Fundamental Studies of Photon Migration in Biological Tissues and Their Application to Optical Tomography

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This paper reviews the studies of photon migration in biological tissues and its application to optical tomography which were conducted in the Mechanical Engineering Laboratory of Japan’s Ministry of International Trade and Industry. The research subjects range from theoretical and experimental studies of photon migration in random media to the development of image reconstruction algorithms and experiments for optical tomography. The most fundamental theoretical study of the photon diffusion equation has proved that the photon diffusion coefficient is independent of the absorption coefficient while the conventional one is dependent on the absorption coefficient. Experimental studies included the time-resolved spectroscopy and the fabrication of realistic human head phantoms which have five tissue types with different optical properties. Several types of reconstruction algorithms have been developed and verified experimentally. These investigations are pioneering work in the field of biomedical optics in Japan.

Key words: photon migration, biological tissue, optical tomography, photon diffusion, time-resolved spectroscopy, optical properties, scattering and absorption, optical phantom

1. Introduction

Fundamental research on photon migration in biological tissues and its application to optical tomography has been conducted in the Mechanical Engineering Laboratory, Agency of Industrial Science and Technology, Japan’s Ministry of International Trade and Industry. Simulations have been made on pulse light propagation in strongly scattering and weakly absorbing media like biological tissues in the near infrared wavelength range using the Monte Carlo method and the finite element method (FEM). During the research on picosecond time-resolved transmittance of impulse light through scattering media, it was found that the conventional equation for the photon diffusion coefficient was physically unreasonable in some cases. Mathematical investigation of the derivation of the photon diffusion equation from the time-dependent equation of radiative transfer then proved that the diffusion coefficient is independent of the absorption coefficient. This result lead to the concept of the microscopic Beer-Lambert law stating that the Beer-Lambert law, which is conventionally applicable only to nonscattering media, holds even in scattering media when one considers the exact light paths in microscale. Theoretical and experimental investigations of pulse light propagation through tissue simulating materials were carried out to determine the fundamental characteristics of pulse light propagation.

Effectively using the characteristics of pulse light propagation or the microscopic Beer-Lambert law, a new algorithm of optical tomography for scattering and absorbing media has been proposed by Monte Carlo simulation. It is the temporally extrapolated absorbance method (TEAM) which uses the conventional algorithm of X-ray CT for image reconstruction by obtaining the difference of the line integral of the absorption coefficient between the object and reference. Cooperative research with Hokkaido University and Shimadzu Corporation experimentally validated TEAM using cylindrical phantoms and a time-resolved spectroscopic measuring system.

Other developed image reconstruction algorithms are essentially based on the technique of inversion problems. One algorithm is called as the zooming method and another is the null-space and maximum a posteriori probability (MAP) reconstruction algorithm. Image reconstruction by simulation and phantom experiments has verified the feasibility of these algorithms.

Realistic human head phantoms were successfully fabricated by use of the rapid prototyping technology. The original MRI images of a human head were classified into five tissue types with different optical properties: scalp, skull, cerebrospinal fluid, gray matter and white matter. The shape data of each tissue type were sent to a rapid prototyping system and five prototypes were fabricated. Then molds of the five tissue types were made, and finally epoxy resins with appropriate optical properties were cast into the molds to make layered human head phantoms. These phantoms were used in time-resolved experiments of photon migration in a human head with a complicated structure.

In the following sections, the subjects introduced above are explained in more detail. Note that the term “optical tomography” in this review refers to “diffuse optical tomography (DOT)” which is very different from “optical coherence tomography (OCT)”.

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2. Studies of Photon Migration in Random Media

2.1 Simulation of Photon Migration

There are two categories of methods for solving photon migration in random media; statistical and deterministic methods.\(^1\) Statistical methods include Monte Carlo methods and random walk methods by which the general behaviors of photon migration or light propagation in random media are statistically described. Deterministic methods solve the time-dependent equation of radiative transfer, the photon diffusion equation, and the telegraph equation (or the wave-diffusion equation). We have used a Monte Carlo method and the photon diffusion equation as major tools to simulate photon migration in random media.

2.1.1 Monte Carlo simulation\(^2\text{--}^9\)

The Monte Carlo method is a statistically direct means of simulating the photon migration in random media. It microscopically traces the trajectories of photon bundles as shown in Fig. 1. The pathlength between two successive interactions, or scattering, \(L\), the deflection angles after interaction in the polar and azimuthal directions \(\theta\) and \(\Psi\) are determined by the following Eq. (1):

\[
L = \frac{-\ln(R_1)}{\mu_t}, \quad \theta = f^{-1}(R_2), \quad \Psi = 2\pi R_3,
\]

where \(R_1\), \(R_2\), and \(R_3\) are uniformly distributed pseudo random numbers between 0 and 1, \(\mu_t = \mu_a + \mu_s\) is the total attenuation coefficient, and the function \(f(\theta)\) is the cumulative probability of scattering phase function \(p(\theta)\). At \(i\)-th interaction event, the bundle is assumed to deposit a fraction, \(\mu_s/\mu_t\), of its current energy, \(E_i\), as absorbed energy, and after interaction its energy \(E_{i+1}\) becomes \(E_{i+1} = (\mu_s/\mu_t)E_i\) with the weighting factor of \(\mu_s/\mu_t\).

The simplest example of the results of a Monte Carlo simulation has been presented for transmittance calculation of an impulse (input of delta-function in time and space) incidence through an infinite and homogeneous slab as shown in Fig. 2.\(^2,3\) The medium has scattering and absorbing coefficients similar to those of biological tissues. As the typical values, the scattering coefficient \(\mu_s\), absorption coefficient \(\mu_a\) and anisotropy parameter \(g\) are given as 10.0 mm\(^{-1}\), 0.1 mm\(^{-1}\), and 0.9, respectively, the reduced scattering coefficient \(\mu'_s\) as 1.0 mm\(^{-1}\), and the slab thickness as 10 mm. Because the mean free path in this case is 0.1 mm and the phase function is not isotropic, it takes a long computing time to obtain results with a satisfactory accuracy even with a supercomputer. Therefore, approximation to isotropic scattering is often adopted using the reduced scattering coefficient. With this approximation, the mean free path is enlarged ten times to 1.0 mm since \(1/\mu'_s = 1/(1-g)\mu_s = 10/\mu_s\) for \(g=0.9\), resulting in a much smaller number of interactions before photon bundles escape from the slab. Also, the approximated isotropic scattering makes the programming much easier with the elimination of conversion of coordinates caused by an anisotropic scattering.

However, some number of initial scattering events is needed for the isotropic scattering approximation to be valid. Figure 2 shows the effect of this number. If we neglect the anisotropic scattering completely an unreasonable sharp peak appears at the ballistic time showing the unscattered component. If the slab material really has an isotropic scattering characteristic \((g=0)\) the sharp peak will appear because \(\mu'_s = (1-g)\mu_a = \mu_a\). However, biological tissues usually have a much higher anisotropy parameter close to unity, and the ballistic component is very small for a 10 mm thickness. As we increase the number of initial anisotropic scattering events the ballistic component becomes smaller and smaller as shown in Fig. 2. The appropriate number of these events depends on the optical properties.

2.1.2 Photon diffusion approximation\(^7,9\text{--}17\)

The most fundamental equation for photon migration