A novel spectral approach to measuring the relative concentrations of two localized chromophores in turbid media

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Introduction

Near infrared (NIR) imaging relies mainly on the absorption of hemoglobin for the source of image contrast, and is highly sensitive to the oxygen saturation of hemoglobin (SO_2). As a result, there are significant research efforts aimed at characterizing the physiological and diagnostic value of spectral data in optical mammography [1-4]. We have recently proposed a novel spectral imaging approach to quantify the oxygen saturation of the hemoglobin in breast tumors [5]. The basic idea is that an appropriate choice of a pair of wavelengths (λ_1, λ_2), which depends on the oxygenation level of the tumor and on the optical properties of the background healthy breast tissue, leads to a measurement of the tumor oxygenation that is largely independent of the tumor size, shape, and location inside the breast [5].

Here, we present Monte Carlo and experimental results to validate such novel spectral approach in the measurement of the relative concentrations of two localized chromophores (mimicking oxy- and deoxy-hemoglobin) within a highly scattering medium (mimicking breast tissue).

Theory

We use black India ink to simulate oxy-hemoglobin, and a blue food dye to simulate deoxy-hemoglobin. By using different combinations of the ink and dye solutions, we can test the ability of our method to measure relative concentrations of known chromophores. Based on the expression for SO_2 in our previous paper [5], the relative concentration of ink is given by:

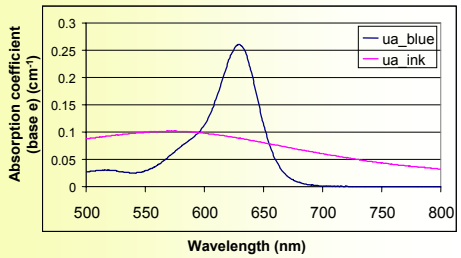
$$\frac{[ink]}{[ink]+[blue]} = \frac{\mu_{a\text{-}blue}(\lambda_2) - \mu_{a\text{-}blue}(\lambda_2)\dfrac{\mu_{s0}'(\lambda_1)}{\mu_{s0}'(\lambda_2)}\dfrac{\Delta I/I_0|_{max}^{(\lambda_1)}}{\Delta I/I_0|_{max}^{(\lambda_2)}}}{[\mu_{a\text{-}blue}(\lambda_2) - \mu_{a\text{-}ink}(\lambda_2)] + [\mu_{a\text{-}ink}(\lambda_1) - \mu_{a\text{-}blue}(\lambda_1)]\dfrac{\mu_{s0}'(\lambda_1)}{\mu_{s0}'(\lambda_2)}\dfrac{\Delta I/I_0|_{max}^{(\lambda_1)}}{\Delta I/I_0|_{max}^{(\lambda_2)}}}$$

where:

- [ink] and [blue] indicate the concentrations of ink and blue dye
- $\mu_{a\text{-}blue}$ and $\mu_{a\text{-}ink}$ are the absorption coefficients of the blue dye and black India ink solutions, respectively
- μ_{s0}' is the background reduced scattering coefficient
- $\Delta I/I_0|_{max}$ is the relative intensity change (where I_0 is the unperturbed intensity measured in the background medium) when the source, detector, and the perturbation are collinear.
- λ_1 and λ_2 are two wavelengths such that:

$$\Delta I/I_0|_{max}^{(\lambda_1)} \approx \Delta I/I_0|_{max}^{(\lambda_2)}$$

Absorption spectra of the aqueous solutions of ink and blue dye



Monte Carlo simulations for various relative concentrations

We have used a Monte Carlo (MC) method to simulate the intensities for different combinations of ink and dye solutions under the following conditions:

- Infinite slab geometry;
- Slab thickness: 6cm;
- Cylindrical defect 1 cm in diameter;
- No scattering mismatch between background medium and defect;
- For the optical properties of the defect and background medium, we have used the following:

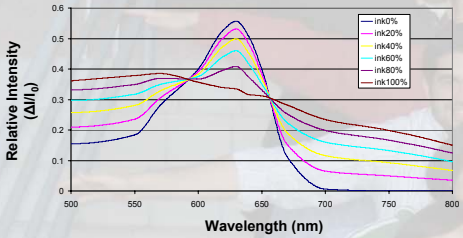
Background absorption: water absorption

Inclusion absorption: A linear combination of the spectra of the ink and dye solutions (see figure in the left column)

Background and inclusion scattering:

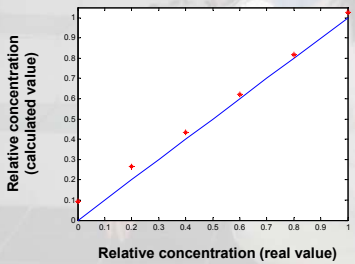
$$\mu_{s0}' = -0.007(\mathrm{cm^{-1}nm^{-1}}) * \lambda(\mathrm{nm}) + 15.4(\mathrm{cm^{-1}})$$

Intensity spectra of the cylindrical ink/dye inclusion in a turbid medium: Monte Carlo



$\Delta I/I_0$ is the relative intensity change cause by the defects, where I_0 is the unperturbed intensity from the background medium.

Calculated vs real values of relative concentrations of ink and blue dye (from Monte Carlo)

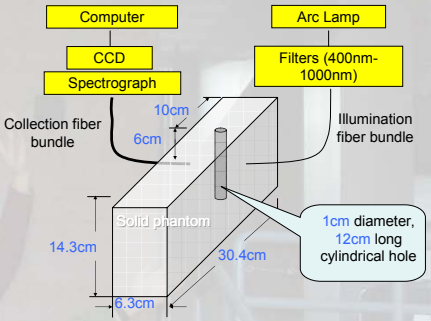


- Blue line implies the real value of relative concentrations of ink solutions.

* Red dots show the calculated relative concentrations for 0%, 20%, 40%, 60%, 80% and 100% ink solutions respectively. The calculations were based on an average of all wavelength pairs for which the error in the relative concentration was below 4%.

Experimental test for various relative concentrations

Experimental Setup



Optical properties of the solid phantom at 690 and 830 nm:

$\mu_a(690\mathrm{nm}) = 0.0110 \pm 0.0003\mathrm{cm^{-1}}$, $\mu_a(830\mathrm{nm}) = 0.0130 \pm 0.0003\mathrm{cm^{-1}}$

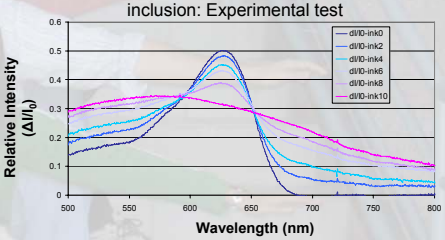
$\mu_{s0}'(690\mathrm{nm}) = 10.6 \pm 0.1\mathrm{cm^{-1}}$, $\mu_{s0}'(830\mathrm{nm}) = 9.5 \pm 0.1\mathrm{cm^{-1}}$

A Liposyn suspension is used as the highly scattering medium in the cylindrical inclusion that contains the ink and dye solutions. The optical properties of the aqueous Liposyn suspension are:

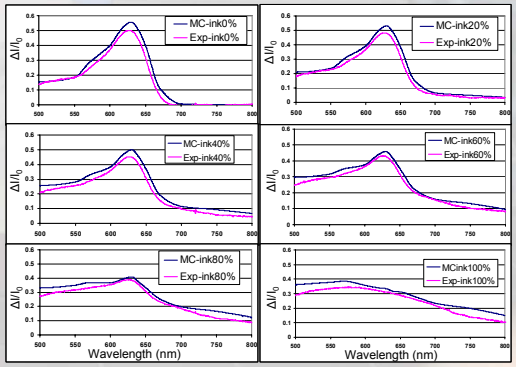
$\mu_a(690\mathrm{nm}) = 0.020 \pm 0.0003\mathrm{cm^{-1}}$ $\mu_a(830\mathrm{nm}) = 0.048 \pm 0.0007\mathrm{cm^{-1}}$

$\mu_{s0}'(690\mathrm{nm}) = 9.6 \pm 0.06\mathrm{cm^{-1}}$ $\mu_{s0}'(830\mathrm{nm}) = 7.0 \pm 0.05\mathrm{cm^{-1}}$

Intensity spectra of the cylindrical ink/dye inclusion: Experimental test



Absolute comparison of the MC and experimental spectra



Discussion

- By using MC spectral data, we obtained average relative concentrations (RC) of ink to within 10% of the actual RC values, and within 5% for RC values >20%.
- The experimental spectra have shapes similar to MC spectra but with lower amplitudes and flatter curves, which may be caused by (1) the difference between the infinite slab geometry used in MC and the finite slab used in experiment, or (2) the scattering mismatch between solid phantom and Liposyn solution used in the experiment.

Conclusions

The proposed two-wavelength spectral approach is capable of quantifying the relative concentrations of two test chromophores inside an inclusion to within an accuracy, based on Monte Carlo spectra data, of 10%. This further proves that the two-wavelength method can be properly used to estimate the relative concentration of inclusions in highly scattering medium.

The tests based on chemically stable and well-characterized dyes such as blue food coloring dye and black India ink provide a proof-of-principle demonstration of the effectiveness of the two-wavelength approach.

Future directions

- Assess the robustness of the method;
- How to select the wavelength pair(s);
- Comparison with other spectral methods;
- Use this method to measure the oxygen saturation of hemoglobin in human breast tumors.

Acknowledgments

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