ABSTRACT

We study frequency-domain spectroscopy for reflectance measurements in two-layered tissues, using a random-walk model of photon migration. We study the phase shift of the reflected light as a function of the source-detector separation, and show that there can be as many as three different types of behavior of this quantity, depending on the relation between the modulated frequency and the absorptivities of both layers. As a result, the possibility of determining the absorptivities of the two layers and the upper layer thickness from the phase shift is different in each regime.

Keywords: Optical diagnostics for medicine; Light propagation in tissues; Layered tissues; Frequency-domain; Phase shift; Random-walk.

1. INTRODUCTION

Recently, a model of random-walk on a lattice has been suggested to describe photon migration in biological tissues [1-5]. In this model, the scattering is simulated by a random change in the direction of travel of each photon on a lattice and the absorption occurring between nodes of the lattice is described by Beer's Law, i.e. exp(-μ) is the survival probability per step on the lattice. This model has been applied to several typical biological systems, in various possible experimental schemes. The assumption was then made that the tissue is homogeneous, i.e. a single set of scattering and absorption parameters is sufficient to describe the entire bulk medium.

However, there are many biological tissues for which the homogeneity assumption is not justified. In particular, many tissues have layered structure, where each layer can be characterized by a different set of physical parameters [6-11]. Examples include skin (epidermis, dermis, subcutaneous fat), brain (scalp, skull, CSF), the walls of arteries (intima, muscle, adventitia), stomach, bladder, intestine and esophagus.

The basic multi-layer model is that of a two-region composite, with a surface layer lying on top of a semi-infinite substrate (see Fig. 1). The two layers are assumed to differ only in their absorption coefficients. The case where the upper layer is the more absorptive one, is typical for most biomedical applications, and has been found to have very interesting properties [4,12-14].

The basic random-walk model for photon migration has been developed for measurements in the time-domain, in which a pulse of light is injected and measurements of the reflected intensity are made at a given distance, at a given time. However, the complex path and multiple scatters experienced by the light within the turbid tissue, result in a loss of amplitude and coherence so that the intensity of the reemitted light is several orders of magnitude smaller than the source intensity. Thus, predictions based on intensity measurements only might be very sensitive to signal-to-noise ratio problems. Contrary to these, measurements in the frequency-domain, seem to suffer less from this drawback. In this domain, one can expect to obtain useful information from the phase-shift of the detected light with respect to the source. Moreover, most of the practical instrumentation are designed in the frequency-domain, where the phase-shift and demodulation of an amplitude-modulated light source is related to the mean transit time in the tissue, which by itself reflects the tissue's absorption and scattering parameters. This also helps to interpret Doppler measurements of blood flow in tissues [see, e.g., 15].

Some aspects of diffusive propagation of intensity-modulated light in tissues, and a corresponding frequency-resolved analysis have been recently studied by several groups [16-22]. In this paper we extend the random walk model of photon migration in two-layered tissues to include frequency-domain analysis. We study the phase shift Φ as a function of the source-detector separation ρ (see Fig. 1), and discuss the possibility of determining the absorptivities of the two layers and the upper layer thickness from the phase shift measurements.
2. METHODOLOGY AND RESULTS

The lattice model is sketched in Fig. 1. The transverse coordinate is \( \rho = (z, y) \), and the positive z-axis is pointing into the tissue. The tissue interface, represented by \( z = 0 \), is assumed to be a totally trapping surface, an assumption which can be justified from the experimental point of view [23]. Radiation is injected into the tissue at the origin. Photons then diffuse randomly within the tissue, eventually either reach the surface \( z = 0 \) where they can be detected, thereafter disappearing from the system, or they suffer internal absorption.

In the two-layer system, the thickness of the upper layer is taken equal to \( W \) (in integer lattice units), and the two layers are distinguished by two different absorption coefficients, \( \mu_1 \) (upper), and \( \mu_2 \) (lower) (Fig. 1).

![Diagram](image)

We now assume that the light source is amplitude-modulated by a factor \( \exp(i\omega n) \), where \( \omega \) is the modulated frequency per step \( n \). We follow the abovementioned random-walk theory, and calculate the phase shift, which is obtained through the Fourier transform of the reflected intensity. In order to present the results, it is convenient to define the following abbreviations, where the index \( i = 1, 2 \) corresponds to the upper and lower layer parameters, respectively:

\[
A_i = \sqrt{6(\omega^2 + \mu_i^2)^{1/4}},
\]

\[
\tau_i = \frac{1}{2} \arctan \left( \frac{\omega}{\mu_i} \right).
\]

Note that in these expressions, the frequency \( \omega \) and the absorption coefficient per step \( \mu_i \) appear to have the same dimensionality, which is a consequence of using the simplified lattice parameters. In an extended version of this work [24] we will refer to real physical values of these parameters.

We next define the following functions which depend on the source-detector separation \( \rho \):

\[
R_i(\rho) = A_i \rho \cos(\tau_i),
\]

\[
S_i(\rho) = \sin(A_i \rho \sin(\tau_i) - \tau_i),
\]

\[
C_i(\rho) = \cos(A_i \rho \sin(\tau_i) - \tau_i).
\]

The last function to be defined is a function which depends on \( \mu_1, \mu_2 \) and \( W \), and, following [13], accounts for the contribution to the reflected light in \( \rho \) from photons who traveled in both layers. This function reads

\[
F(\rho; \mu_1, \mu_2, W) = \exp \left( \frac{-5.2W}{\sqrt{\mu_1}}(\mu_1 - \mu_2) - R_2 + R_1 \right).
\]

In terms of all these functions, the phase shift is found to be given by

\[
\Phi = \arctan \left[ \frac{A_1S_1(\rho) + F(\rho; \mu_1, \mu_2, W)A_2S_2(\rho)}{A_1C_1(\rho) + F(\rho; \mu_1, \mu_2, W)A_2C_2(\rho)} \right].
\]

This general result has been confirmed by numerical calculations for a wide range of the system parameters.
3. ANALYSIS

When the modulated frequency \( \omega \) is small with respect to the absorption (in appropriate units), one obtains that the phase shift of the reflected intensity at \( \rho \) is proportional to the mean path length of this radiation, \( \langle n | \rho \rangle \), a quantity from which one can infer the values of \( \mu_1, \mu_2 \) and \( W \) [4,13]. The specific result in this limit is

\[
\Phi = \omega \langle n | \rho \rangle \approx \frac{1}{2} \sqrt{\frac{6}{\mu_1}} \omega \rho \left( 1 + \alpha(\rho) \right),
\]

(8)

where \( \alpha(\rho) \) is a crossover function which vanishes at small \( \rho \) and is very large for large \( \rho \). This function, which in fact the reduced \( F(\rho; \mu_1, \mu_2, W) \) in this limit, is given by

\[
\alpha(\rho) = \exp\left( -\frac{5.2 W}{\sqrt{\mu_1}}(\mu_1 - \mu_2) - \rho \sqrt{6\mu_2} + \rho \sqrt{6\mu_1} \right).
\]

(9)

The behavior of the phase shift in this limit is shown in Fig. 2. At short distances it is linear in \( \rho \) with a slope determined by the upper layer absorptivity, \( \mu_1 \). At long distances it is also linear in \( \rho \), but with a larger slope, determined by \( \mu_2 \). This is since at these distances the main contribution to the reemitted light comes from deep trajectories in the lower, less absorptive, layer. The sharp crossover between these two slopes occurs at a distance which is a function of the upper layer thickness, \( W \), as can be seen for a few values of this parameter.

From the diagnostic point of view, phase shift measurements performed at several distances from the injection point, can be used for determining \( \mu_1, \mu_2 \) and \( W \). Thus, there appear no two-layer characteristics in the phase shift in this limit, as can be seen in Fig. 3. The phase shift is linear in \( \rho \) with a slope determined by the modulated frequency only, and distinction between curves for different \( W \) is impossible. The periodicity in \( \rho \) which results from the constraint \(-90 \leq \Phi \leq 90 \) (in degrees) and in principle exists in all frequency limits, is observed here already in very short distances.

![Fig. 2.](image-url)  
Fig. 2. The phase shift \( \Phi \) as a function of the source-detector separation \( \rho \), in the low-frequency limit, for various values of the upper layer thickness \( W \). Parameter values are \( \mu_1 = 0.4, \mu_2 = 0.1, \) and \( \omega = 0.01 \), the latter corresponds to modulated frequency of several hundreds MHz as is typical in frequency-domain measurements in tissues.

![Fig. 3.](image-url)  
Fig. 3. The phase shift \( \Phi \) as a function of the source-detector separation \( \rho \), in the high-frequency regime, for various values of the upper layer thickness \( W \). Absorptivities are the same as in Fig. 2 (\( \mu_1 = 0.4, \mu_2 = 0.1 \)). The modulated frequency \( \omega = 10 \) is three orders of magnitude larger than typical frequencies used in biological tissues.
4. SUMMARY

We have studied the phase shift of radiation reflected from two-layered tissues, using a random-walk model of photon migration. We have obtained an analytical result for the phase shift and examined its behavior as a function of the source-detector separation. The behavior depends on the relation between the modulated frequency and the absorptivities, and as many as three typical spatial regimes are possible. However, for most biomedical applications, the phase shift is expected to exhibit a crossover behavior, proportional to the mean path length of the reflected radiation. The crossover behavior enables one to infer the values of \( \mu_1, \mu_2 \) and \( W \) for the tissue under examination. These parameters can then be compared with average values of similar normal tissues, and diagnostic conclusions can be made.

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REFERENCES