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Effects of Anisotropic Optical Parameters on the Penetration of Photons into a Turbid Medium

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Abstract

There are by now many applications of methods based on near-infrared radiation (NIR) used for optical imaging and therapeutic purposes in medical settings. Such optical techniques are appealing in not requiring potentially harmful ionizing radiation, being non-invasive, and generally being easily implementable. Since photons are randomly scattered by cell components, successful use of NIR requires knowledge of the photon trajectories expressed in statistical terminology. Until now the necessary analysis has been based on diffusion theory assuming that the scattering coefficient is an isotropic material property. We analyze the properties of the penetration depth when this assumption is violated. By penetration depth will be meant the depth attained in the turbid medium, given its ultimate emission at the planar surface at a time τ, as a function of the degree of anisotropy of the scattering coefficient. Our analysis will be based on a continuous-time random walk formalism. Properties of both time-gated and continuous-wave experiments will be derived.

Keywords: optical imaging, lattice random walk, continuous-time random walk, transport-corrected scattering coefficient

1 Introduction

Light in all of its manifestations is universal in life as we know it. What is perhaps less well known is that the use of light as a means of biomedical imaging was suggested in a morbidity report as long ago as early nineteenth century as a means for detecting breast tumors, although it was never put to a real test in that era, [1]. A more recent experimental test of this notion was put forth by Cutler, [2], in 1929. Neither of these met with real success because the scientific and technical instrumentation for its successful implementation was obviously unavailable. It was only within the last thirty years that the availability of lasers and sophisticated computing technologies stimulated the development and exploitation of an enormous number of optically-based techniques in biomedical settings, both for imaging and therapy.

Typically, in optical imaging measurements, photons injected by means of a laser into a tissue to be examined, are scattered by various inhomogeneities within the tissue, and then potentially re-emitted through a boundary surface where they are detectable as variations in light intensity. Details of this light intensity encapsulate information related to the physical state of the underlying tissue which can be useful for diagnostic purposes.

The use of optical methods in the near-infrared spectrum is attractive because it is non-invasive and, as far as is presently known, non-carcinogenic [3]. However, since photons are randomly scattered by heterogeneous components of cells, an important requirement in the use of optical techniques corrupted by random scattering is a knowledge of which part of the turbid medium tissue has been interrogated by the photons. Generally properties of photon paths are described in terms of some form of transport theory. In its most general form this can require considerable numerical calculation, since a knowledge of physical properties of the bodies which lead to the scattering is difficult to obtain experimentally. Most often, a straightforward form of diffusion or random walk theory suffices to provide the necessary theory since the types of geometries dealt with are often relatively simple. For example, it is often successfully assumed that the tissue is an infinite slab or a semi-infinite bulk medium. However, when the optical parameters that char-

acterize the underlying tissue are anisotropic with respect to surfaces that separate the tissue from the exterior the mathematical analysis can give rise to considerable complications.

Since transport phenomena in most applications generally imply aspects of randomness, the language and techniques of probability theory provide a natural framework for describing photon motion in turbid media. There are obviously a number of ways of doing this. The specific parameter studied in the present note is the maximum depth reached by a photon which ultimately is re-emitted from the surface of the body being studied. The probability of observing a photon that has visited a given planar depth, or probability of photon reaching certain maximal depth has already been proposed as a parameter characterizing photon penetration earlier in the context of biomedical optics in [11]. Here we extend an analysis in which the photon diffusion in a semi-infinite turbid medium is modeled in terms of a lattice random walk, [4, 5]. The new feature in the present analysis allows for the scattering coefficient to be skewed with respect to a planar boundary rather than being isotropic.

2 Formulation of the model

The three major assumptions in the present analysis are (i), that diffusion in the continuum can be replaced by a random walk on a simple cubic lattice (ii), that the medium and exterior are separated by a plane and that the axes of the lattice are either parallel or perpendicular to boundary plane (iii), that within a given plane parallel to the boundary plane the medium is isotropic. A point of the lattice will be denoted by $\mathbf{r} = (x, y, z)$ where x, y and z are taken to be integers whose ranges are $-\infty < x, y < \infty$ and $0 \leq z < \infty$. That is to say, we consider a semi-infinite medium bounded by a plane $z = 0$, where $z > 0$ corresponds to points within the medium. The optical parameter of greatest interest is μ_s', the transport-corrected scattering coefficient. The lattice coordinate, $\mathbf{r}$, is related to the physical coordinate, $\mathbf{r}_{\rm phys}$, by $\mathbf{r}_{\rm phys} = \mathbf{r}(\sqrt{2}/\mu_s')$ as established in two studies of scaling relations by Gandjbakhche *et al*, [9, 10].

Many results of our investigation will be obtained in a relatively simple form provided that we restrict ourselves to nearest-neighbor random walks. That is to say that a photon at (x, y, z) is permitted, at any step, to move to only one of the six sites $(x \pm 1, y \pm 1, z \pm 1)$. The choice of the particular

site to which the step will be made is determined by the anisotropy, in a manner defined below. The starting point of any analysis related to the trajectory must obviously be based on the propagator. A most convenient way to proceed in the present problem is to use the continuous-time random walk (CTRW), [11, 12]. In the CTRW the time between successive steps is a random variable. Considerable simplification in the analysis is achieved provided that the probability density for this random time, $\psi(t)$, is chosen to have the form

$$\psi(t) = ke^{-kt} = e^{-\tau} \tag{1}$$

in which $k = c\mu_s'$ is a rate constant, and c is the speed of light in the tissue, so that τ is a dimensionless time.

A further assumption is required to define the degree of anisotropy. Note that the anisotropy could have been modeled by using a non-uniform lattice, however, here we treat μ_s', the transport-corrected scattering coefficient, and the rate constant k for the successive steps as being uniform, but the probabilities that such a jump occurs along a specific axis are not. Let the probability that the photon makes a single step along the x axis, i.e., $(x \to x \pm 1)$ be α, $y \to y \pm 1$ be β and $z \to z \pm 1$ be γ so that $2\alpha + 2\beta + 2\gamma = 1$. Isotropy is therefore equivalent to the choice $\alpha = \beta = \gamma = 1/6$. For simplicity we assume that $\alpha = \beta$. The initial position of the photon is taken to be $\mathbf{r}_0 = (0, 0, 1)$. In the absence of boundaries, that is, in free space, the propagator can be shown to be, [15],

$$p^{(F)}(\mathbf{r}; \tau|\mathbf{r}_0) = e^{-\tau} I_x(2\alpha\tau) I_y(2\beta\tau) I_{z-1}(2\gamma\tau) \tag{2}$$

where the $I_m(u)$ are modified Bessel functions of the first kind [14]. At sufficiently long times $p^{(F)}(\mathbf{r}; \tau|\mathbf{r}_0)$ approaches a Gaussian limiting form which is what one expects on the consideration that one is dealing with a random walk for which the central limit theorem holds. What is needed is an expression for the propagator that vanishes on the plane $z = 0$. Since the x and y components of the free-space propagator appear in a factored form, and $\mathbf{r}_0 = (0, 0, 1)$, the propagator that satisfies the boundary condition $p(x, y, 0; \tau|\mathbf{r}_0) = 0$ can be written as [15],

$$p(\mathbf{r}; \tau|\mathbf{r}_0) = ze^{-\tau} I_x(2\alpha\tau) I_y(2\beta\tau) I_z(2\gamma\tau)/(2\gamma\tau) \tag{3}$$

which clearly vanishes at $z = 0$.

In the next section we will use this propagator to calculate the probability that a photon reaches the boundary plane, $z = 0$, and is emitted into

the exterior at time τ, given it has reached the plane $z = Z$ at an earlier time. The utility of the formalism described earlier is that the propagator in Eq.(3) factors into functions of the three spatial variables which allows us to ultimately work with only a single spatial variable at a time.

3 Analysis

3.1 Time-gated experiments

There are two basic types of time-dependent experiments used in biomedical applications; time-gated measurements and continuous-wave (CW) measurements. In the first of these, the optical input can be regarded as a pulse and the output is measured as a function of time, while in CW measurements the input is continuous and the output is a steady-state signal. Information in either case is based on the time-dependent propagator. We therefore begin by studying this function.

Let the time at which the photon escapes through the surface be equal to τ and let two earlier times be $\tau'' < \tau'$ where, of course, $\tau' < \tau$. Denote the probability of observing a photon during the time $\tau, \tau + d\tau$, given that it has at some earlier time visited the plane $z = Z$, by $p(\tau|Z)$. We initiate the calculation by considering the contribution of the time interval $(\tau'', \tau'' + d\tau'')$ to the probability that the photon is at $z = Z$ at τ'', as a function of both Z and τ. To examine this function it will be necessary to examine the entire trajectory from $\mathbf{r}_0$ to an arbitrary point on the surface $\mathbf{R} =(X, Y, 0)$ and lastly, sum over all possible X and Y.

A trajectory which passes through $z = Z$ can be represented schematically as

$$(0, 0, 1; 0) \rightarrow (x, y, Z; \tau'') \rightarrow (X, Y, 1; \tau') \rightarrow (X, Y, 0; \tau) \tag{4}$$

This may be interpreted as follows: At $\tau = 0$ the photon is at $(0, 0, 1)$ from which point it moves to (x, y, Z), arriving there during the time interval $(\tau'', \tau'' + d\tau'')$. The trajectory from $(0, 0, 1)$ to (x, y, Z) is described by the propagator in Eq.(3). The coordinates x and y can take on all possible values, and are to be summed over in the course of the analysis. The random walk occurs on a simple cubic lattice, and has been defined to be a nearest-neighbor random walk terminating at $(X, Y, 0)$ at time τ. Therefore its position just prior to termination $z = 0$ must be at $(X, Y, z = 1)$ at some time τ', such

that $\tau > \tau' > \tau''$. As mentioned, the final step in the derivation consists in summing over X and Y.

The first step in analyzing the sequence in Eq.(4) requires a summation over all x and y using the propagator in Eq.(3). This produces a function $S_1(\tau'')$ defined as

$$S_1(\tau'') = \frac{Ze^{-\tau''}}{2\gamma\tau''} I_Z(2\gamma\tau'') \sum_{x=-\infty}^{\infty} \sum_{y=-\infty}^{\infty} I_x(2\alpha\tau'') I_y(2\beta\tau'') \tag{5}$$

The values of the sums over x and y can be derived from the general formula, [14],

$$\sum_{x=-\infty}^{\infty} I_x(m) = e^m \tag{6}$$

which produces the exponent $\tau''(-1 + 2\alpha + 2\beta) = -2\gamma\tau''$, so that Eq.(5) reduces to a function of the two variables, Z and $2\gamma\tau''$. This will be denoted by $U_Z(\tau'')$ where

$$U_Z(\tau'') = \frac{Ze^{-2\gamma\tau''}}{2\gamma\tau''} I_Z(2\gamma\tau'') \tag{7}$$

The next step in dealing with the sequence in Eq.(4) requires considering the subsequent part of the trajectory, $(x, y, Z; \tau'') \rightarrow (X, Y, 1; \tau')$. To this end we appeal to an argument based on symmetry to derive the contribution from this component. This allows the conclusion that it is basically the same as $S_1(\tau'')$ except that now the time τ'' that appears in Eq.(5) or (7) is to be replaced by the second increment in time, $(\tau' - \tau'')$. Hence the second component takes a form similar to that in Eq.(7) and yields:

$$S_2(\tau' - \tau'') = U_Z(\tau' - \tau'') \tag{8}$$

The final part of the trajectory takes the random walk from the point $(X, Y, 1)$ to $(X, Y, 0)$. The probability density for the time of this event is equal to $\gamma e^{-\gamma(\tau - \tau')}$.

Having now assembled the separate components of the trajectory, we can calculate $p(\tau|Z)$ in terms of convolution integrals and write

$$p(\tau|Z) = \gamma \int_0^{\tau} e^{-\gamma(\tau - \tau')} d\tau' \int_0^{\tau'} U_Z(\tau'') U_Z(\tau' - \tau'') d\tau'' \tag{9}$$

While this expression appears somewhat complicated, an equivalent and simpler looking expression can be found in terms of Laplace transforms. This

has the further advantage of leading directly to the comparable solution for the CW case. Let $\hat{h}(s)$ denote the transform of a generic function of time, $h(\tau)$, i.e., $\hat{h}(s) = \int_0^\infty h(\tau)e^{-s\tau}d\tau$. Using this notation in the transform of Eq.(9) one finds

$$\hat{p}(s|Z) = \frac{\gamma}{s+\gamma}\hat{U}_Z^2(s) \tag{10}$$

The transform of Eq.(7) or (8) can be found from standard tables to be, [16],

$$\hat{U}_Z^2(s) = \frac{1}{2\gamma}\left[\frac{2\gamma}{s+2\gamma+\sqrt{s^2+4\gamma s}}\right]^Z \tag{11}$$

We have not been able to invert this in closed form, but it can be inverted numerically with little difficulty. The long-time behavior of $p(\tau|Z)$ can be determined by passing to the $s \to 0$ limit of the expression in square brackets, which yields an approximation to $\hat{U}_Z^2(s)$ as

$$\hat{U}_Z^2(s) \approx \frac{1}{2\gamma}\left(1+\sqrt{\frac{s}{\gamma}}\right)^{-Z} \tag{12}$$

By taking logarithms of this relation and retaining the lowest order in s we find

$$\ln\left[\hat{U}_Z^2(s)\right] \approx \ln\left(\frac{1}{2\gamma}\right) - Z\ln\left(1+\sqrt{\frac{s}{\gamma}}\right) \approx \ln\left(\frac{1}{2\gamma}\right) - Z\sqrt{\frac{s}{\gamma}} \tag{13}$$

or

$$\hat{U}_Z^2(s) \approx \frac{1}{2\gamma}\exp\left(-Z\sqrt{\frac{s}{\gamma}}\right) \tag{14}$$

An inversion of this transform, together with Eq.(10) leads to an approximation which we expect to be valid at long times

$$p(\tau|Z) \approx \frac{Z}{4\sqrt{\pi(\gamma\tau)^3}}\exp\left(-\frac{Z^2}{4\gamma\tau}\right) \tag{15}$$

has a single maximum as a function of Z at $Z_{\max}(\tau) = (2\gamma\tau)^{1/2}$. It shold be noted that the term $\gamma/(s+\gamma)$ that appears in Eq.(10) is equal to unity for small s in comparison to that in Eq.(12) and its contribution can therefore be neglected in the long-time limit.

Figure 1 compares the numerical Laplace inversion of Eq.(11) with the approximation in Eq.(15) for different values of Z , γ and τ. When τ is large,

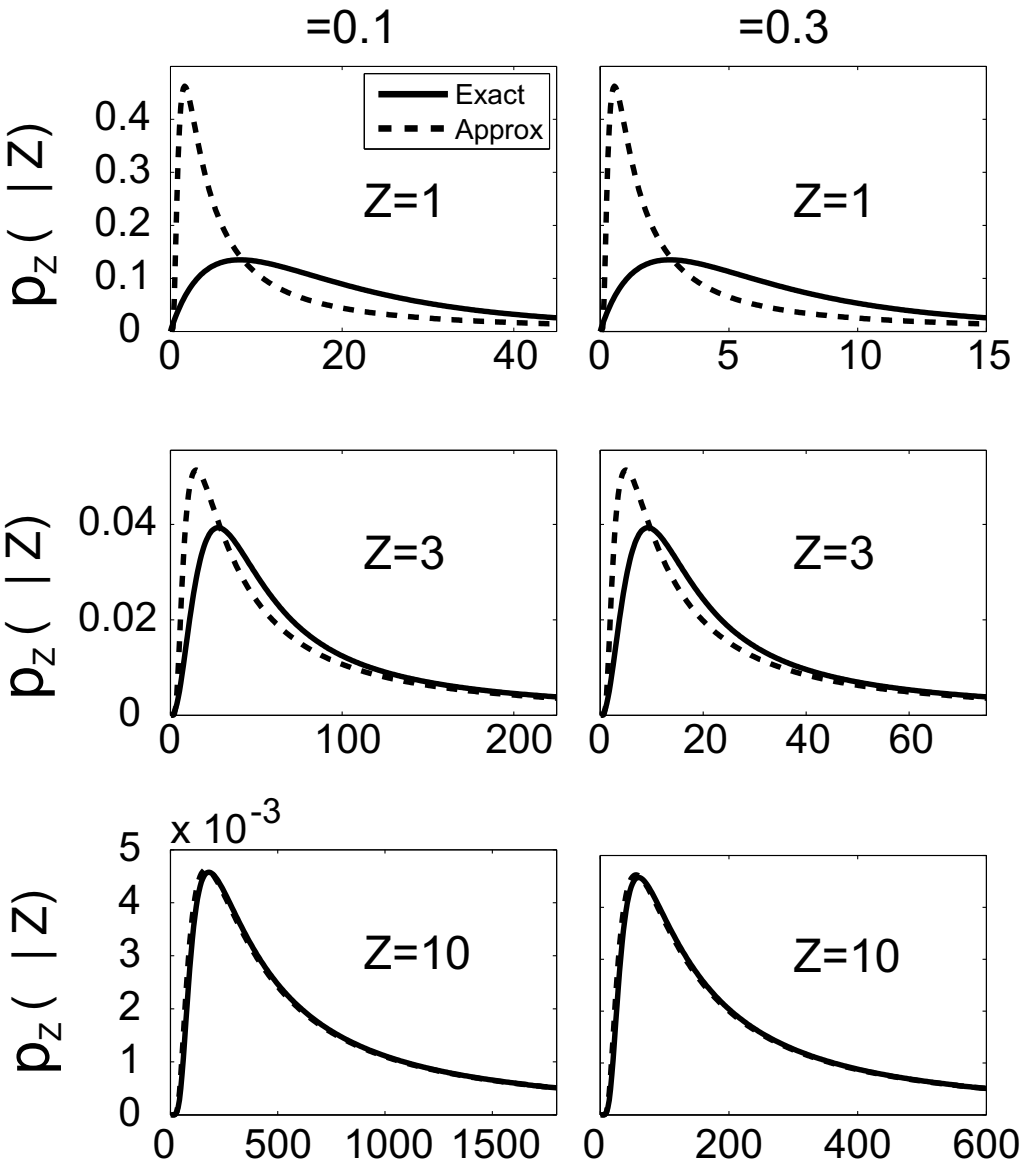

Figure 1: Plot of $p_Z(\tau|Z)$, comparing the numerical Laplace inversion of Eq.(11) with the approximation in Eq.(15), for $\gamma = 0.1$ (left column) and $\gamma = 0.3$ (right column), and for three values of Z, as indicated on each figure. For $\gamma = 0.1$ (0.3) anisotropy is such that the photons are more (less) likely to remain in the plane than in the isotropic tissue ($\gamma = 1/6$).

$p(\tau|Z)$ goes asymptotically to zero as $\tau^{-3/2}$, a power-law behavior predicted by the formula in Eq.(15), which agrees with the exact numerical result. For $Z > 1$ the approximation approaches the exact results quickly and for sufficiently deep penetration, $Z > 10$, the approximation and the exact result are virtually indistinguishable for all values of τ. Further extensions of the present analysis that might be of interest involve calculating the fraction of local time (residence time) spent on an arbitrary set of points to the total time it has taken photon to emerge at the detector τ. Presently, we have not explored all of the difficulties that might have to be overcome to complete such an undertaking in full generality.

3.2 CW experiments

A solution to the time-gated problem is obviously a first step needed to solve the analogous problem for CW experiments. The relation between the two solutions is direct. Let $g(\tau)$ be the probability density for a photon lifetime within the bulk, that is, the time between the photon injection and the time at which it leaves the medium, and let $p_{CW}(Z)$ be the contribution of all photons that have visited given $z = Z$ in a CW measurement. This function can be found in terms of $p(\tau|Z)$ by

$$p_{CW}(Z) = \int_0^\infty p(\tau|Z)g(\tau)d\tau \tag{16}$$

leaving us only with the problem of calculating $g(\tau)$. This can be done by analyzing the trajectory

$$(0, 0, 1; 0) \rightarrow (X, Y, 1; \tau') \rightarrow (X, Y, 0; \tau) \tag{17}$$

which is similar to Eq.(4) omitting the term $(x, y, Z; \tau'')$. An analysis following that in the preceding subsection leads to the expression

$$g(\tau) = \frac{1}{2}\int_0^\tau e^{-2\gamma\tau'}\frac{I_1(2\gamma\tau')}{\tau'}e^{-\gamma(\tau-\tau')}d\tau' \tag{18}$$

While this integral cannot be evaluated exactly, its Laplace transform is found to be, [16],

$$\hat{g}(s) = \frac{s + 2\gamma - \sqrt{s^2 + 4\gamma s}}{4\gamma(s + \gamma)} = \frac{\gamma}{(s + \gamma)\left[s + 2\gamma + \sqrt{s^2 + 4\gamma s}\right]} \tag{19}$$

It is again possible to find $g(\tau)$ from its transform by numerical inversion. A long-time approximation to $g(\tau)$ can be determined by passing to the limit $s \to 0$, leading to the somewhat simplified transform

$$\hat{g}(s) \approx \frac{\sqrt{\gamma}}{2(s+\gamma)\left(\sqrt{s}+\sqrt{\gamma}\right)} \tag{20}$$

The calculation of $\hat{g}(s)$ in the $s \to 0$ follows that in the preceding section, except that the factor Z that appears there is to be replaced by 1, so that

$$g(\tau) \approx \frac{1}{4\sqrt{\pi(\gamma\tau)^3}} \exp\left(-\frac{1}{4\gamma\tau}\right) \tag{21}$$

which decays as $\tau^{-3/2}$. Since $g(\tau)$ is equivalent to $p_z(\tau|Z=1)$ one can see in the top row of Figure 1 ($Z=1$) that this approximation works well only at large values of τ. Nevertheless, using Eqs. 15 and 21 we can arrive at approximate analytic expression for $p_{CW}(Z)$, i.e.,

$$p_{CW}(Z) \approx \frac{Z}{\pi\left(Z^2+1\right)^2\gamma} \tag{22}$$

In Fig. 2 we compare this expression with the accurate result obtained by numerical Laplace inversion and the integral required by the formula in Eq.(16). Figure 2(a) compares numerically accurate and approximate values of $p_{CW}(Z)$ as a function of Z for $\gamma = 0.1$. As Eq.(22) indicates, the approximation has a simple dependence on γ, while the ratio of the approximate and the exact results is insensitive to variation with γ (see Fig. 2(b)). As Z increases the approximation in Eq.(22) approaches the exact result, as can be seen in Figs. 2(a) and 2(b).

4 Conclusions

Optical techniques for biomedical imaging are becoming increasingly popular because they require no potentially dangerous ionizing radiation. Additionally, optical techniques in the NIR regime (photon wavelenghts roughly between 400 and 1100 nm) are potentially sensitive to metabolic processes and blood flow. However, a drawback is that photons are also scattered in that range of wave lengths. Consequently, the problem of establishing

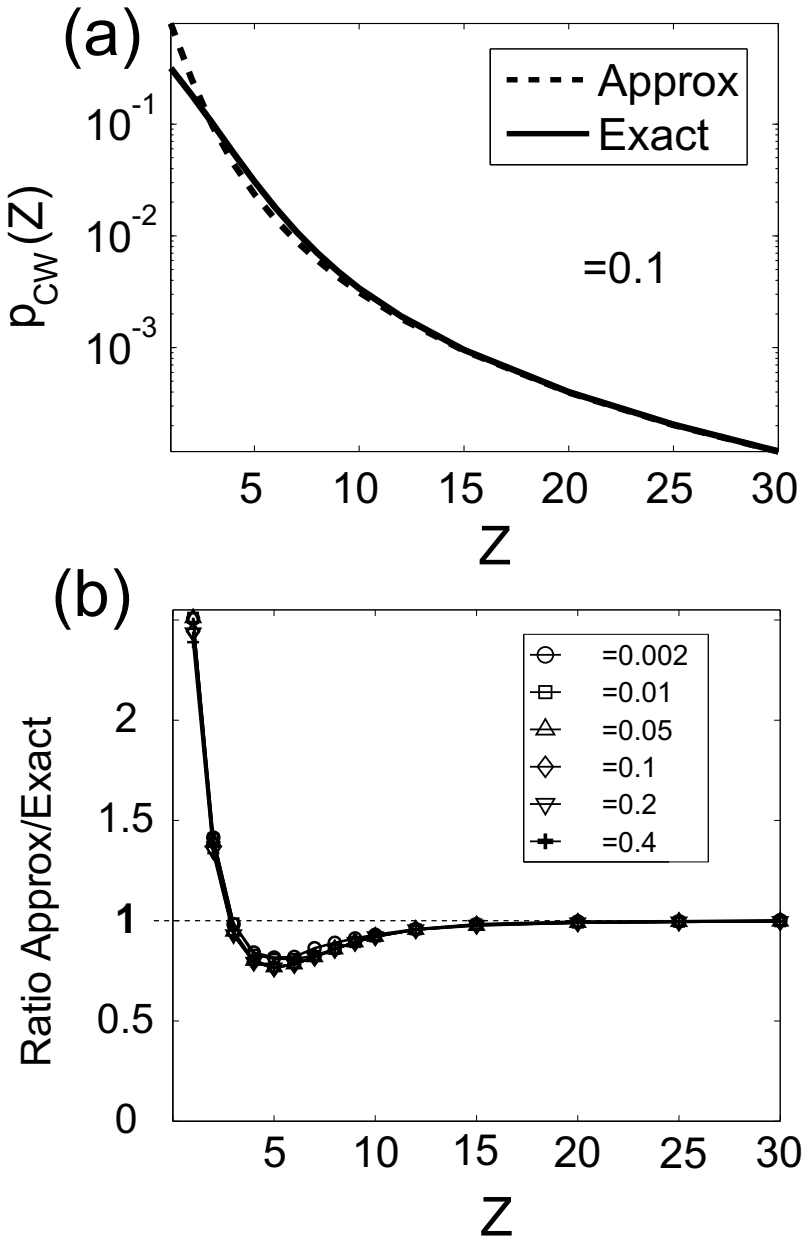

Figure 2: (a) Plot of $p_{CW}(Z)$, comparing the approximate result in Eq.(22) to exact numeric evaluation for $\gamma = 0.1$. The results are plotted on semi-logarithmic plot to emphasize the agreement at larger values of Z. (b) Plot of the ratio of the approximate result and the exact numeric result as a function of Z, for six different values of γ.

precisely which volumes have been interrogated by photon trajectories in biological tissues is an important one. In view of the fact that many tissues have been identified as having anisotropic optical properties it is worthwhile to investigate the effects of this class of properties.

To investigate at least one aspect of this general problem we have worked with a model in which the diffusion is represented by a CTRW on a simple cubic lattice in which the anisotropy is represented by differences in transition probabilities for movement along different axes of the lattice. This model was first suggested and several of its properties analyzed in [17]. We investigated the probability of observing a photon being emitted through the plane $z = 0$ during the time interval $(\tau, \tau + d\tau)$ conditional on visiting the plane $z = Z$ at some earlier time. A complete solution for this conditional probability density for both time-gated and continuous wave measurements is given in terms of Laplace transforms. The asymptotic ($\tau \to \infty$) solution is shown to have a single maximum as a function of Z and is proportional to $\tau^{-3/2}$ in the case of time-gating and has a single maximum as a function of Z in the case of both measurements techniques. More complicated problems can also be addressed, for example, by calculating the joint probability of the exit time and the exit site. This, however, requires considerable further computation and leads to more complicated results. We have therefore not pursued this additional complication at the present time.

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