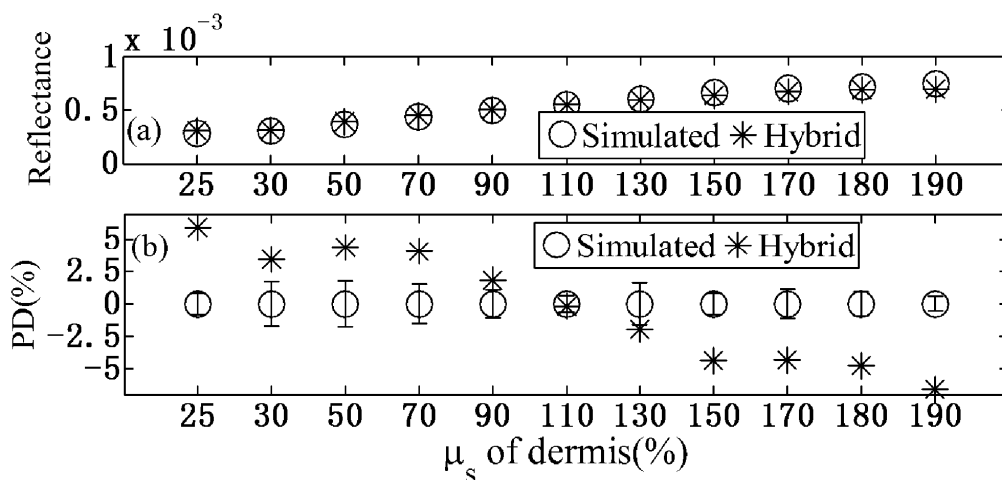


Fig.4. Comparison in (a) diffuse reflectance and (b) percent deviation, between the hybrid method, i.e. “Hybrid”, and independent MC simulations, i.e. “simulated”, with varying μ_s in the tumor. “PD” refers to percent deviation. The error bars in (b) indicates the 95% CI of the percent deviations for diffuse reflectance values from independent MC simulations as calculated by Eq. (2).

4. DISCUSSION

In summary, we have developed a hybrid method, which combines a multi-layered scaling method and a perturbation method, for fast MC simulation of diffuse reflectance from a multi-layered tissue model with tumor-like heterogeneities. In the hybrid method, one needs to perform the multi-layered scaling first to find the exit weight and exit distance for every survival photon in the multi-layered tissue model without considering the tumor-like heterogeneity, then use the photon trajectory information recorded for the entire baseline medium to determine the portions of the optical path and number of collisions in the tumor region and scale them to perform perturbation for the multi-layered tissue model with an arbitrary tumor-like heterogeneity. The latter step is different from all the perturbation methods that have been reported in the literature to our best knowledge, which is the key step that distinguishes the hybrid method from the simple addition of the two existing methods. The hybrid method takes advantage of the proven high accuracy of the multi-layered scaling method in the simulation of a multi-layered tissue model so that the perturbation method is applied to only the heterogeneities instead of the entire tissue model. This feature significantly expands the range of applicable tissue models compared to pMC methods alone. Moreover, the hybrid method only requires a single baseline simulation to generate the photon trajectory information required and applies to a multi-layered tissue model embedded with tumor like heterogeneities, in which all tissue layers and tumors could have arbitrary absorption and scattering coefficients and dimensions. This advantage will speed up the computation by several orders of magnitude. Therefore the method is suitable for simulating diffuse reflectance spectra or creating a MC database to extract optical properties of a multi-layered tissue model with tumor-like heterogeneities from diffuse reflectance measurement. Such a method can be useful in the early diagnosis of epithelial cancer using diffuse reflectance spectroscopy.

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