Optimal wavelength selection for optical spectroscopy of hemoglobin and water within a simulated light-scattering tissue

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Abstract. An algorithm that selects optimal wavelengths for spectral fitting of diffuse light reflectance spectra using a nonnegative least squares method is presented. Oxyhemoglobin, deoxyhemoglobin, and water are considered representative absorbers, but the approach is not constrained or limited by absorber selection provided native basis spectra are available. The method removes wavelengths iteratively from a scattering-modulated absorption matrix by maximizing the product of its singular values and offers considerable improvements over previously published wavelength selection schemes. Resulting wavelength selections are valid for a broad range of optical properties and yield lower RMS errors than other wavelength combinations. The method is easily modified and broadly applicable to tissue optical spectroscopy. Adaptation of the algorithm to select optimal light-emitting diodes for fitting blood is described. © The Authors. Published by SPIE under a Creative Commons Attribution 3.0 Unported License. Distribution or reproduction of this work in whole or in part requires full attribution of the original publication, including its DOI. [DOI: 10.1117/1.IJO.23.7.071202]

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1 Introduction
Multispectral reflectance is a broadly established method for estimating concentrations of multiple absorbers in tissue. It is often used to decouple and estimate quantities of oxyhemoglobin (HbO2), deoxyhemoglobin (HbR), and water (H2O), among other absorbers, through spectral fitting based on least squares, provided the acquisition of multiple wavelengths is available (a minimum of three wavelengths is needed for HbO2, HbR, and H2O). The wavelengths acquired have a considerable effect on the accuracy of the concentration estimates that are generated. In the approach presented here, wavelengths are selected by maximizing the product of the singular values of the scattering-modulated absorption matrix. Analysis shows that this selection method is robust and stable over a wide range of optical properties and that it improves the accuracy of the resulting estimates relative to algorithms previously published. Finally, a practical application where optimal light-emitting diodes (LEDs) are chosen to estimate blood concentrations is described.

2 Methods

2.1 Spectral Fitting
Concentrations of multiple absorbers in tissue can be estimated from its wavelength-dependent reflectance signal. For each wavelength, the fraction of reflectance collected can be modeled with Beer’s law

\[ R(\lambda) = \exp[-\mu_a(\lambda)L(\lambda)], \]  

where \( \mu_a(\lambda) \) is the wavelength-dependent absorption coefficient represented in the medium as a linear combination of the absorption coefficients of all components present. To illustrate the benefits of our approach, we consider oxyhemoglobin, deoxyhemoglobin, and water, and, accordingly, the absorption coefficient is

\[ \mu_a(\lambda) = BS\mu_{oxy}(\lambda) + B(1-S)\mu_{deoxy}(\lambda) + W\mu_{water}(\lambda), \]  

where \( L(\lambda) \) is the average path length of photons in the medium at wavelength \( \lambda \), which varies according to the absorption (\( \mu_a \)) and scattering (\( \mu_s' \)) coefficients of the tissue, and is computed using an adaption of the diffusion model described by Farrell et al. B, S, and W quantify the blood concentration, oxygen saturation, and water concentration, respectively. Parameter estimation can be refined through more advanced models. For example, adding specific layers of tissue can be advantageous if the laminar distribution of chromophores is known (e.g., in the case of epidermial melanin). Additionally, correction factors accounting for vessel size can be added depending on the underlying structures that are being considered (notably, blue light does not penetrate to the center of large vessels and, therefore, underestimates blood content). The optical depth is defined as the natural logarithm of the reflectance signal and is needed to extract information about concentration through spectral fitting

\[ -\ln R(\lambda) = \mu_a(\lambda)L(\lambda). \]  

Given an optical depth equation for each wavelength, the problem is decomposed into a matrix system
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RMS errors generated when fitting with wavelengths chosen by different selection criteria were compared in Fig. 2. As a control, the RMS error associated with wavelengths selected randomly and linearly within the 480- to 1000-nm range was also computed. These results demonstrate that using the product of the singular values yields improved results over condition number or smallest singular value, especially when selecting a larger number of wavelengths. Interestingly, random and linearly spaced wavelength selection outperformed those based on condition number and the smallest singular value. Methods that rely on the smallest singular values are affected by spectra that are highly disproportioned (as is the case here, with water having an absorption coefficient that is orders of magnitude lower than blood).

3.2 Optimal Wavelengths

Using our selection algorithm based on maximizing the product of singular values, the three optimal wavelengths for estimating blood concentration and saturation in tissue were computed for a wide variety of optical properties. For the majority (76%) of optical property combinations tested, the same trio of optimal wavelengths was selected. These wavelengths are shown in Fig. 3.

In the other cases, which were mostly when oxygen saturation was lower than 60%, the center wavelength selected switched from 604 to 596 nm. Variations in the wavelengths picked are expected when modifying optical properties since they alter the shape of the absorption spectra used to compute the optimal wavelengths. Even if, for some combinations of optical properties, the selection algorithm found wavelengths that differed slightly from the ones in Fig. 3, these choices generated similar RMS errors. The concentration estimates generated with the set of optimal wavelengths highlighted in Fig. 3 yielded RMS errors that were smaller than the ones generated with other wavelength trios, on average. The region of low RMS error was constant for a radius of about 10 nm around the optimal wavelengths, as shown in Fig. 4, in which the change in RMS error relative to the error generated with the optimal wavelengths is presented.

Interestingly, some wavelengths can be moved with greater freedom than others. For example, increasing the 578-nm...
wavelength changes RMS error nominally, while decreasing it produces RMS errors that are orders of magnitude greater.

### 3.3 Additional Chromophores

Depending on the tissue being imaged, more (or different) absorbers may need to be considered. They can easily be included in the selection process by adding their associated spectra to the matrix of pathlength-modulated bases ($μ_aL$) used to compute the singular values. As a demonstration, the spectra of ICG (for a concentration of $1290 \mu$M), lipids, and a linear offset (which removes linear background sources) were added to the basis spectra matrix, and 6 wavelengths were selected with these additional components. As in the 3 wavelength selection case, optical properties and concentrations were chosen randomly 10 times within the ranges outlined in Table 1 for concentrations of ICG and lipids varying between 0.02 and 0.06 (%). The optimal wavelengths found by our algorithm are presented in Fig. 5. The average RMS error of the concentration estimates generated with these wavelengths was compared with the average errors generated with other algorithms, and the results are summarized in Table 2.

<table>
<thead>
<tr>
<th>Selection method</th>
<th>Linear spacing</th>
<th>Random selection</th>
<th>Condition number</th>
<th>Smallest singular value</th>
<th>Product of singular value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average RMS error</td>
<td>0.39</td>
<td>1.45</td>
<td>0.37</td>
<td>0.30</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Once again, selecting wavelengths based on the product of singular values yielded the smallest RMS error and outperformed previously published algorithms.

### 4 Practical Application

The selection algorithm outlined in this paper is easily adapted to multiple practical situations. As an example, it is used to select the 3 best LEDs for fitting HbO$_2$, HbR, and H$_2$O from an inventory of 20 possibilities. The input set of LEDs was taken from Gareau. Although LED emission spectra usually have varying amplitudes, they have been normalized for this analysis to account only for their emission wavelength. The normalized spectra are shown in Fig. 6.

LEDs were selected by the algorithm outlined in this paper, by replacing the $μ_aL$ matrix with the following LED matrix

$$
\begin{bmatrix}
\int μ_{a,oxy}LLED_1dλ \\
\int μ_{a,deoxy}LLED_1dλ \\
\int μ_aLLED_1dλ \\
\int μ_aLLED_2dλ \\
\int μ_aLLED_2dλ \\
\int μ_{a,water}LLED_2dλ \\
\vdots \\
\int μ_{a,oxy}LLED_{20}dλ \\
\int μ_{a,deoxy}LLED_{20}dλ \\
\int μ_aLLED_{20}dλ \\
\int μ_aLLED_{20}dλ
\end{bmatrix}
$$

where LED$_i$ is the emission spectrum of LED $i$. This matrix considers the bandwidth of the LED’s emission as well as the modulated absorption spectra of the components fitted.

Executing the selection algorithm on this matrix returned the 3 best LEDs: LED# 9, LED# 17, and LED# 20 centered at 496, 668, and 935 nm, respectively, and yielded wavelength peaks having slight variations from the optimal wavelengths picked by our algorithm. This outcome is explained by the fact that,
5 Conclusion

This paper presented and evaluated a wavelength selection criterion that produced improved results relative to previously published strategies by maximizing the product of singular values of the scattering-modulated absorption matrix. Using this approach, three optimal wavelengths were found for diffuse reflectance spectral fitting of HbO₂, HbR, and H₂O. These optimal wavelengths proved to be stable over a wide range of optical absorption and scattering properties. The method is easily extended to more and different absorbers and achieved similarly improved results. Modifications to the algorithm were demonstrated to account for LED broadband emission spectra instead of distinct discrete wavelengths, and the process was used to select LEDs that are optimal for fitting blood components. While this paper prioritized the diffuse reflectance fitting of blood, the algorithm is readily applied to applications that require spectral fitting of other absorbers and/or fluorophores.

Disclosures

The authors have no conflicts of interests to disclose.

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References


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