MODELING THE SPATIAL HAEMODYNAMIC RESPONSE ON PROPAGATING NEURONAL ACTIVITY PATTERNS

Valery Pilipchuk (1), Chin-An Tan (1), and Stefan Posse (2)

(1) Department of Mechanical Engineering
(2) Department of Psychiatry and Behavioral Neurosciences
Wayne State University
Detroit, MI

INTRODUCTION

In this work, a neurovascular network approach is employed to mathematically model the temporal and spatial behavior of coupled neuronal spiking activity and the corresponding blood/oxygen delivery. Neuronal spiking and the vascular response represent processes of different time scales: few milliseconds and few seconds, respectively. Their spatial network architectures and biophysics (-mechanics) are also quite different so that different physical and mathematical tools are required to study both systems (for example, see the related articles in the book [1].) However, theoretical significance and practical importance of a uniform approach to this complex problem are motivated by the necessity to understand how the human brain functions and biomedical interpretations of functional neuroimaging diagrams obtained by functional MR imaging (fMRI) and positron emission tomography (PET). Although several substances have been identified that mediate neuronal activity-induced increases in cerebral blood flow [2,3], the mechanisms that regulate the time course and the spatial extent of the vascular response to neuronal activity remain insufficiently characterized. Recent studies using optical imaging suggest that the vascular response spreads spatially within seconds after initiation of neuronal activation [4]. Our own fMRI studies and those of other groups indicate that both the amplitude and the time course of the haemodynamic response function are strongly dependent on global cerebral blood flow [5]. These findings have major implications for event-related studies of brain function and contribute to the growing evidence that there are fundamental physiological limits to the spatial and temporal resolution of functional neuroimaging techniques. It is of interest to estimate these limits using neurovascular modeling. Several recent studies have attempted to describe the spatial and temporal characteristics of the hemodynamic response using physiologically based models of blood vessel dynamics [6,7]. Other groups and we have modeled the effect of blood oxygenation changes in venules on the fMRI signal [8,9]. However, the link between spatial-temporal activity patterns of the neuronal network and the reaction of the vascular network is missing, since the majority of works done in this area follow the so-called 'mean field' approach. Note that energetic aspects of signaling in the grey matter of the brain have been extensively investigated in recent studies based on anatomic and physiologic data regardless neural or vascular network architectures [10,11]. By contrast, modeling of spiking activity of biological neurons and their networks is well established, but does not describe the energy delivery mechanisms (for introduction and references, see books [1,12-14]). To bridge this gap, we consider both networks as coupled dynamical systems. The mechanism of thermodynamic coupling between the networks constitutes an essential part of the modeling. A novel phenomenological approach is based on energetic considerations in order to ease the modeling, which is inherently complex due to numerous regulatory mechanisms (biochemical transformations and neuronal feedback) involved.

MODELING AND SAMPLE RESULTS

In this research, the neuronal component of the model is represented by a two-dimensional array of the FitzHugh-Nagumo neurons coupled locally via diffusion [15]. A single FitzHugh-Nagumo neuron of the network is described by one nonlinear and one linear differential equations as follows

$$\dot{V}(t) = -[V^3(t)/3 - V(t) + W(t)] + I(t)$$
$$\dot{W}(t) = \varepsilon[V(t) + a] \qquad (1)$$

where $V(t)$ is a membrane potential, $W(t)$ is a slow auxiliary variable responsible for a spiking behavior, ε is a parameter of the temporal scale of recovery processes, and a is a positive parameter such that when $a>1$ the system has a single fixed point, whereas a limit cycle occurs when $a<1$. The excitation $I(t)$ is due to the coupling between the nearest neurons and possibly external stimulus. The diffusion coupling used in reference [15] is generalized by randomizing the strength of interaction between the neurons around the couples. At small ε and $a>1$, the temporal shape of spikes resembles that of the biological neurons. Also, such a simplified neuron still gives a good description of the refractory period of biological neurons. The

dynamics of the vascular component is governed by diffusion in a discrete two-dimensional lattice. The activation function of the vascular lattice is assumed to depend monotonically on the power of spiking in such a fashion that the diffusion is intensified as the power increases. The power can be estimated by using the mechanical or electrical analogues of the system (1). The oxygen concentration is chosen as a basic state variable of the vascular network. The latter is due to the presumably linear coupling between cerebral blood flow and oxygen consumption in activated human cortex [16]. In our simulations, neural and vascular components are represented by the quadratic arrays of 476 neurons/elements. The cyclic boundary conditions are formulated for the boundaries of both arrays. This makes the two-dimensional network surfaces topologically toroidal. However, from the physical point of view, such a formulation describes the spatially periodic states in infinite two-dimensional arrays. In our numerical simulations, the neural network is subjected to a rapidly oscillating periodic square-well current. Such an external stimulus is acting synchronously on four and six nearest neurons in two spatially separated areas. (Location of the stimulated neurons can be identified from the diagrams for the oxygen flow represented in Figure 1.) The figure shows two different snapshots of the maps of neuronal and haemodynamic activities.

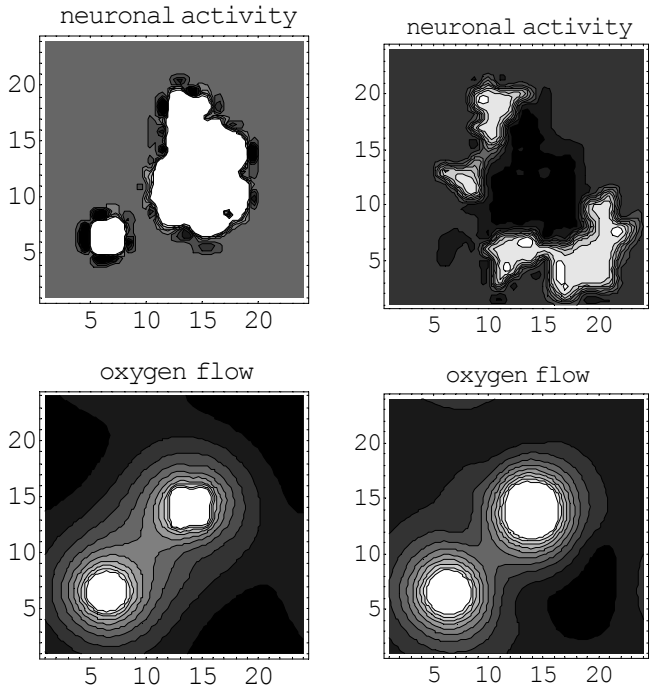

Figure 1. Maps of neuronal activity and the corresponding oxygen flow' levels at two consecutive sampling times

The time period between the two states is approximately equal to that of a single neuronal spike. Due to a large spatial resolution, the neuronal activity patterns are propagating very fast whereas distribution of the oxygen flow remains practically unchanged. As a result, the map of the oxygen flow may not reflect the local temporal behavior of neuronal activity. Moreover, the computer simulations show that, if meeting each other, the patterns of neuronal activity annihilate. A possible explanation of this phenomenon is that a front of activity cannot penetrate into the refractory zone behind another front. Note that self-supported propagating waves in active (self excited) distributed structures are known in the physical literature as 'autowaves.' In neurodynamic studies, patterns of neuronal activity in large-scale inhibitory neuronal networks were described in the article [17] based on 200 Hodgkin-Huxley neurons, however, the spatial haemodynamic was not considered.

The neurovascular system modeling based on the Hodgkin-Huxley neurons is currently being tested.

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