# DIFFUSION EQUATION REPRESENTATION OF PHOTON MIGRATION IN TISSUE

Michael S. Patterson, Steen J. Madsen,
J. David Moulton and Brian C. Wilson

Hamilton Regional Cancer Center and McMaster University
711 Concession St., Hamilton, Ontario, Canada L8V 1C3

A time dependent diffusion model of photon migration in tissue is used to develop analytic expressions for the diffusely reflected pulse detected some distance from a delta function input. Particular attention is paid to the nature of the boundary between the tissue and the surrounding non-scattering medium, and it is shown that the pulse shape is relatively insensitive to the nature of this boundary. Monte Carlo simulation and experimental results are presented which confirm the accuracy of the diffusion model.

## 1. INTRODUCTION

Mathematical models of light propagation in tissue are required for two purposes. The first is to estimate the radiation field in tissue given its optical properties and the irradiation conditions. Such "forward" calculations are necessary to predict the biological effect of therapeutic interventions such as laser surgery or photodynamic therapy. The second purpose is to infer the optical properties of the tissue from measurements of the light field. These "inverse" calculations are characteristic of diagnostic techniques which use changes in the optical properties as indicators of physiological or pathological processes. Solution of the inverse problem usually involves iterative applications of a forward calculation of the light field to improve estimates of the optical properties (1).

In this paper we will be concerned with perhaps the simplest of inverse problems, illustrated in Fig.1. The object is to estimate the absorption and scattering coefficients of the tissue, where these properties are assumed to be spatially invariant. Our estimate relies on the fact that a short light pulse is temporally broadened as it propagates in a multiple scattering medium such as soft tissue. Hence the shape of the diffusely reflected pulse detected some distance from the source depends on both the absorption and scattering properties of the medium.

In this paper we will present a simple model, based on diffusion theory, which provides an analytical expression for the detected pulse as a function of the tissue optical properties. We will discuss the influence of the boundary between the tissue and the surrounding medium on the pulse shape and will compare the diffusion model with more accurate Monte Carlo simulation. Finally we will show representative experimental data illustrating the solution of this inverse problem and discuss some problems in clinical implementation.

## 2. THEORY

It is generally agreed (2) that the propagation of light in a strongly scattering medium such as tissue is accurately described by the equation of radiative transfer. The radiation field at any point is characterized by the energy radiance, which is the energy transported by photons per unit time in a given direction per unit solid angle per unit area normal to that direction. If the radiance is not strongly dependent on direction, it is possible to derive a much simpler equation for the fluence rate $\phi(\underline{r},t)$ which is simply the integral of the radiance over all solid angles. This diffusion equation is

$$\frac{1}{c}\frac{\partial\phi(\underline{r},t)}{\partial t} - D\underline{\nabla}^2\phi(\underline{r},t) + \mu_a\phi(\underline{r},t) = s(\underline{r},t) \qquad (1)$$

where c is the speed of light, $\mu_a$ is the linear absorption coefficient, $s(\underline{r},t)$ is a fluence source and the diffusion coefficient $D = \{3[\mu_a + (1-g)\mu_s]\}^{-1}$ where $\mu_s$ is the linear scattering coefficient and g is the mean cosine of the scattering angle. The solution of Eq.(1) for the case of a unit point source $s(\underline{r},t) = \delta(0,0)$ in an infinite uniform medium is

$$\phi(\underline{r},t) = \frac{c}{(4\pi Dct)^{3/2}}\exp\left(-\frac{r^2}{4Dct}\right)\exp(-\mu_a ct) \qquad (2)$$

We now consider the problem posed in Fig.1 where light is introduced by a small source (such as an optical fiber) at the surface of a semi-infinite uniform medium and collected by another fiber at a distance ρ. We will ignore the finite size of source and detector and further assume that all incident photons are scattered at a depth $z_0 = [(1-g)\mu_s]^{-1}$, an equivalent mean free path for isotropic scattering. We seek an expression for

$$R(\rho,t) = -D\frac{\partial}{\partial z}\phi(\rho,z,t)\Big|_{z=0} \qquad (3)$$

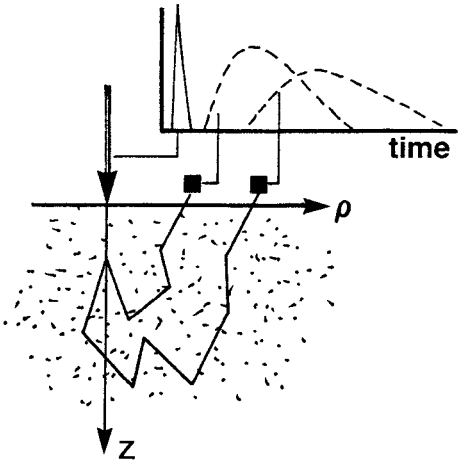


Fig. 1 Formulation of the inverse problem in which the optical properties of a uniform semi-infinite medium are to be estimated from measurements of the time resolved diffuse reflectance R(ρ,t).



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the light energy reaching the surface per unit area per unit time per unit incident energy when the tissue is in contact with a non-scattering medium in which the speed of light is $c_o$. We will consider the solution of Eq.(1) subject to three boundary conditions.

## 2.1 Partial Current Boundary Condition

The most correct formulation (3) of the boundary condition relates the flow of energy across the surface in both directions by the expression

$$\frac{1}{4}\phi(0,t) - \frac{D}{2\kappa}\frac{\partial\phi}{\partial z}\bigg|_{z=0} = 0 \tag{4}$$

where

$$\kappa = \frac{(1-R_0)(1-\mu_c^2)}{(1+R_0) + (1-R_0)\mu_c^3} \tag{5}$$

$$R_0 = \left(\frac{c_0-c}{c_0+c}\right)^2 \tag{6}$$

$$\mu_c = \cos\left[\sin^{-1}\left(\frac{c}{c_0}\right)\right] \tag{7}$$

The solution for R(ρ,t) under these conditions is

$$R(\rho,t) = \frac{1}{2}\frac{c\kappa}{(4\pi Dct)^{3/2}}\exp\left(-\frac{\rho^2+z_0^2}{4Dct}\right) \cdot \left\{2 - \kappa\sqrt{\pi}\sqrt{\frac{ct}{D}}\exp\left[\frac{(z_0+\kappa ct)^2}{4Dct}\right]erfc\left[\frac{z_0+\kappa ct}{\sqrt{4Dct}}\right]\right\}\exp(-\mu_a ct) \tag{8}$$

which is somewhat inconvenient because of the need to numerically evaluate the complementary error function.

## 2.2 Zero Fluence Boundary Condition

A much simpler approach, which we presented in an earlier publication (4), is to assume the fluence is zero on the boundary. While not physically correct, this allows the solution of Eq.(1) by the method of images (5) leading to

$$R(\rho,t) = \frac{z_0}{(4\pi Dc)^{3/2}}t^{-5/2}\exp\left(-\frac{\rho^2+z_0^2}{4Dct}\right)\exp(-\mu_a ct) \tag{9}$$

This simple expression can be rapidly evaluated and is suitable for estimating $\mu_a$ and D by least-squares fitting.

## 2.3 Extrapolated Boundary Condition

A compromise solution which is physically plausible and also allows solution by the method of images is to assume that the fluence is zero at an extrapolated boundary a distance $z_e$ from the actual boundary. It is well known in transport theory (6) that this artifice provides much more accurate estimates of the fluence in the medium near a boundary. In diffusion theory the correct choice of $z_e$ is

$$z_e = \frac{2D}{\kappa} \tag{10}$$

and the resulting expression for the reflectance is

$$R(\rho,t) = \frac{1}{2(4\pi Dc)^{3/2}}t^{-5/2}\exp(-\mu_a ct) \cdot \left\{z_0\exp\left(-\frac{\rho^2+z_0^2}{4Dct}\right) + z_p\exp\left(-\frac{\rho^2+z_p^2}{4Dct}\right)\right\} \tag{11}$$

where $z_p = z_o + 2z_e$.

## 2.4 Comparison of Solutions with Different Boundary Conditions

Extensive comparison of solutions based on the partial current and extrapolated boundary condition (7) has shown that they are in very close agreement. A typical example is shown in Fig.2 where R(ρ,t) has been calculated using all three boundary conditions. Therefore Eq.(11) appears to be adequate for most purposes. In fact, as evident in Fig.2, even the solution based on the zero fluence boundary gives an almost identical pulse shape. Inspection of Eqs.(9) and (11) shows that for $\rho^2 >> z_o^2, z_p^2$, the zero fluence and extrapolated boundary solutions are related by a constant factor 1 + 2/3κ.

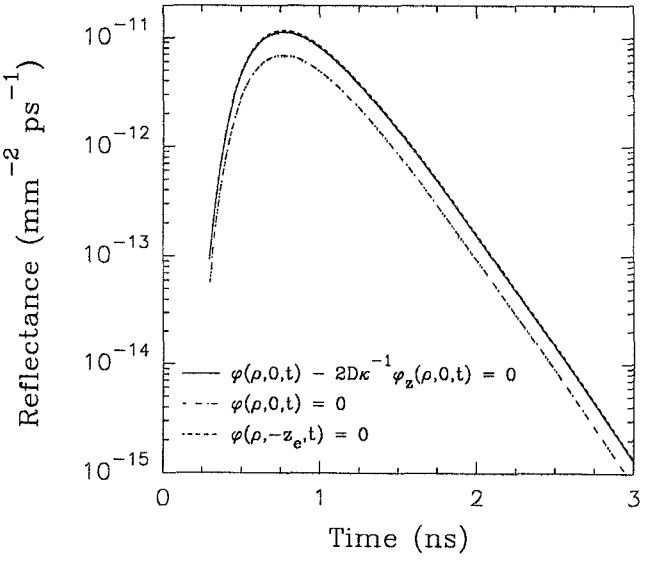


Fig. 2 Evaluation of R(ρ,t) using the three boundary conditions discussed in the text. Calculations performed for ρ = 30 mm, $\mu_a$ = 0.02 mm$^{-1}$, (1-g)$\mu_s$ = 1.5 mm$^{-1}$.

## 2.5 Influence of Index of Refraction on Pulse Shape

From the preceding discussion it is clear that $R(\rho,t)$ depends on both c and $c_o$, and we must consider how uncertainty in these two quantities affects estimates of $\mu_a$ and (1-g) $\mu_s$. Studies of the index of refraction of tissue (8) suggest that a value of c = 0.214 mm $ps^{-1}$ is unlikely to be in error by more than a few per cent for any soft tissue in the visible and near infrared spectral regions. Examination of Eqs. (8,9,11) reveals that an error in c results in a proportional error in the estimates of $\mu_a$ and (1-g) $\mu_s$, i.e. a 5% overestimate of c results in a 5% underestimate of the absorption coefficient and a 5% overestimate of the scattering coefficient.

If the tissue is in contact with air only, the value of $c_o$ is obvious. If a probe used to hold the source and detector fibers is in contact with the tissue, it is not clear what value of $c_o$ to assume. The influence of this parameter is illustrated in Fig.3 where in one case we have assumed that $c_o$ = c = .214 mm $ps^{-1}$ ( a so-called matched boundary) and in the other case $c_o$ = 0.300 mm $ps^{-1}$ (a mismatched boundary). While the absolute value of $R(\rho,t)$ depends on c and $c_o$, the pulse shape is rather insensitive to a mismatch at the boundary. In fact for $\rho^2 >> z_o^2, z_\rho^2$, $R(\rho,t)$ for a mismatched boundary is related to the reflectance for a matched boundary ($\kappa = 1$) by a multiplicative constant $0.60 + 2/5\kappa$. In summary, estimates of the absorption and scattering coefficients do not require complete knowledge of the light propagation speed in the tissue or the surrounding medium.

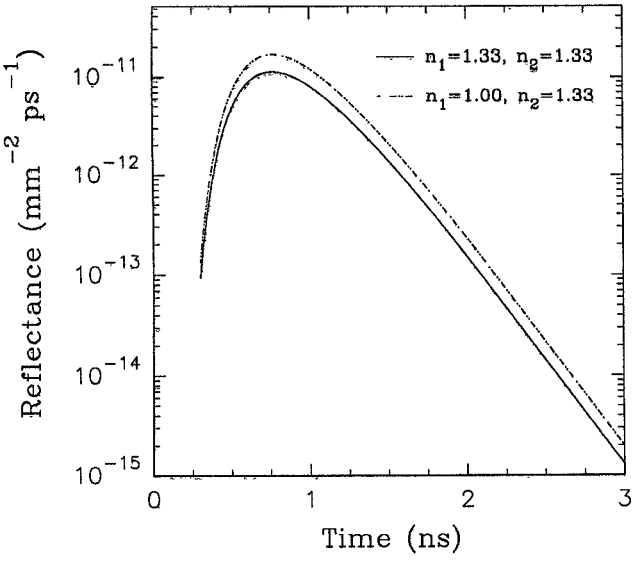


Fig. 3 Calculation of $R(\rho,t)$ using Eq. (8) for matched and mismatched boundaries. Other parameters as described in Fig. 2.

## 3. TESTS OF THE DIFFUSION MODEL

In this section we will show representative comparisons of the diffusion model with Monte Carlo simulations of radiation transport and with experimental results obtained with well-characterized tissue substitutes. In Fig.4 the expression for $R(\rho,t)$ given in Eq. (11) is compared with the result of a Monte Carlo simulation (9). We

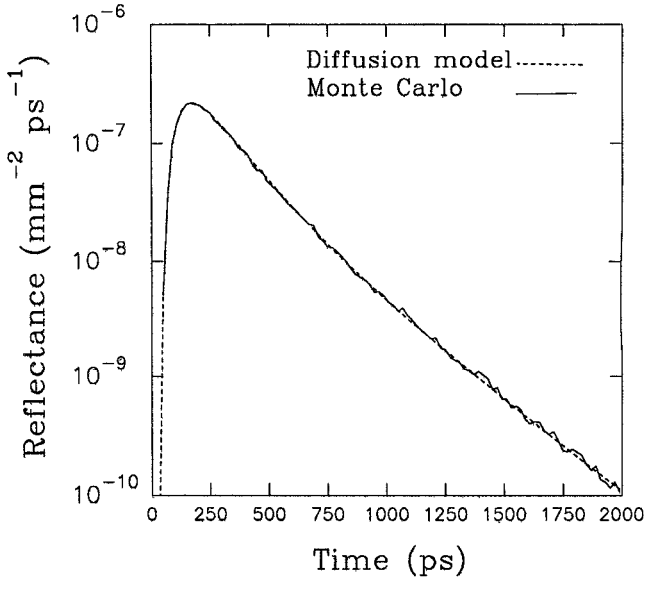


Fig. 4 Comparison of Monte Carlo simulation and Eq. (11) for conditions described in the text.

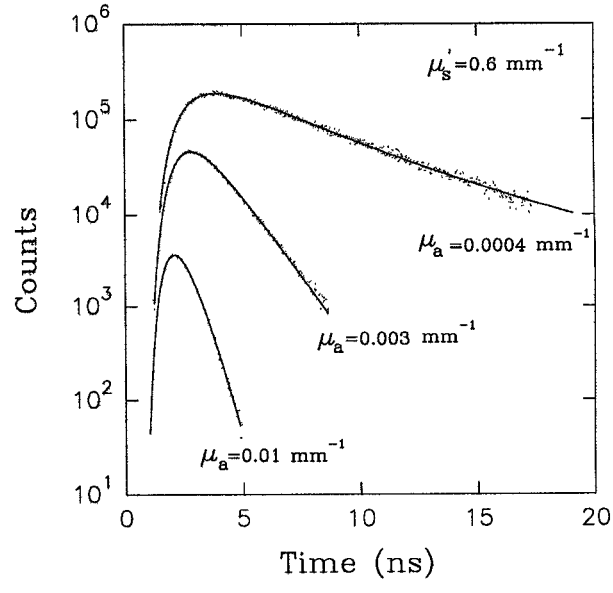


Fig. 5 Experimental data obtained for tissue-simulating materials with optical properties as stated. Smooth lines are best weighted least-squares fit of Eq. (9) to the data. (Use of experimental facilities at the Harrison Spectroscopy Lab, MIT, is gratefully acknowledged).

assumed $\rho$ = 10mm, $\mu_a$ = 0.02 $mm^{-1}$, $\mu_s$ = 1.5 $mm^{-1}$, c = $c_o$ = 0.225 mm $ps^{-1}$, g = 0. Not only does the diffusion model accurately predict the full pulse shape under these conditions, but the absolute value of $R(\rho,t)$ is also within the statistical uncertainty of the simulation. Other simulations showed that realistic detector sizes (1-3 mm) did not significantly change the pulse shape. The only conditions under which the diffusion model has been found to give inaccurate results is at early times, when the detected photons have not been multiply scattered.

In Fig.5 we present some typical experimental results showing best fits of Eq.(9) to data obtained from a scattering emulsion (Intralipid, Kabi Vitrum, CA) to which increasing amounts of India ink were added. Pulse shapes were recorded using time correlated single photon counting and the light source was a picosecond pulsed dye laser. The experiments and data analysis have been completely described elsewhere (10). As seen in Fig.5, good fits to the data can be obtained and the estimates of absorption and scattering coefficients obtained in this manner agreed to better than 10% with independent steady-state measurements.

## 4. DISCUSSION AND CONCLUSIONS

In this paper we have demonstrated that a diffusion model of photon migration can provide an accurate description of the diffusely reflected pulse observed at the surface of a uniform, semi-infinite medium. Furthermore, a detailed analysis showed that the pulse shape is not sensitive to the exact nature of the interface between the tissue and the surrounding medium. Experimental tests have confirmed that the absorption and scattering coefficients derived by using the model are accurate to 10% or better.

In real biological situations, however, the technique must be applied to finite tissue volumes and the assumption of semi-infinite extent may not be justified. The influence of other boundaries is illustrated in Fig.6 where the pulse shape recorded for a thick slab (100 mm) is compared to that observed when the thickness is reduced to 10 mm. Absorption of light at the other face of the slab causes a dramatic change in pulse shape, introducing a more rapid decay and a shift in the peak to earlier times. Application of the semi-infinite model to this data would result in a large overestimate of $\mu_a$ and an underestimate of (1-g) $\mu_s$. It is possible to solve Eq.(1) for the slab geometry as well as for finite cylinders and spheres (7). These solutions are much more cumbersome to use in fitting routines

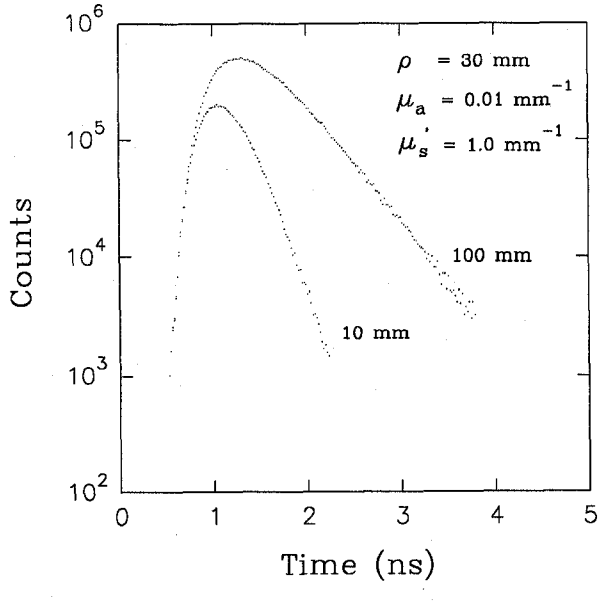


Fig. 6 Experimental data for tissue-simulating slabs showing the influence of slab thickness on the measured pulse shape.

however, as the solution involves the numerical evaluation of series with many terms. We are currently examining the conditions under which simple solutions such as Eqs.(9,11) can be employed with acceptable accuracy.

Finally we note that application of the technique as described here requires an expensive pulsed laser system. Pulsed diode lasers may offer a practical clinical alternative if the desired wavelength is available. Another possibility is to perform the measurements in the frequency domain where cw light sources can be easily modulated at frequencies up to a few hundred megahertz. Analytical expressions for the phase and modulation have been published by Patterson et al. (11) which allow the determination of $\mu_a$ and (1-g) $\mu_s$. This approach may also permit faster data acquisition and simpler correction for instrument response.

## 5. ACKNOWLEDGEMENTS

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