Quantitative spectroscopy of superficial turbid media

Sheng-Hao Tseng, Carole Hayakawa, Bruce J. Tromberg, Jerome Spanier, and Anthony J. Durkin

Laser Microbeam and Medical Program, Beckman Laser Institute, University of California, Irvine, Irvine, California 92617

Received April 28, 2005; revised manuscript received July 22, 2005; accepted July 25, 2005

We report a novel diffuse optical spectroscopy probe design for determining optical properties of superficial volumes of turbid samples. The fiber-based probe employs a highly scattering layer placed in contact with the sample’s surface. This modified two-layer diffusion model results in highly diffused light and enables us to employ a MTL diffusion model to predict the optical properties of superficial volumes of interest.

The MTL model is an extension of a general two-layer diffusion model proposed by Kienle et al. Following Kienle’s derivation of a two-layer model, the diffusion equation can be written as

$$ \phi_2(z, Q) = \frac{\sinh[\alpha_1(z_b + z_0)]\exp[\alpha_2(l - z)]}{D_1\alpha_1 \cosh[\alpha_1(l + z_b)] + D_2\alpha_2 \sinh[\alpha_1(l + z_b)]} $$

where

[Diagram of source and detector configurations]

Optical techniques such as diffuse optical spectroscopy (DOS) promise a fast and noninvasive way to quantify tissue composition and function in vivo. DOS can be used for accurate determination of optical absorption ($\mu_a$) and reduced scattering properties ($\mu_s'$) and for access to functional information, such as water and lipid concentrations and blood oxygen saturation of bulk biological tissues. In a typical DOS measurement, a volume of tissue can be probed by use of a source–detector geometry similar to that illustrated in Fig. 1(a). We compare the performance of this modified two-layer diffusion model with Monte Carlo simulations. A set of experiments that demonstrate the feasibility of this method in turbid tissue phantoms is also presented. Optical properties deduced by this approach are in good agreement with those derived by use of a benchmark method for determining optical properties. The average interrogation depth of the probe design investigated here is estimated to be less than 1 mm. © 2005 Optical Society of America

OCIS codes: 170.3660, 170.5270, 170.5280

© 2005 Optical Society of America

Quantitative spectroscopy of superficial turbid media

Sheng-Hao Tseng, Carole Hayakawa, Bruce J. Tromberg, Jerome Spanier, and Anthony J. Durkin

Laser Microbeam and Medical Program, Beckman Laser Institute, University of California, Irvine, Irvine, California 92617

Received April 28, 2005; revised manuscript received July 22, 2005; accepted July 25, 2005

We report a novel diffuse optical spectroscopy probe design for determining optical properties of superficial volumes of turbid samples. The fiber-based probe employs a highly scattering layer placed in contact with the sample’s surface. This modified two-layer diffusion model results in highly diffused light and enables us to employ a MTL diffusion model to predict the optical properties of superficial volumes of interest.

The MTL model is an extension of a general two-layer diffusion model proposed by Kienle et al. Following Kienle’s derivation of a two-layer model, the diffusion equation can be written as

$$ \phi_2(z, Q) = \frac{\sinh[\alpha_1(z_b + z_0)]\exp[\alpha_2(l - z)]}{D_1\alpha_1 \cosh[\alpha_1(l + z_b)] + D_2\alpha_2 \sinh[\alpha_1(l + z_b)]} $$

where

[Diagram of source and detector configurations]

Optical techniques such as diffuse optical spectroscopy (DOS) promise a fast and noninvasive way to quantify tissue composition and function in vivo. DOS can be used for accurate determination of optical absorption ($\mu_a$) and reduced scattering properties ($\mu_s'$) and for access to functional information, such as water and lipid concentrations and blood oxygen saturation of bulk biological tissues. In a typical DOS measurement, a volume of tissue can be probed by use of a source–detector geometry similar to that illustrated in Fig. 1(a). We compare the performance of this modified two-layer diffusion model with Monte Carlo simulations. A set of experiments that demonstrate the feasibility of this method in turbid tissue phantoms is also presented. Optical properties deduced by this approach are in good agreement with those derived by use of a benchmark method for determining optical properties. The average interrogation depth of the probe design investigated here is estimated to be less than 1 mm. © 2005 Optical Society of America

OCIS codes: 170.3660, 170.5270, 170.5280

© 2005 Optical Society of America

Quantitative spectroscopy of superficial turbid media

Sheng-Hao Tseng, Carole Hayakawa, Bruce J. Tromberg, Jerome Spanier, and Anthony J. Durkin

Laser Microbeam and Medical Program, Beckman Laser Institute, University of California, Irvine, Irvine, California 92617

Received April 28, 2005; revised manuscript received July 22, 2005; accepted July 25, 2005

We report a novel diffuse optical spectroscopy probe design for determining optical properties of superficial volumes of turbid samples. The fiber-based probe employs a highly scattering layer placed in contact with the sample’s surface. This modified two-layer diffusion model results in highly diffused light and enables us to employ a MTL diffusion model to predict the optical properties of superficial volumes of interest.

The MTL model is an extension of a general two-layer diffusion model proposed by Kienle et al. Following Kienle’s derivation of a two-layer model, the diffusion equation can be written as

$$ \phi_2(z, Q) = \frac{\sinh[\alpha_1(z_b + z_0)]\exp[\alpha_2(l - z)]}{D_1\alpha_1 \cosh[\alpha_1(l + z_b)] + D_2\alpha_2 \sinh[\alpha_1(l + z_b)]} $$

where

[Diagram of source and detector configurations]

Optical techniques such as diffuse optical spectroscopy (DOS) promise a fast and noninvasive way to quantify tissue composition and function in vivo. DOS can be used for accurate determination of optical absorption ($\mu_a$) and reduced scattering properties ($\mu_s'$) and for access to functional information, such as water and lipid concentrations and blood oxygen saturation of bulk biological tissues. In a typical DOS measurement, a volume of tissue can be probed by use of a source–detector geometry similar to that illustrated in Fig. 1(a). We compare the performance of this modified two-layer diffusion model with Monte Carlo simulations. A set of experiments that demonstrate the feasibility of this method in turbid tissue phantoms is also presented. Optical properties deduced by this approach are in good agreement with those derived by use of a benchmark method for determining optical properties. The average interrogation depth of the probe design investigated here is estimated to be less than 1 mm. © 2005 Optical Society of America

OCIS codes: 170.3660, 170.5270, 170.5280

© 2005 Optical Society of America
\[ \phi_2(z, Q) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \Phi_2(x, y, z) \exp(i(Q_1 x + Q_2 y)) \, dx \, dy, \]

\[ \omega_2^2 = (D_2 Q^2 + \mu_\omega + j \omega c_2)/D_2, \]

\( \omega \) is the source modulation frequency, \( l \) is the thickness of the first layer, and \( Q^2 = Q_1^2 + Q_2^2 \). By numerically performing an inverse Fourier transformation of the solution, we obtain the fluence rate in the bottom layer. The spatially resolved reflectance is the integral of radiance \( L \) in the bottom layer, \( L_2 = \Phi_2 + 3D_2(a \Phi_2/\partial z) \cos \theta \), over the backward hemisphere: \( R(\rho) = \int_2 \left[ 1 - R_\text{Fres}^2(\theta) \right] \cos \theta \, d\Omega \), where \( R_\text{Fres}^{(2)}(\theta) \) is the Fresnel reflection coefficient for a photon with incident angle \( \theta \) relative to the normal to the boundary. In this Letter we compare the performance of the MTL diffusion model with Monte Carlo simulation. Experimental results that demonstrate the feasibility of a MTL method that uses turbid phantoms are also presented.

Monte Carlo simulations of the MTL measurement geometry [Fig. 1(b)] were carried out to validate our modeling approach. The optical properties of the top layer (scattering layer) and the bottom layer (sample) were \( \mu_{\omega_1} = 1 \times 10^{-6} / \text{mm}, \) \( \mu_{\omega_1}' = 50 / \text{mm}, \) \( n_1 = 1.33, \) \( \mu_{\omega_2} = 0.04 / \text{mm}, \) \( \mu_{\omega_2}' = 0.7 / \text{mm}, \) and \( n_2 = 1.33, \) respectively. The numerical apertures of the source fiber and of the detection fiber were both set at 1.33 to be consistent with our MTL diffusion model. The top layer's thickness and the source–detector separation were set to 3 and 2.5 mm, respectively. The sample thickness for this simulation was semi-infinite. The amplitude and phase data from a Monte Carlo simulation (asterisks) and from a MTL diffusion model (solid curves) are shown in Fig. 2. Amplitude and phase differences between the Monte Carlo simulation and the MTL diffusion model are within 1.3% and 4.6%, respectively, over the source modulation frequency range 50–500 MHz. Small differences between amplitude and phase data generated from Monte Carlo simulation and two-layer diffusion model were also observed by Kienle et al.\(^3\) By fitting the Monte Carlo simulated data to the MTL diffusion model with a nonlinear regression algorithm, we recovered the optical properties of the sample layer to be \( \mu_{\omega_2} = 0.03156 / \text{mm} \) and \( \mu_{\omega_2}' = 0.7 / \text{mm}, \) which deviate from the designed values by 21% and 5%, respectively. We calculated the probe depth from the simulation by averaging and weighting the depths of scattering events in the sample layer experienced by detected photons. Probe depths of 676 and 658 \( \mu \)m were obtained when the source modulation frequencies were 50 and 500 MHz, respectively.

We performed an additional Monte Carlo simulation to illustrate that the MTL geometry is relatively insensitive to shallow sample optical properties. In this simulation, the sample itself is stratified, with an upper-layer thickness of 2 mm (optical properties as used in the previous simulation) and an underlying semi-infinite layer that has distinctly different optical properties of \( \mu_{\omega_3} = 0.08 / \text{mm}, \) \( \mu_{\omega_3}' = 1.4 / \text{mm}, \) and index of refraction \( n = 1.33. \) Optical properties of the semi-infinite layer are not meant to represent those of any particular in vivo tissues but were chosen to illustrate the superficial probing aspects of the MTL probe design. Monte Carlo simulated amplitude and phase in this geometry are shown as squares in Fig. 2, and the recovered optical properties of the sample were \( \mu_{\omega_2} = 0.03268 / \text{mm} \) and \( \mu_{\omega_2}' = 0.706 / \text{mm}, \) which correspond closely to the uppermost 2 mm of the sample. The maximum differences in amplitude and phase between the two Monte Carlo simulations (asterisks and squares) are 6.1% and 1.1%, respectively, and illustrate that the influence of the third layer on the recovered sample’s optical properties is small and that the majority of photons detected by use of our MTL geometry have traveled within the most superficial 2 mm of the sample.

Next, we carried out experiments on tissue phantoms, using a frequency-domain photon migration instrument that has been described in detail elsewhere.\(^1\) Six laser diodes, 661, 681, 783, 806, 823, and 850 nm, were used in all our measurements, and a fiber-coupled avalanche photodiode was used for detection.

We fabricated five homogeneous liquid phantoms with different optical properties by using 10% Lyposin (Abbott Laboratories, Chicago, Ill.) as a scatterer, the water-soluble dye Nigrosin (Sigma, St. Louis, Mo.) as an absorber, and water. We determined the benchmark properties for each phantom by placing each phantom in a 1500 ml beaker. Source and detector fibers were submerged 80 mm below the surface and 70 mm from the sides of the container to prevent the occurrence of boundary effects. Measurements of amplitude and phase were carried out with source and detection fibers separated by 8 and by 10 mm. Source modulation frequencies ranged from 50 to 500 MHz in 400 equal steps. The optical properties of the five phantoms at 660 nm are listed in Table 1.

Next, we carried out measurements of each phantom in the semi-infinite and MTL geometries. For MTL measurements, the source fiber (610 \( \mu \)m; N.A., 0.37) was glued with epoxy to the top of a 70 mm \( \times \) 70 mm, 3 mm thick Spectralon layer (Labsphere, North Sutton, NH). A small hole was
drilled through the Spectralon layer such that the center-to-center distance for the source and detection fibers (610 μm; N.A., 0.37) was 2.5 mm. We placed the probe in gentle contact with the surface of each sample and carried out frequency-domain photon migration measurements. The index mismatch between the probe and the phantom is small because the index refraction of Spectralon is 1.35 and the water-based phantoms have refractive indices of ~1.33. The modulation frequencies ranged from 50 to 300 MHz in 200 equal steps. Inasmuch as Spectralon is highly attenuating, with μs = 10−7/mm and μ's = 4.735/mm at 661 nm, the reflectance data collected at modulation frequencies higher than 300 MHz were noisy and were therefore neglected for this set of measurements. For semi-infinite measurements, the source–detector separation was 5 mm and the source modulation frequency range and the diameters of the source and detection fibers were the same as those used in MTL measurements.

We determined instrument response by measuring a liquid phantom with known optical properties and subsequently used it to calibrate the raw data from each phantom. We employed a MTL diffusion model and a P 3 diffusion model to recover the optical properties from MTL and semi-infinite geometry measurements, respectively. A least-squares fit to amplitude demodulation and phase shift based on these models was used to recover the optical properties for each sample.

Figure 3 shows the results of using three different measurement geometries for liquid phantom 3, which has optical properties similar to those of oral cheek tissue. The properties determined in the MTL geometry (circles) are in good agreement with those determined from infinite-medium measurements (asterisks), and the deviations between the results of the two measurement geometries are less than 5%. Error bars for MTL and infinite measurement results are not apparent in Fig. 3 because the error bars are smaller than the symbols used to identify the data. We calculated the deviation of optical properties deduced by MTL measurements from benchmark properties for all five phantoms at 661 nm. MTL measurement results showed small deviations (less than 8%) from benchmark results for all phantoms studied here, as listed in Table 1. The deviations do not demonstrate a noticeable dependence on a samples’ optical properties.

In conclusion, the MTL approach provides an efficient and reliable way to quantify the optical properties of superficial volumes of samples. The average interrogation depth of the MTL probe given the parameters investigated here is less than 1 mm. Our future research will include a detailed characterization of the probe’s performance as a function of parameters such as top-layer scattering coefficient, source–detector separation, range of source modulation frequencies, and sample optical properties.

This research was supported by National Institutes of Health grant P41-RR01192, the Beckman Foundation, and U.S. Air Force Office of Scientific Research grants F49620-00-2-0371 and FA9550-04-1-0101. S.-H. Tseng’s e-mail address is shenghat@uci.edu.

### References


### Table 1. Benchmark Optical Properties at 661 nm of Five Liquid Phantoms and Deviations of Optical Properties Determined by Use of MTL Measurements from Benchmark Values

<table>
<thead>
<tr>
<th>Phantom</th>
<th>μa (mm⁻¹)</th>
<th>μ's (mm⁻¹)</th>
<th>Deviation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>μa</td>
</tr>
<tr>
<td>LP1</td>
<td>0.0198</td>
<td>1.0865</td>
<td>-2.07</td>
</tr>
<tr>
<td>LP2</td>
<td>0.0396</td>
<td>1.0746</td>
<td>-3.58</td>
</tr>
<tr>
<td>LP3</td>
<td>0.0367</td>
<td>0.6896</td>
<td>-6.94</td>
</tr>
<tr>
<td>LP4</td>
<td>0.0118</td>
<td>1.1098</td>
<td>1.87</td>
</tr>
<tr>
<td>LP5</td>
<td>0.0195</td>
<td>0.6698</td>
<td>3.90</td>
</tr>
</tbody>
</table>

Fig. 3. (a) Reduced scattering coefficients μ's and (b) absorption coefficients μa of the liquid phantom recovered from infinite-medium (asterisks), MTL (circles), and 5 mm semi-infinite (triangles) measurements at six wavelengths.