Simulating the light propagation in brain tissues using ray tracing with a dynamic and heterogeneous tissue model

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Thomas J. Sauer[1], Peifang Tian[1,2], Anna Devor[2,3,4], Qianqian Fang[4], Hana Uhlirova[3], Payam A. Saisan[2], Anders M. Dale[2,3], David A. Boas[4], and Sava Sakadzic[4]

[1]Department of Physics, John Carroll University, University Heights, OH 44118, Departments of Neurosciences[2] and Radiology[3], UCSD, La Jolla, CA 92093,

[4]Martinos Center for Biomedical Imaging, MGH/HMS, Charlestown, MA 02129

INTRODUCTION

- Cortical neuronal activities, metabolism, and hemodynamics on the level of single cell and vessel can be measured by two-photon laser scanning microscopy (TPLSM) *in vivo*.
- Relatively large hemodynamic changes often accompany neuronal activities and metabolism changes, thus distort the signal of interest, such as the cerebral metabolic activities measured through β-nicotinamide adenine dinucleotide (NADH) fluorescence change.
- Prior work: Baraghis et al modeled the hemodynamic distortion on TPLSM NADH fluorescence with precise maps of cortical microvasculature, however, they only did it at some specific locations and did not estimate the hemodynamic distortion throughout the cortical tissue where NADH fluorescence would be measured [1].
- Our goal: simulate the effect of hemodynamic changes and correct its distortion in the signal of interest in cortical tissue of 0.3x0.3x0.3mm^3. To illustrate the principle, we calculate the distortion in the NADH signal measured by TPLSM using ray tracing implemented in Matlab.

METHODS

Light propagation consists of excitation and fluorescence (Fig 1a) [1]

- **Excitation (only consider scattering due to blood vessels)**
  - Incident laser light (740nm): multiple rays uniformly distributed on the cortical surface within the excitation cone determined by NA (0.95) and n_{tissue} (1.36); initial intensity of each ray determined by Gaussian distribution.
  - Each ray has a probability to experience a scattering event from a red blood cell if a blood vessel intercepts its path. The ray intensity contributes to the excitation of NADH if scattering does not deviate its trajectory such that the ray misses a disk of radius R_E=1.08ω_0 at the focal spot. (R_E corresponds to a radius where intensity falls to 10% of the peak intensity)
- **Fluorescence (only consider absorption due to blood vessels)**
  - Each ray within the same excitation cone and emitted from the focal point is considered; it experiences a series absorption events due to blood vessels before exiting the tissue.

Tissue optical properties (Fig 1b depicts extinction and emission spectra.)

- Non-vascular tissue: homogeneous and constant ➡ ignore its effect
- Blood vessels:
  - heterogeneous ➡ use microvasculature stack from TPLSM imaging; absorption: $\mu_a \propto Hematocrit[SO_2\varepsilon_{HbO}(\lambda) + (1-SO_2)\varepsilon_{Hb}(\lambda)]$ oxygen saturation SO2: 0.75; hematocrit: determined by diameter scattering [2]: $\mu_s \propto (1-Hematocrit)Hematocrit$
  - time-varying ➡ simultaneously image and simulate a functional inert dye (Sulforhodamine 101, S101)

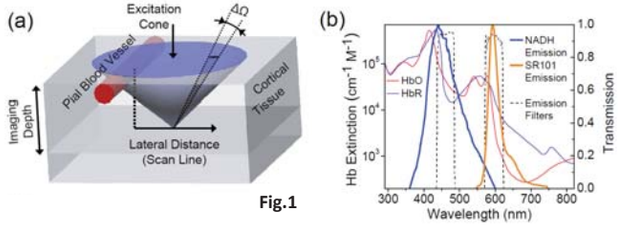


Fig.1

RESULTS

Fig.2 NADH and S1010 fluorescent intensity profiles calculated by ray tracing are comparable to those from experiment

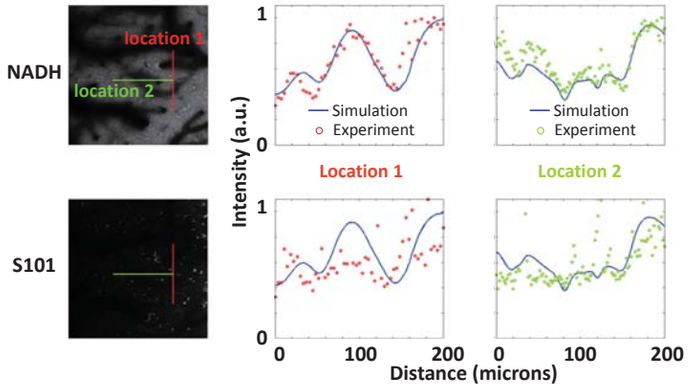
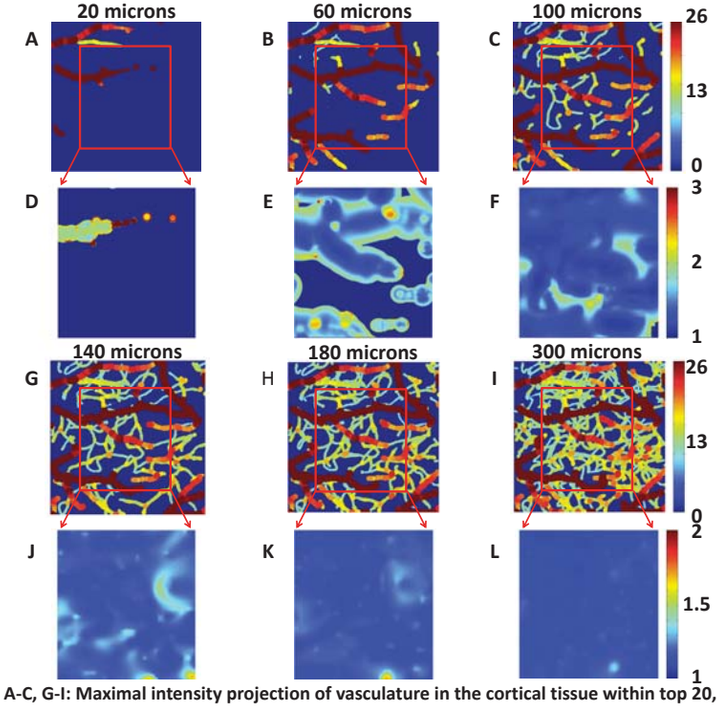


Fig.3 Correction factor K is heterogeneous within the top 140 microns and becomes more homogeneous deeper down.

K: ratio of relative change of NADH fluorescence over relative change of S101 fluorescence due to hemodynamic change ➡

$$\frac{\Delta C_{NADH}}{C_{NADH}} = \frac{\Delta I_{NADH}}{I_{NADH}} - K\frac{\Delta I_{S101}}{I_{S101}} \quad \text{Eq (1)}$$

- $\frac{\Delta C_{NADH}}{C_{NADH}}$: true relative NADH concentration change
- $\frac{\Delta I_{NADH}}{I_{NADH}}$: measured relative NADH fluorescence change
- $\frac{\Delta I_{S101}}{I_{S101}}$: measured relative S101 fluorescence change



A-C, G-I: Maximal intensity projection of vasculature in the cortical tissue within top 20, 60, 100, 140, 180, and 300 microns, respectively. D-F, J-L: K at the corresponding cortical depths. The area of each K graph is 0.3x0.3 mm².

CORRECTING HEMODYNAMIC DISTORTION

Correction schemes (refer to Fig.3-5)

Many TPLSM NADH images are taken within the top 300 microns below cortical surface.

- Near surface: K varies greatly near large vessels ➡ avoid these areas; no correction needed in other areas
- ~ 60-140 microns: position-specific K needs to be simulated and used in Eq (1) in many areas; otherwise, it may lead to large error (See Fig.4)
- ~ 160-300 microns: a single value K of 1.14 (See Fig.5) may be used in Eq (1) for most areas, thus no need to calculate K unless one is interested in the few locations where K deviates significantly from 1.14.

Fig.4 Contour plot of percent error when a single value K_0 = 1.14 is used in Eq (1) instead of the true value K_{true}

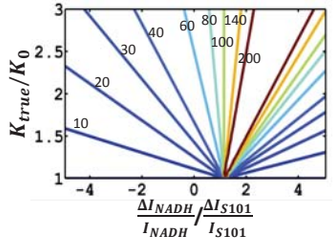
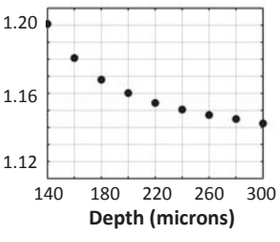


Fig.5 Averaged K reaches a plateau of 1.14 from 140-300 microns



SUMMARY AND FUTURE WORK

- The relative changes of the signal (NADH) and functional inert dye (S101) due to hemodynamic changes have been simulated using ray tracing implemented in Matlab.
- The correction factor K (used to recover the true relative NADH concentration change from the simultaneously measured relative NADH and S101 fluorescence changes) has been obtained using realistic microvasculature.
  - K is heterogeneous and critically dependent on the vessel locations within the top 140 microns; position-specific K needs to be used in correcting distortions.
  - K is more homogeneous and its average value within the same depth reaches a plateau from 160 to 300 microns, indicating that a single value correction scheme may be sufficient in deeper tissues.
- Future work: simulate K using the more accurate Monte Carlo method; compare results obtained from both approaches.

REFERENCES

1. Baraghis et al, J. Biomed Optics 16, 106003 (2011)
2. Twersky, J. Opt. Soc. Am 60, 1084 (1970)

ACKNOWLEDGEMENT

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