

NIRS Brain Studies with a New Hemodynamic Model: Coherent Hemodynamics Spectroscopy and Functional Neuroimaging

Sergio Fantini

*Department of Biomedical Engineering, Tufts University
4 Colby St., Medford, MA 01890, USA
sergio.fantini@tufts.edu*

Abstract: A new hemodynamic model relates tissue hemoglobin concentration to blood volume, flow, and oxygen consumption. It affords a quantitative analysis of hemodynamic oscillations (Coherent Hemodynamics Spectroscopy) and transients in neuroimaging.

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1. Basic approach to the derivation of the new hemodynamic model

Electrical or fluid dynamic equivalent networks have been commonly used to model the cerebral vasculature [1]. These approaches must necessarily introduce a number of approximations to the complex structure of the microvascular cerebral network, and their refinements may result in a large number of model parameters. The model presented here is based on a conceptually new approach that results in a set of equations that relate fNIRS (functional near-infrared spectroscopy) and fMRI (functional magnetic resonance imaging) signals to a set of steady state and dynamic parameters that characterize the cerebral hemodynamics and metabolic rate of oxygen. The detailed description of this hemodynamic model has been reported in [2,3].

The basic idea behind this new model is to conceptually separate the arterial, capillary, and venous vascular compartments in the brain, considering that each individual red blood cell in the blood stream will travel sequentially through these three compartments and that oxygen diffusion from blood to tissue only occurs in the capillary compartment. The two key parameters of this model are the mean blood transit time in the capillaries ($t^{(c)}$) and the rate constant for oxygen diffusion (α), which fully determine the desaturation of hemoglobin in the capillary compartment. In this approach, the complexity of the vascular network architecture and of the blood microcirculation is irrelevant because the only thing that matters is the average time that each red blood cell spends in the capillary compartment. The model quantitatively describes the desaturation of hemoglobin as it flows through the capillary compartment, and determines how such dynamic desaturation is related to changes in the blood flow velocity and the rate of oxygen diffusion. The cerebral microvasculature is treated as a linear time-invariant system whose inputs are the cerebral blood volume (CBV), cerebral blood flow (CBF), and cerebral metabolic rate of oxygen (CMRO₂), and whose outputs are the tissue concentrations of deoxy-hemoglobin (D) and oxy-hemoglobin (O), from which the fMRI BOLD signal can also be derived.

2. Model equations in the time-domain: Functional neuroimaging

In the general case of time-varying physiological signals (such as those measured with fNIRS or fMRI) the hemodynamic model yields the following equations for the time-dependent concentrations of deoxy-hemoglobin [$D(t)$] and oxy-hemoglobin [$O(t)$] in terms of the perturbations in the arterial and venous blood volume [$cbv^{(a)}(t)$ and $cbv^{(v)}(t)$, respectively], and the difference between the perturbations in cerebral blood flow [$cbf(t)$] and cerebral metabolic rate of oxygen [$cmro_2(t)$] [2,3]:

$$\begin{aligned}
 D(t) = & ctHb \left[(1 - S^{(a)})CBV_0^{(a)} + (1 - \langle S^{(c)} \rangle)F^{(c)}CBV_0^{(c)} + (1 - S^{(v)})CBV_0^{(v)} \right] + \\
 & + ctHb \left[(1 - S^{(a)})CBV_0^{(a)}cbv^{(a)}(t) + (1 - S^{(v)})CBV_0^{(v)}cbv^{(v)}(t) \right] + \\
 & - ctHb \left[\frac{\langle S^{(c)} \rangle}{S^{(v)}} (\langle S^{(c)} \rangle - S^{(v)})F^{(c)}CBV_0^{(c)}h_{RC-LP}^{(c)}(t) + (S^{(a)} - S^{(v)})CBV_0^{(v)}h_{G-LP}^{(v)}(t) \right] * [cbf(t) - cmro_2(t)], \quad (1)
 \end{aligned}$$

$$\begin{aligned}
 O(t) = & ctHb \left[S^{(a)}CBV_0^{(a)} + \langle S^{(c)} \rangle F^{(c)}CBV_0^{(c)} + S^{(v)}CBV_0^{(v)} \right] + ctHb \left[S^{(a)}\Delta CBV^{(a)}(t) + S^{(v)}\Delta CBV^{(v)}(t) \right] + \\
 & + ctHb \left[\frac{\langle S^{(c)} \rangle}{S^{(v)}} (\langle S^{(c)} \rangle - S^{(v)})F^{(c)}CBV_0^{(c)}h_{RC-LP}^{(c)}(t) + (S^{(a)} - S^{(v)})CBV_0^{(v)}h_{G-LP}^{(v)}(t) \right] * [cbf(t) - cmro_2(t)], \quad (2)
 \end{aligned}$$

where ctHb is the concentration of hemoglobin in blood, CBV_0 is the baseline blood volume, $F^{(c)}$ is the ratio of capillary to large vessel hematocrit (Fåhræus factor), S is the blood oxygen saturation, α is the rate constant of oxygen diffusion from blood to tissue, and the $*$ operator indicates a convolution product. Superscripts (a) , (c) , (v) indicate the arterial, capillary, and venous compartments, respectively. The low-pass (LP) impulse responses associated with the capillary [$h_{RC-LP}^{(c)}(t)$] and venous [$h_{G-LP}^{(v)}(t)$] compartments are given by [2]:

$$h_{RC-LP}^{(c)}(t) = H(t) \frac{e}{t^{(c)}} e^{-et/t^{(c)}} ; \quad h_{G-LP}^{(v)}(t) = \frac{1}{0.6(t^{(c)}+t^{(v)})} e^{-\pi[t-0.5(t^{(c)}+t^{(v)})]^2/[0.6(t^{(c)}+t^{(v)})]^2} , \quad (3)$$

where $t^{(c)}$ and $t^{(v)}$ are the capillary and venous blood transit times, and $H(t)$ is the Heaviside unit step function [$H(t) = 0$ for $t < 0$; $H(t) = 1$ for $t \geq 0$].

3. Model equations in the frequency-domain: Coherent hemodynamics spectroscopy (CHS)

The general time-dependent equations [Eqs. (1)-(2)] can be expressed in the frequency domain by replacing time-varying quantities with phasors (identified in bold face) defined by the amplitude and phase of the associated oscillations at a frequency ω , and by replacing convolution products with regular products. The frequency-domain equations are [2,3]:

$$\mathbf{D}(\omega) = \text{ctHb} \left[(1 - S^{(a)}) \text{CBV}_0^{(a)} \mathbf{cbv}^{(a)}(\omega) + (1 - S^{(v)}) \text{CBV}_0^{(v)} \mathbf{cbv}^{(v)}(\omega) \right] + \\ - \text{ctHb} \left[\frac{(S^{(c)})}{S^{(v)}} ((S^{(c)}) - S^{(v)}) F^{(c)} \text{CBV}_0^{(c)} \mathcal{H}_{RC-LP}^{(c)}(\omega) + (S^{(a)} - S^{(v)}) \text{CBV}_0^{(v)} \mathcal{H}_{G-LP}^{(v)}(\omega) \right] [\mathbf{cbf}(\omega) - \mathbf{cmro}_2(\omega)] , \quad (4)$$

$$\mathbf{O}(\omega) = \text{ctHb} \left[S^{(a)} \text{CBV}_0^{(a)} \mathbf{cbv}^{(a)}(\omega) + S^{(v)} \text{CBV}_0^{(v)} \mathbf{cbv}^{(v)}(\omega) \right] + \\ + \text{ctHb} \left[\frac{(S^{(c)})}{S^{(v)}} ((S^{(c)}) - S^{(v)}) F^{(c)} \text{CBV}_0^{(c)} \mathcal{H}_{RC-LP}^{(c)}(\omega) + (S^{(a)} - S^{(v)}) \text{CBV}_0^{(v)} \mathcal{H}_{G-LP}^{(v)}(\omega) \right] [\mathbf{cbf}(\omega) - \mathbf{cmro}_2(\omega)] , \quad (5)$$

where $\mathcal{H}_{RC-LP}^{(c)}(\omega)$ and $\mathcal{H}_{G-LP}^{(v)}(\omega)$ are complex transfer functions [given by the Fourier transform of the impulse response functions of Eq. (3)] describing the capillary and venous low-pass (LP) effects. They are [2]:

$$\mathcal{H}_{RC-LP}^{(c)}(\omega) = \frac{1}{1 + i\omega t^{(c)}/e} ; \quad \mathcal{H}_{G-LP}^{(v)}(\omega) = e^{-\frac{\ln 2}{2}[\omega 0.281(t^{(c)}+t^{(v)})]^2} e^{-i\omega 0.5(t^{(c)}+t^{(v)})} . \quad (6)$$

4. Cerebral autoregulation

Cerebral autoregulation is a dynamic process that maintains a stable cerebral blood flow by regulating the vascular resistance in response to variations in perfusion pressure. Since autoregulation can only respond to relatively slow perfusion pressure changes, it may be modeled as a high-pass filter response to perfusion pressure changes. By considering blood volume changes as a surrogate for perfusion pressure changes, cerebral autoregulation may be described by the following relationships in the time domain and frequency domain:

$$\text{cbf}(t) = k h_{HP}^{(\text{AR})}(t) * \text{cbv}(t) , \quad (7)$$

$$\mathbf{cbf}(\omega) = k \mathcal{H}_{HP}^{(\text{AR})}(\omega) \mathbf{cbv}(\omega) , \quad (8)$$

where k is a constant, $\omega_c^{(\text{AR})} = 1/t_c^{(\text{AR})}$ (with $\omega_c^{(\text{AR})}$ and $t_c^{(\text{AR})}$ cutoff frequency and critical time constant for autoregulation), and the high-pass impulse response and transfer function (related by a Fourier transformation) are given by:

$$h_{HP}^{(\text{AR})}(t) = H(t) \left[\delta(t) - \frac{1}{t_c^{(\text{AR})}} e^{-t/t_c^{(\text{AR})}} \right] ; \quad \mathcal{H}_{HP}^{(\text{AR})}(\omega) = \frac{i\omega/\omega_c^{(\text{AR})}}{1 + i\omega/\omega_c^{(\text{AR})}} . \quad (9)$$

A phasor representation of the oscillations of cerebral blood flow (\mathbf{cbf}), cerebral blood volume (\mathbf{cbv}), deoxy-hemoglobin concentration (\mathbf{D}), and oxy-hemoglobin concentration (\mathbf{O}) provides a convenient illustration of their phase relationships. Figure 1 shows such a phasor representation in the presence and in the absence of cerebral autoregulation according to the model presented here.



Fig. 1. Phasor diagrams representing oscillations of blood volume (**cbv**), blood flow (**cbf**), and tissue concentrations of deoxy- (**D**) and oxy-hemoglobin (**O**) at a frequency of 0.15 Hz. In the presence of autoregulation (left) (cutoff frequency: 0.15 Hz), blood flow oscillations lead blood volume oscillations, whereas in the absence of autoregulation (right) they are in phase. Notice the greater phase lag of **D** with respect to **O** in the absence of autoregulation. These phasor diagrams have been computed using typical values for the model parameters [2].

5. Coherent hemodynamics spectroscopy (CHS)

The frequency-domain equations allow for the quantitative analysis of frequency-resolved measurements of the amplitude and phase of cerebral hemodynamic oscillations measured with NIRS. Because of the requirement of a high coherence between the measured hemodynamic oscillations and the driving oscillatory physiological processes (for reliable phase measurements and for the applicability of transfer function analysis on which the hemodynamic model is based), this technique is called coherent hemodynamics spectroscopy (CHS) [2]. Figure 2 shows representative CHS spectra obtained from Eqs. (4) and (5) by using typical values for the model parameters [2]. The frequency of cerebral hemodynamic oscillations may be controlled by inducing them with paced breathing [4,5] or with cyclic inflation-deflation of a pneumatic cuff placed around the subject's thigh [6].

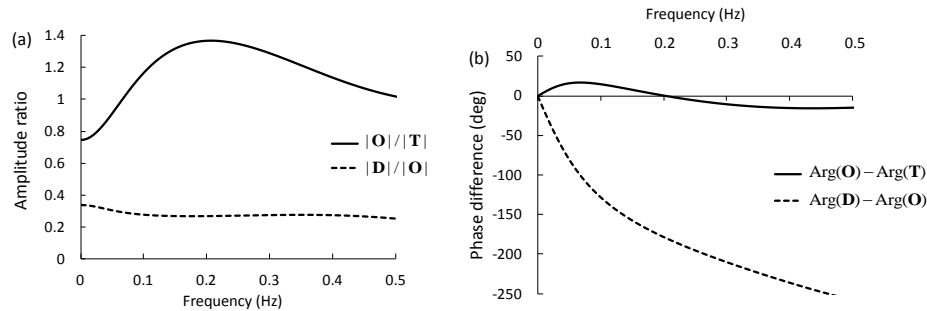


Fig. 2. Representative CHS spectra. (a) Frequency dependence of the amplitude ratio of phasors **O** and **T** (solid line), and **D** and **O** (dashed line). (b) Frequency dependence of the phase difference of phasors **O** and **T** (solid line), and **D** and **O** (dashed line). $T = D + O$ is the total hemoglobin concentration phasor.

6. Conclusion

The new model presented here provides a quantitative framework for the analysis of hemodynamic based neuroimaging methods such as fNIRS and fMRI [4,7]. Furthermore, it can translate coherent hemodynamics spectra such as those of Fig. 2 into a set of physiological parameters related to the cerebral microvascular flow and autoregulation [5,7]. This capability has been demonstrated in the clinical setting of a hemodialysis unit [6].

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7. References

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