## Near-IR Optical Calibration of the BOLD Signal

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**Introduction.** Although the simultaneous collection of multimodal data is becoming more common, relatively little progress has been made in advancing analysis methods to take the advantage of this unique form of data. We hypothesize that multimodal data can be better utilized by developing specific analysis methods that account for the differing sources of error, assumptions, and limitations of each method and that attempt to define an underlying physiology that is jointly and simultaneously consistent with all of the acquired signals. In this work, we describe a bottom-up analysis model for fusing multimodal data from concurrently measured fMRI BOLD and diffuse optical tomoghaphy (DOT) measurements. Our model is used to combine multimodal data into a single estimate of underlying hemodynamic changes that is simultaneously consistent with both sets of measurements. This method is based on an image reconstruction routine involving the simultaneous inversion of both the optical and fMRI measurement models to create a combined estimate of oxy- and deoxy-hemoglobin changes. This approach allows us to incorporate both the high temporal information of the optical data with the spatial information of the fMRI method.

By combining optical and BOLD measurements into a single model, we show that the complimentary spatial and spectroscopic information in these two methods allows a cross-calibration of the measurements. Alone, neither of these methods is considered to be quantitatively accurate. However, we find that combining these methods provides a more quantitatively accurate estimation of deoxy- and oxy-hemoglobin changes. We present both simulation and empirical results from simulations optical and BOLD imaging of the human motor cortex at 3.0 T (Siemens Allegra scanner) to demonstrate how our method can be used to provide more quantitatively accurate estimates of oxy- and deoxy-hemoglobin.

**Theory.** Our model is based on the inversion of a simultaneous observation model of both fMRI and optical methods. We use a linear model to describe the underlying spatial and temporal distribution of oxy- and deoxy-hemoglobin changes. We use a multimodal observation model to relate both of the measurement types to this common underlying physiology. This joint-observation model is given by the equation

$$\begin{bmatrix} \Delta BOLD(t) \\ \Delta OD_{830nm}(t) \\ \Delta OD_{690nm}(t) \end{bmatrix} = \begin{bmatrix} 0 & -\alpha \cdot I \\ \varepsilon_{830nm|HbO2} \cdot \mathbf{A}_{830nm} & \varepsilon_{830nm|HbR} \cdot \mathbf{A}_{830nm} \\ \varepsilon_{690nm|HbO2} \cdot \mathbf{A}_{690nm} & \varepsilon_{690nm|HbR} \cdot \mathbf{A}_{690nm} \end{bmatrix} \cdot \begin{bmatrix} \Delta HbO_2(t) \\ \Delta HbR(t) \end{bmatrix}$$
(1)

The first row in the observation operator represents the extra-vascular BOLD observation model, which includes an unknown calibration factor for the BOLD signal ( $\alpha$ ), which is estimated within the model based on the data. The bottom two rows of the observation operator in Eqn 1 capture the optical forward model, where  $\varepsilon$  is the spectroscopic extinction coefficient for oxy- and deoxy-hemoglobin and A is the spatial sensitivity of the array of optical measurement pairs.  $\Delta$ OD is defined as the change in optical density (or absorption) of the underlying tissue. Eqn 1 is solved by using a pseudo-Bayesian linear inverse formula, which allows appropriate weighting of the multimodal data using prior estimates of the noise in each signal.

**Results.** We applied our new analysis method to both simulated and experimental multimodality data sets. We demonstrate the use of this model to reconstruct the changes in oxy and deoxy-hemoglobin concentrations from concurrently measured optical and fMRI experimental data and examine the improvements made with this model. In Fig. 1, we show the BOLD-alone, DOT-alone, and fusion reconstructions for a representative subject recorded during a brief (2-sec) finger-tapping task. The BOLD calibration factor ( $\alpha$  in Eqn 1) was estimated based on an iterative approach as shown in the table below.

**Conclusions.** We described a multimodal fusion model for analyzing simultaneous optical and BOLD measurements. Our results demonstrate that by combining both BOLD and DOT measurement models, multimodality data can be used to provide more quantitative estimates of evoked changes in oxy- and deoxy-hemoglobin.



Hemoglobin Changes			BOLD Calibration ( $\alpha$ )
Subject	$\Delta$ HbO <sub>2</sub>	ΔHbR	
А	6.1 μM	-1.2 μM	0.41 %-BOLD/µM
В	3.9 µM	-1.5 μM	0.52 %-BOLD/µM
С	4.4 μΜ	-0.7 µM	1.24 %-BOLD/µM
D	4.5 μΜ	-0.3 µM	0.19 %-BOLD/µM
Е	1.6 μM	-0.5 µM	0.39 %-BOLD/µM
Group	4.1 μΜ	-0.9 µM	0.55 %-BOLD/µM

**Fig 1/Table 1.** This figure and table show the model reconstructions using the DOT alone, BOLD alone, and fusion datasets for deoxy- and oxy-hemoglobin changes recorded during a finger-tapping exercise. Functional changes are shown masked at the half-max amplitude. The right-most images show the projections of the activation patterns onto the surface of the brain. The maximum amplitude of the responses and BOLD calibration estimates are shown in the table above.