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A stochastic mechanism for signal propagation in the brain: Force of rapid random fluctuations in membrane potentials of individual neurons

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HIGHLIGHTS

- We propose a stochastic differential equation (SDE) model as a framework for signal propagation in the brain, based on leaky integrate-and-fire equations for individual neurons.
- Using the proposed SDE model, we give a general characterization of rapid random fluctuations (RRF) in membrane potentials of individual neurons.
- By the SDE model and the characterization of RRF, we provide analytic evidence for the existence of a force behind signal propagation in the brain. Here, Q2 the force—an analogue of Casimir force—is caused by RRF in membrane potentials of individual neurons with a synaptic delay.

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ABSTRACT

There are two functionally important factors in signal propagation in a brain structural network: the very first synaptic delay–a time delay about 1 ms–from the moment when signals originate to the moment when observation on the signal propagation can begin; and rapid random fluctuations in membrane potentials of every individual neuron in the network at a timescale of microseconds. We provide a stochastic analysis of signal propagation in a general setting. The analysis shows that the two factors together result in a stochastic mechanism for the signal propagation as described below. A brain structural network is not a rigid circuit rather a very flexible framework that guides signals to propagate but does not guarantee success of the signal propagation. In such a framework, with the very first synaptic delay, rapid random fluctuations in every individual neuron in the network cause an "alter-and-concentrate effect" that almost surely forces signals to successfully propagate. By the stochastic mechanism we provide analytic evidence for the existence of a force behind signal propagation in a brain structural network caused by rapid random fluctuations in every individual neuron in the network at a timescale of microseconds with a time delay of 1 ms.

1. Introduction

Many advances have been made in the study of the brain connectivity. Nonetheless, a major open question in neuroscience is to understand how a vast repertoire of brain functional networks can arise from a fixed brain structural network. The reader is referred to Park and Friston (2013) for a recent review where the authors call for theoretical models of neuronal information processing that underlies cognition. Search for such a model is extremely challenging. Cognitive functions require signal propagation in a brain structural network. Here, signals are understood as propagating in a brain structural network where the nodes are neurons, each of which has connections from and to presynaptic and postsynaptic neurons, respectively. The difficulty in the study of signal propagation in a brain structural network has been to explain how the signal propagation can be stable (see Vogels et al., 2005, pp. 368–371). Signal propagation in a brain structural network can in principle be observed by monitoring membrane potentials of every individual neuron in the network. Signals propagate via spike trains which are physiologically limited to a timescale of 10^{-3} s. The dynamics of the membrane potential of an individual neuron is characterized by a leaky integrate-and-fire equation. Thus, signal propagation in a brain structural network has been studied, using leaky integrate-and-fire equations at a timescale of 10^{-3} s; and the

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focus of inquiry has been on network structures that ensure stable signal propagation.

We take a different approach to study signal propagation in a brain structural network, not focusing on network structures. It was inspired by the idea that neuronal information processing is stochastic. The reader is referred to McDonnell and Abbott (2009) and Friston (2010) for detailed discussions of the idea. We begin with a stochastic differential equation (SDE) model, i.e., we model signal propagation in a brain structural network by stochastic process. Since every single trial of signal propagation in a brain structural network counts, we use a strong solution of SDE to describe what may be observed in a single trial. As it turns out, signal propagation in a brain structural network in repeated trials may be explained using weak solutions of SDE. The reader is referred to Karatzas and Shreve (1991) for a detailed discussion of strong and weak solutions of SDE and how these solutions are models that follow the principle of causality for dynamic systems. Our SDE model is based on studies in neuroscience. The irregular openings and closings of ionic channels underlie all neural activities (see, e.g., Glass, 2001). The rate constants of these openings and closings can be up to 10^{-6} s; see Schröder et al. (2005) and Schröder and Harlfinger (2007). In a brain structural network, rapid random fluctuations (RRF) in membrane potentials of every individual neuron are therefore present at a timescale of 10^{-6} s. Our SDE model of signal propagation in a brain structural network is built by simply adding RRF in every individual neuron in a brain structural network to the leaky integrate-and-fire equations for the individual neurons in the network.

Using the SDE model, we formulate a general characterization of RRF in every individual neuron in a brain structural network. Also, regarding signal propagation in a brain structural network as activity over the entire network, we formulate a general characterization of the stability of signal propagation in a brain structural network as follows: In a single trial, observed values of membrane potentials of every individual neuron in the network are close to their expected values (expectations). By the two characterizations, we analyze signal propagation in a brain structural network without specifications of network structures, although, as shown in our analysis, the structures are indeed critical. In what follows, we use the term "the underlying synaptic connection" for the network structure in a brain structural network through which signals propagate. A key step in our analysis is to take the very first synaptic delay into account. Here the term "the very first synaptic delay" means a time delay about 1 ms from the moment when signals originate to the moment when the propagation of the signals starts emerging from membrane potentials of neurons. An actual synaptic delay typically is in the range [0.5, 0.75] ms with the rest being spread in declining fashion to 4 ms (Katz and Miledi, 1965). However, we may count the very first synaptic delay as follows. No matter how long an actual synaptic delay is, always wait for 1 ms and then let observation of signal propagation in a brain structural network begin. (Such a time delay in the observation is acceptable in experiments in neuroscience.)

We analyze signal propagation in a brain structural network as integration of activities at two spatiotemporal scales. Globally, at a large spatiotemporal scale, signals propagate in the network at a timescale of 10^{-3} s. Locally, at a small spatiotemporal scale, RRF in each individual neuron in the network are present at a timescale of 10^{-6} s. The gap between the two timescales can be characterized as 10^{-3}–10^{-6} s $= (10^3)$. Crucially, the gap creates a lag as the very first synaptic delay takes 10^{-3} s$=(10^3)\times 10^{-6}$ s. Our analysis shows that by the lag, i.e., with the very first synaptic delay, RRF in every individual neuron can cause an "alter-and-concentrate effect" that almost surely forces signals to successfully propagate under a very flexible support provided by the underlying synaptic connection. The flexibility can be described as follows. With probability that virtually can take any value in $(0, 1]$, the underlying synaptic connection ensures observed values of membrane potentials of each individual neuron to be close their expectations. A key method in our analysis is applying a fundamental result by Talagrand (1995) in concentration of measure (Ledoux, 2001) to show how signal propagation in a brain structural network is stochastic and yet stable in general.

Clinical study (Kuiken et al., 2007) and experimental research (Suminski et al., 2010) have demonstrated that neural motor control can be enhanced by time-delayed sensory feedback. Milton (2011), for the first time, proposed a theoretical framework of how interplay between the internal noise and time delay–modeled by delayed random walk–can enhance neural motor control; and the author raised a question: "has the nervous system learned through evolution to take advantage of time delays in some, as yet to be discovered, manner?" The results of this paper show that with the very first synaptic delay, RRF in every individual neuron in a brain structural network cause a force behind signal propagation in the network. Random fluctuations may cause forces, which was first discovered in quantum physics (Casimir, 1948). Recently, it was discovered that random fluctuations of a classical rather than a quantum nature may also cause forces (see Balibar, 2008). The brain's dark energy (Raichle, 2006)–a considerable portion of the energy consumed by the brain which was found for functions unaccounted for–may be the physical evidence for the force shown in this paper.

2. Methods

2.1. An SDE model for signal propagation in a brain structural network

We consider a brain structural network containing n (about 10^{12}) neurons. Each neuron is labeled by $(i), i = 1, \ldots, n$. Let $X_t = (x_t^{(1)} \ldots x_t^{(i)} \ldots x_t^{(n)})$ represent membrane potentials of the n neurons over time t. Each $x_t^{(i)}$, a mathematical function of time t, represents membrane potentials of neuron (i) over time t. A group of signals to propagate in the brain structural network is given. The signal propagation is observed by monitoring $(x_t^{(1)} \ldots x_t^{(i)} \ldots x_t^{(n)})$ at a timescale with τ being the unit. The signals originate at the same time $t=0$ and have the same length $L\tau \cdot N\tau$ denotes the very first synaptic delay. The duration of observing the signal propagation is $t \in [0, (\ell N + L)\tau]$. Nine parameters, including n, τ, L, N and ℓ, used in this paper are explain in Section 3.2 when the parameters are used to present the results.

Signal propagation in a brain structural network can in principle be observed by monitoring membrane potentials of each individual neuron in the network over time, which can be mathematically expressed as follows. An ordinary differential equation (ODE)

$$dX_t = f(t, X_t)dt, \quad t \in [0, (\ell N + L)\tau], \tag{1}$$

is a master equation for signal propagation in a brain structural network. An ODE (1) can be written as

$$\begin{pmatrix} dx_t^{(1)} \\ dx_t^{(2)} \\ \vdots \\ dx_t^{(n)} \end{pmatrix} = \begin{pmatrix} f_1 \\ f_2 \\ \vdots \\ f_n \end{pmatrix} dt, \tag{2}$$

where

$$dx_t^{(i)} = f_i(t, x_t^{(1)}, \ldots, x_t^{(n)})dt \tag{3}$$

is the general form of a leaky integrate-and-fire equation for neuron (i) for each $1 \le i \le n$, and $f = (f_1 \ldots f_i \ldots f_n)^T$ is a deterministic

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