Neural Networks 49 (2014) 1–10

Contents lists available at ScienceDirect

Neural Networks

journal homepage: www.elsevier.com/locate/neunet

Modeling the BOLD correlates of competitive neural dynamics

James Bonaiuto [a,b,c,*], Michael A. Arbib [b,c,d]

[a] Division of Biology, California Institute of Technology, Pasadena, CA 91225, USA
[b] Neuroscience Program, University of Southern California, Los Angeles, CA 90089-2520, USA
[c] USC Brain Project, University of Southern California, Los Angeles, CA 90089-2520, USA
[d] Computer Science Department, University of Southern California, Los Angeles, CA 90089-2520, USA

ARTICLE INFO

Article history:
Received 13 June 2013
Received in revised form 2 September 2013
Accepted 4 September 2013

Keywords:
Neural network model
FMRI, decision-making
Winner-take-all
Synthetic brain imaging

ABSTRACT

Winner-take-all models are commonly used to model decision-making tasks where one outcome must be selected from several competing options. Related random walk and diffusion models have been used to explain such processes and apply them to psychometric and neurophysiological data. Recent model-based fMRI studies have sought to find the neural correlates of decision-making processes. However, due to the fact that hemodynamic responses likely reflect synaptic rather than spiking activity, the expected BOLD signature of winner-take-all circuits is not clear. A powerful way to integrate data from neurophysiology and brain imaging is by developing biologically plausible neural network models constrained and testable by neural and behavioral data, and then using *Synthetic Brain Imaging* — transforming the output of simulations with the model to make predictions testable against neuroimaging data. We developed a biologically realistic spiking winner-take-all model comprised of coupled excitatory and inhibitory neural populations. We varied the difficulty of a decision-making task by adjusting the contrast, or relative strength of inputs representing two response options. Synthetic brain imaging was used to estimate the BOLD response of the model and analyze its peak as a function of input contrast. We performed a parameter space analysis to determine values for which the model performs the task accurately, and given accurate performance, the distribution of the input contrast–BOLD response relationship. This underscores the need for models grounded in neurophysiological data for brain imaging analyses which attempt to localize the neural correlates of cognitive processes based on predicted BOLD responses.

1. Introduction

A continuing challenge for systems and cognitive neuroscience is to integrate data from animal neurophysiology and human brain imaging. While neurophysiological studies provide detailed information on the properties of a sample of neurons in a single region, brain imaging data reflects global brain activity resulting from neural population activation. Although these two sources of information are often used in developing *conceptual* models of cognitive processes, more refined analysis requires an explicit account of the coupling between these levels of data. One method that has begun to shed light on this coupling is synthetic brain imaging. This technique uses computational models of the brain regions in question based on neurophysiological data to generate simulated neuroimaging signals such as regional cerebral blood flow (rCBF) and blood oxygen level-dependent (BOLD) responses. These can then be compared with experimental neuroimaging data in order to reinterpret imaging data in computational terms and to validate and update models of macaque circuitry.

Winner-take-all (WTA) or race models are frequently used to account for psychophysical data in decision-making tasks. Given multiple inputs, these models converge on an output corresponding to the strongest input. This makes them well suited for decision-making tasks where evidence for multiple alternatives is integrated and one must be selected. Many types of WTA models have been proposed. Neural field models implement WTA dynamics through the use of recurrent excitation and surround inhibition (Amari, 1977). Leaky accumulator models assume that evidence for different response options is integrated over time with some decay factor and a decision is made once one accumulator reaches a threshold (Usher & McClelland, 2001). Similar models have been used to interpret data from perceptual decision making tasks such as the random dot motion direction discrimination (RDMDD) task (Palmer, Huk, & Shadlen, 2005). In this task the subject observes a field of moving dots and must decide in which direction (right or left) the majority of dots are moving, and then make a saccade to the right or left target stimulus to indicate their choice. In different conditions the percentage of dots moving in the same direction, or

* Corresponding author at: Division of Biology, California Institute of Technology, Pasadena, CA 91225, USA. Tel.: +1 6263955851.
E-mail address: bonaiuto@caltech.edu (J. Bonaiuto).

0893-6080/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neunet.2013.09.001

coherence, is varied from 0% to 100%. Response time and accuracy vary predictably as a function of coherence (Palmer et al., 2005), allowing it to serve as an indication of task difficulty. In this paper, we perform synthetic brain imaging on a neural WTA network in order to determine the likelihood that such a model would exhibit a particular relationship between coherence and peak BOLD response.

The generic structure of a synthetic brain imaging model involves coupled neural and synaptic models that are grouped into virtual voxels or larger aggregates. The output of each synapse is summed and input to a model of neurovascular coupling, which then feeds into a vascular model to generate simulated rCBF or BOLD responses. The choice of neural and synaptic model depends on the data that the overall model is intended to address. Early synthetic brain imaging approaches used simple firing rate neural models (Arbib, Bischoff, Fagg, & Grafton, 1995) while later models used mean field approximations (Corchs & Deco, 2002, 2004), leaky integrate-and-fire models (Deco, Rolls, & Horwitz, 2004), and compartmental models (Riera, Wan, Jimenez, & Kawashima, 2006). A suggestion of the earliest synthetic brain imaging study (Arbib et al., 1995) which was used by later approaches (Riera et al., 2006; Tagamets & Horwitz, 1998) was that the hemodynamic response reflected synaptic activity rather than the spiking output of a region. This is in agreement with recent studies in monkeys and rats that suggest that the BOLD response reflects synaptic activity in both pyramidal cells and interneurons (Cauli et al., 2004; Goense & Logothetis, 2008; Pelled et al., 2009). Our model of synthetic brain imaging therefore uses integrated synaptic activity in pyramidal cells and interneurons to generate the blood flow inducing signal. We also tested the effect of using only integrated excitatory synaptic activity, but the results were not significantly different and we therefore do not report on these simulations here.

1.1. Neural and synaptic models

Synaptic models in previous approaches have ranged from the absolute values of connection weights multiplied by presynaptic firing rate (Arbib et al., 1995; Tagamets & Horwitz, 1998) to simple models of synaptic conductances for basic receptor types (AMPA, NMDA, $GABA_A$, $GABA_B$) (Deco et al., 2004). Given the assumption that activity-driven increase in blood flow is triggered by synaptic activity, models that generate simulated BOLD responses should incorporate synapses with, to the extent that data permits, realistic conductance amplitudes and time courses. The recent rise of fMRI on awake, behaving monkeys (Kagan, Wilke, & Andersen, 2009; Nelissen, Luppino, Vanduffel, Rizzolatti, & Orban, 2005) provides a unique opportunity to calibrate models using synthetic brain imaging since both neurophysiological and hemodynamic data are available. Several studies have performed fMRI on monkeys while administering neuropharmacological drugs such as muscimol, a GABA agonist (Wilke, Kagan, & Andersen, 2009, 2010). These conditions can be directly simulated by synaptic models that allow the conductance of a particular synapse type to be altered.

In this paper we will apply synthetic brain imaging to networks which employ conductance-based synapse models for AMPA, NMDA, $GABA_A$, and $GABA_B$ synapse types. We sum the synaptic currents of each type (AMPA, NMDA, $GABA_A$, and $GABA_B$) and input the total synaptic current into the adaptive exponential leaky integrate-and-fire (LIF) neural model (Brette & Gerstner, 2005). Neurons are grouped into excitatory and inhibitory populations with projections within and between populations.

1.2. Neurovascular coupling

Early approaches to modeling the neurovascular coupling mechanism focused on the metabolic basis for the BOLD signal (Jueptner & Weiller, 1995). Based on the reasoning that increased synaptic activity resulted in increased neural metabolism with a consequent increase in local blood flow, these models integrated the total synaptic activity in a modeled region in order to compute a qualitative measure of rCBF (Arbib et al., 1995; Tagamets & Horwitz, 1998). In order to compute synaptic activity in a voxel or volume, $p(t)$, these models summed the product of each neuron's input with the absolute value of its connection weight (to include the effects of inhibitory synapses on rCBF). Similarly, later models used the sum of the absolute value of synaptic currents (Deco et al., 2004). However this may not be an appropriate measure of synaptic activity since each synaptic current goes to zero as the membrane potential approaches its associated reversal potential. Therefore, Izhikevich and Edelman (2008) use the sum of synaptic conductances:

$$p(t) = \sum_m \left(g^m_{\mathrm{AMPA}}(t) + g^m_{\mathrm{NMDA}}(t) + g^m_{\mathrm{GABAa}}(t) + g^m_{\mathrm{GABAb}}(t)\right) \quad (1)$$

where $g^m_n(t)$ is the synaptic conductance of receptor type n in neuron m at time t. More detailed studies have modeled neural metabolism, including glucose and oxygen (Sotero, Trujillo-Barreto, Jimenez, Carbonell, & Rodriguez-Rojas, 2009) and ATP consumption (Aubert, Pellerin, Magistretti, & Costalat, 2007), however these studies did not involve networks of neurons. To date, no studies have compared how sensitive the overall rCBF or BOLD predictions are to these alternatives.

The output of the neurovascular coupling module is a blood flow-inducing signal, l, that serves as the input signal for the vascular model. Many early synthetic brain imaging studies simply used the synaptic activity measure p. However it is known that synaptic activity does not directly drive changes in blood flow, but several mechanisms coexist to regulate blood flow in response to neural activity including the neuron–astrocyte pathway (Koehler, Gebremedhin, & Harder, 2006), vasomotor GABAergic interneurons (Cauli et al., 2004), and nitric oxide (NO) diffusion (Metea & Newman, 2006). It is therefore becoming increasingly popular to use a generic blood flow-inducing signal that subsumes these different mechanisms as input to a vascular model, as suggested by Friston, Mechelli, Turner, and Price (2000). We use a modified version of Riera et al.'s (2006) formulation of this signal that normalizes the synaptic activity signal to account for differences in the number of neurons in the model region compared to the actual brain region (see Section 2).

Poznanski and Riera (2006) review synthetic brain imaging approaches and argue for the need to model networks of astrocytes connected via gap-junctions and connected to the vascular system. While we agree in principle, the data needed to construct models of integrated neurons, glia and blood supply is not available. Instead, our primary concern is to base our predictions of imaging results on models of neural circuitry underlying some range of human behavior which make contact with related data from animal neurophysiology on the activity of single neurons. Moreover, it is possible to gain significant insight into the large scale organization of the brain by modeling the neural networks alone, and at a coarser grain, if the model is constrained by enough experimental data. Synthetic brain imaging (Arbib, Fagg, & Grafton, 2003) on the FARS model of primate control of grasping (Fagg & Arbib, 1998) predicted the influence of PFC on the anterior intraparietal area AIP ten years before it was verified anatomically (Borra et al., 2007) and functionally (Baumann, Fluet, & Scherberger, 2009).

1.3. Vascular signal generation

The first synthetic brain imaging approaches (Arbib et al., 1995; Tagamets & Horwitz, 1998) were applied to PET data since it measures rCBF and therefore does not include some of the nonlinearities of the BOLD signal which also involves changes in blood