

Validity conditions for the radiative transfer equation

Luis Martí-López and Jorge Bouza-Domínguez

Centro de Neurociencias de Cuba, Apartado Postal 6412, C. P. 10600, La Habana, Cuba

Jeremy C. Hebden

Department of Medical Physics and Bioengineering, University College London, 11-20 Capper Street, London WC1E 6JA, UK

Simon R. Arridge

Department of Computer Science, University College London, Gower Street, London WC1E 6BT, UK

René A. Martínez-Celorio

Centro de Investigaciones en Óptica, Loma del Bosque 115, Col. Lomas del Campestre León, Apartado Postal 1-948, Guanajuato 150, México

Received May 28, 2003; revised manuscript received July 1, 2003; accepted July 14, 2003

We compare the radiative transfer equation for media with constant refractive index with the radiative transfer equation for media with spatially varying refractive indices [J. Opt. A Pure App. Opt. **1**, L1 (1999)] and obtain approximate conditions under which the former equation is accurate for modeling light propagation in scattering media with spatially varying refractive indices. These conditions impose restrictions on the variations of the refractive index, the gradient of the refractive index, the divergence of the rays, the frequency of modulation, and the widths of light pulses, which are related to the mean refractive index, the absorption coefficient, and the reduced scattering coefficient of the medium. Each condition is geometrically interpreted. Some implications of the results are discussed. © 2003 Optical Society of America

OCIS codes: 170.5280, 290.7050, 290.1990.

1. INTRODUCTION

Optical tomography (OT) deals with the problem of retrieving spatial functions of internal physical properties of a body from a set of optical measurements.¹ Examples of such functions are scattering and absorption coefficients (in biomedical applications) or the refractive index (in plasma physics research). Since biological tissues are relatively low absorbing in the optical window ranging from $\lambda = 700$ nm to $\lambda = 1000$ nm, most medical applications of OT are carried out in that range. Unfortunately, most biological tissues also strongly scatter light, which represents a serious problem for viewing the body's internal structures and characterizing biological processes by optical methods.²⁻⁴

A thorough theoretical description of low-power light propagation in biological tissues should utilize Maxwell's equations (or equations derived from them), taking into account the high inhomogeneity and anisotropy of biological media. However, this leads to highly complex mathematical problems.⁵ A simpler mathematical approach is to employ the radiative transfer theory; the differential radiative transfer equation (RTE) represents the theory's main equation.⁴⁻⁷ The RTE has been applied with quite significant success for solving forward and inverse problems and for Monte Carlo simulations in OT.⁷⁻⁹ The RTE

can be derived from the Boltzmann transport equation or from an optical model.⁴⁻⁹ In stratified tissues, where multiple light fluxes are present, more complicated models should be used.⁶

One of the main assumptions of the model leading to the RTE is that ray trajectories are straight lines and any change of direction of propagation is due to scattering. This assumption is supported by qualitative arguments. It implies, among other things, that the velocity of photons inside the body is constant or, equivalently, that the refractive index of the body is constant. Nevertheless, it is a well-known fact that the refractive index of biological tissues depends on the type of tissue and that a section of a biological body may be composed of many different tissues having different refractive indices. For example, some values of refractive index of human tissues at $\lambda = 633$ nm are 1.38 (lung), 1.39 (muscle), and 1.45 (normal adipose tissue).¹⁰ The refractive index of a tissue may be related to biological processes that take place within it. A change of the refractive index of tissues produces a change in the optical path of the propagating light that can be measured by techniques of time-of-flight¹¹ or phase-resolved spectroscopy.¹² On the other hand, accurate simulations in the approximation of the diffusion equation (DE) show that a mismatch of refractive index at

a tissue boundary leads to large errors in retrieved optical properties of the tissue.¹³ This result suggests that the spatial variations of refractive index could have a nonnegligible influence on the propagation of light through tissue boundary. Obviously, the study of the effects of spatially varying refractive index on light propagation would be of great interest for the development of OT for biomedical applications. In particular, a generalization of the RTE is needed.

In a study by Ferwerda,¹⁴ the RTE for a medium with spatially varying refractive index (RTEvri) was proposed. In the model leading to the RTEvri, the scattering medium was assumed to consist of a background medium with variable refractive index in which scattering centers are randomly distributed. Recently Khan and Jiang¹⁵ showed that Ferwerda's RTEvri presents a redundant term and proposed a DE derived from the RTEvri. It is easy to show that the RTE is a particular case of the RTEvri.

A drawback of the DE derived from the RTE is that it gives wrong results in the vicinity of sources.^{16,17} It has been suggested that the perturbations introduced by the optical fibers are among the causes of the observed discrepancies between experimental and theoretical results.^{16,17} Another possible cause for such discrepancies may be a nonnegligible divergence of rays in the vicinity of a point source. In this regard the RTEvri contains a term accounting for the divergence of the rays that could be used to give an alternative explanation for the inaccuracy of the DE in the vicinity of sources.

The goal of the present paper is to determine the conditions under which, in biological tissues, the RTE can be considered an accurate equation for modeling light propagation in turbid media with spatially varying refractive indices and in the vicinity of sources. To achieve that goal, we compare the RTE with the RTEvri in connection with OT problems for nonnull coefficients of absorption and reduced scattering, deduce the conditions under which the RTE is accurate, and interpret the results geometrically.

2. COMPARISON OF THE RADIATIVE TRANSFER EQUATION WITH THE RADIATIVE TRANSFER EQUATION FOR A MEDIUM WITH SPATIALLY VARYING REFRACTIVE INDEX

The time-dependent RTEvri is given by the expression^{14,15}

$$\begin{aligned} & \frac{n(\mathbf{r})}{c} \frac{\partial}{\partial t} L(\mathbf{r}, \boldsymbol{\Omega}, t) + \boldsymbol{\Omega}(\mathbf{r}) \cdot \nabla_{\mathbf{r}} L(\mathbf{r}, \boldsymbol{\Omega}, t) \\ & + [\mu_a(\mathbf{r}) + \mu_s(\mathbf{r})] L(\mathbf{r}, \boldsymbol{\Omega}, t) + [\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})] L(\mathbf{r}, \boldsymbol{\Omega}, t) \\ & + \nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \nabla_{\boldsymbol{\Omega}} L(\mathbf{r}, \boldsymbol{\Omega}, t) \\ & = \mu_s(\mathbf{r}) \int_{4\pi} L(\mathbf{r}, \boldsymbol{\Omega}', t) \theta(\boldsymbol{\Omega}, \boldsymbol{\Omega}') d\omega + \epsilon(\mathbf{r}, \boldsymbol{\Omega}, t), \quad (1) \end{aligned}$$

where $L(\mathbf{r}, \boldsymbol{\Omega}, t)$ is the radiance at a point \mathbf{r} in the direction $\boldsymbol{\Omega}$, $n(\mathbf{r})$ is the refractive index, c is the speed of light in vacuum, $\mu_a(\mathbf{r})$ and $\mu_s(\mathbf{r})$ are the absorption and scat-

tering coefficients, respectively, $\theta(\mathbf{r}, \boldsymbol{\Omega}, \boldsymbol{\Omega}')$ is the normalized scattering function, $d\omega$ is a differential of solid angle, $\epsilon(\mathbf{r}, \boldsymbol{\Omega}, t)$ is a source distribution per unit volume, and symbols $\nabla_{\mathbf{r}}$ and $\nabla_{\boldsymbol{\Omega}}$ denote gradient operators with respect to coordinates \mathbf{r} and the direction of propagation $\boldsymbol{\Omega}$, respectively. Here we used the identity $\nabla_{\mathbf{r}} n(\mathbf{r})/n(\mathbf{r}) = \nabla_{\mathbf{r}} \ln[n(\mathbf{r})]$. The explicit form of the term $\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$ will be discussed later in the paper.

The vector field of unit vectors $\boldsymbol{\Omega}(\mathbf{r})$ is perpendicular to wave fronts and tangent to ray trajectories. Accordingly, it can be found with the expression¹⁸

$$\boldsymbol{\Omega}(\mathbf{r}) = \frac{\nabla_{\mathbf{r}} \mathcal{L}(\mathbf{r})}{|\nabla_{\mathbf{r}} \mathcal{L}(\mathbf{r})|} = \frac{\nabla_{\mathbf{r}} \mathcal{L}(\mathbf{r})}{n(\mathbf{r})}, \quad (2)$$

where $\mathcal{L}(\mathbf{r})$ is the eikonal given by the equation

$$\nabla_{\mathbf{r}} \mathcal{L}(\mathbf{r}) \cdot \nabla_{\mathbf{r}} \mathcal{L}(\mathbf{r}) = n^2(\mathbf{r}). \quad (3)$$

A wave front is described by the expression¹⁸

$$\mathcal{L}(\mathbf{r}) = \text{const}. \quad (4)$$

Alternatively, vector $\boldsymbol{\Omega}(\mathbf{r})$ along a ray trajectory $\mathbf{r} = \mathbf{R}(s)$, where s is the length of arc, can be found through the equation¹⁸

$$\boldsymbol{\Omega}[\mathbf{R}(s)] = \frac{d}{ds} \mathbf{R}(s). \quad (5)$$

The trajectory of a ray is given by the equation¹⁸

$$\frac{d}{ds} \left\{ n[\mathbf{R}(s)] \frac{d}{ds} \mathbf{R}(s) \right\} = \nabla_{\mathbf{r}} n[\mathbf{R}(s)]. \quad (6)$$

The term $\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$ requires a special comment. It was calculated to be¹⁴

$$\begin{aligned} \nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r}) &= \frac{1}{n(\mathbf{r})} \left[\frac{1}{\Omega_x} \frac{\partial n(\mathbf{r})}{\partial x} + \frac{1}{\Omega_y} \frac{\partial n(\mathbf{r})}{\partial y} + \frac{1}{\Omega_z} \frac{\partial n(\mathbf{r})}{\partial z} \right] \\ & - \frac{3}{n(\mathbf{r})} \nabla_{\mathbf{r}} n(\mathbf{r}) \cdot \boldsymbol{\Omega}(\mathbf{r}), \quad (7) \end{aligned}$$

where Ω_x , Ω_y , and Ω_z are the Cartesian components of vector $\boldsymbol{\Omega}$.

From expression (7), it follows that in a medium of a constant refractive index the divergence is always zero. Therefore expression (7) takes into account the effect of a spatially varying refractive index on the divergence, ignoring that in the vicinity of a source the wave front may not be a plane. To illustrate this point, we consider the following example. For an isotropic point source placed at the origin of a Cartesian coordinate system in a medium of a constant refractive index, the eikonal, the ray directions, and the divergence are

$$\mathcal{L}(\mathbf{r}) = nr, \quad (8)$$

$$\boldsymbol{\Omega}(\mathbf{r}) = \frac{\nabla_{\mathbf{r}} \mathcal{L}(\mathbf{r})}{n(\mathbf{r})} = \frac{\mathbf{r}}{r}, \quad (9)$$

$$\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r}) = \frac{2}{r} \neq 0. \quad (10)$$

Therefore expression (7) gives wrong results for this particular case. We can find an alternative expression for the divergence of the vector field $\boldsymbol{\Omega}(\mathbf{r})$, free from this drawback, by using expression (2). It yields

$$\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r}) = \frac{\nabla_{\mathbf{r}}^2 \mathcal{L}(\mathbf{r})}{n(\mathbf{r})} - \mathbf{\Omega}(\mathbf{r}) \cdot \nabla_{\mathbf{r}} \ln n(\mathbf{r}). \quad (11)$$

Note that for plane waves propagating in a medium of a constant refractive index, $\nabla_{\mathbf{r}}^2 \mathcal{L}(\mathbf{r}) = 0$, $\nabla_{\mathbf{r}} \ln n(\mathbf{r}) = 0$, and, consequently, $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r}) = 0$, as we could expect. The consequences of using expression (11) instead of expression (7) for the divergence $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})$ are as follows. First, this term now implicitly accounts for wave-front curvature, and, second, the second equation of the P_1 approximation of the RTEvri adopts a form different from that obtained by Khan and Jiang.¹⁵

Let us rearrange RTEvri (1). To do that, we introduce the following magnitudes and functions:

$$\bar{n} = \frac{1}{V} \int_V n(\mathbf{r}) dV, \quad (12)$$

where V is the volume of the body,

$$\tilde{n}(\mathbf{r}) = n(\mathbf{r}) - \bar{n}, \quad (13)$$

$$\begin{aligned} \epsilon_L(\mathbf{r}, \mathbf{\Omega}, t) = & -\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \nabla_{\mathbf{\Omega}} L(\mathbf{r}, \mathbf{\Omega}, t) \\ & - \frac{\tilde{n}(\mathbf{r})}{c} \frac{\partial}{\partial t} L(\mathbf{r}, \mathbf{\Omega}, t). \end{aligned} \quad (14)$$

Substituting expressions (12)–(14) into Eq. (1), we get an equivalent form of the RTEvri, given by the expression

$$\begin{aligned} & \frac{\bar{n}}{c} \frac{\partial}{\partial t} L(\mathbf{r}, \mathbf{\Omega}, t) + \mathbf{\Omega} \cdot \nabla_{\mathbf{r}} L(\mathbf{r}, \mathbf{\Omega}, t) \\ & + [\mu_a(\mathbf{r}) + \mu_s(\mathbf{r}) + \nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})] L(\mathbf{r}, \mathbf{\Omega}, t) \\ & = \mu_s(\mathbf{r}) \int_{4\pi} L(\mathbf{r}, \mathbf{\Omega}', t) \theta(\mathbf{\Omega}, \mathbf{\Omega}') d\omega' + \epsilon(\mathbf{r}, \mathbf{\Omega}, t) \\ & + \epsilon_L(\mathbf{r}, \mathbf{\Omega}, t). \end{aligned} \quad (15)$$

If $\tilde{n}(\mathbf{r}) = 0$ and $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r}) = 0$ for any $\mathbf{r} \in V$, the ray trajectories are straight parallel lines and RTEvri (15) assumes the form of the RTE

$$\begin{aligned} & \frac{\bar{n}}{c} \frac{\partial}{\partial t} L(\mathbf{r}, \mathbf{\Omega}, t) + \mathbf{\Omega} \cdot \nabla_{\mathbf{r}} L(\mathbf{r}, \mathbf{\Omega}, t) \\ & + [\mu_a(\mathbf{r}) + \mu_s(\mathbf{r})] L(\mathbf{r}, \mathbf{\Omega}, t) \\ & = \mu_s(\mathbf{r}) \int_{4\pi} L(\mathbf{r}, \mathbf{\Omega}', t) \theta(\mathbf{\Omega}, \mathbf{\Omega}') d\omega' + \epsilon(\mathbf{r}, \mathbf{\Omega}, t). \end{aligned} \quad (16)$$

Let us compare RTEvri (15) with RTE (16).

1. In RTEvri (15), vector $\mathbf{\Omega}(\mathbf{r})$ is related to the refractive index and its spatial derivatives through Eq. (2) or Eqs. (5) and (6), whereas in RTE (16) it is treated as an independent variable.

2. The term $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})$ can be interpreted as an absorption coefficient if $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r}) > 0$ or as an amplification coefficient if $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r}) < 0$. Of course, no actual attenuation or amplification takes place. The effect of the divergence on the shape of the elementary scattering volume is illustrated in Fig. 1 for the RTEvri and the RTE.

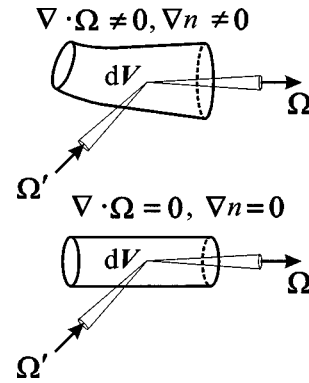


Fig. 1. Elementary scattering volumes. $\nabla \cdot \mathbf{\Omega} \neq 0, \nabla n \neq 0$: elementary scattering volume for the RTEvri. $\nabla \cdot \mathbf{\Omega} = 0, \nabla n = 0$: elementary scattering volume for the RTE.

3. The term $\epsilon_L(\mathbf{r}, \mathbf{\Omega}, t)$ can be interpreted as a radiance-dependent source. This term is related to the gradient of the logarithm of the refractive index.

4. In time-dependent problems the refractive index $n(\mathbf{r})$ and its spatial derivatives contribute terms to the RTEvri, whereas in time-independent problems only the spatial derivatives of $n(\mathbf{r})$ do.

5. Existing experimental arrangements for medical applications of OT do not facilitate measurement or characterization of $\mathbf{\Omega}$, $n(\mathbf{r})$, $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})$, and other related functions.³ The RTEvri suffers from this lack of information, whereas the RTE simply ignores it.

6. RTEvri (15) shares all the problems related to uniqueness and ill-posedness of RTE (16). These issues of the RTE have been analyzed elsewhere.⁸

7. Condition

$$|\tilde{n}(\mathbf{r})| \ll \bar{n}, \quad (17)$$

for any $\mathbf{r} \in V$, does not suffice for using the RTE instead of the RTEvri for solving inverse or forward problems in media with spatially varying refractive indices, since it does not impose restrictions on the properties of the vector field $\mathbf{\Omega}$ or on the spatial derivatives of $n(\mathbf{r})$.

Points 1–4 strongly suggest that RTE (16) is a rough approximation to RTEvri (15), whereas point 5 suggests that new experimental approaches are needed for gathering additional information to use the RTEvri. Point 6 suggests that further studies on uniqueness and ill-posedness of both the RTE and the RTEvri are needed. Point 7 indicates that complementary mathematical conditions should be determined for specifying when the RTE is an accurate approximation to the RTEvri.

To analyze the effect of using the RTE instead of the RTEvri for a medium with a spatially varying refractive index, we assume that $L_{\text{vri}}(\mathbf{r}, \mathbf{\Omega}, t)$ is a known solution to RTEvri (15) for certain boundary and initial conditions in a convex region V with spatially varying refractive index $n(\mathbf{r})$. We also assume that the mean refractive index \bar{n} and functions $\theta(\mathbf{r}, \mathbf{\Omega}, \mathbf{\Omega}')$ and $\epsilon(\mathbf{r}, \mathbf{\Omega}, t)$ are known. If we substitute radiance $L_{\text{vri}}(\mathbf{r}, \mathbf{\Omega}, t)$ into RTEvri (15), we obtain

$$\begin{aligned}
& \frac{\bar{n}}{c} \frac{\partial}{\partial t} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) + \boldsymbol{\Omega}(\mathbf{r}) \cdot \nabla_{\mathbf{r}} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& + [\mu_{\text{a}}(\mathbf{r}) + \mu_{\text{s}}(\mathbf{r}) + \nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})] L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& = \mu_{\text{s}}(\mathbf{r}) \int_{4\pi} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}', t) \theta(\mathbf{r}, \boldsymbol{\Omega}, \boldsymbol{\Omega}') d\omega' + \epsilon(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& + \epsilon_L(\mathbf{r}, \boldsymbol{\Omega}, t), \tag{18}
\end{aligned}$$

where $\mu_{\text{a}}(\mathbf{r})$, $\mu_{\text{s}}(\mathbf{r})$, and $\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$ are unknown functions.

Now we assume that there exists an algorithm based on RTE (16), which retrieves functions $\mu_{\text{a}}(\mathbf{r})$ and $\mu_{\text{s}}(\mathbf{r})$ with negligible uncertainties from function $L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t)$. To avoid any confusion, we denote retrieved absorption and scattering coefficients by $\mu_{\text{ar}}(\mathbf{r})$ and $\mu_{\text{sr}}(\mathbf{r})$, respectively. Substituting radiance $L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t)$ and retrieved functions $\mu_{\text{ar}}(\mathbf{r})$ and $\mu_{\text{sr}}(\mathbf{r})$ into Eq. (16), we obtain

$$\begin{aligned}
& \frac{\bar{n}}{c} \frac{\partial}{\partial t} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) + \boldsymbol{\Omega} \cdot \nabla_{\mathbf{r}} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& + [\mu_{\text{ar}}(\mathbf{r}) + \mu_{\text{sr}}(\mathbf{r})] L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& = \mu_{\text{sr}}(\mathbf{r}) \int_{4\pi} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}', t) \theta(\mathbf{r}, \boldsymbol{\Omega}, \boldsymbol{\Omega}') d\omega' \\
& + \epsilon(\mathbf{r}, \boldsymbol{\Omega}, t). \tag{19}
\end{aligned}$$

If we combine Eq. (18) with Eq. (19) and rearrange the resulting equation, we get

$$\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r}) = \frac{\epsilon_L(\mathbf{r}, \boldsymbol{\Omega}, t)}{L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t)}, \tag{20}$$

where we assume that $L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) \neq 0$. From the definition of $\epsilon_L(\mathbf{r}, \boldsymbol{\Omega}, t)$ [Eq. (14)] and Eq. (20), it follows that $\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$ depends on $L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t)$ and its derivatives, $\boldsymbol{\Omega}(\mathbf{r})$, $n(\mathbf{r})$, and $\nabla_{\mathbf{r}} n(\mathbf{r})$. But this result is physically meaningless, since $\boldsymbol{\Omega}(\mathbf{r})$ and, consequently, its divergence depend only on the eikonal and the refractive index of the background medium as seen from Eq. (2) or on ray trajectories, as seen from Eq. (5). Therefore no algorithm based on RTE (16), which retrieves coefficients $\mu_{\text{ar}}(\mathbf{r})$ and $\mu_{\text{sr}}(\mathbf{r})$ will lead to physically correct values of $\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$.

Another difficulty related to the use of the RTE for OT problems for a medium with a spatially varying refractive index is that the RTEvri has a form similar to that of the RTE. To illustrate this issue we rearrange Eq. (15) in the form

$$\begin{aligned}
& \frac{\bar{n}}{c} \frac{\partial}{\partial t} L(\mathbf{r}, \boldsymbol{\Omega}, t) + \boldsymbol{\Omega} \cdot \nabla_{\mathbf{r}} L(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& + [\mu_{\text{a mod}}(\mathbf{r}) + \mu_{\text{s}}(\mathbf{r})] L(\mathbf{r}, \boldsymbol{\Omega}, t) \\
& = \mu_{\text{s}}(\mathbf{r}) \int_{4\pi} L(\mathbf{r}, \boldsymbol{\Omega}', t) \theta(\mathbf{r}, \boldsymbol{\Omega}, \boldsymbol{\Omega}') d\omega' \\
& + \epsilon_{\text{mod}}(\mathbf{r}, \boldsymbol{\Omega}, t), \tag{21}
\end{aligned}$$

where $\mu_{\text{a mod}}(\mathbf{r}) = \mu_{\text{a}}(\mathbf{r}) + \nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$ is the modified absorption coefficient and $\epsilon_{\text{mod}}(\mathbf{r}, \boldsymbol{\Omega}, t) = \epsilon(\mathbf{r}, \boldsymbol{\Omega}, t) + \epsilon_L(\mathbf{r}, \boldsymbol{\Omega}, t)$ is the modified source distribution. Note that Eq. (21) has the form of RTE (16).

From a comparison of RTE (16) with Eq. (21), it follows that an algorithm for solving OT problems based on RTE (16) cannot distinguish the modified absorption coefficient $\mu_{\text{a mod}}(\mathbf{r})$ from the actual absorption coefficient $\mu_{\text{a}}(\mathbf{r})$ unless some complementary information on $\nabla_{\mathbf{r}} \cdot \boldsymbol{\Omega}(\mathbf{r})$ is provided. On the other hand, in practical situations $\epsilon(\mathbf{r}, \boldsymbol{\Omega}, t)$ is known (for example, as a result of illuminating the surface of the object with light by use of an optical fiber), but the modified source distribution $\epsilon_{\text{mod}}(\mathbf{r}, \boldsymbol{\Omega}, t)$ is unknown.

Despite the above analysis, we can expect that, under some restrictions on the vector field $\boldsymbol{\Omega}(\mathbf{r})$ (or, equivalently, on wave fronts and rays) and on the refractive index $n(\mathbf{r})$, RTE (16) could retrieve functions $\mu_{\text{ar}}(\mathbf{r})$ and $\mu_{\text{sr}}(\mathbf{r})$, which are good approximations to $\mu_{\text{a}}(\mathbf{r})$ and $\mu_{\text{s}}(\mathbf{r})$, respectively.

3. CONDITIONS FOR USING THE RADIATIVE TRANSFER EQUATION IN OPTICAL TOMOGRAPHY PROBLEMS

Consider an expansion of the radiance $L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t)$ and the source distribution $\epsilon_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t)$ in a series of spherical harmonics of $\boldsymbol{\Omega}$, where only the first two terms are retained (P_1 approximation):

$$L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) = \frac{1}{4\pi} I_{\text{vri}}(\mathbf{r}, t) + \frac{3}{4\pi} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t), \tag{22}$$

$$\epsilon(\mathbf{r}, \boldsymbol{\Omega}, t) = \frac{1}{4\pi} \epsilon_0(\mathbf{r}, t) + \frac{3}{4\pi} \boldsymbol{\Omega} \cdot \boldsymbol{\epsilon}_1(\mathbf{r}, t), \tag{23}$$

where $I_{\text{vri}}(\mathbf{r}, t)$ is the irradiance and $\mathbf{J}_{\text{vri}}(\mathbf{r}, t)$ is the radiative flux density vector. They are given by the expressions

$$I_{\text{vri}}(\mathbf{r}, t) = \int_{4\pi} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) d\omega, \tag{24}$$

$$\mathbf{J}_{\text{vri}}(\mathbf{r}, t) = \int_{4\pi} L_{\text{vri}}(\mathbf{r}, \boldsymbol{\Omega}, t) \boldsymbol{\Omega} d\omega. \tag{25}$$

$\epsilon_0(\mathbf{r}, t)$ and $\boldsymbol{\epsilon}_1(\mathbf{r}, t)$ are given by the expressions

$$\epsilon_0(\mathbf{r}, t) = \int_{4\pi} \epsilon(\mathbf{r}, \boldsymbol{\Omega}, t) d\omega, \tag{26}$$

$$\boldsymbol{\epsilon}_1(\mathbf{r}, t) = \int_{4\pi} \epsilon(\mathbf{r}, \boldsymbol{\Omega}, t) \boldsymbol{\Omega} d\omega. \tag{27}$$

In expressions (22) and (23) it is assumed that the conditions for the P_1 approximation hold well. See elsewhere.⁵

Further, we assume that the phase function is independent of the direction of incident photons so that $\theta(\mathbf{r}, \boldsymbol{\Omega}, \boldsymbol{\Omega}') \equiv \theta(\mathbf{r}, \boldsymbol{\Omega} \cdot \boldsymbol{\Omega}')$. Consequently, it can be expanded in a series of Legendre polynomials.⁹ Approximating that expansion by its first two terms, we obtain

$$\theta(\mathbf{r}, \boldsymbol{\Omega} \cdot \boldsymbol{\Omega}') \approx \frac{1}{4\pi} + \frac{3g(\mathbf{r})}{4\pi} \boldsymbol{\Omega} \cdot \boldsymbol{\Omega}', \tag{28}$$

where $g(\mathbf{r})$ is the asymmetry factor, given by the expression

$$g(\mathbf{r}) = \int_{4\pi} \boldsymbol{\Omega} \cdot \boldsymbol{\Omega}' \theta(\mathbf{r}, \boldsymbol{\Omega}, \boldsymbol{\Omega}') d\omega'. \tag{29}$$

The assumption of a normalized phase function independent of the direction of incident photons seems to be valid for nonstructured biological tissues and may fail for structured tissues such as muscle.⁶ If the normalized phase function depends on the direction of incident photons, we can expand separately it in the directions $\mathbf{\Omega}$ and $\mathbf{\Omega}'$ by using spherical harmonics $Y_{l,m}^*(\mathbf{\Omega}')Y_{l,m}(\mathbf{\Omega})$.⁹ It leads to far more complicated equations, which limits its wide use in OT problems. Note also that for a phase function independent of the direction of incidence we can transform the expansion in spherical harmonics into a Legendre series by using the addition theorem for spherical harmonics. Here we study only the scattering independent of the direction of incident photons.

Integrating Eq. (1) over 4π sr and applying expressions (22), (23), and (29), we obtain (see Appendix A)

$$\begin{aligned} & \frac{\bar{n}}{c} \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t) + \nabla_{\mathbf{r}} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) + \mu_a(\mathbf{r}) I_{\text{vri}}(\mathbf{r}, t) \\ & + 2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \\ & = \epsilon_0(\mathbf{r}, t) - \frac{\bar{n}(\mathbf{r})}{c} \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t). \end{aligned} \quad (30)$$

To obtain a second equation, we substitute expressions (24)–(27) into Eq. (1), multiply the result by $\mathbf{\Omega}$, and integrate again over a solid angle of 4π sr. This yields (see Appendix B)

$$\begin{aligned} & \frac{\bar{n}}{c} \frac{\partial}{\partial t} \mathbf{J}_{\text{vri}}(\mathbf{r}, t) - \frac{1}{3} [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I_{\text{vri}}(\mathbf{r}, t) + \frac{1}{3} \nabla_{\mathbf{r}} I_{\text{vri}}(\mathbf{r}, t) \\ & + [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r}) + \mu_d(\mathbf{r})] \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \\ & = \frac{1}{\bar{n}} \boldsymbol{\epsilon}_1(\mathbf{r}, t) - \frac{\bar{n}(\mathbf{r})}{c} \frac{\partial}{\partial t} \mathbf{J}_{\text{vri}}(\mathbf{r}, t), \end{aligned} \quad (31)$$

where $\mu'_s(\mathbf{r})$ and $\mu_d(\mathbf{r})$ are the reduced scattering coefficient and the coefficient of divergence, respectively, defined by the expressions

$$\mu'_s(\mathbf{r}) = [1 - g(\mathbf{r})] \mu_s(\mathbf{r}), \quad (32)$$

$$\mu_d(\mathbf{r}) = \frac{\nabla_{\mathbf{r}}^2 \mathcal{L}(\mathbf{r})}{n(\mathbf{r})}. \quad (33)$$

Note that P_1 Eqs. (30) and (31) give the well-known P_1 approximation of the RTE if $\nabla_{\mathbf{r}} \ln n(\mathbf{r}) = \mathbf{0}$ and $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega} = 0$.

In the following analysis we consider three separate cases: the time-independent case, the pulsed case (for time-domain OT systems), and the periodic case (for frequency-domain OT systems).

A. Time-Independent Case

For $\partial I_{\text{vri}}(\mathbf{r}, t)/\partial t = 0$, $\partial \mathbf{J}_{\text{vri}}(\mathbf{r}, t)/\partial t = \mathbf{0}$, $\partial \epsilon_0(\mathbf{r}, t)/\partial t = 0$, and $\partial \boldsymbol{\epsilon}_1(\mathbf{r}, t)/\partial t = \mathbf{0}$, Eqs. (30) and (31) transform into the equations

$$\begin{aligned} \nabla_{\mathbf{r}} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}) + \mu_a(\mathbf{r}) I_{\text{vri}}(\mathbf{r}) + 2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}) \\ = \epsilon_0(\mathbf{r}), \end{aligned} \quad (34)$$

$$\begin{aligned} -\frac{1}{3} [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I_{\text{vri}}(\mathbf{r}) + \frac{1}{3} \nabla_{\mathbf{r}} I_{\text{vri}}(\mathbf{r}) + [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r}) \\ + \mu_d(\mathbf{r})] \mathbf{J}_{\text{vri}}(\mathbf{r}) = \boldsymbol{\epsilon}_1(\mathbf{r}). \end{aligned} \quad (35)$$

We must analyze the terms $2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_{\text{vri}}(\mathbf{r})$, $[\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I_{\text{vri}}(\mathbf{r})/3$, and $\mu_d(\mathbf{r}) \mathbf{J}_{\text{vri}}(\mathbf{r})$ to decide whether they can be discarded to obtain simpler equations corresponding to the P_1 approximation of the RTE. Negligible, but nonzero, terms $2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_{\text{vri}}(\mathbf{r})$, $[\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I_{\text{vri}}(\mathbf{r})/3$, and $\mu_d(\mathbf{r}) \mathbf{J}_{\text{vri}}(\mathbf{r})$ contribute errors, affecting the results from any OT algorithm based on the P_1 approximation of the RTE, drawn from Eqs. (34) and (35). In this regard we adopt a self-consistent approach: We consider that errors due to those terms do not significantly affect any algorithm derived from the P_1 approximation of the RTE if they are much less than the corresponding contributions that contain retrieved coefficients, such as $\mu_a(\mathbf{r}) I_{\text{vri}}(\mathbf{r})$, $\mu_a(\mathbf{r}) \mathbf{J}_{\text{vri}}(\mathbf{r})$, and $\mu'_s(\mathbf{r}) \mathbf{J}_{\text{vri}}(\mathbf{r})$. This reasoning leads to the following conditions:

$$|\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_{\text{vri}}(\mathbf{r})| \ll \frac{1}{2} |\mu_a(\mathbf{r}) I_{\text{vri}}(\mathbf{r})|, \quad (36)$$

$$|[\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I_{\text{vri}}(\mathbf{r})| \ll 3 |\min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \mathbf{J}_{\text{vri}}(\mathbf{r})|, \quad (37)$$

$$|\mu_d(\mathbf{r}) \mathbf{J}_{\text{vri}}(\mathbf{r})| \ll |\min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \mathbf{J}_{\text{vri}}(\mathbf{r})|, \quad (38)$$

for $I_{\text{vri}}(\mathbf{r}) \neq 0$ and $\mathbf{J}_{\text{vri}}(\mathbf{r}) \neq \mathbf{0}$.

Using the relation

$$\begin{aligned} |\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_{\text{vri}}(\mathbf{r})| & \leq |\nabla_{\mathbf{r}} \ln n(\mathbf{r})| |\mathbf{J}_{\text{vri}}(\mathbf{r})| \\ & \leq |\nabla_{\mathbf{r}} \ln n(\mathbf{r})| I_{\text{vri}}(\mathbf{r}), \end{aligned} \quad (39)$$

we can transform condition (36) to obtain a more practical (but less general) expression. Conditions (37) and (38) can be transformed also. Assuming that $I_{\text{vri}}(\mathbf{r}) \neq 0$ and $|\mathbf{J}_{\text{vri}}(\mathbf{r})| \neq 0$, we obtain

$$|\nabla_{\mathbf{r}} \ln n(\mathbf{r})| \ll \frac{\mu_a(\mathbf{r})}{2}, \quad (40)$$

$$|\nabla_{\mathbf{r}} \ln n(\mathbf{r})| \ll 3\eta \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})], \quad (41)$$

$$|\mu_d(\mathbf{r})| \ll |\mu_{d \max}| = \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})], \quad (42)$$

where $\eta = |\mathbf{J}_{\text{vri}}(\mathbf{r})|/I_{\text{vri}}(\mathbf{r})$ and $|\mu_{d \max}|$ is the upper bound of the modulus of $|\mu_d(\mathbf{r})|$.

Conditions (40) and (41) can be combined to give

$$|\nabla_{\mathbf{r}} \ln n(\mathbf{r})| \ll \min \left\{ \frac{\mu_a(\mathbf{r})}{2}, 3\eta \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \right\}. \quad (43)$$

Most biological tissues in the spectral range from $\lambda = 700$ nm to $\lambda = 1000$ nm have absorption and reduced scattering coefficients so that $\mu_a(\mathbf{r}) < \mu'_s(\mathbf{r})$. Therefore for them condition (43) has the form $|\nabla_{\mathbf{r}} \ln n(\mathbf{r})| \ll \mu_a(\mathbf{r}) \min[1/2, 3\eta]$. Nevertheless, we keep it with no change for the sake of generality.

The geometrical meanings of inequalities (42) and (43) are simple. The modulus of the curvature vector \mathbf{K} of the rays is $|\mathbf{K}| = 1/R = \mathbf{v} \cdot \nabla_{\mathbf{r}} \ln n(\mathbf{r}) \leq |\nabla_{\mathbf{r}} \ln n(\mathbf{r})|$, where R is the radius of curvature and \mathbf{v} is the unitary principal normal vector at the point \mathbf{r} of the ray.¹⁸ Therefore condition (43) imposes restrictions on the minimum curvature of rays as follows:

$$R \geq R_{\min} = \max \left\{ \frac{2}{\mu_a(\mathbf{r})}, \frac{1}{3\eta} \max \left[\frac{1}{\mu_a(\mathbf{r})}, \frac{1}{\mu'_s(\mathbf{r})} \right] \right\}, \quad (44)$$

where R_{\min} is the minimum radius of curvature of the rays allowed by condition (43).

If we define the mean free path for absorption l_a and the mean free path for scattering l'_s as $l_a = 1/\mu_a(\mathbf{r})$ and $l'_s = 1/\mu'_s(\mathbf{r})$, we can rewrite expression (44) in the form

$$R \geq R_{\min} = \max \left[2l_a, \frac{1}{3\eta} \max(l_a, l'_s) \right]. \quad (45)$$

The coefficient $\mu_d(\mathbf{r})$ is related to the curvature of the wave front [see expression (33)]. For example, for a plane wave front, $\mu_d(\mathbf{r}) = 0$. Therefore condition (42) restricts the departure of a wave front propagating in the medium from an ideally plane one. Another interpretation can be derived from expression (11). From the latter expression it follows that

$$|\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})| \leq |\mu_d(\mathbf{r})| + |\nabla_{\mathbf{r}} \ln n(\mathbf{r})|. \quad (46)$$

Combining expression (45) with conditions (42) and (43), we obtain

$$\begin{aligned} |\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})| &\leq |\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})|_{\max} \\ &= \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \\ &\quad + \min \left\{ \frac{\mu_a(\mathbf{r})}{2}, 3\eta \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \right\}, \end{aligned} \quad (47)$$

where $|\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})|_{\max}$ is the maximum modulus of the divergence. Consequently, the fulfillment of conditions (42) and (43) implies the existence of an upper bound for the modulus of the ray divergence.

B. Pulsed (Time-Domain) Case

From an inspection of Eqs. (30) and (31), it follows that in the time-domain case the RTE is a reasonable good approximation to the RTE_{vri} if, in addition to conditions (36)–(38), conditions on the time derivatives are imposed. Applying the reasoning leading to conditions (36)–(38), we obtain the following set of inequalities:

$$\frac{1}{c} \left| \tilde{n}(\mathbf{r}) \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t) \right| \leq \frac{\tilde{n}(\mathbf{r})}{c} \left| \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t) \right|, \quad (48)$$

$$\frac{\tilde{n}(\mathbf{r})}{c} \left| \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t) \right| \leq \mu_a(\mathbf{r}) I_{\text{vri}}(\mathbf{r}, t), \quad (49)$$

$$\frac{\tilde{n}(\mathbf{r})}{c} \left| \frac{\partial}{\partial t} \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \right| \leq \frac{1}{c} \left| \tilde{n} \frac{\partial}{\partial t} \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \right|, \quad (50)$$

$$\left| \frac{\tilde{n}(\mathbf{r})}{c} \frac{\partial}{\partial t} \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \right| \leq [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r})] \mathbf{J}_{\text{vri}}(\mathbf{r}, t). \quad (51)$$

From conditions (48) or (50), condition (17) can be derived. Conditions (49) and (51) are not practical because they involve functions and time derivatives that are difficult to visualize. To obtain more practical expressions, we assume that at an arbitrary point $\mathbf{r} \in V$, during a time interval Δt centered at t_0 , the radiance is Gaussian shaped; that is,

$$L_{\text{vri}}(\mathbf{r}, \mathbf{\Omega}, t) = L_i(\mathbf{r}, \mathbf{\Omega}) \exp \left[-\frac{(t - t_0)^2}{w_0^2(\mathbf{r})} \right], \quad (52)$$

where $w_0 > 0$ is the half-width at e^{-1} maximum and is measured in seconds.

This is a very simple model of the radiance, but considering a more realistic radiance adds extra mathematical complexity and does not lead to essentially different physical conclusions. Substituting expression (52) into definitions (22) and (23) we obtain

$$I_{\text{vri}}(\mathbf{r}, t) = I_i(\mathbf{r}) \exp \left[-\frac{(t - t_0)^2}{w_0^2(\mathbf{r})} \right], \quad (53)$$

$$\mathbf{J}_{\text{vri}}(\mathbf{r}, t) = \mathbf{J}_i(\mathbf{r}) \exp \left[-\frac{(t - t_0)^2}{w_0^2(\mathbf{r})} \right]. \quad (54)$$

Substituting expressions (53) and (54) into conditions (49) and (51), respectively, we obtain

$$\begin{aligned} &\left| \frac{2(t - t_0)\tilde{n}(\mathbf{r})}{cw_0^2} I_{\text{vri}}(\mathbf{r}) \exp \left[-\frac{(t - t_0)^2}{w_0^2} \right] \right| \\ &\leq \left| \mu_a(\mathbf{r}) I_{\text{vri}}(\mathbf{r}) \exp \left[-\frac{(t - t_0)^2}{w_0^2} \right] \right|, \end{aligned} \quad (55)$$

$$\begin{aligned} &\left| \frac{2(t - t_0)\tilde{n}(\mathbf{r})}{cw_0^2} \mathbf{J}_{\text{vri}}(\mathbf{r}) \exp \left[-\frac{(t - t_0)^2}{w_0^2} \right] \right| \\ &\leq \left| [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r})] I_{\text{vri}}(\mathbf{r}) \exp \left[-\frac{(t - t_0)^2}{w_0^2} \right] \right|, \end{aligned} \quad (56)$$

for $I_{\text{vri}}(\mathbf{r}) \neq 0$, $\mathbf{J}_{\text{vri}}(\mathbf{r}) \neq 0$.

The left-hand sides of inequalities (55) and (56) reach their maxima at $t = t_0 \pm w_0/2$. Consequently, those terms contribute a negligible error to Eqs. (30) and (31) at their maxima if

$$\frac{|\tilde{n}(\mathbf{r})|}{w_0(\mathbf{r})} \leq \frac{2|\tilde{n}(\mathbf{r})|}{w_{\min}} = c \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})], \quad (57)$$

where w_{\min} is the minimum allowable pulse full width.

To illustrate the geometrical meaning of condition (57), we define the mean displacement of the light pulse in the medium during a pulse width $2w_0$, $l_{\text{width}} = 2cw_0/\tilde{n}$. Dividing expression (57) by \tilde{n} , rearranging the result, and substituting the definitions of l_a , l'_s , and l_{width} , we obtain

$$\frac{|\tilde{n}(\mathbf{r})|}{\tilde{n}} \leq \frac{l_{\text{width}}}{2 \max[l_a, l'_s]}. \quad (58)$$

Therefore condition (57) imposes implicitly a restriction on the relative spatial fluctuation of the refractive index, which is related to the traveled distance of the pulse during a half-width and the mean free paths for absorption and reduced scattering.

Although our analysis was addressed to a single pulse, it is valid for each pulse of a train of pulses of a frequency-domain OT system. Since the period T of such train of pulses must be $T > 2w_0$, we can employ expression (57)

to find an upper bound for the maximum pulse rate (or, equivalently, the maximum modulation frequency). It yields

$$f_{\max} < \frac{1}{w_{\min}} = \frac{c}{2|\tilde{n}(\mathbf{r})|} \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})], \quad (59)$$

where f_{\max} is the maximum pulse repetition rate or modulation frequency.

C. Periodic Case (Frequency-Domain)

In Subsection 3.B we obtained the allowed maximum pulse rate (modulation frequency) for which the RTE is a good approximation of the RTEvri in a frequency-domain OT system. In the present subsection we derive a more precise expression for this magnitude by using a completely different approach. This tests the basis of our analysis for self-consistency.

For the sake of simplicity, we consider real functions $\epsilon_0(\mathbf{r}, t)$ and $\epsilon_1(\mathbf{r}, t)$ of the form

$$\epsilon_0(\mathbf{r}, t) = \epsilon_{0i}(\mathbf{r})[1 + \gamma \cos(2\pi ft)], \quad (60)$$

$$\epsilon_1(\mathbf{r}, t) = \epsilon_{1i}(\mathbf{r})[1 + \gamma \cos(2\pi ft)], \quad (61)$$

where $0 < \gamma \leq 1$ is the modulation depth.

Functions (60) and (61) are a superposition of time-independent terms $\epsilon_{0i}(\mathbf{r})$, $\epsilon_{1i}(\mathbf{r})$ and time-dependent terms $\gamma\epsilon_{0i}(\mathbf{r})\cos(2\pi ft)$ and $\gamma\epsilon_{1i}(\mathbf{r})\cos(2\pi ft)$. Because of the linearity of Eqs. (30) and (31), their solutions are also a superposition of time-independent and time-dependent terms as follows:

$$I_{\text{vri}}(\mathbf{r}, t) = I_i(\mathbf{r}) + I_d(\mathbf{r}, t), \quad (62)$$

$$\mathbf{J}_{\text{vri}}(\mathbf{r}, t) = \mathbf{J}_i(\mathbf{r}) + \mathbf{J}_d(\mathbf{r}, t), \quad (63)$$

where $I_i(\mathbf{r})$ and $\mathbf{J}_i(\mathbf{r})$ are solutions to the time-independent equations

$$\nabla_{\mathbf{r}} \cdot \mathbf{J}_i(\mathbf{r}) + \mu_a(\mathbf{r})I_i(\mathbf{r}) + 2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_i(\mathbf{r}) = \epsilon_{0i}(\mathbf{r}), \quad (64)$$

$$-\frac{1}{3}[\nabla_{\mathbf{r}} \ln n(\mathbf{r})]I_i(\mathbf{r}) + \frac{1}{3}\nabla_{\mathbf{r}} I_i(\mathbf{r}) + [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r})]\mathbf{J}_i(\mathbf{r}) = \epsilon_{1i}(\mathbf{r}) \quad (65)$$

and $I_d(\mathbf{r}, t)$ and $\mathbf{J}_d(\mathbf{r}, t)$ are solutions to the time-dependent equations

$$\begin{aligned} \frac{\bar{n}}{c} \frac{\partial}{\partial t} I_d(\mathbf{r}, t) + \frac{\tilde{n}(\mathbf{r})}{c} \frac{\partial}{\partial t} I_d(\mathbf{r}, t) + \nabla_{\mathbf{r}} \cdot \mathbf{J}_d(\mathbf{r}, t) \\ + \mu_a(\mathbf{r})I_d(\mathbf{r}, t) + 2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}_d(\mathbf{r}, t) \\ = \gamma\epsilon_{0i}(\mathbf{r})\cos(2\pi ft), \quad (66) \end{aligned}$$

$$\begin{aligned} \frac{\bar{n}}{c} \frac{\partial}{\partial t} \mathbf{J}_d(\mathbf{r}, t) - \frac{1}{3}[\nabla_{\mathbf{r}} \ln n(\mathbf{r})]I_d(\mathbf{r}, t) + \frac{1}{3}\nabla_{\mathbf{r}} I_d(\mathbf{r}, t) \\ + [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r}) + \mu_d(\mathbf{r})]\mathbf{J}_d(\mathbf{r}, t) + \frac{\tilde{n}(\mathbf{r})}{c} \frac{\partial}{\partial t} \mathbf{J}_d(\mathbf{r}, t) \\ = \gamma\epsilon_{1i}(\mathbf{r})\cos(2\pi ft). \quad (67) \end{aligned}$$

It is straightforward to show that both $I_d(\mathbf{r}, t)$ and $\mathbf{J}_d(\mathbf{r}, t)$ are periodic functions with period $T = 1/f$ and

$$\overline{I_{\text{vri}}(\mathbf{r}, t)} = I_i(\mathbf{r}), \overline{I_d(\mathbf{r}, t)} = 0, \quad (68)$$

$$\overline{\mathbf{J}_{\text{vri}}(\mathbf{r}, t)} = \mathbf{J}_i(\mathbf{r}), \overline{\mathbf{J}_d(\mathbf{r}, t)} = 0, \quad (69)$$

where the overbar denotes the mean value over a period of the signal.

From a comparison of Eqs. (64)–(67) with Eqs. (34) and (35), it follows that conditions (36)–(38) can be applied to both the time-independent and the time-dependent equations, but they do not suffice for approximating the RTEvri by the RTE, since they do not restrict the time behavior of possible solutions to the RTEvri. To find those complementary conditions, we need to compare the term $\tilde{n}(\mathbf{r})c^{-1}\partial I_d(\mathbf{r}, t)/\partial t$ with the terms $\bar{n}c^{-1}\partial I_d(\mathbf{r}, t)/\partial t$ and $\mu_a(\mathbf{r})I_d(\mathbf{r}, t)$ in Eq. (66) and the term $\tilde{n}(\mathbf{r})c^{-1}\partial \mathbf{J}_d(\mathbf{r}, t)/\partial t$ with the terms $\bar{n}c^{-1}\partial \mathbf{J}_d(\mathbf{r}, t)/\partial t$ and $[\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r})]\mathbf{J}_i(\mathbf{r})$ in Eq. (67). From the comparison of the terms containing time derivatives, $\tilde{n}(\mathbf{r})c^{-1}\partial I_d(\mathbf{r}, t)/\partial t$ with $\bar{n}c^{-1}\partial I_d(\mathbf{r}, t)/\partial t$ and $\tilde{n}(\mathbf{r})c^{-1}\partial \mathbf{J}_d(\mathbf{r}, t)/\partial t$ with $\bar{n}c^{-1}\partial \mathbf{J}_d(\mathbf{r}, t)/\partial t$, condition (17) follows, as we could expect.

The comparisons of the remaining terms require a particular analysis. Functions $I_d(\mathbf{r}, t)$ and $\mathbf{J}_d(\mathbf{r}, t)$ are periodic. Consequently, their time derivatives $\partial I_d(\mathbf{r}, t)/\partial t$ and $\partial \mathbf{J}_d(\mathbf{r}, t)/\partial t$ are also periodic, but out of phase with respect to them, so that when $I_d(\mathbf{r}, t) = 0$ or $\mathbf{J}_d(\mathbf{r}, t) = \mathbf{0}$, their derivatives are different from zero and vice versa. Consequently, conditions similar to conditions (49) or (51) cannot be applied. Taking into account this property of periodic signals and repeating the reasoning leading to conditions (36)–(38), we propose that the terms $\tilde{n}(\mathbf{r})c^{-1}\partial I_d(\mathbf{r}, t)/\partial t$ and $\tilde{n}(\mathbf{r})c^{-1}\partial \mathbf{J}_d(\mathbf{r}, t)/\partial t$ can be neglected if

$$\left[\frac{\tilde{n}(\mathbf{r})}{c} \right]^2 \left| \frac{\partial I_d(\mathbf{r}, t)}{\partial t} \right|^2 \ll \mu_a^2(\mathbf{r}) \overline{I_d^2(\mathbf{r}, t)}, \quad (70)$$

$$\left[\frac{\tilde{n}(\mathbf{r})}{c} \right]^2 \left| \frac{\partial \mathbf{J}_d(\mathbf{r}, t)}{\partial t} \right|^2 \ll [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r})]^2 \overline{|\mathbf{J}_d(\mathbf{r}, t)|^2}. \quad (71)$$

Like conditions (49) and (51), conditions (68) and (69) are difficult to use. To obtain a practical estimate of the maximum modulation frequency, we consider real functions $I_d(\mathbf{r}, t)$ and $\mathbf{J}_d(\mathbf{r}, t)$, of the forms

$$I_d(\mathbf{r}, t) = \alpha I_i(\mathbf{r}) \cos[2\pi ft + \phi_I(\mathbf{r})], \quad (72)$$

$$\mathbf{J}_d(\mathbf{r}, t) = \beta \mathbf{J}_i(\mathbf{r}) \cos[2\pi ft + \phi_J(\mathbf{r})], \quad (73)$$

where $0 < \alpha \leq 1$ and $0 < \beta \leq 1$ are modulation depths and $0 \leq \phi_I(\mathbf{r}) < 2\pi$ and $0 \leq \phi_J(\mathbf{r}) < 2\pi$ are phases.

Substituting expressions (72) and (73) into conditions (70) and (71), we obtain

$$f \ll f_{\max} = \frac{c}{2\pi|\tilde{n}(\mathbf{r})|} \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})], \quad (74)$$

for any $\mathbf{r} \in V$. Note that this result is consistent with expression (59), as we could expect.

To illustrate the geometrical meaning of condition (74), we define the mean displacement of light in the medium

during a period of modulation $l_{\text{period}} = cf^{-1}/\bar{n}$. Repeating the procedure that leads to expression (58), we obtain

$$\frac{|\tilde{n}(\mathbf{r})|}{\bar{n}} \ll \frac{c \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})]}{2\pi\bar{n}} = \frac{l_{\text{period}}}{2\pi \max[l_a, l'_s]}. \quad (75)$$

4. ESTIMATES OF $|\nabla_{\mathbf{r}} \ln n(\mathbf{r})|_{\text{max}}$, R_{min} , $|\mu_d(\mathbf{r})|_{\text{max}}$, w_{min} , AND f_{max} FOR THE VALIDITY OF THE RADIATIVE TRANSFER EQUATION

The obtained conditions define the boundaries of a region of trust of the parameters $|\nabla_{\mathbf{r}} \ln n(\mathbf{r})|$, R_{min} , $\mu_d(\mathbf{r})$, f , and w_0 as dependences on c , $\tilde{n}(\mathbf{r})$, \bar{n} , $\mu_a(\mathbf{r})$, $\mu'_s(\mathbf{r})$, and η , in which the RTE is a reasonable good approximation to the RTEvri. The absorption and reduced scattering coefficients of biological tissues have been widely reported (as reviewed by Cheong *et al.*¹⁹), and values of the typical refractive index have also been measured (Bolin *et al.*¹⁰). Roggan *et al.*²⁰ pointed out that even for the same type of tissue the absorption and reduced scattering coefficients reported in the literature vary in a wide range, owing to different preparation techniques of specimens, experimental setups, and calculation methods. Obviously, this circumstance affects any estimate based on the use of reported data.

For obtaining worst-case estimates, we assume that for biological tissues in the spectral range from $\lambda = 700$ nm to $\lambda = 1000$ nm we have $\min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] = \mu_a(\mathbf{r}) \approx 0.01 \text{ mm}^{-1}$, $\bar{n} \approx 1.4$, and $|\tilde{n}(\mathbf{r})| \approx 0.05$. The speed of light in vacuum is $c \approx 3 \times 10^{11} \text{ mm/s}$. For the validity of the series expansion (22) it has been suggested that $3|\mathbf{J}_{\text{vri}}(\mathbf{r}, t)| \ll I_{\text{vri}}(\mathbf{r}, t)$.⁵ Therefore we have to impose the condition $\eta \ll 1/3$. Assuming $\eta < 1/6$ in expressions (43) and (44), we obtain

$$|\nabla_{\mathbf{r}} \ln n(\mathbf{r})| \ll 3\eta\mu_a(\mathbf{r}) = 0.03\eta \text{ mm}^{-1}, \quad (76)$$

$$R \geq R_{\text{min}} = \frac{33}{\eta} \text{ mm}. \quad (77)$$

From expressions (76) and (77), it follows that if η approaches zero, then $|\nabla_{\mathbf{r}} \ln n(\mathbf{r})|$ must approach zero also, making it more difficult to meet condition (43) for approximating the RTEvri by the RTE. If we assume $1/6 \leq \eta < 1/3$, conditions (43) and (44) transform into the expressions

$$|\nabla_{\mathbf{r}} \ln n(\mathbf{r})| \ll \frac{\mu_a(\mathbf{r})}{2} = 0.005 \text{ mm}^{-1}, \quad (78)$$

$$R \geq R_{\text{min}} = \frac{2}{\mu_a(\mathbf{r})} = 200 \text{ mm}. \quad (79)$$

From condition (42), it follows that the maximum modulus of the coefficient of divergence is

$$|\mu_d(\mathbf{r})| \ll |\mu_{d \text{ max}}| = 0.01 \text{ mm}^{-1}, \quad (80)$$

and if conditions (42) and (43) are met, the maximum modulus of divergence is

$$\begin{aligned} |\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})| &\leq |\mu_d(\mathbf{r})|_{\text{max}} + |\nabla_{\mathbf{r}} \ln n(\mathbf{r})|_{\text{max}} = \mu_a(1 + 3\eta) \\ &= 0.01(1 + 3\eta) \text{ mm}^{-1}, \end{aligned} \quad (81)$$

for $\eta < 1/6$, and

$$|\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}(\mathbf{r})| \leq |\mu_d(\mathbf{r})|_{\text{max}} + |\nabla_{\mathbf{r}} \ln n(\mathbf{r})|_{\text{max}} = 0.015 \text{ mm}^{-1}, \quad (82)$$

for $1/6 \leq \eta < 1/3$.

From conditions (57) and (74), it follows that the minimum pulse width and maximum modulation frequency are

$$2w_0(\mathbf{r}) \geq w_{\text{min}} = \frac{2|\tilde{n}(\mathbf{r})|}{c \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})]} \approx 33.3 \text{ ps}, \quad (83)$$

$$\begin{aligned} f \leq f_{\text{max}} &= \frac{c}{2\pi|\tilde{n}(\mathbf{r})|} \min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \\ &\approx 9.5 \text{ GHz}. \end{aligned} \quad (84)$$

The worst-case estimate of the minimum pulse width (83) is based on chosen values of $\mu_a(\mathbf{r}) < \mu'_s(\mathbf{r})$, and $|\tilde{n}(\mathbf{r})|$ is of the order of the pulse widths typically employed by experimental time-of-flight tomographic systems. For example, Eda *et al.*,²¹ Benaron *et al.*,²² and Schmidt *et al.*²³ used ~ 100 ps, 60 ps, and \sim ps pulse full widths, respectively. Therefore the assumed values of $|\tilde{n}(\mathbf{r})|$ and $\mu_a(\mathbf{r})$ predict that the RTE could fail to be a good approximation of the RTEvri for OT problems.

The worst-case estimate (84) of the maximum modulation frequency is many orders larger than the modulation frequency of reported frequency-domain systems.^{12,24–28} Accordingly, condition (84) predicts that the RTE is a good approximation of the RTEvri for such systems if, in addition, conditions (36)–(38) are met.

5. CONCLUSIONS

It is considered that radiative transfer theory and its basic equation, the differential radiative transfer equation (RTE), are correct when scattering centers are sufficiently separated from one another.⁴ The sets of conditions derived above show that this assumption does not ensure the validity of the RTE for OT problems. Our results have the form of conditions for the accuracy of the RTE in the presence of a spatially varying refractive index. All conditions were obtained for the P_1 approximation. Conditions (17), (36)–(38), (49), (51), (70), and (71) were derived by use of a self-consistency principle: In any of the equations of the P_1 approximation of the RTEvri, the error due to a negligible (but nonzero) term, containing $\tilde{n}(\mathbf{r})$, $\nabla_{\mathbf{r}} \ln n(\mathbf{r})$, or $\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}$, should be much less than the contribution any of the terms containing \bar{n} , $\mu_a(\mathbf{r})$, or $\mu'_s(\mathbf{r})$. Conditions (70) and (71), in addition, take into account the periodicity of the irradiance and the radiative flux density vector in frequency-domain systems. Using simplified models of the optical signals, we obtained expressions for the minimum allowable pulse width w_{min} [expression (57)] and the maximum allowable modulation frequency f_{max} [expression (74)]. Worst-case estimates of minimum allowable pulse widths yield $w_{\text{min}} \approx 33.3$ ps,

suggesting that the RTE may be a rough approximation to the RTEvri at the pulse widths used in some reported time-of-flight systems. Worst-case estimates for the maximum allowable modulation frequencies yield $f_{\max} \approx 9.5$ GHz, suggesting that the RTE is an accurate approximation of the RTEvri for reported frequency-domain systems. It should be noted that the estimates given in Section 4 depend on the optical parameters of the medium.

Our results provide us with an alternative explanation of the inaccuracy of the DE in the vicinity of sources. Rinzema *et al.*¹⁶ experimentally estimated the radius R_{inac} of the inaccuracy region of the DE as

$$R_{\text{inac}} \sim 0.25/\mu_t, \quad \sim 2/\mu_t, \quad (85)$$

where $\mu_t = \mu_a + \mu'_s$, whereas Martelli *et al.*¹⁷ for the same magnitude obtained

$$R_{\text{inac}} \sim 2/\mu'_s. \quad (86)$$

Consider now a point isotropic source located within a medium of optical parameters μ_a , μ'_s , and $n = \text{constant}$, at the origin of a coordinate system. Then the eikonal, the vector field $\mathbf{\Omega}$, and its divergence are given by formulas (8), (9), and (10), respectively. From the expression for the divergence [Eq. (10)] and from condition (42), it follows that the RTE and, consequently, the DE are valid if

$$r \gg R_{\text{inac}} \sim 2/\min[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})]. \quad (87)$$

This result is consistent with the estimates given by expressions (85) and (86) and points to another possible cause of inaccuracy of the DE at short distances from sources. Note that expression (7), derived by Ferwerda¹⁴ and employed by Khan and Jiang¹⁵ for the divergence term, cannot explain the behavior of wave fronts and rays in the vicinity of sources.

Our estimates of the allowed maximum values of $|\tilde{n}(\mathbf{r})|$, $|\nabla_{\mathbf{r}} \ln n(\mathbf{r})|$, and $|\nabla_{\mathbf{r}} \cdot \mathbf{\Omega}|$ were obtained for the condition $\mu'_s(\mathbf{r}) \gg \mu_a(\mathbf{r})$, which is met by most biological tissues. However in the so-called void regions of a biological body there is little scattering; the medium in those regions does not meet the condition $\mu'_s(\mathbf{r}) \gg \mu_a(\mathbf{r})$, and the DE becomes inaccurate.²⁸ Consequently, our estimates (83) and (84) must be recalculated for those regions. Note also that for some combinations of optical properties of void regions the RTE may become inaccurate also.

Finally, we would like to add that Firbank *et al.*²⁹ noticed that some plastics, after curing, present small fluctuations of refractive index. They concluded that such fluctuations of refractive index are one of the factors that make it difficult to predict their scattering properties and prevent the use of those plastics as tissue like material for phantoms for near-infrared spectroscopy and imaging. Our results explain how the fluctuations of refractive index could affect the scattering properties of a medium and confirm that conclusion.

APPENDIX A

Using the vector identity

$$\nabla_{\mathbf{r}} \cdot [\mathbf{\Omega}L(\mathbf{r}, \mathbf{\Omega}, t)] = \mathbf{\Omega} \cdot \nabla_{\mathbf{r}}L(\mathbf{r}, \mathbf{\Omega}, t) + (\nabla_{\mathbf{r}} \cdot \mathbf{\Omega})L(\mathbf{r}, \mathbf{\Omega}, t), \quad (A1)$$

we rewrite expression (1) in the following way:

$$\begin{aligned} & \frac{n(\mathbf{r})}{c} \frac{\partial}{\partial t} L(\mathbf{r}, \mathbf{\Omega}, t) + \nabla_{\mathbf{r}}[\mathbf{\Omega}L(\mathbf{r}, \mathbf{\Omega}, t)] \\ & + [\mu_a(\mathbf{r}) + \mu'_s(\mathbf{r})]L(\mathbf{r}, \mathbf{\Omega}, t) \\ & + \nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \nabla_{\mathbf{\Omega}}L(\mathbf{r}, \mathbf{\Omega}, t) \\ & = \mu_s(\mathbf{r}) \int_{4\pi} L(\mathbf{r}, \mathbf{\Omega}', t) \theta(\mathbf{\Omega}, \mathbf{\Omega}') d\omega + \epsilon(\mathbf{r}, \mathbf{\Omega}, t). \end{aligned} \quad (A2)$$

Integrating Eq. (A2) over 4π sr and using the expressions

$$\begin{aligned} & \frac{n(\mathbf{r})}{c} \int_{4\pi} \frac{\partial}{\partial t} L(\mathbf{r}, \mathbf{\Omega}, t) d\omega \\ & = \frac{n(\mathbf{r})}{c} \frac{\partial}{\partial t} \int_{4\pi} L(\mathbf{r}, \mathbf{\Omega}, t) d\omega = \frac{n(\mathbf{r})}{c} \frac{\partial}{\partial t} I(\mathbf{r}, t), \end{aligned} \quad (A3)$$

$$\begin{aligned} & \int_{4\pi} \nabla_{\mathbf{r}} \cdot [\mathbf{\Omega}L(\mathbf{r}, \mathbf{\Omega}, t)] d\omega \\ & = \nabla_{\mathbf{r}} \cdot \int_{4\pi} \mathbf{\Omega}L(\mathbf{r}, \mathbf{\Omega}, t) d\omega = \nabla_{\mathbf{r}} \cdot \mathbf{J}(\mathbf{r}, t), \end{aligned} \quad (A4)$$

$$\begin{aligned} & \int_{4\pi} [\mu_a(\mathbf{r}) + \mu_s(\mathbf{r})]L(\mathbf{r}, \mathbf{\Omega}, t) d\omega \\ & = [\mu_a(\mathbf{r}) + \mu_s(\mathbf{r})]I(\mathbf{r}, t), \end{aligned} \quad (A5)$$

$$\begin{aligned} & \int_{4\pi} \nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \nabla_{\mathbf{\Omega}}L(\mathbf{r}, \mathbf{\Omega}, t) d\omega \\ & = 2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \int_{4\pi} \mathbf{\Omega}L(\mathbf{r}, \mathbf{\Omega}, t) d\omega \\ & = 2\nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \mathbf{J}(\mathbf{r}, t), \end{aligned} \quad (A6)$$

$$\begin{aligned} & \int_{4\pi} \mu_s(\mathbf{r}) \int_{4\pi} L(\mathbf{r}, \mathbf{\Omega}', t) \theta(\mathbf{\Omega}, \mathbf{\Omega}') d\omega' d\omega \\ & = \mu_s(\mathbf{r})I(\mathbf{r}, t), \end{aligned} \quad (A7)$$

we obtain Eq. (30). Note that no approximation was used, and, consequently, Eq. (30) is exact.

APPENDIX B

Substituting expression (22) into Eq. (1), multiplying by $\mathbf{\Omega}$, and integrating over 4π sr, we obtain

$$\begin{aligned}
& \frac{\bar{n}}{4\pi c} \int_{4\pi} \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega + \frac{3\bar{n}}{4\pi c} \int_{4\pi} \frac{\partial}{\partial t} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega + \frac{1}{4\pi} \int \boldsymbol{\Omega} \cdot \nabla_{\mathbf{r}} I_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega + \frac{3}{4\pi} \int_{4\pi} \boldsymbol{\Omega} \\
& \quad \cdot \nabla_{\mathbf{r}} [\boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t)] \boldsymbol{\Omega} d\omega \\
& + \frac{1}{4\pi} \int_{4\pi} [\mu_{\text{d}}(\mathbf{r}) - \nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \boldsymbol{\Omega}] I_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega + \frac{3}{4\pi} \int_{4\pi} [\mu_{\text{d}}(\mathbf{r}) - \nabla_{\mathbf{r}} \ln n(\mathbf{r}) \cdot \boldsymbol{\Omega}] [\boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t)] \boldsymbol{\Omega} d\omega \\
& + \frac{[\mu_{\text{a}}(\mathbf{r}) + \mu_{\text{s}}(\mathbf{r})]}{4\pi} \int_{4\pi} I_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega + \frac{3[\mu_{\text{a}}(\mathbf{r}) + \mu_{\text{s}}(\mathbf{r})]}{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega \\
& + \frac{3}{4\pi} \int_{4\pi} [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] \cdot \nabla_{\boldsymbol{\Omega}} [\boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t)] \boldsymbol{\Omega} d\omega \\
& = \frac{\mu_{\text{s}}(\mathbf{r})}{4\pi} \int_{4\pi} \int_{4\pi} I_{\text{vri}}(\mathbf{r}, t) \theta(\boldsymbol{\Omega}, \boldsymbol{\Omega}') \boldsymbol{\Omega} d\omega d\omega' + \frac{3\mu_{\text{s}}(\mathbf{r})}{4\pi} \int_{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \theta(\boldsymbol{\Omega}, \boldsymbol{\Omega}') \boldsymbol{\Omega} d\omega d\omega' + \boldsymbol{\epsilon}_1(\mathbf{r}, t). \quad (\text{B1})
\end{aligned}$$

In Eq. (B1) we used expressions (11) and (27). After straightforward calculation that used the expressions attached below, we obtain Eq. (31):

$$\frac{\bar{n}}{4\pi c} \int_{4\pi} \frac{\partial}{\partial t} I_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega = \mathbf{0}, \quad (\text{B2})$$

$$\begin{aligned}
& \frac{3\bar{n}}{4\pi c} \int_{4\pi} \left[\frac{\partial}{\partial t} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \right] \boldsymbol{\Omega} d\omega \\
& = \frac{3\bar{n}}{4\pi c} \frac{\partial}{\partial t} \int_{4\pi} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega \\
& = \frac{n(\mathbf{r})}{c} \frac{\partial}{\partial t} \mathbf{J}(\mathbf{r}, t), \quad (\text{B3})
\end{aligned}$$

$$\frac{1}{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot \nabla_{\mathbf{r}} I_{\text{vri}}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega = \frac{1}{3} \nabla_{\mathbf{r}} I_{\text{vri}}(\mathbf{r}, t), \quad (\text{B4})$$

$$\frac{3}{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot \nabla_{\mathbf{r}} [\boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t)] \boldsymbol{\Omega} d\omega = \mathbf{0}, \quad (\text{B5})$$

$$\int_{4\pi} \mu_{\text{d}}(\mathbf{r}) I(\mathbf{r}, t) \boldsymbol{\Omega} d\omega = \mathbf{0}, \quad (\text{B6})$$

$$\frac{3}{4\pi} \int_{4\pi} \mu_{\text{d}}(\mathbf{r}) \boldsymbol{\Omega} \cdot \mathbf{J}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega = \mu_{\text{d}}(\mathbf{r}) \mathbf{J}(\mathbf{r}, t) \quad (\text{B7})$$

[in expressions (B6) and (B7) we assume that $\mu_{\text{d}}(\mathbf{r})$ does not depend on $\boldsymbol{\Omega}$],

$$\begin{aligned}
& \frac{1}{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I(\mathbf{r}, t) \boldsymbol{\Omega} d\omega \\
& = \frac{1}{3} [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] I(\mathbf{r}, t), \quad (\text{B8})
\end{aligned}$$

$$\begin{aligned}
& \frac{3}{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] \boldsymbol{\Omega} \cdot \mathbf{J}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega \\
& = \mathbf{0}, \quad (\text{B9})
\end{aligned}$$

$$\frac{3}{4\pi} \int_{4\pi} [\mu_{\text{a}}(\mathbf{r}) + \mu_{\text{s}}(\mathbf{r})] \boldsymbol{\Omega} \cdot \mathbf{J}(\mathbf{r}, t) \boldsymbol{\Omega} d\omega = [\mu_{\text{a}}(\mathbf{r}) + \mu_{\text{s}}'(\mathbf{r})] \mathbf{J}(\mathbf{r}, t), \quad (\text{B10})$$

$$\frac{3}{4\pi} \int_{4\pi} [\nabla_{\mathbf{r}} \ln n(\mathbf{r})] \cdot \nabla_{\boldsymbol{\Omega}} [\boldsymbol{\Omega} \cdot \mathbf{J}(\mathbf{r}, t)] \boldsymbol{\Omega} d\omega = \mathbf{0}, \quad (\text{B11})$$

$$\int_{4\pi} \int_{4\pi} I_{\text{vri}}(\mathbf{r}, t) \theta(\boldsymbol{\Omega}, \boldsymbol{\Omega}') \boldsymbol{\Omega} d\omega d\omega' = \mathbf{0}, \quad (\text{B12})$$

$$\frac{3\mu_{\text{s}}(\mathbf{r})}{4\pi} \int_{4\pi} \int_{4\pi} \boldsymbol{\Omega} \cdot \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \theta(\boldsymbol{\Omega}, \boldsymbol{\Omega}') \boldsymbol{\Omega} d\omega d\omega' = \mu_{\text{s}}'(\mathbf{r}) \mathbf{J}_{\text{vri}}(\mathbf{r}, t) \quad (\text{B13})$$

[in the latter expression we used expression (28) and the definition of reduced scattering coefficient $\mu_{\text{s}}'(\mathbf{r})$ (32)].

ACKNOWLEDGMENTS

L. Martí-López and J. C. Hebden express their gratitude to The British Council for a traveling grant. R. A. Martínez-Celorio thanks Consejo de Ciencia y Tecnología del Estado de Guanajuato for a traveling grant under contract 02-04-203-073. The authors acknowledge the Cuban Neuroscience Center and the Department of Medical Physics and Bioengineering of University College London for creating the conditions for this study. The authors are also indebted to V. V. Tuchin, M. S. Patterson, and K. Stannes for providing references and to H. A. Ferwerda for a fruitful exchange of ideas. We are also grateful to the reviewers for constructive criticism.

L. Martí-López, J. Bouza-Domínguez, J. C. Hebden, S. R. Arridge, and R. Martínez-Celorio can be reached by e-mail at marti@cneuro.edu.cu, jorge@cneuro.edu.cu, jem@medphys.ucl.ac.uk, s.arridge@cs.ucl.ac.uk, and rcelorio@cio.mx, respectively.

REFERENCES

1. G. G. Levin and G. N. Vishnyakov, *Optical Tomography* (Radio i Svyaz', Moscow, 1989) (in Russian).
2. J. Beuthan, O. Minet, J. Helfmann, M. Herrig, and G. Müller, "The spatial variation of refractive index in biological cells," *Phys. Med. Biol.* **41**, 369–382 (1996).
3. J. C. Hebden, S. R. Arridge, and D. T. Delpy, "Optical imaging in medicine: I. Experimental techniques," *Phys. Med. Biol.* **42**, 825–840 (1997).
4. V. V. Tuchin, "Light interaction with biological tissues (overview)," in *Static and Dynamic Light Scattering in Medicine and Biology*, R. J. Nossal, R. Pecora, and A. V. Priezzhev, eds., *Proc. SPIE* **1884**, 234–272 (1994).
5. A. Ishimaru, *Wave Propagation and Scattering in Random Media* (Academic, New York, 1978).
6. M. S. Patterson, B. S. C. Wilson, and D. R. Wyman, "The propagation of optical radiation in tissue I. Models of radiation transport and their application," *Lasers Med. Sci.* **6**, 155–168 (1991).
7. S. R. Arridge and J. C. Hebden, "Optical imaging in medicine: II. Modelling and reconstruction," *Phys. Med. Biol.* **42**, 841–853 (1997).
8. S. R. Arridge, "Optical tomography in medical imaging," *Inverse Probl.* **15**, R41–R93 (1999).
9. S. R. Arridge, "Diffusion tomography in dense media," in *Scattering and Inverse Scattering in Pure and Applied Science*, R. Pike and P. Sabatier, eds. (Academic, San Diego, Calif., 2002), pp. 920–936.
10. F. P. Bolin, L. E. Preuss, R. C. Taylor, and R. J. Ference, "Refractive index of some mammalian tissues using a fiber optic cladding method," *App. Opt.* **28**, 2297–2303 (1989).
11. D. T. Delpy, M. Cope, P. van der Zee, S. R. Arridge, S. Wray, and J. S. Wyatt, "Estimation of optical pathlength through tissue from direct time of flight measurements," *Phys. Med. Biol.* **33**, 1433–1442 (1988).
12. A. Duncan, J. H. Meek, M. Clemence, C. E. Elwell, L. Tyszczyk, M. Cope, and D. T. Delpy, "Optical pathlength measurements on adult head, calf and forearm and the head of the newborn infant using phase resolved optical spectroscopy," *Phys. Med. Biol.* **40**, 295–304 (1995).
13. B. Chen, K. Stamnes, and J. Stamnes, "Validity of the diffusion approximation in bio-optical imaging," *App. Opt.* **40**, 6356–6366 (2001).
14. H. A. Ferwerda, "The radiative transfer equation for scattering media with spatially varying refractive index," *J. Opt. A Pure Appl. Opt.* **1**, L1–L2 (1999).
15. T. Khan and H. Jiang, "A new diffusion approximation to the radiative transfer equation for scattering media with spatially varying refractive indices," *J. Opt. A Pure Appl. Opt.* **5**, 137–141 (2003).
16. K. Rinzema, L. H. P. Murrer, and W. M. Star, "Direct experimental verification of light transport theory in an optical phantom," *J. Opt. Soc. Am. A* **15**, 2078–2088 (1998).
17. F. Martelli, M. Bassani, L. Alianelli, L. Zanghaeri, and G. Zaccanti, "Accuracy of the diffusion equation to describe photon migration through an infinite medium: numerical and experimental investigation," *Phys. Med. Biol.* **45**, 1359–1373 (2000).
18. M. Born and E. Wolf, *Principles of Optics* (Pergamon, Oxford, UK, 1975).
19. W. F. Cheong, S. A. Prah, and A. J. Welch, "A review of the optical properties of biological tissues," *IEEE J. Quantum Electron.* **26**, 2166–2185 (1990). Available also at <http://omlc.ogi.edu/pubs/pdf/cheong90a.pdf>.
20. A. Roggan, D. Schädel, U. Netz, J.-P. Ritz, C.-T. Germer, and G. Müller, "The effect of preparation technique on the optical parameters of biological tissue," *Appl. Phys. B* **69**, 445–453 (1999).
21. H. Eda, I. Oda, Y. Ito, Y. Wada, Y. Oikawa, Y. Tsunazawa, M. Takada, Y. Tsuchiya, Y. Yamashita, M. Oda, A. Sassaroli, Y. Yamada, and M. Tamura, "Multichannel time-resolved optical tomographic system," *Rev. Sci. Instrum.* **70**, 3595–3602 (1999).
22. D. A. Benaron, S. R. Hintz, A. Villringer, D. Boas, A. Kleinschmidt, J. Frahm, C. Hirth, H. Obrig, J. C. van Houten, E. L. Kermit, W.-F. Cheong, and D. K. Stevenson, "Noninvasive functional imaging of human brain using light," *J. Cereb. Blood Flow Metab.* **20**, 469–477 (2000).
23. F. E. W. Schmidt, M. E. Fry, E. M. C. Hillman, J. C. Hebden, and D. T. Delpy, "A 32-channel time-resolved instrument for medical optical tomography," *Rev. Sci. Instrum.* **71**, 256–265 (2000).
24. B. W. Pogue, M. Testorf, T. McBride, U. Osterberg, and K. Paulsen, "Instrumentation and design of a frequency-domain diffuse optical tomography imager for breast cancer detection," *Opt. Express* **1**, 391–403 (1997).
25. M. A. Franceschini, V. Toronov, M. E. Filiaci, E. Gratton, and S. Fantini, "On-line optical imaging of the human brain with 160-ms temporal resolution," *Opt. Express* **6**, 49–57 (2000).
26. M. A. O'Leary, D. A. Boas, B. Chance, and A. G. Yodh, "Experimental images of heterogeneous turbid media by frequency-domain diffusing-photon tomography," *Opt. Lett.* **20**, 426–428 (1995).
27. J. B. Fishkin, O. Coquoz, E. R. Anderson, M. Brenner, and B. J. Tromberg, "Frequency-domain photon migration measurements of normal and malignant tissue optical properties in a human subject," *App. Opt.* **36**, 10–20 (1997).
28. H. Dehghani, S. R. Arridge, M. Schweiger, and D. T. Delpy, "Optical tomography in the presence of void regions," *J. Opt. Soc. Am. A* **17**, 1659–1670 (2000).
29. M. Firbank, M. Oda, and D. T. Delpy, "An improved design for a stable and reproducible phantom material for use in near-infrared spectroscopy and imaging," *Phys. Med. Biol.* **40**, 955–961 (1995).