Three Dimensional Vascular Anatomical Network Model of Dynamic Oxygen Delivery  
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1. Motivation
We have recently developed a vascular model with a distributed network of branching vessels to explore the spatial point spread function of the hemodynamic response to brain activation. With this distributed network model, we found that blood flow in the surrounding vessels could passively decrease in response to a center arterial dilatation driving greater blood flow increase in the center. The model suggests, however, that this passive response is not sufficient to explain the surrounding negativity observed in our recent experiments in the rat whisker barrel cortex, that active surround vaso-constrictive mechanisms are additionally required.

We are now extending this vascular network model to three dimensional space to more accurately model oxygen advection and diffusion given the connectivity of experimentally measured networks from rodents. This model will guide interpretation of recent experiments measuring the spatial extent of tissue oxygen changes during brain activation, help validate Windkessel model estimates of oxygen consumption, help us understand tissue zones most at risk to reduced oxygen delivery, and help understand oxygen efflux.

We present our present progress on obtaining 3D vascular anatomical networks from rat brains obtained with 2 photon microscopy, the graphing of these networks for the computer model, and implementation of oxygen advection-diffusion on these graphed networks.

2. Windkessel Model Estimates of Oxygen Metabolism
Analogous to a circuit model with oxygen diffusion

- Flow/Volume changes are driven by changes in arteriole resistance
- Oxygen diffusion between central and extra-vascular tissue
- Mitochondrial metabolism drains tissue PO2

We are able to precisely estimate relative CMRO2 change from NIRS/fMRI data and fMRI data alone with unprecedented temporal resolution. It is accurate?

3. Parallel Vascular Network
To explore accuracy of our Windkessel model estimates of oxygen consumption and arteriole dilatation, we are developing a microscopic model of the vascular network based on physically measurable parameters.

The model produces spatio-temporal responses comparable to experimental data. It suggests that passive blood steal does occur, but that active mechanisms are required to observe our observed surround negativity.

We still need to properly handle 3D diffusion of oxygen. Spatio-temporal response to local dilatation

4. 3D Advection Diffusion of Oxygen

\[ \frac{\partial C}{\partial t} = \nabla \cdot (\nabla C + \nabla^2 C - G(C)) \]

- \( C \) = free oxygen concentration
- \( v \) = blood velocity
- \( D \) = oxygen diffusion coefficient
- \( G \) = cerebral metabolic rate of oxygen
- \( c_{Hb} \) = hemoglobin concentration
- \( S_a \) = hemoglobin oxygen saturation

Solve using finite difference iteratively time stepping over advection terms (multiple small time steps) and diffusion/consumption terms (larger time step) [1].

Simulation Parameters
- \( \alpha = 1.0 \text{ mm/s} \)
- \( D = 2.4 \times 10^{-9} \text{ m}^2/\text{s} \)
- \( \rho = 10 \times 10^{-6} \text{ g} \)
- \( H = 0.40 \text{ [1]} \)

Volume is 100 x 100 x 100 mm3

5. Building the 3D VAN Model

- Particles launched and tracked from a seed point. Movement based on local intensity variation. Summed tracks serve to segment vessels.
- Tracks are centered in Imaris and diameters estimated.
- Tracks launched from multiple seed points. Prune by selecting track that connect with other seed points.
- Algorithms automatically remove small loops. Then we manually correct a small number of vessel connections.

6. Summary
Advection-Diffusion of oxygen applied to a 3D single vessel and 3D vascular network. We observe a biphasic PO2 response 10 µm from vessel when CMRO2 and flow increase simultaneously. If CMRO2 precedes flow then biphasic response seen in vessel. We have a semi-automatic method to graph vascular network and can solve velocities within network. Our preliminary analysis of vessel diameter to vessel suggests that oxygen needs to diffuse no more than 25 µm from a vessel. More to come on characteristics of oxygen delivery and validation of Windkessel estimates by using microscopic network to simulate OIS and fMRI signals thus giving ground truth for Windkessel analysis.