The Propagation of Optical Radiation in Tissue I. Models of Radiation Transport and their Application

MICHAEL S. PATTERSON, BRIAN C. WILSON, DOUGLAS R. WYMAN

Hamilton Regional Cancer Centre and McMaster University, 711 Concession Street, Hamilton, Ontario, Canada L8V 1C3

Correspondence to Dr. M.S. Patterson

Abstract. This paper is the first of two reviewing the propagation of electromagnetic radiation of wavelength 0.25–10 μm in tissue. After a brief discussion of light/tissue interactions, a mathematical description of light propagation in terms of radiative transfer is developed. Formal solutions of the resulting equation are outlined, but the emphasis is on approximate method of solution—namely the discrete ordinates method, the technique of functional expansion and Monte Carlo simulation. The application of the simplest of these approximate methods, namely the 2-flux and diffusion models, to tissue optics is discussed in some detail. The second paper deals with the optical properties of tissue and the salient characteristics of light fluence distributions in these tissues.

INTRODUCTION

The rapidly increasing use of ultra-violet, visible and infra-red radiation in both diagnostic and therapeutic medicine has created a need to understand how this radiation propagates in tissue. Such knowledge is necessary for the optimum development of therapeutic techniques and for the quantitative analysis of diagnostic measurements. For example, the local tissue temperature is of prime importance in laser surgery and depends, in turn, on the spatial distribution of the incident radiation. This variable is also of central importance in photodynamic therapy of cancer where the local biological effect is directly related to the light fluence. Diagnostic methods which use fluorescent, scattered, or transmitted light to measure parameters such as drug concentration and blood oxygenation also require detailed information about the propagation of the excitation and observed light. The general problem is illustrated in Fig. 1. A tissue of arbitrary geometry, whose optical properties (to be defined and discussed) may be functions of position and time, is irradiated by external and/or internal sources of light. A complete solution describes the time dependence of the electromagnetic field at any point. There are three basic requirements in solving this problem. These are:

(i) a mathematical description of the interaction of optical radiation with tissue;
(ii) information about the optical properties of the irradiated tissue (usually provided by experiment) and;
(iii) workable solutions of the mathematical equations to provide sufficiently accurate calculations under circumstances of biomedical interest.

It is the purpose of this paper and a companion article (1) to examine each of these requirements for electromagnetic radiation in the wavelength range of 0.25–10 μm. The first paper begins with a brief discussion of the possible mechanisms of light interaction with tissue, but attention will be focused on linear problems with time independent optical properties. We will describe two mathematical constructs which have been used to study radiation propagation in scattering media, multiple scattering electromagnetic theory and radiative transfer theory. Detailed discussion will be limited to the latter, as multiple scattering theory has yet to be fruitfully applied to tissue optics. We will then review methods by which useful solutions to the radiative transfer equation may be obtained. Although many techniques have been applied, only those which have proved most useful in tissue optics, namely 2-flux models, diffusion theory and Monte Carlo simulation will be discussed in detail. For the most part, steady-state (time-independent) transport problems will be considered, but we will also show some instances where models of pulse propagation have been essential.

In the second paper we will summarize the

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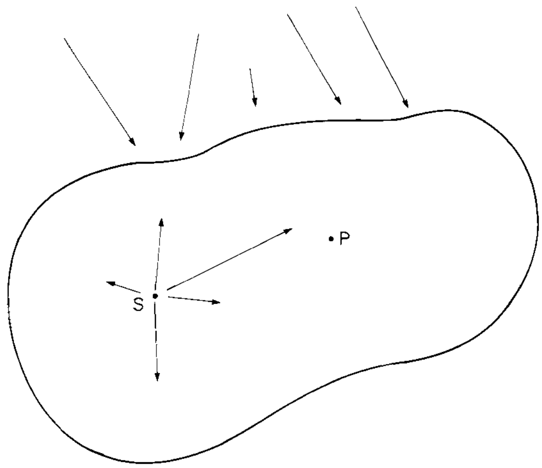

Fig. 1. Solution of the general problem in tissue optics gives the electromagnetic field at an arbitrary location, P, as a function of time. The tissue has an arbitrary geometry and optical properties which may be functions of position and time. The tissue may be irradiated by external or internal (S) sources of light.

current knowledge of tissue optical properties in the wavelength range 0.25–10 μm. These properties can be measured in a variety of ways ranging from direct measurements of interaction coefficients on excised, optically thin samples, to indirect non-invasive methods suitable for in vivo application. A review of these methods and their limitations will be presented. Finally, we will identify wavelength regimes where absorption processes dominate scattering, where scattering is dominant, and where the two are comparable. The nature of the light fluence distribution in tissue in these different regimes is described, along with the radiation propagation models which may be successfully employed in each.

THE MATHEMATICAL DESCRIPTION OF RADIATION PROPAGATION

In an excellent review paper, Boulnois (2) identified four categories of photophysical processes in light/tissue interactions: photochemical, thermal, photoablative and electromechanical. Photochemical interactions involve the absorption of light by specific molecules present in, or added to, the tissue. Such interactions are the basis for photodynamic therapy. Thermal interactions are those where the observed biological effect is due to the deposition of heat in the tissue. Most current laser surgery falls into this category. Photoablative interactions can occur in the ultra-violet where photons possess sufficient energy to cause the dissociation of biopolymers and the subsequent desorption of fragments. This effect is observed for 10 ns pulses at a threshold fluence rate of about 10^8 W cm^{-2}. The fourth category is the electromechanical interaction which occurs at fluence rates of approximately 10^{10} W cm^{-2} for nanosecond pulses and 10^{12} W cm^{-2} for picosecond pulses. The intense electric field present during these pulses causes dielectric breakdown of the tissue and the formation of a small volume plasma. The expansion of this plasma creates a shock wave which can mechanically rupture tissue. The last two classes of interaction are complex, threshold, nonlinear effects and we will not consider them further in this paper. Instead, we will confine our attention to situations where the optical properties of the tissue are time invariant and independent of the light field so that the local absorbed energy rate is proportional to the local energy fluence rate.

Light which enters tissue can be scattered and absorbed. The relative probability of these processes in a given tissue depends on wavelength as will be discussed in detail in Part II of this review (1). In most problems in tissue optics, multiple light scattering is important and any useful theory must account for this.

Multiple scattering electromagnetic theory (3) can, in principle, be used to describe the propagation of light in tissue. Tissue could be considered as a random medium whose permittivity, $\epsilon(r)$, fluctuates with position about some mean value ϵ_1, so that

$$\epsilon(r) = \epsilon_1 + \epsilon_2(r) \tag{1}$$

where $\epsilon_2(r)$ is a random process whose important characteristics (i.e. variance and correlation length) are known. The statistical behaviour of the electric field can then be described using Maxwell's equations. While physically appealing, this formalism has yet to find application in tissue optics because of its complexity, the lack of readily applied solutions and the lack of information about $\epsilon_2(r)$.

The usual approach, and the one which we shall follow in this review, is called radiative transfer theory. The important variable in this description is the energy radiance, $L(r, \hat{\Omega})$ which is defined such that, at position r, the energy carried per unit time by photons in an elemental solid angle $d\hat{\Omega}$ about a direction $\hat{\Omega}$ through an infinitesimal area dA oriented normal to $\hat{\Omega}$ is $L(r, \hat{\Omega})\, dA\, d\hat{\Omega}$. This quantity has also been called the specific intensity in the astrophysical literature. To avoid such confusion, we have compiled in Table 1 a list of definitions and symbols for quantities we will use in our discussion of radiative transfer.

In stating the equation of radiative transfer, we will restrict our attention to monochromatic light and avoid the complications of inelastic scatter and fluorescence (although these could be incorporated). We must also define a set of interaction coefficients (see Table 1). The absorption coefficient, μ_a, is the probability per infinitesimal path length that a photon will be absorbed by the tissue. The scatter coefficient μ_s is similarly defined. To complete the description of scatter, we must also include the angular dependence through the differential scattering cross-section $d\mu_s(r, \hat{\Omega}' \rightarrow \hat{\Omega})$, which is the probability that a photon moving initially in a direction $\hat{\Omega}'$ is scattered to a new direction $\hat{\Omega}$. It is customary to assume that the differential scat-

Table 1. Brief definitions of physical quantities used in this paper and their associated symbols and SI units

Name of quantity	Definition	Symbol	Unit
Photon number	Number of photons emitted, transferred or received	N	
Radiant energy	Energy of photons emitted, transferred or received ($h\nu N$)		J
Radiant energy flux	$\frac{dN}{dt}$		W
Radiant energy fluence	$\frac{dN}{dA}$ Where dN photons are incident on a sphere of cross-sectional area dA	Ψ	$J\,m^{-2}$
Radiant energy fluence rate		ψ	$W\,m^{-2}$
Energy radiance	Energy transported by photons in direction $\hat{\Omega}$ per unit solid angle per unit time per unit area	$L(\hat{\Omega})$	$W\,m^{-2}\,sr^{-1}$
Linear absorption coefficient	Probability of photon absorption per infinitesimal pathlength	μ_a	m^{-1}
Linear scattering coefficient	Probability of photon scatter per infinitesimal pathlength	μ_s	m^{-1}
Linear attenuation coefficient	$\mu_a + \mu_s$	μ_t	m^{-1}
Mean free path	$1/\mu_t$		m
Single scattering albedo	μ_s/μ_t	a	
Differential scattering coefficient	Probability of scatter from an initial direction $\hat{\Omega}'$ to a final direction $\hat{\Omega}$ per unit solid angle per infinitesimal path length	$d\mu_s(\hat{\Omega}' \rightarrow \hat{\Omega})$	$m^{-1}\,sr^{-1}$
Scattering phase function	The differential scattering coefficient normalized so that $\int_{4\pi} f(\hat{\Omega}' \rightarrow \hat{\Omega})\, d\hat{\Omega} = 1$	$f(\hat{\Omega}' \rightarrow \hat{\Omega})$	sr^{-1}
Mean cosine of scattering angle or anisotropy parameter		g	
Transport scattering coefficient	$(1 - g)\mu_s$		m^{-1}
Specular reflectance	Fraction of incident light flux reflected by irradiated surface	R_{sp}	
Scattered reflectance	Fraction of incident light flux scattered through irradiated surface	R_s	
Total reflectance	$R_{sp} + R_s$	R_t	
Internal reflectance	Fraction of internal light flux incident on tissue surface and reflected back into the tissue	R_i	
Primary transmittance	Fraction of incident light flux transmitted without interaction	T_p	
Scattered transmittance	Fraction of incident light flux transmitted after scattering	T_s	
Total transmittance	$T_p + T_s$	T_t	

tering coefficient is independent of incident photon direction so that

$$d\mu_s(\hat{\Omega}' \rightarrow \hat{\Omega}) = d\mu_s(\hat{\Omega}'\cdot\hat{\Omega}). \quad (2)$$

This assumption is probably valid for 'randomly' organized soft tissues but may not be true for highly structured tissues such as muscle (4). Clearly, the total scattering coefficient is given by the integral over solid angle

$$\mu_s = \int_{4\pi} d\mu_s(\hat{\Omega}' \rightarrow \hat{\Omega})d\hat{\Omega}. \quad (3)$$

In radiative transfer theory a normalized version of the differential scattering coefficient, called the phase function, is often used. This probability density function is defined by

$$f(\hat{\Omega}'\cdot\hat{\Omega}) = \frac{1}{\mu_s}d\mu_s(\hat{\Omega}'\cdot\hat{\Omega}). \quad (4)$$

The mean cosine of scattering angle (sometimes called the anisotropy factor) is the average value of $(\hat{\Omega}'\cdot\hat{\Omega})$ and is denoted by g. Note that for isotropic scattering $g = 0$ and that $g \rightarrow 1$ as scattering becomes more forward peaked. The total interaction or attenuation coefficient, μ_t is given by

$$\mu_t = \mu_a + \mu_s \quad (5)$$

and to complete the mathematical description, we include a source of photons, $s(r, \hat{\Omega})$.

The equation of radiative transfer can be derived by considering the radiant energy balance in an arbitrary elemental volume of tissue. The details of this derivation have been given by many authors and the final result is

$$\hat{\Omega}\cdot\nabla L(r, \hat{\Omega}) + \mu_t(r)L(r, \hat{\Omega}) = \int_{4\pi} d\hat{\Omega}' d\mu_s(r, \hat{\Omega}' \rightarrow \hat{\Omega})L(r, \hat{\Omega}') + s(r, \hat{\Omega}) \quad (6)$$

where the first term represents the net change due to energy flow, the second term radiance lost due to absorption and scatter, the third term the gain in radiance due to scatter from all other directions, and the fourth term the radiance source defined above.

Two other complexities have been omitted from Eq. (4), namely time dependent radiance and polarization. The first simplification is unimportant unless we are interested in the evolution of $L(r, \hat{\Omega})$ or other time dependent quantities during a short light pulse. If the incident pulse is long compared to photon lifetimes in the medium, then the steady-state solution is probably adequate. Even if this condition is not met, the quantity of interest is often the time integral of a radiance dependent parameter, for example the total absorbed energy. It can be shown that, for linear transport, such time integrals can be determined from knowledge of the steady-state solution. However, recent developments in diagnostic applications of picosecond light pulses (5) has spurred the development of time-dependent models, and some specific applications will be discussed below.

Polarization can be included in the formulation of radiative transfer. This is done by using the Stokes parameters (6) to describe the polarization and deriving four, instead of one, radiative transfer equations. In an intensely scattering medium such as tissue, Svaasand and Gomer (7) have shown evidence that incident light rapidly becomes unpolarized and polarization effects are therefore generally unimportant.

The basic assumption in radiative transfer theory is that we can ignore the wave nature of light and simply consider the flow of energy within the medium. The physical foundation of this theory is, therefore, not as satisfactory as that for multiple scattering theory. Ishimaru (3) and Fante (8) have shown that, under certain conditions, the energy radiance can be equated to the average Poynting vector and that the two treatments are mathematically equivalent. It is not clear whether these conditions are met for optical radiation in tissue but to date only one experiment has demonstrated a macroscopic effect which cannot be predicted by radiative transfer. Yoo et al (9) reported the observation of a coherent peak in the light backscattered by tissue—an interference phenomenon which has been observed with a variety of dense scattering materials. In the next section, we will examine methods by which useful solutions of the radiative transfer equation can be obtained.

SOLUTIONS OF THE RADIATIVE TRANSFER EQUATION

Problems in radiative transfer similar to those in tissue optics are encountered in many fields of science. The propagation of light in planetary and stellar atmospheres (10), in the ocean (11), and the propagation of neutrons in a reactor (12), have all been described by the equation of radiative transfer or its equivalent, the linearized Boltzmann particle transport equation. Many different mathematical approaches have been used in solving this equation. The best method depends on the information sought and the accuracy required. For example, an astronomer might be most interested in the light reflected by a planetary atmosphere and not the radiance within the atmosphere. On the other hand, this variable is of prime importance to the oceanographer or the investigator in tissue optics. A complete review of the mathematical solution of the radiative transfer equation is beyond the scope of this paper. The interested reader might consult the review articles by Hansen and Travis (6), Irvine (13), or Hunt (14) for more complete discussions. Other works restricted to one method will be referred to in the following subsections. While we will briefly discuss general methods for solving the equation of radiative transfer, we will focus on methods which have been successfully applied in tissue optics—the 2-flux, diffusion and Monte Carlo techniques.

Formal solutions of the radiative transfer equation

In this section, we briefly describe methods by which analytic solutions of the radiative transfer equation have been obtained. While these solutions are 'exact' in the sense that the radiance can be expressed in mathematical terms (usually in integral form), the actual evaluation of the solution usually involves numerical methods and may lead to results which are no more accurate than so-called approximate solutions.

Method of successive orders

One 'brute force' method of solving for the radiance is to consider contributions at a point due to light which has been propagated unscattered from the source, that which has been scattered once, that which has been scattered twice, etc. These contributions are shown schematically in Fig. 2. The radiance can then be formally written as the sum of all these contributions

$$L(r, \hat{\Omega}) = \sum_{n} L_n(r, \hat{\Omega}) \tag{7}$$

where $L_n(r, \hat{\Omega})$ is the radiance due to photons scattered n times. In practice, one calculates a source function for nth order scatter by integration over all incident directions of the $(n - 1)$th order radiance multiplied by the phase function. The nth order radiance term is then calculated by integration of the nth order source function over all space.

This method is practical for relatively thin layers but converges very slowly for thick layers unless the single scattering albedo ($a = \mu_s/\mu_t$) is much less than one. Van de Hulst and Irvine (15) have noted that the ratio of successive terms approaches a constant so that the sum in Eq. (7) can be terminated after a finite number of terms and the remainder replaced with a geometric series. One very attractive feature of the successive orders method is that if a problem is solved for a specific albedo, then the solution for any other albedo is easily obtained. The detailed application of the method to homogeneous media with arbitrary phase functions is discussed by Irvine (16).

Solution in terms of X, Y functions

This classical method of solving the equation of radiative transfer has been fully developed for the case of a homogeneous slab with a phase function that can be expanded in a series of Legendre polynomials. This method has evolved from the early work of Chandrasekhar, Busbridge, Mullikin and Sobolev, and has been summarized by van de Hulst (10).

In this technique, the radiance at the entrance and exit surfaces of the slab is expressed in terms of X and Y functions. These functions are themselves the solution of non-linear integral equations which, while not presented here, can be assigned a simple physical meaning as de-

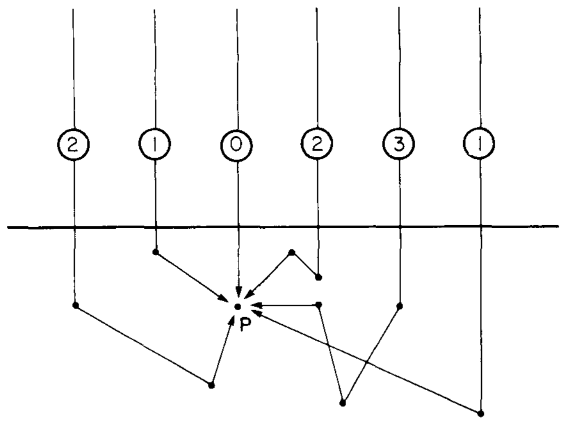

Fig. 2. Schematic illustration of the method of successive orders. The radiance at P can be expressed as the sum of all contributions due to unscattered photons, photons which have been scattered once, those which have been scattered twice, etc.

scribed by Chandrasekhar (17). Using the polar angle θ, the azimuthal angle ϕ, and the depth variable, z, the radiance is $L(z, \theta, \phi)$. If radiation

$$L_{inc}(0, \theta, \phi) = \frac{L_o}{|\cos \theta|} \quad (8)$$

is incident on the top face of the slab, the total radiance at the surface will be the sum of this term and a diffusely reflected term, $L_{ref}(0, \theta, \phi)$. The relative change in radiance due to the presence of the slab is given by $X(d, \theta)$ where

$$X(d, \theta) = \frac{L_{inc}(0, \theta, \phi) + L_{ref}(0, \theta, \phi)}{L_{inc}(0, \theta, \phi)} \quad (9)$$

and d is the slab thickness. Similarly $Y(d, \theta)$ represents the relative change in radiance at the exit surface of the slab.

X and Y functions have been tabulated for isotropic and linearly anisotropic phase functions, but the numerical evaluation of the integral expressions becomes very complex if more than three terms are retained in the Legendre expansion of the phase function. Van de Hulst (10) questions the value of the method for highly anisotropic scattering. While the method has been used most extensively to study the radiance at the slab surfaces, Sobolev (18) has solved for the radiance at depth in terms of X and Y functions.

Method of eigenfunction expansion

This method, developed by Case and Zweifel (19) for a slab geometry leads to a general solution for the radiance at arbitrary depth within the slab. The solution of the radiative transfer equation is obtained as an expansion in a series of solutions to the homogeneous part of the equation. Particular solutions of the form

$$e^{-z\mu_t/\nu}\, \Phi_\nu^m (\cos \theta)(1 - \cos^2 \theta)^{m/2} \cos m\phi \quad (10)$$

can be found where Φ_ν^m is the radiance eigenfunction and ν is the corresponding eigenvalue. The method consists of finding the eigenvalues and eigenfunctions, proving that they form a complete set, and expanding the solution of the complete equation of transfer in terms of these eigenfunctions by imposing the correct boundary conditions.

While elegant in principle, the method requires extensive mathematical manipulation and has found limited application. Van de Hulst (10) has suggested that the final equations are, in fact, equivalent to a solution in terms of X and Y functions. It is interesting to note that the largest discrete eigenvalue and corresponding eigenfunction give, respectively, the diffusion exponent and diffusion pattern deep within the medium. The importance of these parameters in tissue optics is discussed in the subsection, Asymptotic radiation and hybrid methods.

Approximate solutions of the radiative transfer equation

In this section, we will discuss practical methods by which the equation of radiative transfer may be solved. As detailed below, these may involve approximate numerical solutions to the full equation, or physical assumptions which simplify the equation to one which can, itself, be solved analytically or numerically.

Adding method

The adding method is a powerful technique for computing the radiance at the entrance and exit surface of a slab. Because it is incapable of providing the radiance at arbitrary positions within the slab, its application to tissue optics is limited. Nonetheless, it is accurate and serves

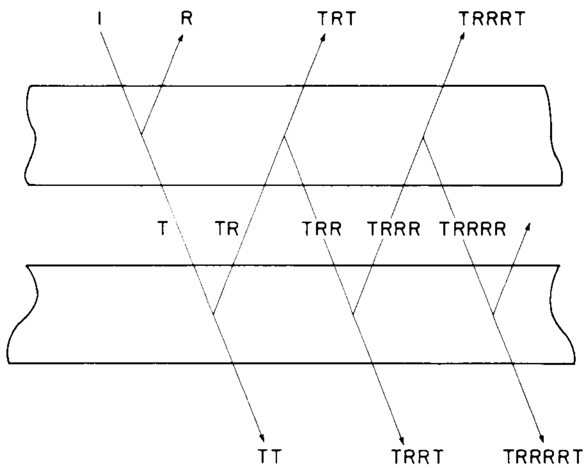

Fig. 3. Schematic illustration of the doubling method for calculating the radiance at the surfaces of an infinite slab. It is assumed that the radiance at the entrance (R) and exit (T) surfaces is known for irradiation from any direction (I). The radiance for a slab which is twice as thick can be calculated by considering the interplay between the two constituent slabs. A gap is shown between the slabs for the sake of clarity. This method will also yield the radiance at mid-depth in the thicker slab.

as a useful check of other methods. The principle, as first proposed by van de Hulst (20), is illustrated in Fig. 3. For a very thin slab (say of thickness equal to $2^{-20/\mu_t}$) one can write the radiance at the two surfaces from knowledge of the phase function, since multiple scattering is negligible. If one now adds an identical slab, the radiance at the surfaces of this thicker slab can be calculated by considering the successive scattering back and forth between the component layers. Computation for thicker slabs can be carried out by adding other thin layers or, more efficiently, by doubling the total thickness with each iteration. This doubling method has been used by van de Hulst (10) to generate a very useful set of results for slabs with a wide range of thickness, albedo and mean cosine of scattering angle. Another advantage of this technique is that slabs of different optical properties can be combined. This sort of inhomogeneity would constitute a reasonable model of the skin (21).

Invariance methods

These methods were pioneered by Ambartsumian (22) and will not be described in detail as the emphasis has again been placed on calculating the radiance external to a slab. The basic idea is to consider the changes in radiance at the two surfaces of the slab in question when an infinitesimally thin layer is added to one of the surfaces. Because the added layer is thin, multiple scattering within it can be ignored and one can find the partial derivative of the function of interest with respect to slab thickness. Numerical integration then yields the radiance at the surface. Moaveni and Razani (23) have applied this method to the propagation of light in blood and Orchard (24) has used it to calculate the reflectance of suspensions of scattering particles.

Discrete ordinates methods

The essence of this technique is the conversion of the radiative transfer equation to a system of linear algebraic equations suitable for numerical solution. To do this, the radiance $L(r, \hat{\Omega})$ is represented only by its value at discrete values of the independent variables. In addition, the operations of differentiation and integration are replaced by their discrete counterparts, finite differences and summation (or quadrature).

For example, if we discretize the direction variable, $\hat{\Omega}$, at N values in the equation of transfer so that

$$L(r, \hat{\Omega}) \rightarrow L(r, \hat{\Omega}_N) \equiv \ell_N(r) \qquad (11)$$

then integrals over $d\hat{\Omega}$ become summations

$$\int_{4\pi} d\hat{\Omega}\, L(r, \hat{\Omega}) \simeq \sum_{n=1}^{N} w_n\, \ell_n(r) \qquad (12)$$

where w_n are the appropriate weighting factors for the numerical integration. The discretized equation of radiative transfer is thus

$$\hat{\Omega}_n \cdot \nabla \ell_n(r) + \mu_t\, \ell_n(r) = \sum_{n'=1}^{N} w_{n'}\, d\mu_s(\hat{\Omega}_{n'} \rightarrow \hat{\Omega}_n) \ell_{n'}(r) + s_n(r). \qquad (13)$$

This set of equations is known as the S_N equations in the neutron transport literature (12). This method of discretizing the angular dependence of the radiance has also been referred to as the N-flux method and has been lucidly described for the slab geometry by Mudgett and Richards (25). The idea of discretizing the radiance is an old one and was first proposed by Schuster (26) who considered only the forward and backward flux. This 2-flux model was used in the familiar work of Kubelka and Munk (27) and, because of its wide application to tissue optics, is discussed in some detail below. Chandrasekhar (17) generalized the scheme and applied the Gaussian quadrature technique now commonly used in the discrete ordinates method.

We will now examine the 2-flux model using, initially, the formulation of Kubelka and Munk (27). These authors considered a forward flux i and a reverse flux j propagating in an infinite slab of thickness d. The differential equations describing i and j are

$$-di = -(S + K)i\,dx + Sj\,dx \qquad (14)$$

$$dj = -(S + K)j\,dx + Si\,dx \qquad (15)$$

where x = 0 at the unilluminated face of the slab and S and K are modified scattering and absorption coefficients respectively. There are a number of explicit and implicit assumptions in the derivation of Eqs (14) and (15). These are:

(i) The forward and reverse fluxes are integrals of the radiance over the appropriate hemisphere. Specifically

$$i(x) = \int_0^{\pi/2} \int_0^{2\pi} L(x, \hat{\Omega}) \cos\theta \sin\theta\, d\theta d\phi \qquad (16)$$

$$j(x) = \int_{\pi/2}^{\pi} \int_0^{2\pi} L(x, \hat{\Omega}) \cos\theta \sin\theta\, d\theta d\phi. \qquad (17)$$

(ii) The modified scattering and absorption coefficients are not identical to those defined in Table 1. Rather, Kdx represents the fraction of flux (i or j) which is absorbed by a layer of infinitesimal thickness dx. K is related to the true absorption coefficient, μ_a, by

$$K = \mu_a \frac{\int_0^{\pi/2} \int_0^{2\pi} L(x, \hat{\Omega}) \sin\theta \, d\theta d\phi}{\int_0^{\pi/2} \int_0^{\pi/2} L(x, \hat{\Omega}) \cos\theta \sin\theta \, d\theta d\phi}. \quad (18)$$

Note that, in general, there is no simple relation between K and μ_a and, in fact, K is even depth dependent if the radiance is not separable in x and $\hat{\Omega}$. This distinction has not been appreciated by some investigators who have applied the model to tissue optics and this has resulted in some confusion in the literature.

(iii) The original assumption by Kubelka and Munk was that the radiance is isotropic in each hemisphere at all depths. Under this rather unrealistic assumption K and S are the same for the forward and reverse fluxes and are given by

$$K = 2\mu_a \quad (19)$$

$$S = \mu_s \quad (20)$$

where Sdx represents the fraction of, say, forward flux which is scattered into the backward hemisphere by a layer of infinitesimal thickness dx.

With these rather restrictive assumptions the differential equations can be solved subject to the appropriate boundary conditions which, for a slab in vacuo, are

$$i(x = d) = I_0 \quad (21)$$

$$j(x = 0) = 0 \quad (22)$$

where I_0 is the incident forward flux. The solutions are given by Kubelka (28) as

$$i = I_0 \frac{a \sinh(bSx) + b \cosh(bSx)}{a \sinh(bSd) + b \cosh(bSd)} \quad (23)$$

$$j = I_0 \frac{\sinh(bSx)}{a \sinh(bSd) + b \cosh(bSd)} \quad (24)$$

where

$$a = \frac{S + K}{S} \quad (25)$$

and

$$b = \sqrt{a^2 - 1}. \quad (26)$$

It is also possible to derive explicit expressions for the scattered (or diffuse) reflectance, R_s, and the scattered (or diffuse) transmittance, T_s

$$R_s = \frac{j(x = d)}{I_0} = \frac{\sinh(bSd)}{a \sinh(bSd) + b \cosh(bSd)} \quad (27)$$

$$T_s = \frac{i(x = 0)}{I_0} = \frac{b}{a \sinh(bSd) + b \cosh(bSd)} \quad (28)$$

Equations (27) and (28) have been the chief appeal of the Kubelka–Munk model because S and K, and hence μ_s and μ_a, can be directly calculated from measurements of R_s and T_s. Of course the convenience of these formulas must be weighed against the very likely possibility that the assumptions made in deriving them are incorrect!

Various modifications to the Kubelka–Munk 2-flux model have been made by van Gemert and Star (29), Mudgett and Richards (30), Reichman (31), Klier (32), Brinkworth (33) and Meador and Weaver (34). These authors have derived differential equations similar to Eqs (14) and (15) directly from the radiative transfer equation. These more general models have incorporated the effects of collimated beam incidence, anisotropic scatter and radiance, and internal specular reflection at the slab boundaries. Several authors have pointed out that Eqs (27) and (28) relating S and K to R_s and T_s can be retained if a simple physical definition of S and K is abandoned. Separate equations can be derived relating S and K to the true absorption and scattering coefficients but there is no general agreement among the various authors on the exact form of these equations. For the case of $\mu_a \ll (1 - g)\mu_s$, however, all these equations reduce to

$$K = 2\mu_a \quad (29)$$

$$S = \tfrac{3}{4}(1 - g)\mu_s. \quad (30)$$

As absorption increases, the radiance becomes more anisotropic and a 2-flux model may be inadequate. Mudgett and Richards (30) have advocated the use of a 4-flux model in an excellent didactic paper on the discrete ordinates method, and have shown that this model gives excellent predictions for R_s and T_s when the angular direction bins are properly chosen. The relative simplicity of this model suggests that its application to tissue optics should be further explored. Welch et al (35) have also reported the use of a 7-flux model in slabs with tissue-like optical properties.

Functional expansion methods

As in the discrete ordinates method, the goal of this technique is to reduce the integro-differential equation of radiative transfer to a set of coupled differential equations which can be solved by standard techniques. As opposed to the discrete ordinates method, where a number of discrete directions of the radiance are considered, the angular dependence of the radiance is here approximated by a finite series expansion of orthogonal functions. While several functional expansions have been used, a popular and general set is the spherical harmonics. For a homogeneous slab the radiance may be expanded in terms of the Legendre polynomials $P(\mu)$, where μ is the cosine of the angle, θ, between the direction vector $\hat{\Omega}$ and the inward normal to the surface. In this case the phase function $f(\hat{\Omega}'\cdot\hat{\Omega})$ is expanded in a series of Legendre polynomials

$$f(\hat{\Omega}'\cdot\hat{\Omega}) = \frac{1}{4\pi}\sum_{n=0}^{\infty}(2n+1)b_n\, P_n(\hat{\Omega}'\cdot\hat{\Omega}) \quad (31)$$

where orthogonality of the P_n implies that

$$b_n = \int_{4\pi} f(\hat{\Omega}'\cdot\hat{\Omega})P_n(\hat{\Omega}'\cdot\hat{\Omega})d\hat{\Omega}'. \quad (32)$$

Note that $b_1 = g$, the average cosine of scattering angle.

As an example, consider the case of an infinite homogeneous slab irradiated by a normally incident beam. Star et al (36) have shown that the equation of radiative transfer can be written as

$$\mu\frac{\partial}{\partial z}L(z,\mu) + \mu_t\, L(z,\mu) = \frac{\mu_s}{4\pi}\int_{4\pi} L(z,\mu')\sum_{n=0}^{\infty}(2n+1)b_n\, P_n(\hat{\Omega}'\cdot\hat{\Omega})d\hat{\Omega}' + \frac{\mu_s}{4\pi}\sum_{n=0}^{\infty}(2n+1)b_n\, P_n(\mu)e^{-\mu_t z}. \quad (33)$$

The various terms in Eq. (33) can be identified by comparison with Eq. (6). The last term represents the internal source of photons since it describes the initial scatter from the incident beam. In this formulation $L(z, \mu)$ describes only photons which have been scattered at least once, and the uncollided beam must be added to $L(z, \mu)$ to obtain the total radiance. An identical total radiance would be obtained by solving Eq. (33) with a zero source term and a non-zero incidence boundary condition. For most functional expansions, the former alternative is more convenient.

If Eq. (33) is multiplied by $(2m + 1)P_m(\mu)$ and integrated over all directions $\hat{\Omega}$, one can generate, with the aid of a recurrence relation for Legendre polynomials, a set of equations

$$\frac{\partial}{\partial z}\int_{-1}^{1}[(m+1)P_{m+1}(\mu) + mP_{m-1}(\mu)]L(z,\mu)d\mu + \mu_t\int_{-1}^{1}(2m+1)P_m(\mu)L(z,\mu)d\mu = \mu_s\int_{-1}^{1}(2m+1)b_m\, P_m(\mu')L(z,\mu')d\mu' + \frac{(2m+1)}{2\pi}\mu_s\, b_m e^{-\mu_t z}. \quad (34)$$

If we also expand the radiance $L(z, \mu)$ in a series of Legendre polynomials so that

$$L(z,\mu) = \frac{1}{4\pi}\sum_{n=0}^{\infty}(2n+1)L_n(z)P_n(\mu) \quad (35)$$

and substitute in Eq. (34) we can derive, again using the orthogonality of $P_m(\mu)$, a set of ordinary differential equations for the coefficients $L_n(z)$ of this expansion

$$\frac{\partial}{\partial z}[(m+1)L_{m+1}(z) + mL_{m-1}(z)] = -[\mu_a + (1-b_m)\mu_s](2m+1)L_m(z) + (2m+1)\mu_s\, b_m e^{-\mu_t z}. \quad (36)$$

By truncating this set after $m = N$, we obtain a set of $(N + 1)$ equations in the $(N + 1)$ unknowns $L_n(z)$, $n = 0$ to N.

This truncated set of equations is known as the P_N equations in the literature of neutron transport (12). A special case of interest is that where the expansion is terminated after two terms so that the radiance is assumed to depend only linearly on μ and is said to be linearly anisotropic. In this case we have two differential equations:

$$\frac{\partial}{\partial z}L_1(z) = -\mu_a\, L_0(z) + \mu_s e^{-\mu_t z} \quad (37)$$

$$\frac{\partial}{\partial z}L_0(z) = -[\mu_a + (1-g)\mu_s]3L_1(z) + 3\mu_s\, g e^{-\mu_t z}. \quad (38)$$

We can eliminate $L_1(z)$ to yield one equation in $L_0(z)$:

$$\frac{\partial^2}{\partial z^2}L_0(z) - 3\mu_a\, \mu_{tr}\, L_0(z) = -3\mu_s\, \mu_{tr}e^{-\mu_t z} - 3\mu_s\, \mu_t\, g e^{-\mu_t z} \quad (39)$$

where we have defined the transport coefficient

$$\mu_{tr} = \mu_a + (1-g)\mu_s. \quad (4)$$

Now

$$L_0(z) = 2\pi\int_{-1}^{1} L(z,\mu)d\mu = \psi(z) \quad (41)$$

so that we have derived a differential equation for the energy fluence rate $\psi(z)$. This equation is equivalent to the diffusion equation which, in general, may be written as

$$\nabla^2 \psi(r) - \frac{\mu_a}{D} \psi(r) = \frac{-S_o(r)}{D} + 3\nabla \cdot S_1(r) \quad (42)$$

where D, the diffusion coefficient, is given by

$$D = \frac{1}{3\mu_{tr}} \quad (43)$$

and S_0 and S_1 are the first two coefficients in the Legendre expansion of the general source function $s(r, \hat{\Omega})$.

The diffusion or P_1 model has been used by several investigators in tissue optics including Reynolds et al (37), Takatani and Graham (38), Hemenger (39), Groenhius et al (40), Jacques and Prahl (41) and Star et al (36). The equation may be solved analytically for simple geometries such as a slab illuminated by a collimated beam or a point or cylindrical source in an infinite medium. These cases have been summarized by McKenzie (42) and a more exact treatment has been published by Star et al (36). For more complex geometries or for inhomogeneous media, standard numerical methods for solving such differential equations may be used. It is worth reiterating that the basic assumption of this useful model is that the radiance is at most linearly anisotropic. This will not be the case near sources or boundaries or if there is significant absorption in the tissue. We also note that boundary conditions cannot usually be exactly fulfilled in the diffusion approximation (12). More exact methods must be employed if detailed knowledge of the fluence is required under circumstances of strongly anisotropic radiance. Extension of the functional expansion method to higher P_n approximations is uncommon and it is more usual to use the discrete ordinates method. However, Storchi (43) has detailed the application of the method to the slab geometry, and Star et al (36) have published results of a P_{29} calculation for a slab with tissue-like properties.

One additional attractive feature of the diffusion approximation is the straightforward extension to time dependent problems. The appropriate equation is

$$\frac{1}{c}\frac{\partial}{\partial t} \psi(r, t) - D\nabla^2 \psi(r, t) + \mu_a \psi(r, t) = s(r, t). \quad (44)$$

Patterson et al (5) have solved this equation for the case of an infinitesimally narrow pulse $\delta(r, t)$ incident on a homogeneous semi-infinite medium. Analytic solutions can also be written (44) for slab, cylindrical and spherical geometries, and, as discussed above, finite difference methods could be used to tackle more complex geometries. As will be discussed in Part II (1), the impetus for developing these models has been the possibility of non-invasively probing tissue by measuring time resolved scattered transmittance or reflectance.

Monte Carlo particle simulation method

In general, the term 'Monte Carlo method' refers to numerical evaluations or simulations based on random sampling from appropriate probability distributions. The two most common applications are particle transport simulation and numerical integration. While numerical integration could be used to evaluate the scattering integral in the radiative transfer equation, Eq. (6), particle simulations represent the great majority of Monte Carlo applications in radiative transfer. We will therefore restrict our discussion of Monte Carlo to particle simulations, noting that a simulation is not actually a direct solution to the radiative transfer equation.

In the simplest algorithm, referred to as 'analog Monte Carlo', photons are injected into the medium one-by-one and their history is traced until they are either absorbed or permanently scattered out of the region of interest. Parameters such as the injection position, pathlength between interactions, and scattering angle are randomly sampled from probability distributions based on the known physics of the problem. Quantities of interest, such as absorbed energy, are scored at desired locations. The data required (i.e. μ_a, μ_s, $f(\hat{\Omega}' \cdot \hat{\Omega})$) are identical to those required for solution of the radiative transfer equation.

The Monte Carlo particle simulation method has the advantages of being conceptually simple and allowing direct handling of complex geometries and optical inhomogeneities. The chief disadvantage is that the method can be computationally expensive, and while faster and cheaper computers will help, a limiting consideration is that the accuracy of scored quantities increases only with the square root of the number of photon histories. Techniques to improve the accuracy of Monte Carlo simulations, known as variance reduction methods, have

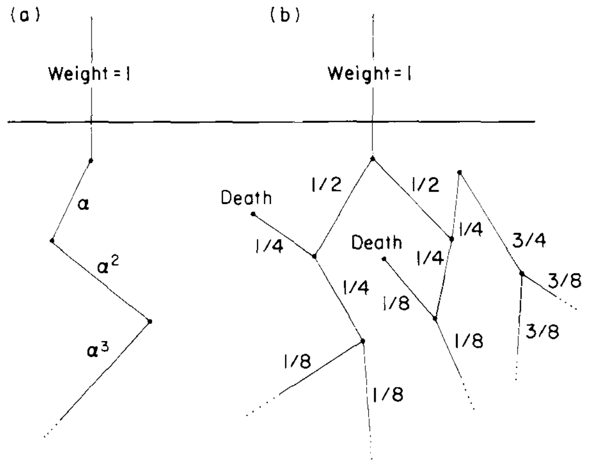

Fig. 4. Depiction of variance reduction techniques used in Monte Carlo particle transport simulation.
(a) Survival weighting with factor $\alpha = \mu_s/\mu_t$.
(b) Splitting of forward directed photons with parameter $v_{split} = 2$, and rouletting of reverse directed photons with parameter $v_{roulette} = 1/3$. Note that only one in three reverse directed photons survives but that its weight is tripled.

been reviewed by Carter and Cashwell (45). One very useful method, particularly applicable to situations where scatter dominates absorption, is survival weighting. In this method, simulated photons are never totally absorbed but rather are transported through the medium with an associated weight, as depicted in Fig. 4(a). At each interaction, the fraction μ_a/μ_t of a photon's weight represents deposited energy while the remaining fraction, μ_s/μ_t, is the factor by which the photon's weight is reduced.

Two other common variance reduction techniques are splitting and Russian roulette. Splitting involves increased sampling in regions or directions that are likely to contribute to scoring, while roulette involves decreased sampling for unfavourable photons, such as those that are poorly located, directed, or have a very low weight. In the splitting technique, a favourably located or directed photon is split into v 'subphotons', each of weight v^{-1}, thereby increasing the number of trajectories while conserving total photon weight. Likewise, Russian roulette involves random sampling that terminates an unfavourable photon with a probability $1 - v$ $(0 < v < 1)$, so that the photon survival probability of v is accompanied by a compensating weight increase factor of v^{-1}. A simulation involving splitting and roulette is depicted in Fig. 4(b).

Another common variance reduction technique is the exponential transformation (46), which can be viewed as either an artificial expansion of the interaction mean free path or a contraction of the medium. Typically, μ_t is multiplied by a parameter, $b(0 < b < 1)$, which may be constant or directionally dependent. This increases randomly sampled distances by the factor b, thereby increasing the probability of large distances between interactions. As with all variance reduction methods, the photon weight must be appropriately adjusted.

While other variance reduction methods exist (45), the above methods involving biased sampling can be used simply and effectively to reduce computation time. Each method should be applied, however, with some caution. A typical problem arises from setting the roulette parameter, v, too small or the exponential parameter, b, larger than unity, resulting in particles of large weight that can actually increase the variance in scored quantities. Biased sampling results should therefore be initially checked against regular sampling results.

The Monte Carlo method has been applied to tissue optics by Wilksch et al (4), Wilson and Adam (47), Jacques and Prahl (41), Groenhuis et al (40), Flock et al (48), and Peters et al (49). This technique is finding increased application as computing power becomes more cheaply available. The method is also useful for checking the validity of approximate methods like diffusion theory under circumstances where other numerical methods are not feasible.

As shown by Wilson et al (50), Jacques (51) and Hebden and Kruger (52), the Monte Carlo method also provides a conceptually simple approach to time dependent problems involving the propagation of short light pulses. Simply maintaining a running total of path-length travelled allows the calculation of time resolved parameters such as the scattered reflectance. It is worth noting that time resolved Monte Carlo methods have some advantages even in calculating steady-state quantities. For example, suppose the desired quantity is the scattered transmittance through a slab, T_s. A time-resolved Monte Carlo simulation can be performed to estimate $T_{so}(t)$, the transmittance for an incident short pulse when the slab has no absorption. The steady-state transmittance for any absorbance can then be calculated as

$$T_s = \int_0^\infty T_{so}(t)\, e^{-\mu_a c t}\, dt \qquad (45)$$

so that one simulation provides T_s for the full range of single scattering albedo. (This is similar in concept to the successive orders method disussed above.)

Random walk model

In recent years Bonner and colleagues have published a number of interesting papers (53–56) in which a random walk model of photon propagation was used to solve for quantities such as the spatial dependence of scattered reflectance arising from a point source. In the original paper (53), photon random walks occurred on a cubic lattice where the lattice spacing was equal to the root mean square distance between scattering events and absorption occurred in the intervening space. This is equivalent to isotropic scattering, but later publications extended the application to anisotropic scattering through the use of 'constrained walks'.

In the limit of a large number of steps in the walk, it is possible to derive analytic expressions for quantities of interest—such as the probability of finding a photon at a certain distance from a point source. It should be noted, however, that a large number of steps corresponds physically to a low probability of absorption. This model is therefore most useful in the wavelength regime where diffusion theory is also successful. In fact, Chandrasekhar (57) has formally shown the correspondence between these two descriptions of particle transport. It is not clear that there is any advantage in using one approach over the other.

Asymptotic radiation and hybrid methods

As summarized by van de Hulst (10), a number of authors have shown that deep within a homogeneous medium and far from any radiation sources, the fluence falls off with distance, r, as a single exponential $e^{-\mu_{eff}r}$, where μ_{eff} is the effective attenuation coefficient, and that the radiance assumes a fixed angular dependence. This so-called asymptotic field has been demonstrated in oceanographic measurements by Jerlov (11) and, on a smaller scale, in aqueous suspensions of polyvinyl acetate and ink (58). In Fig. 5 we have used the Monte Carlo technique to illustrate the transition from a 'transient' radiance distribution near the surface of a semi-infinite medium irradiated by an infinite collimated beam to the asymptotic field at sufficient depth. The region of asymptotic radiation occurs when the log radiance verus depth curves become parallel straight lines.

Under conditions where diffusion theory applies, the coefficient of exponential fall-off can be simply calculated by

$$\mu_{eff}^2 = 3\mu_a[\mu_a + (1 - g)\mu_s] \quad (46)$$

and the fixed radiance pattern, also known as the diffusion pattern, $L_{dif}(\theta)$, is given by

$$L_{dif}(\theta) = \frac{[1 + 3g(1 - a)\dfrac{\mu_t}{\mu_{eff}}\cos\theta]}{[1 - \dfrac{\mu_{eff}}{\mu_t}\cos\theta]}. \quad (47)$$

Under more general conditions, it is still possible to find μ_{eff} and $L_{dif}(\theta)$ from the integral equation

$$\left(1 - \frac{\mu_{eff}}{\mu_t}\cos\theta\right) L_{dif}(\theta) = a \int_{-1}^{1} f[\cos\theta\cos\beta + (1 - \cos^2\theta)^{\frac{1}{2}}(1 - \cos^2\beta)^{\frac{1}{2}}]L_{dif}(\beta)d(\cos\beta) \quad (48)$$

but the numerical solution is rather difficult if the phase function is highly anisotropic (10).

The qualitative behaviour of the radiance at depth is, therefore, easily determined, but an absolute calculation of the radiance is much more difficult. This suggests that hybrid models might be developed which use more accurate numerical methods near the surface but 'couple' these solutions at sufficient depth to the ex-

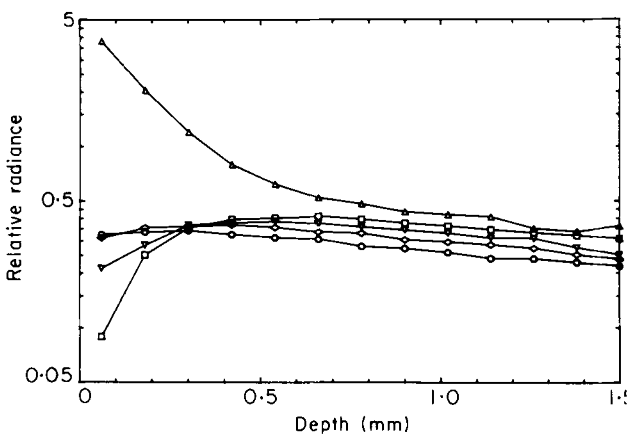

Fig. 5. Monte Carlo calculations of radiance showing the change from a transient radiance pattern near the surface of a semi-infinite slab irradiated by an infinite collimated beam, to a stable radiance or diffusion pattern at depth. The direction angle is relative to the direction of the incident collimated beam. The optical properties are typical of soft tissue in the scatter-dominated wavelength regime. $\mu_s = 33\,mm^{-1}$; $\mu_a = 0.033\,mm^{-1}$; g = 0.95. Direction: △, 0°; □, 63°; ▽, 90°; ◇, 153°; ○, 180°.

pression for the asymptotic field. Flock et al (48) have published the framework for such a model which combines Monto Carlo and diffusion calculations.

SUMMARY AND DISCUSSION

In this paper we have reviewed the mathematical description of light propagation in a medium in which the optical properties do not depend on the local electromagnetic field and the effects of multiple scattering are important. These conditions apply to many of the important uses of light in medicine. While a mathematical description of this situation in terms of Maxwell's equation is theoretically possible, the detailed knowledge of tissue dielectric properties necessary is not currently available. Radiation transfer theory, which essentially ignores wave-like phenomena such as interference, has instead been used to formulate an equation for the radiance in terms of absorption and differential scattering coefficients. While less satisfying from a theoretical standpoint, this formalism has been adequate to describe almost all experimental results.

The solution of the radiative transfer equation is a formidable task which has been the subject of several textbooks. While we have referred to the classical methods of solution, our emphasis has been mainly on methods which have proven their utility in tissue optics. The oldest of these is the 2-flux model which can still provide accurate results for tissue slabs with high scattering to absorption ratio. Currently more popular is the diffusion or P_1 model which is easily generalized to arbitrary 3-D geometries and which again provides accurate results far from sources and boundaries when scattering dominates absorption. There are, however, wavelength ranges where neither of these models provides reliable radiance or fluence calculations (1). The only method which is presently capable of dealing with arbitrary 3-D geometries in this regime is the Monte Carlo simulation. While conceptually simple, this method usually requires substantial computer resources for precise calculations. These resources are becoming more widely available, however, and it is likely that tissue optics will follow the trend seen in other fields of radiation physics with such simulation studies becoming more prevalent.

In the second part of this review, we will summarize current knowledge of the optical properties of tissues in the wavelength range 0.25–10 μm. We will also discuss the methods, both direct and indirect, by which this information may be obtained. Both scattering and absorption coefficients of tissue vary with wavelength and there are regimes where the propagation is dominated by the effect of one of these processes. At other wavelengths, both processes must be considered in calculating the fluence distribution in tissue. We will discuss the characteristics of the fluence distribution in tissue under these different circumstances and how the models discussed in Part I can be most effectively applied.

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