MODELING THE NON-NEURONAL CONTRIBUTION TO THE BLOOD OXYGENATION LEVEL DEPENDENT FMRI SIGNAL OSCILLATIONS

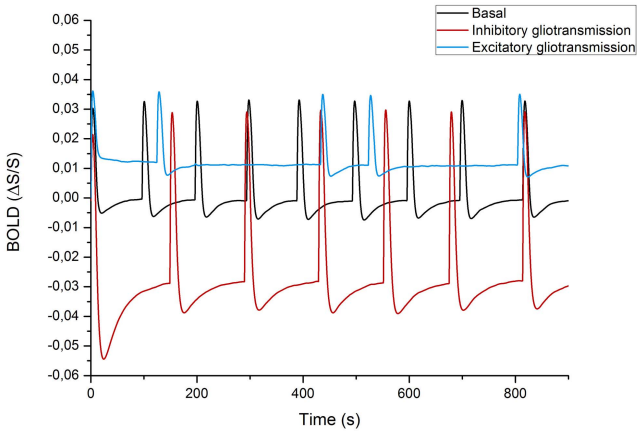
M. DiNuzzo[1], F. Giove[1,2], and B. Maraviglia[1,2]
[1]Physics, Sapienza University of Rome, Rome, RM, Italy, [2]MARBILab, "Enrico Fermi" Center, Rome, RM, Italy

Purpose

Resting oscillatory patterns in cortical activity are a common feature of the human brain. It has been suggested that the temporal coordination of regional activity across the cortex emerges from the physical architecture of neuronal networks. However, it is now recognized that slow periodic changes in cortical activity can originate by both network- and metabolism-related mechanisms [1]. Specifically, the metabolic state of neuronal and non-neuronal (astroglial) cells is thought to have an important role in the balance of recurrent excitation and local inhibition, much likely via astrocytic intracellular calcium (Ca^{2+})-mediated gliotransmission, which can also occur spontaneously [2]. Astrocytes are primary intermediary in synaptic transmission-mediated functional hyperaemia. Since the hemodynamic changes induced by synaptic activity form the basis of functional magnetic resonance imaging (fMRI), it is important to examine how the blood oxygenation level dependent (BOLD) signal is influenced by astrocyte-neuron interactions and spontaneous astrocytic activation. The aim of the present study is to examine theoretically the contribution of astrocytes in the generation of the fMRI signal changes in the absence of focal neuronal stimulations.

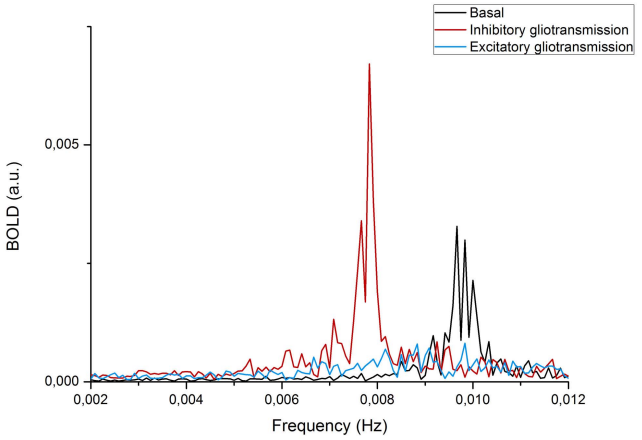
Methods

We integrated previous kinetic models of functional brain metabolism and intracellular calcium (Ca^{2+}) dynamics in astrocytes and calcium-dependent astrocytic transmitter release [3,4,5]. Briefly, neuronal electrical activity increases energy consumption as adenosine triphosphate (ATP) hydrolysis by the Na+/K+-ATPase (sodium pump) in both neurons and astrocytes. Furthermore, cell stimulation enhance Ca^{2+} entry into astrocytes resulting in inhibitory and excitatory gliotransmission, which in turn exerts feedback on the neuronal element. The overall energy demand activates cellular metabolism (glycolysis and respiration) as well as vascular response via increased cerebral blood flow (CBF).



Results

We found that the impact of Ca^{2+} dynamics on cerebral metabolism is high enough to evoke detectable spontaneous BOLD fluctuations. In the presence of a basal level of neuronal activity, these oscillations are in the low-frequency range (around 0.01 Hz). Simulations (200 mins) show that inhibitory gliotransmission induces a decrease in the frequency of BOLD oscillations. Interestingly, excitatory gliotransmission coupled to increased neuronal activation is characterized by desynchronization of the stimulation/metabolism BOLD slow-wave.



Discussion

Recent evidences suggest that the cell metabolic state exert an indirect control over the intrinsic network responsivity of the brain [1]. Possible physiological roles for the spontaneous oscillations in cerebral activity includes the maintenance of functional connectivity among different cortical areas, and the preservation of the excitatory tone in relation to external (i.e. thalamic) input [2], consistent with the recently observed reduction in BOLD oscillation frequency during eyes-open condition with respect to eyes-closed condition [6]. While the elucidation of the details underlying these aspects of the partnership between neurons and glia requires further experimental research, this modeling work indicates that oscillations in brain electrical, metabolic and vascular activity, as revealed by the BOLD-fMRI signal, can be qualitatively and quantitatively explained by calcium-mediated coupling between neuroglial activation and metabolism.

References

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