Random walk analysis of time-resolved transillumination measurements in optical imaging

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Data relating photon migration in human tissue can be obtained from experiments in which laser light is injected into one face of a finite slab of tissue and detected at the opposite face. From the results of such experiments one would like to infer optical properties of the underlying tissue which are related to its biological properties. Random walk theory has been successfully applied to the translation of such data into the physical parameters that characterize properties of the tissue. We here outline a technique based on the theory of random walks for analyzing how well time-resolved transillumination experiments may be expected to perform for detecting hidden inclusions which have a greater absorption than surrounding tissue. We use an asymptotic evaluation of exact results to determine the degree to which detection is possible.

1. Introduction

The possibility of medical imaging by optical techniques is a very appealing one because of the presumed safety of such modalities as compared, say, with those based on the use of X-rays. Indeed, there is considerable research activity in this area, both theoretical and experimental, a good sampling of which is summarized in [1,2]. In particular, imaging systems have been proposed as a possible means to screen for tumors that have optical properties differing from those of normal tissue [3–9]. Imaging based on conventional transillumination methods (i.e., methods using cw light beams) are generally found to have intrinsically poor resolution. In contrast, time-gated optical detection which measures the earliest-arriving photons at a detector following a brief pulse of light can enhance the detectability of absorbing objects hidden in normal tissue because the intensity of light detected in the short-travel time regime will generally depend on the optical properties of a narrow volume in the tissue. Hence, when one scans along a tissue and detects light transmitted
Fig. 1. A schematic diagram of the configuration of a transillumination measurement. As shown, the positive $z$ coordinate points into the slab and $x$ and $y$ are coordinates transverse to $z$, with $\mathbf{r} = (x, y)$.

through the tissue, an observable change in signal strength is possible when an absorbing object is located between the source and the detector, as is illustrated in idealized form in fig. 1.

A common technique for performing such time-resolved imaging is through the use of a streak camera [4]. In such a system a pumped dye laser provides a very short pulse having a duration of several picoseconds. The repetition rate is generally of the order of a small number of megahertz, and the wavelength is selected to be that at which the streak camera is most sensitive. Generally this is of the order of 600 nm. The incident beam is divided into two separate pulses, as indicated in fig. 2. The first is a reference pulse which arrives at the streak camera without passing through the sample, and the second beam is delivered to the imaged object and focussed before being collected at the input slit of the streak camera. The streak camera system produces a two-dimensional image which is a measure of the intensity of the light emerging from a small region of the optically turbid medium centered on the optical axis.

In order to examine the efficiency of any optical imaging scheme it is necessary to have a model for the motion of photons through a biological tissue. Since such tissue is generally quite complex it is generally assumed that
one is in a multiply scattering regime. There are a number of approaches to modelling the motion of photons through a turbid medium, and different authors have chosen to model such motion in terms of transport theory [10], diffusion theory [11], a lattice random walk model [12], and by different simulation techniques [13,14]. Somewhat surprisingly, the lattice random walk model does a quite good job in fitting data which have been generated both from experiments and from computer simulations based on a more realistic physical picture of photon motion that includes anisotropic scattering effects [12]. These cannot be incorporated directly into a diffusion model but some recent work has been directed towards establishing the relation between a theory that contains anisotropic scattering effects and the diffusion theory which is equivalent to it at sufficiently long times [15,16].

The work to be described in this paper is aimed at giving a mathematical formalism based on a random walk picture that allows a simple evaluation of some of the properties suggesting as being important by the physical problem. We will discuss what is most likely the simplest of a hierarchy of imaging models, leaving for future work embellishments on this most basic of models. The problem to be analyzed relates to light transmission through a finite slab bounded by two parallel planes. The internal structure of the slab is modelled in terms of a simple cubic lattice and the distance between the bounding planes is assumed to be an integer number of lattice sites, which will be denoted by \( L \). A single point of this lattice is taken to be completely absorbing, which will be regarded as a model of an inclusion in the tissue. The system of coordinates is indicated in fig. 1. Our investigation is aimed at determining the effect on photon transmission of the presence of an inclusion which absorbs photons more heavily than does the surrounding tissue. The present paper emphasizes imaging in terms of time-gated measurements. There already exist accurate computer simulations of much more complicated versions of this model [14],

![Diagram of the instrumental implementation of the time-resolved transillumination experiment.](image-url)
2. Formulation of the model

We will assume that the laser beam impinges on the slab at a single lattice point as shown in fig. 1. The coordinate pointing into the slab will be designated as \( z > 0 \), as shown, and the transverse coordinates will be denoted by \( \rho = (x, y) \). Material properties of the tissue are assumed to be isotropic which excludes an insignificant number of specific applications. Under this assumption the quantities of interest will depend only on the magnitude \( \rho = (\rho \cdot \rho)^{1/2} \). The coordinates \( x \) and \( y \) are integers which range from \(-\infty\) to \(+\infty\). In our model the surfaces at \( z = 0 \) and \( z = L \) will be assumed to be trapping surfaces necessitating the assumption that the initial position of a typical photon or random walker is \( r_0 = (x_0, y_0, 1) \), i.e., \( z_0 = 1 \). The absorbing point is set at \( s = (0, 0, s) \). The total number of photons that eventually reach the point \( z = L \) within \( n \) steps constitute the measured output of time-gated experiments. As previously shown the dimensionless parameters \( L, n \) and \( \rho \) can be related to real space and time variables and the optical parameters of the medium [16].

A mathematical formulation of this model is therefore equivalent to determining a number of properties of a lattice random walk in which a single point has been excluded. Properties of such random walks have been studied earlier but only on a lattice unbounded in all directions [18].

3. Analysis

We will need to define a number of functions before proceeding to the analysis. Let \( p_n(r|r_0) \) be the probability that a random walker initially at \( r_0 \) is at \( r \) at step \( n \) in the presence of trapping boundaries at \( z = 0 \) and \( z = L \), and let \( f_n(r|r_0) \) be the first passage time probability for the displacement from \( r_0 \) to \( r \) in \( n \) steps again in the presence of trapping boundaries. Finally, let \( q_n(r|r_0) \) be the probability that the photon, in the absence of internal absorption, reaches \( r \) excluding visits to the absorbing point at \( s \). This restriction is equivalent to the identification of \( s \) as a trapping point. The probability \( q_n(r|r_0) \) is related to \( p_n(r|r_0) \) and \( f_n(r|r_0) \) by
\[ q_n(r|r_0) = p_n(r|r_0) - \sum_{k=0}^{n} f_k(s|r_0) \ p_{n-k}(r|s) \]  

(1)

since this relation subtracts from the expression for \( p_n(r|r_0) \) the contribution from all walks that would ordinarily pass through \( s \) before reaching \( r \) at step \( n \). Because of the convolution in this last equation it is convenient to introduce a generating function with respect to the step parameter. We define this function as

\[ \hat{q}_\xi(r|r_0) = \sum_{n=0}^{\infty} q_n(r|r_0) e^{-\xi n} \]  

(2)

with a similar notation applying to the remaining functions in eq. (1). Under this convention, eq. (1) is equivalent to the relation

\[ \hat{q}_\xi(r|r_0) = \hat{p}_\xi(r|r_0) - \hat{f}_\xi(s|r_0) \hat{p}_\xi(r|s) \]  

(3)

One can show by a straightforward argument [19] that

\[ \hat{f}_\xi(s|r_0) = \hat{p}_\xi(s|r_0)/\hat{p}_\xi(s|s) \]  

(4)

so that the generating function which will be central to our analysis is \( \hat{p}_\xi(r|r_0) \) since all of the terms in eq. (3) can be made up of terms of this form. In fact, since we deal with nearly ballistic photons we will mainly be interested in the behavior of this function in the large \( \xi \) limit.

For convenience we will assume that the random walk is to nearest neighbors only, so that in an unrestricted three-dimensional space the displacement probabilities are equal to \( \frac{1}{6} \) in all allowed directions. The generating function or the Fourier series of the transition probabilities for this walk in an unbounded space, \( \lambda(\theta) \), is therefore equal to

\[ \lambda(\theta) = \frac{1}{3} \left( \cos \theta_1 + \cos \theta_2 + \cos \theta_3 \right) \]  

(5)

which, by a separation of variables in the evolution equation, allows us to write an explicit representation of \( p_n(r|r_0) \) in the form

\[ p_n(r|r_0) = \frac{1}{2\pi^2 L} \int_{-\pi}^{\pi} \int_{-\pi}^{\pi} \sum_{j=1}^{L} \lambda^n(\theta_1, \theta_2, \frac{\pi j}{L}) \sin\left(\frac{\pi j z_0}{L}\right) \sin\left(\frac{\pi j z}{L}\right) \times \exp[i(x_0 - x)\theta_1 + i(y_0 - y)\theta_2] \ d\theta_1 \ d\theta_2 . \]  

(6)

We will be interested in the case of large \( L \) (the physiologically interesting
range begins at about $L = 10$) so that the values of $n$ must be at least that large. This suggests that the physically interesting results can be found by restricting attention to small values of the components of $\theta$. Since these are small the limits on the integrals in eq. (6) can be extended to $\pm \infty$ and the upper limit of the sum in eq. (6) can also be extended to $\infty$. In fact we write

$$\lambda^L(\theta_1, \theta_2, \frac{\pi j}{L}) \sim \exp\left(-\frac{n\theta_1^2}{6} - \frac{n\theta_2^2}{6} - \frac{\pi^2 j^2}{6L^2}\right), \quad (7)$$

and, by evaluating the integrals over the $\theta$'s, one finds that $p_n(r|r_0)$ can be represented as

$$p_n(r|r_0) \sim \frac{3}{\pi Ln} \exp\left(-\frac{3|\rho - \rho_0|^2}{2n}\right) \sum_{j=1}^\infty \exp\left(-\frac{n\pi^2 j^2}{6L^2}\right) \sin\left(\frac{\pi jz_0}{L}\right) \sin\left(\frac{\pi jz}{L}\right),$$

(8)
in which $\rho_0 = (x_0, y_0)$. The approximations which we have adopted have allowed the decoupling of the $(x, y)$ coordinates from the $z$ coordinate in the expression for $p_n(r|r_0)$. An alternative expression for the sum in eq. (8) can be given either by means of a Poisson transformation or by the method of images but will not be used in any of the following analysis. In the transillumination experiments illustrated in fig. 1 it is always the case that $\rho = \rho_0$ so that the exponential multiplying the sum in eq. (8) is equal to 1.

Recall that the principal tool for calculating $q_n(r|r_0)$ is the generating function given in eq. (2). The difficulty in finding this function from the formal expression in eq. (3) is the fact that $\hat{f}_\xi(s|r_0)$ is a ratio of transforms as shown in eq. (4) and its inverse is not readily calculated. We make use of a relatively crude approximation to find results which are easily evaluated. The key observation is that physical properties in the short time limit can also be found in terms of the large-$\xi$ limit of the generating function. In the model of photon migration as a random walk on a simple cubic lattice the flux at step $n$ can be expressed in terms of the state probabilities as

$$j(n) = \frac{1}{\xi} q_{n-1}(\rho, L - 1|\rho, 1)$$

(9)
in the presence of an absorber, which is to say that our attention need only be directed towards a calculation of properties of the propagator $p_n(r|r_0)$, or, equivalently, its generating function $\hat{p}_\xi(r|r_0)$. In the transillumination experiment (i.e., $\rho = \rho_0$) a convenient expression for $\hat{p}_\xi(r|r_0)$ based on eq. (8) is found to be
\[ \hat{p}_\xi(r|r_0) = \frac{3}{\pi L} \sum_{j=1}^{\infty} \ln \left( \frac{1}{1 - \exp \left( -\xi - \frac{j^2}{6L^2} \right)} \right) \sin \left( \frac{\pi j z_0}{L} \right) \sin \left( \frac{\pi j z}{L} \right). \] (10)

The suggested approximation based on taking the large-\( \xi \) limit of \( \hat{p}_\xi(s|s) \), is found from this expression to be

\[ \hat{p}_\xi(s|s) \sim e^{-\xi} \sum_{j=1}^{\infty} \exp \left( -\frac{j^2}{6L^2} \right) \sin^2 \left( \frac{j s}{L} \right) + O(e^{-2\xi}). \] (11)

The use of this asymptotic form in eqs. (3) and (4) leaves just a product of two generating functions in eq. (3), which is equivalent to an easily evaluated convolution of a transformation back to the time domain.

A consequence of the expressions in eqs. (1)-(4) and (8) is that \( q_n(r|r_0) \) is unchanged when the position of the absorber is reflected through the line \( z = \frac{1}{2}L \) so that only results for \( s > \frac{1}{2}L \) need to be calculated. The symmetry property is a consequence of the isotropy of the random walk, since when the input and output points are interchanged the random walk is exactly reversible. It is trivially verified that the expression for \( \hat{p}_\xi(s|s) \) also has this property.

Numerical calculations of this function regarded as a function of \( s \) for a fixed value of \( L \) indicate that it is very nearly constant (exhibiting variations of much less than 1% across the slab) for values of \( L \geq 10 \). If we express the lowest order term in eq. (11) by \( \hat{p}_\xi(s|s) \sim A(L) e^{-\xi} \), the function \( A(L) \) is, to a good approximation, given by

\[ A(L) = 0.35L - 0.05, \quad L > 10, \] (12)

and the expression for \( \hat{q}_\xi(r|r_0) \) is approximated by

\[ \hat{q}_\xi(r|r_0) = \hat{p}_\xi(r|r_0) - \frac{e^\xi}{A(L)} \hat{p}_\xi(r|s) \hat{p}_\xi(s|r_0). \] (13)

The photon flux itself is not measured directly but rather the cumulative number of photons transmitted through the slab is measured as a function of time at the point on the opposite face of the slab having the same value of \( x \) and \( y \) as the input point. That is to say, the experimentally detectable output is a cumulative intensity, \( \Gamma_t(n) \), which, according to our approximation in eq. (13), is given by the sum
\[ \Gamma_a(n) = \sum_{k=1}^{n-1} j(k) \sum_{k=1}^{n-1} p_{k-1}(0, L-1|0, 1) \]
\[ - \frac{1}{A(L)} \sum_{m=1}^{n-2} p_{n-\gamma-m}(0, s|0, 1) p_{m}(0, L-1|0, s) \]  
(14)

where the shift in the index of the last term on the right-hand side comes from the factor \( e^\xi \) in eq. (13).

4. Results

A measure of the detectability of the absorber in the transillumination experiment is provided by the ratio of \( \Gamma_a(n) \) in the presence of an absorber to the same function in the absence of the absorber. This ratio will be denoted by \( R(n) (=\Gamma_a(n)/\Gamma_0(n)) \) and, from the physical picture, one can deduce that this function is necessarily less than 1. In fig. 3a we compare a plot of this function with the data generated by exact enumeration when the source, the absorber and the detector are all collinear, which is where one expects the greatest effect. The sensitivity of \( \Gamma_a(n) \) at relatively short times to the presence of an absorbing point is clearly evident in the curve shown. On the other hand, when both the illumination and detection points are not collinear with the absorbing point the sensitivity falls very rapidly to zero with increasing distance from that point. This effect is illustrated in fig. 3b. These qualitative results can be understood in terms of the physical picture in which photons which arrive at the detector at long times are those which have wandered away from the axis connecting the photon source and the detector and therefore are not likely to

![Fig. 3.](image-url)
encounter the absorber. The ballistic and short path photons are those most likely to encounter the absorbing point and consequently measurements made at short times are most likely to detect a region of enhanced absorption. At very long times the effect of the absorbing point is very weak, which is an indication of the superiority of the time-resolved transillumination experiment over the cw experiment in the context of imaging.

A final point to be made about the present calculations is that in the present formulation, as already mentioned, an absorbing point located at a distance \( \frac{1}{2}L + \sigma \) gives effects indistinguishable from those at \( \frac{1}{2}L - \sigma \). One possible way of resolving this ambiguity in the location of the absorber is to choose a value of \( \rho \) unequal to \( \rho_0 \), which is to say, to remove the restriction to the experiment described by fig. 1. The problem with this modified experiment is that the number of photons affected by the absorber is considerably reduced and may therefore not be of practical use.

5. Discussion

A number of generalizations of the current model can be analyzed by a similar mathematical formalism. The most straightforward of these is the inclusion of the internal absorption of photons into the present model. This is usually modelled in terms of a Beer's law picture, which requires a replacement of the functions \( q_n(r|r_0) \) by \( q_n(r|r_0) e^{-\mu r} \), \( \mu \) being a constant that measures absorption. This is equivalent to replacing the parameter \( \xi \) by \( \xi + \mu \) in the transform domain. It is our expectation that the effect of internal absorption is to enhance the effectiveness of the transillumination experiment as described here since this absorption tends to filter out photons which would ordinarily have long trajectories within the slab.

A second relatively simple extension of the present analysis is to include the effect of an imperfect absorber, which is to say that a photon impinging on the designated site is absorbed with probability equal to \( \eta < 1 \) rather than \( \eta = 1 \) as assumed till now. Including this possibility allows us to study the transition between the case of an absorber-free medium and one with a perfect absorber. The mathematical formalism required to take this possibility into account is based on the inclusion of a set of other functions derived from the first passage time probability \( f_k(s|r_0) \) that appears in eq. (1). The difference in the physical picture introduced by imperfect absorption is that the photon may be at the absorbing site an arbitrary number of times before being absorbed. The
formalism developed in this paper can be extended to yield an expression in closed form for the function $R(n)$ in the case of partial absorption.

Since the results of our analysis are all expressible in terms of generating functions they can be used without approximation to find the expressions necessary for interpreting data from frequency-resolved experiments [20,21]. Finally, we mention that while we have only described the mathematical development relevant for the detection problem as formulated in terms of a single absorbing point it is also possible to extend the analysis to deal with multiple absorbing points. This treatment makes use of formalism developed in [22]. Applications of such an analysis can be made to the problem of resolving different absorbers. This will be discussed in a future publication.

References