Estimation of Dynamic CMRO$_2$ Changes from Dynamic CBF and BOLD fMRI Data

Alberto Vazquez*, Vikas Gulan*i, Luis Hernandez*, Douglas Noll*  
* FZI Research Laboratory, University of Karlsruhe, Karlsruhe, Germany  
† Physical Department, University of Würzburg, Würzburg, Germany

Motivation

The changes in CMRO$_2$ that take place as a result of changes in neural activity have been difficult to understand due to the non-trivial interplay between oxygen consumption and cerebral blood flow and volume. Further, the dynamics of oxygen delivery and oxygen consumption are not well known. Various methods have been proposed to estimate the steady-state changes in CMRO$_2$, that take place due to prolonged changes in neuronal activity [1,2,3].

The objective of this work is to estimate the dynamic changes in CMRO$_2$ that result from evoked neural activation using CBF and BOLD MRI data along with dynamic models of the hemodynamics involved.

Dynamic Model

Blood Flow and Blood Volume

The changes in blood flow that result from changes in neural activity originate in the arterial vasculature by changes in the vessel caliber. The changes in blood flow are assumed to follow first-order dynamics with respect to the changes in oxygen consumption and propagate through the local capillaries and veins. In the veins, changes in blood flow produce changes in blood volume due to the elastic nature of the venous vessels (for further details refer to [2]).

Oxygen Delivery and Consumption

The amount of oxygen in the capillaries depends on the amount entering and leaving the capillaries by convection and the amount that exchanges with tissue. In the tissue, the amount of oxygen depends also on the amount exchanging with the capillary and the amount consumed. Oxygen is assumed to exchange with blood plasma instantaneously and described by the Hill equation (for further details please refer to [3]):

\[
\frac{dV}{dt} = \frac{F \cdot (V - F_{\text{sat}})}{K_{\text{sat}} - V}
\]

Deoxy-hemoglobin and MRI Signal

The sensitivity of the MRI signal to changes in oxygenation stems from the changes in venous deoxy-hemoglobin. In a gradient-echo acquisition, the amount of deoxy-hemoglobin is approximately proportional to R$_2^*$ [1].

\[
\frac{dM_{\text{deoxy}}}{dt} = C_{\text{deoxy}} \cdot F_{\text{deoxy}} \cdot F_a \cdot \frac{V}{T} \cdot S \cdot k_1 \cdot \left[1 - q/\eta\right]
\]

MRI Data Acquisition

A two-echo gradient-echo FAIR acquisition was used to obtain simultaneous CBF (8 ms TE) and BOLD (28 ms TE) functional MRI data with temporal resolution of 2 seconds [4]. The data from each echo in both FAIR inversion conditions were linearly interpolated to each TR to subtraction images using CBF images and additional yield BOLD images at each TR. All scans were performed in a 3 Tesla GE scanner.

The stimulation paradigm consisted of a visually cued motor task with stimulation and rest periods of 60 sec each. Region-of-interest vessels were determined from the correlation of the FAIR data with the stimulus waveform. A hypercapnia challenge was also performed in order to calibrate the BOLD signal changes to steady-state changes in blood oxygenation.

CMRO$_2$ Estimation Methods

The goal of this work is to determine the CMRO$_2$ at every point given the CBF and BOLD MRI data. The large number of parameters/unknowns in the model makes it difficult to accurately determine the dynamic changes in CMRO$_2$.

The estimation process consisted of three steps:

Step 1: Determine the steady-state change in CMRO$_2$ using the hypercapnia challenge data [1].

Step 2: Estimate PS and the baseline $C_{\text{baseline}}$, $C_{\text{sat}}$, and $F_{\text{sat}}$ using a constrained simplex search algorithm where the average physiological solution was selected.

Step 3: Dynamic CMRO$_2$ changes were estimated from the average CBF and BOLD MRI data using two approaches:

- Model the CMRO$_2$ changes with selected functions (rectangular, trapezoidal, local field potential) such that the CMRO$_2$ changes are summarized by a small number of parameters.
- Model-less estimation of CMRO$_2$ during the transition periods (determined from the data) whereas the steady-state periods were fitted by the steady-state solution.

Steps 1, 2 and 3 were carried out using the CBF and BOLD MRI functional data with 60 sec stimulation and rest periods.

Model Sensitivity

The model sensitivity to different venous volume behaviors was examined. These out-flow vs. volume characteristics were investigated: histidines (blue), linear (green) and exponential (blue). Histidines: The CBF response is slow compared to CBF. The predicted BOLD response is very similar to the actual responses. Linear: The CBF changes are proportional to CBF. The effect on the BOLD response is to accentuate the transition periods. Exponential: A fast CBF response onset is observed followed by a slow offset. The changes during onset are greatly accentuated.

The differences between various models for CMRO$_2$ were also examined. The following functions for CMRO$_2$ were investigated: rectangular (blue), trapezoidal (red), local field potential (green). Rectangular: A simple model, represented by 3 parameters (width, height and onset), with very fast transition periods. Trapezoidal: Allows for variability in the onset and offset ramps individually. A slower offset causes the BOLD response to return slower to baseline. Local field potential: Perhaps representative of the neuronal response, this function provides a larger increase in both CBF and BOLD during onset. Overall, the difference in the CBF and BOLD responses from these functions are not very significant.

Dynamic CMRO$_2$ estimation

Motor stimulation produced changes in CBF and BOLD of 63.5% and 3.6%, respectively, averaged over the last 10 sec of the rest and stimulation conditions. The average cmrostimation factor M in the motor cortex of the subjects tests was 0.1884.

Step 1: Steady-state changes in CMRO$_2$ were estimated to be 24.5%

Step 2: A likely solution for the parameters PS and the baseline $C_{\text{baseline}}$, $C_{\text{sat}}$, and $F_{\text{sat}}$ was determined to be 64.58 mmHg, 90.0 mmHg, 54.8 mmHg and 50.9 mmHg.

Note that using steady-state models to estimate dynamic changes in CMRO$_2$ suggest that blood oxygen delivery and consumption is instantaneous processes and the dynamics of oxygen consumption are directly related to the changes in blood flow.

Step 3a: CMRO$_2$ was modeled as a rectangular, trapezoidal and local field potential-like function and fit to the CBF and BOLD MRI data (rectangular function results shown).

Although these functional allow for fast changes at stimulation onset and offset, discrepancies are observed in the transition periods of both CBF and BOLD fMRI.

Step 3b: CMRO$_2$ was estimated during the transition periods. A slower CMRO$_2$ evolution was necessary to improve the fit of the CBF response. It is possible that the CMRO$_2$ evolution is relatively slow, however, model and/or data inaccuracies also affects the CMRO$_2$ estimates.

Inaccuracies in the model description of the arterial response is likely to be incorrect. Another possibility is that the FAIR data represents changes in tissue perfusion that do not accurately represent the changes in arterial blood flow.

Conclusions

It may be possible to determine dynamic CMRO$_2$ changes from functional CBF and BOLD MRI data:

- Model-less approaches are necessary in order to estimate the unknown dynamics of the CMRO$_2$ changes.
- Inaccuracies in the model description affect the estimation of CMRO$_2$, since it is likely that these discrepancies are incorrectly captured by the CMRO$_2$ evolution.

A physiological model of the cerebral hemodynamics can be used to expand our knowledge of brain physiology by generating and testing hypotheses, especially for different physiological conditions.

For example, consider these 3 cases: slower CBF response, no CMRO$_2$ response, and no CBF response to evoked stimulation.