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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 a stochastic differential equation model, we provide analytic evidence for the existence of a force behind signal propagation in the brain.

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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.

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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

mathematical function that characterizes the underlying synaptic connection of a brain structural network. By the existence and uniqueness theorem for ODE, f is uniquely determined by $f_i, i=1,\ldots,n$, in Eq. (3). The above ODE model has been applied in studies of signal propagation in a brain structural network; see Vogels and Abbott (2005, 2009). We notice that in these studies, a brain structural network is generated in a random way, and leaky integrate-and-fire equations are used to express that activity in a brain structural network *in vivo* is generated through a dynamic balance of excitations and inhibitions received by every individual neuron in the network as reported in Shu et al. (2003) and Haider et al. (2006). These studies showed that signal propagation in a brain structural network can be studied without knowing details of the network structure.

We propose an SDE model for signal propagation in a brain structural network by adding a term $\sigma(t,X_t)dB_t$ to ODE (1):

$$dX_t = f(t,X_t)dt + \sigma(t,X_t)dB_t, \quad t\in[0,(\ell N+L)\tau], \tag{4}$$

where $\sigma(t,X_t)dB_t$ is to represent RRF in every individual neuron in a brain structural network. Eq. (4) is called Itô equation. In general, both the drift coefficient f and the diffusion coefficient σ in Itô equation are stochastic processes. In this paper the drift coefficient f is a deterministic mathematical function as f is inherited from ODE (1). Continuous Markov processes in applications–for example, Markov processes with their transition probability density functions characterized by the Fokker–Planck equation also termed as the Kolmogorov forward equation used in physics and chemistry (Van Kampen, 2007)–can be constructed by using Itô equation; see Stroock (2003). (In other words, such a Markov process is the solution of an Itô equation.) An SDE (4) can be written as

$$\begin{pmatrix} dx_t^{(1)} \\ dx_t^{(2)} \\ \vdots \\ dx_t^{(n)} \end{pmatrix} = \begin{pmatrix} f_1 \\ f_2 \\ \vdots \\ f_n \end{pmatrix} dt + \begin{pmatrix} \sigma_{1,1} & \sigma_{1,2} & \cdots & \sigma_{1,\alpha} \\ \sigma_{2,1} & \sigma_{2,2} & \cdots & \sigma_{2,\alpha} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{n,1} & \sigma_{n,2} & \cdots & \sigma_{n,\alpha} \end{pmatrix} \begin{pmatrix} dB_t^{(1)} \\ dB_t^{(2)} \\ \vdots \\ dB_t^{(\alpha)} \end{pmatrix}, \tag{5}$$

where for $i=1,\ldots,n$,

$$dx_t^{(i)} = f_i(t,x_t^{(1)},\ldots,x_t^{(n)})dt + \sum_{r=1}^{\alpha}\sigma_{i,r}(t,x_t^{(1)},\ldots,x_t^{(n)})dB_t^{(r)}$$

is obtained by adding $\sum_{r=1}^{\alpha}\sigma_{i,r}(t,x_t^{(1)},\ldots,x_t^{(n)})dB_t^{(r)}$ to the leaky integrate-and-fire equation for neuron (i) in Eq. (3). Here, an α-dimensional Brownian motion $\left\{B_t=\left(B_t^{(1)}\ldots B_t^{(r)}\ldots B_t^{(\alpha)}\right)^T : t\in[0,(\ell N+L)\tau]\right\}$ models the source that causes RRF in every individual neuron $(i), i=1,\ldots,n$. The dimension α of the Brownian motion is huge so that as many random factors as necessary, each of which is modeled by a 1-dimensional Brownian motion $B_t^{(r)}$, are taken into account. In this way the source represents random disturbance in synaptic inputs to each individual neuron (i) and in converting the synaptic inputs to membrane potential of each neuron (i). We denote the underlying probability space of an SDE (5) by $(\Omega,\mathcal{F},\mathbb{P})$ where $\mathcal{F}$ is the Brownian filtration generated by the Brownian motion in the SDE (5).

We use strong solution of SDE (5) to model single trial of signal propagation in a brain structural network. As it turns out, signal propagation in a brain structural network in repeated trials can accordingly be explained by using weak solutions of SDE (5) (see Appendix A). Thus, we use SDE (5) as a general model for signal propagation in a brain structural network. Let

$$\left\{X_t=(x_t^{(1)}\ldots x_t^{(i)}\ldots x_t^{(n)}) : t\in[0,(\ell N+L)\tau]\right\} \tag{6}$$

denote strong solution of SDE (5). Stochastic process (6) gives a general description of a single trial of signal propagation in a brain structural network. Observations on signal propagation in a brain structural network are at a timescale of 10^{-6} s with τ being the unit. Accordingly, the discrete version of stochastic process (6),

$$\left\{X_{k\tau}=(x_{k\tau}^{(1)}\ldots x_{k\tau}^{(i)}\ldots x_{k\tau}^{(n)}) : k=0,\ldots,(\ell N+L)\right\}, \tag{7}$$

gives a general description of what may be observed in a single trial of signal propagation in a brain structural network at the timescale with τ being the unit; and for each $i=1,\ldots,n$, the discrete stochastic process

$$\left\{x_{k\tau}^{(i)} : k=0,\ldots,(\ell N+L)\right\}, \tag{8}$$

i.e., the ith projection of stochastic process (7), gives a general description of the dynamics of membrane potential of neuron (i). Accordingly, a sample path in stochastic process (7),

$$\left\{X_{k\tau}(\omega)=(x_{k\tau}^{(1)}(\omega)\ldots x_{k\tau}^{(i)}(\omega)\ldots x_{k\tau}^{(n)}(\omega)) : k=0,\ldots,(\ell N+L)\right\}, \tag{9}$$

$\omega\in\Omega$, specifies what may be observed in a single trial of the signal propagation; and a sample path in stochastic process (8),

$$\left\{x_{k\tau}^{(i)}(\omega) : k=0,\ldots,(\ell N+L)\right\}, \tag{10}$$

specifies what may be observed on membrane potentials of neuron (i) in a single trial.

By using stochastic processes (7) and (8) as well as sample paths (9) and (10), we analyze signal propagation in a brain structural network. The essence of our approach is to analyze what may be observed on membrane potentials of every individual neuron in a brain structural network during signal propagation. Thus we can count the very first delay simply as a time delay in observation, i.e., count the delay in the above stochastic processes. Therefore, we do not need to introduce a delay factor in equations used in this paper.

In what follows, whenever there is no confusion about a brain structural network and signals to propagating in the network being given, we use a short term "the signal propagation" for signal propagation in a brain structural network; and we use a short term "a single trial" for a single trial of the signal propagation. In Section 2.2, using the proposed SDE model, we formulate a general characterization of RRF in individual neurons.

2.2. A general characterization of RRF in individual neurons

Suppose that in a single trial it is observed that signals successfully propagate in a brain structural network, i.e., a stochastic process (6) exhibits a pattern of success of the signal propagation. Although the same pattern may never duplicate in repeated trials, such a pattern validates information transfer by the signal propagation at a timescale of 10^{-3} s. Thus, a pattern of success of the signal propagation has a deterministic aspect at a timescale of 10^{-3} s, which is confirmed by the fact that such a pattern can be characterized by leaky integrate-and-fire equations as expressed by Eq. (2) at a timescale of 10^{-3} s. As far as the information transfer is the concern, RRF in individual neurons at a timescale of 10^{-6} s can be treated as negligible. This indicates that RRF in individual neurons in a certain way go along with the information transfer. In a single trial, for each $1\le i\le n$, the sequence

$$\left\{(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}]) : k=1,\ldots,(\ell N+L)\right\} \tag{11}$$

is determined. It is the sequence of expected increments in membrane potential of neuron (i) which describes the following. In each of the time intervals, $[(k-1)\tau,k\tau], k=1,\ldots,(\ell N+L)$, membrane potential of neuron (i) is expected either to be beyond the threshold to fire or to stay below the threshold not to fire. RRF in neuron (i) cause $\left\{(x_{k\tau}^{(i)}-x_{(k-1)\tau}^{(i)}) : k=1,\ldots,(\ell N+L)\right\}$, a sequence of

random variables corresponding to sequence (11). From a view of probability, sequence (11) gives a special case of stochastic independence where each $(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}])$ is viewed as a random variable taking a fixed value with probability 1. Therefore we may formulate "RRF in neuron (i) in a certain way go along with the information transfer" by claiming that

$$(x_{k\tau}^{(i)}-x_{(k-1)\tau}^{(i)}),\quad k=1,\ldots,(\ell N+L) \text{ are stochastically independent.} \tag{12}$$

Below we argue that independence (12) is a mathematical formulation of the resilience of neuronal membrane under random disturbance at a timescale of 10^{-6} s.

The resilience can be interpreted as membrane of each individual neuron $(i), 1\le i\le n$, having no memory of the random disturbance during the signal propagation. By Eq. (5) we have

$$x_t^{(i)}=x_0^{(i)}+\int_0^t f_i(s,x_s^{(1)},\ldots,x_s^{(n)})\,ds+\sum_{r=1}^{\alpha}\int_0^t \sigma_{i,r}(s,x_s^{(1)},\ldots,x_s^{(n)})dB_s^{(r)},\quad t\in[0,(\ell N+L)\tau]. \tag{13}$$

Eq. (13) describes the dynamics of membrane potential of neuron (i) from time $t=0$ to time $t=(\ell N+L)\tau$. Given a time $t=k\tau, 1\le k\le(\ell N+L)\tau$, taking the random variable $x_{k\tau}^{(i)}$ obtained by Eq. (13) as the initial condition, let us consider

$$x_t^{(i)}=x_{k\tau}^{(i)}+\int_{k\tau}^t f_i(s,x_s^{(1)},\ldots,x_s^{(n)})\,ds+\sum_{r=1}^{\alpha}\int_{k\tau}^t \sigma_{i,r}(s,x_s^{(1)},\ldots,x_s^{(n)})dB_s^{(r)},\quad t\in[k\tau,(\ell N+L)\tau]. \tag{14}$$

By the uniqueness of strong solution of SDE, with probability 1, Eq. (14) describes the same dynamics of membrane potential of neuron (i) from time $t=k\tau$ to time $t=(\ell N+L)\tau$ as Eq. (13) does. Using Eqs. (13) and (14), we show that independence (12) is a formulation of "membrane of each individual neuron $(i), 1\le i\le n$, having no memory of the random disturbance during the signal propagation". In Eqs. (13) and (14), two stochastic processes,

$$\sigma_i[0,(\ell N+L)\tau]=\{(\sigma_{i,1}(s,x_s^{(1)},\ldots,x_s^{(n)})\ldots\sigma_{i,\alpha}(s,x_s^{(1)},\ldots,x_s^{(n)})):\ s\in[0,(\ell N+L)\tau]\}$$

and

$$\sigma_i[k\tau,(\ell N+L)\tau]=\{(\sigma_{i,1}(s,x_s^{(1)},\ldots,x_s^{(n)})\ldots\sigma_{i,\alpha}(s,x_s^{(1)},\ldots,x_s^{(n)})):\ s\in[k\tau,(\ell N+L)\tau]\}$$

describe how membrane of neuron (i) interacts with the Brownian motion

$$\left\{B_t=(B_t^{(1)}\ldots B_t^{(r)}\ldots B_t^{(\alpha)})^T : t\in[0,(\ell N+L)\tau]\right\},$$

which models the source that causes RRF in neuron (i). Recall that the source represents the random disturbance. Thus, "having no memory of the random disturbance" can be formulated as the stochastic process $\sigma_i[k\tau,(\ell N+L)\tau]$ being stochastically independent of $\mathcal{F}_u\in\mathcal{F}$ for $0\le u<k\tau$ where $\mathcal{F}$ is the Brownian filtration $\mathcal{F}=\{\mathcal{F}_t : t\in[0,(\ell N+L)\tau]\}$ generated by the Brownian motion $\left\{B_t=\left(B_t^{(1)}\ldots B_t^{(r)}\ldots B_t^{(\alpha)}\right)^T : t\in[0,(\ell N+L)\tau]\right\}$. Moreover, f_i in Eq. (2) as well as in Eq. (5) is the deterministic mathematical function in the leaky integrate-and-fire equation for neuron (i). Hence, Eq. (14) can be defined by only using the filtration $\mathcal{F}(k\tau)=\{\mathcal{F}_t : t\in[k\tau,(\ell N+L)\tau]\}$. This implies for $t\in[k\tau,(\ell N+L)\tau]$, $(x_t^{(i)}-x_{k\tau}^{(i)})$ is stochastically independent of $\mathcal{F}_u\in\mathcal{F}=\{\mathcal{F}_t : t\in[0,(\ell N+L)\tau]\}$ for $0\le u<k\tau$, which consequently yields independence (12).

During the signal propagation, in each of the time intervals $[(k-1)\tau,k\tau], k=1,\ldots,(\ell N+L)$, RRF in neuron (i) cause deviation in the expected increment, $\left((x_{k\tau}^{(i)}-x_{(k-1)\tau}^{(i)})-(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}])\right)$. Using a parameter b, we formulate bounded effect of RRF in neuron (i) by

$$\left|(x_{k\tau}^{(i)}-x_{(k-1)\tau}^{(i)})-(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}])\right|\le b\tau \quad \text{with probability 1.} \tag{15}$$

How to assign a value to the parameter b is discussed in Section 3.2. Independence (12) and inequality (15) together formulate a general characterization of RRF in individual neurons. This characterization follows from the notion of "weak noise" appeared in our previous work (Hong and Man, 2010).

2.3. The stability of signal propagation in a brain structural network

As signal propagation in a brain structural network is a key basic operation in neuronal information processing, the stability of the signal propagation should be understood as follows. What observed in a single trial does not occur by chance rather than with probability close to 1. In a single trial, observation on the signal propagation is by recording the sequences $\left\{x_{k\tau}^{(i)}(\omega) : k=N,\ldots,(\ell N+L)\right\}, i=1,\ldots,n$, each of which is the segment of sample path (10) observed in the very first synaptic delay $N\tau$. Given a single trial, the sequences $\phi_i=\left\{\mathbb{E}[x_{k\tau}^{(i)}] : k=N,\ldots,(\ell N+L)\right\}, i=1,\ldots,n$, are the only deterministic quantities in regard to the signal propagation. This implies that in any case–whether the signal propagation succeeds or fails–, with probability close to 1, it holds that

$$\left|x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]\right|\le\delta,\quad i=1,\ldots,n \text{ and } k=N,\ldots,(\ell N+L). \tag{16}$$

Here δ is a parameter that specifies a bound of deviations in neuronal membrane potentials which are tolerable in signal propagation in a brain structural network. Since $\mathbb{E}[x_{k\tau}^{(i)}]=x_0^{(i)}+\mathbb{E}\left[\int_0^{k\tau} f_i(s,x_s^{(1)},\ldots,x_s^{(n)})ds\right]$ by Eq. (13), expression (16) states what observed in a single trial should with probability close to 1 follow the initial state represented by $x_0^{(i)}$ and the support provided by the underlying synaptic connection characterized by $f_i, i=1,\ldots,n$.

Using the sequences $\phi_i, i=1,\ldots,n$, introduced earlier, we define an event in probability space $(\Omega,\mathcal{F},\mathbb{P})$,

$$\mathcal{E}(\phi)=\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\left\{\omega\in\Omega : |x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]|\le\delta\right\},$$

$\omega\in\mathcal{E}(\phi)$, specifies what observed in a signal trial as follows. In the very first synaptic delay–a time delay $N\ \tau$–, membrane potentials $x_{k\tau}^{(i)}(\omega)$ of every neuron $(i), i=1,\ldots,n$, are within $\mathbb{E}[x_{k\tau}^{(i)}]\pm\delta$, at times $t=k\tau, k=N,\ldots,(\ell N+L)$ where τ is about 10^{-6} s. In this way, event $\mathcal{E}(\phi)$ characterizes the stability of signal propagation in a brain structural network.

The stability of signal propagation in a brain structural network discussed above can be applied to repeated trials. For the same brain structural network and the same signals, patterns of success of the signal propagation never duplicate in repeated trials, and yet, all these patterns as different responses to the same signals can be reliable; see Fellous et al. (2004) and references therein. In repeated trials, the brain structural network and the signals may remain but the source that causes RRF in every individual neuron certainly is a variable, which can be modeled by weak solutions of SDE. Using these weak solutions, we may explain how, by the stability, different responses to the same signals in the same brain structural network can all be reliable; see Appendix A.

3. Results

3.1. The alter-and-concentrate effect of RRF in individual neurons

How can the stability of signal propagation in a brain structural network be established? Event $\mathcal{E}(\phi)$–that characterizes the stability–occurs if and only if all sub-events $\left\{\omega\in\Omega: |x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]|\le\delta\right\}, i=1,\ldots,n$, and $k=N,\ldots,(\ell N+L)$, occur. The number of these sub-events is $n\times(\ell N+L)$, which is about 10^{17} as shown in Section 3.2. It seems difficult to establish the stability, i.e., $\mathbb{P}\{\mathcal{E}(\phi)\}\approx 1$. However, the characterization by event $\mathcal{E}(\phi)$ reveals two factors which may be useful. One factor is a time delay, that is, $|x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]|\le\delta$ is required after the very first synaptic delay $N\tau$. Another factor is $\left|(x_{k\tau}^{(i)}(\omega)-x_{(k-1)\tau}^{(i)}(\omega))-(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}])\right|$ caused by RRF in neuron (i). Using Fig. 1 below, we illustrate how the two factors together may be utilized to establish the stability of signal propagation in a brain structural network. Suppose that signals originate at time $t=0$. The observation of the signal propagation starts at time $t=1$ ms (which is counted as the very first synaptic delay $N\tau$). The expectations of membrane potential of neuron (i) over time $t\in[1,51]$ ms–the ideal dynamics of membrane potential of neuron (i) for the stability of the signal propagation–are depicted in Fig. 1(a). The bold curve in Fig. 1(b) is obtained by adding ± 1.000 mV to the curve in Fig. 1(a), which is based on the following. In regard to signal propagation in a brain structural network, two patterns of membrane potential of a neuron, which agree with each other within ± 1.000 mV in every 1 μs, can be treated as the same. Thus, the bold curve in Fig. 1 (b) represents a collection of patterns of membrane potential of neuron (i), each of which is a trace that can be embedded into the bold cure, under the stability of the signal propagation. RRF in neuron (i) over time $t\in[0,51,000]$μs, which cause the bold curve in Fig. 1(b), are depicted in Fig. 1(c).

From time $t=0$ μs to time $t=1000$ μs (which is counted as a time delay from the moment when signals originate to the moment when observation of the signal propagation starts), RRF in individual neuron $(i), i=1,\ldots,n$, consume energy. We will show

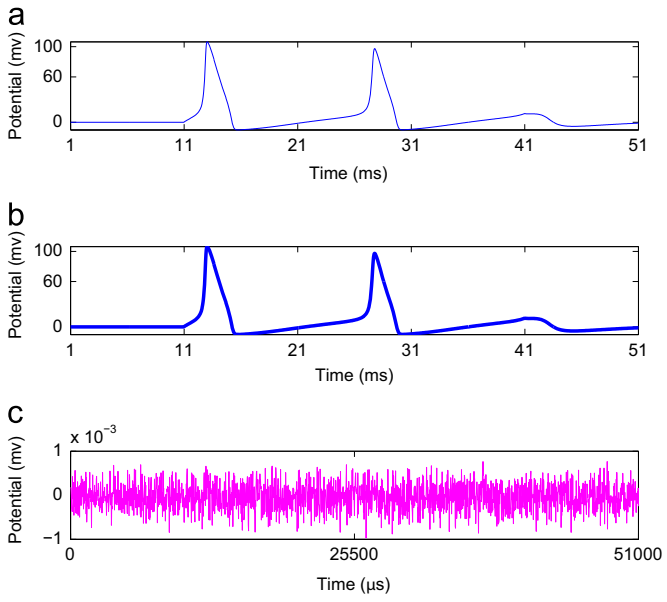

Fig. 1. (a) The expectations of membrane potential of neuron (i) over time $t\in[1,51]$ ms. (b) Under the stability of the signal propagation, what observed on membrane potential of neuron (i) over time $t\in[1,51]$ ms in a single trial may be a trace that can be embedded into the bold curve. (c) RRF in neuron (i) over time $t\in[0,51,000]$ μs. Notice that the duration here is [0, 51] ms which is 1 ms longer than the duration in (a) and (b) to count the very first synaptic delay.

that, by the energy consumption, RRF in every individual neuron cause an alter-and-concentrate effect to establish the stability of the signal propagation. Indeed, the following phenomenon may occur. The underlying synaptic connection, with non-zero probability p_1, ensures that some traces which are around the curve in Fig. 1(a) within ± 0.500 mV in every 1 μs may be observed in a single trial. This provides a basis to observe a trace which is around the curve in Fig. 1(a) within ± 1.000 mV in every 1 μs with probability p_2. By definition we have $p_2\ge p_1$. In the case of $p_2>p_1$, the difference (p_2-p_1) gives a quantitative description of what a purpose the energy consumption by RRF in neuron (i) may be for. Our analysis will show that p_2 can be close to 1 even when p_1 is close to 0. This reveals that the energy consumed by RRF in every individual neuron $(i), i=1,\ldots,n$, in a brain structural network–in particular during the very first synaptic delay (a time delay of 1 ms)–has a profound impact on the stability of signal propagation in the network. To describe such an impact, in the rest of this section, we formulate the alter-and-concentrate effect by RRF in neuron $(i), i=1,\ldots,n$. And, using the formulation, we analyze the alter-and-concentrate effect in Section 3.2.

Our formulation of the alter-and-concentrate effect involves all nine parameters used in this paper. To express the relation among these parameters, we use a symbol for each parameter in the formulation. Values assigned to these parameters are discussed in Section 3.2. For each $1\le i\le n$ and each $N\le k\le(\ell N+L)$, we introduce an event

$$\mathcal{E}_{i,k}^{net}(\phi)=\left\{\tilde{\omega}\in\Omega: |x_{k\tau}^{(i)}(\tilde{\omega})-\mathbb{E}[x_{k\tau}^{(i)}]|\le\frac{\delta}{2}\right\}$$

with a condition

$$\mathbb{P}\left\{\mathcal{E}_{i,k}^{net}(\phi)\right\}\ge\exp\left(-\frac{N^{2\lambda}}{4}\right),\quad \lambda\in[0,0.48]. \tag{17}$$

It will become clear in Section 3.2 why the parameter λ is in the range of $[0,0.48]$. Here we use events $\mathcal{E}_{i,k}^{net}(\phi), i=1,\ldots,n$ and $k=N,\ldots,(\ell N+L)$, to represent traces that can be embedded into the bold curve in Fig. 1(b) as follows. The joint event $\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{net}(\phi)$ states that from time $t=N\tau$ to $(\ell N+L)\tau$, for every $i=1,\ldots,n$, membrane potential of neuron (i) is within $\pm\frac{\delta}{2}$ of its expectation in every τ s. (As shown in Section 3.2, $\frac{\delta}{2}=0.500$ mV and $\tau=10^{-6}$ s.) Notice that, according to condition (17), for each $1\le i\le n$ and each $N\le k\le(\ell N+L)$, probability of event $\mathcal{E}_{i,k}^{net}(\phi)$, i.e. $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$, may take any value in $[\exp\left(-\frac{N^{0.96}}{4}\right),1]$, and values taken by $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$ may vary for different i and $k, 1\le i\le n$ and $N\le k\le(\ell N+L)$. This implies that probability of the joint event $\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{net}(\phi)$ may be $\exp\left(-\frac{N^{0.96}}{4}\right)$ or even smaller (as shown in Section 3.2, the probability can virtually take any value in $(0,1]$). Thus, the events $\mathcal{E}_{i,k}^{net}(\phi), i=1,\ldots,n$ and $k=N,\ldots,(\ell N+L)$, with condition (17) together give a description of a minimal requirement on the support provided by the underlying synaptic connection for the stability of the signal propagation.

The above minimal requirement raises a question: How can the signal propagation proceed if at some time $t=k\tau, N\le k\le(\ell N+L)$, $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$ is much less than 1 for some neuron $(i), 1\le i\le n$? To answer the question, for each $1\le i\le n$ and each $N\le k\le(\ell N+L)$, we introduce a companion of event $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$,

$$\mathcal{E}_{i,k}^{noise}(\phi)=\left\{\omega\in\Omega:\exists\tilde{\omega}\in\mathcal{E}_{i,k}^{net}(\phi)\left(|x_{k\tau}^{(i)}(\tilde{\omega})-x_{k\tau}^{(i)}(\omega)|\le\frac{\delta}{2}\right)\right\}.$$

As the initial network state X_0 is deterministic in a single trial, we have for each $1\le i\le n, N\le k\le(\ell N+L)$ and for almost every $\omega\in\Omega, x_{k\tau}^{(i)}(\omega)=\sum_{q=1}^{k}\left(x_{q\tau}^{(i)}(\omega)-x_{(q-1)\tau}^{(i)}(\omega)\right)+x_0^{(i)}$, which can be

rewritten as for each $1 \le i \le n$ and each $N \le k \le (\ell N+L)$,

$$(x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]) = \sum_{q=1}^{k} \left((x_{q\tau}^{(i)}(\omega)-x_{(q-1)\tau}^{(i)}(\omega))-(\mathbb{E}[x_{q\tau}^{(i)}]-\mathbb{E}[x_{(q-1)\tau}^{(i)}])\right)$$

for almost every $\omega \in \Omega$. (18)

To have a shorthand notation, we let

$$m_q^{(i)}(\omega) = \left((x_{q\tau}^{(i)}(\omega)-x_{(q-1)\tau}^{(i)}(\omega))-(\mathbb{E}[x_{q\tau}^{(i)}]-\mathbb{E}[x_{(q-1)\tau}^{(i)}])\right)$$

and then express equality (18) by

$$(x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]) = \sum_{q=1}^{k} m_q^{(i)}(\omega). \quad (19)$$

At time $t = k\tau, N \le k \le (\ell N+L)$, the expectation $\mathbb{E}[x_{k\tau}^{(i)}]$ is determined. By equality (19), an observed value $x_{k\tau}^{(i)}(\omega)$ is determined by a sequence

$$\left\{m_q^{(i)}(\omega) : q = 1, \ldots, k\right\}. \quad (20)$$

Here, $N\ \tau$ represents the very first synaptic delay which is about 10^{-3} s, and τ represents the unit of a timescale of 10^{-6} s. Thus, N is about 10^3, which means that the length of a sequence (20) is a large number $k(\ge N)$.

The fact that k is a large number provides a physical basis for the alter-and-concentrate effect. The underlying synaptic connection ensures

$$\left\{m_q^{(i)}(\tilde{\omega}) : q = 1, \ldots, k\right\}, \quad \tilde{\omega} \in \mathcal{E}_{i,k}^{net}(\phi), \quad (21)$$

to take place such that a possibly observed value $x_{k\tau}^{(i)}(\tilde{\omega})$ of membrane potential of neuron (i) would ideally be within $\mathbb{E}[x_{k\tau}^{(i)}] \pm \frac{\delta}{2}$ at time $t = k\tau$. Although probability $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$ of such a case may take any value between $\exp(-\frac{N^{0.96}}{4})$ and 1 as indicated by condition (17), RRF in neuron (i) can affect any sequence (21) for a large number $k(\ge N)$ times by altering $m_q^{(i)}(\tilde{\omega})$ in each time interval $[(q-1)\tau, q\tau], q = 1, \ldots, k$. Then, it is possible that an altered version of some sequence (21) is almost surely observed, i.e., a sequence (20) that actually takes place in a single trial very likely is an altered version of some sequence (21). The intuition is consistent with the fact that signals in the brain are always observed as "noisy" and that the brain is developed to better process "noisy signals" (McIntosh et al., 2008). At the same time, because $k(\ge N)$ is large, effects of RRF in neuron (i) over the k time intervals $[(q-1)\tau, q\tau], q = 1, \ldots, k$, may cancel each other, which results in the concentration of an actually observed value $x_{k\tau}^{(i)}(\omega)$ on its expectation so that $|x_{k\tau}^{(i)}(\omega)-\mathbb{E}[x_{k\tau}^{(i)}]| \le \delta$ with high probability. We formulate such an observed value $x_{k\tau}^{(i)}(\omega), \omega \in \Omega$, by $\exists \tilde{\omega} \in \mathcal{E}_{i,k}^{net}(\phi)\left(|x_{k\tau}^{(i)}(\tilde{\omega})-x_{k\tau}^{(i)}(\omega)| \le \frac{\delta}{2}\right)$. By definition it holds that

$$\mathcal{E}(\phi) \supseteq \bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L} \mathcal{E}_{i,k}^{noise}(\phi) \supseteq \bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L} \mathcal{E}_{i,k}^{net}(\phi). \quad (22)$$

Using relation (22) we formulate the alter-and-concentrate effect of RRF in neuron $(i), i = 1, \ldots, n$. The event $\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{net}(\phi)$, the rightmost term of relation (22), gives a description of how the underlying synaptic connection of a brain structural network supports signal propagation in the network: For each individual neuron $(i), i = 1, \ldots, n$, the underlying synaptic connection ensures event $\mathcal{E}_{i,k}^{net}(\phi)$ to physically take place at each time $k\tau, k = N, \ldots, (\ell N+L)$, with probability $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\} \ge \exp\left(-\frac{N^{2\lambda}}{4}\right), \lambda \in [0, 0.48]$. The event $\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{noise}(\phi)$, the middle term of relation (22), gives a description of how RRF in neuron $(i), i = 1, \ldots, n$, may help to stochastically establish the stability of the signal propagation: For each individual neuron $(i), i = 1, \ldots, n$, at each time $k\tau, k = N, \ldots, (\ell N+L)$, as long as the underlying synaptic connection ensues event $\mathcal{E}_{i,k}^{net}(\phi)$ with probability $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\} \ge \exp\left(-\frac{N^{2\lambda}}{4}\right), \lambda \in [0, 0.48]$, an observed value of membrane potential of neuron (i) in a single trial may be $x_{k\tau}^{(i)}(\omega)$ with $\omega \in \mathcal{E}_{i,k}^{noise}(\phi)$ by the alter-and-concentrate effect of RRF in neuron (i). Notice that the alter-and-concentrate, as a procedure, takes place locally at a small spatiotemporal scale–in each individual neuron at a timescale with τ (i.e. 10^{-6} s) being the unit. The local activity, as our analysis shown in Section 3.2, is vital in establishing the stability of the signal propagation which is a global activity at large spatiotemporal scale–at timescale of 10^{-3} s, signals of length 10^{-1} s propagate in a brain structural network that may contain up to 10^{12} neurons.

3.2. A stochastic mechanism of signal propagation in a brain structural network

A characterization of the alter-and-concentrate effect of RRF in individual neuron $(i), i = 1, \ldots, n$, is as follows. Suppose that condition (17) is met and $\delta = 4bN^{\theta}\tau, \theta \in (0, 1)$. Then it holds that

$$\mathbb{P}\{\mathcal{E}(\phi)\} \ge 1-n((\ell-1)N+L+1)\left[\exp\left(-\frac{N-N^{2\lambda}}{4}\right)+4\exp\left(-2N^{\theta}\right)\right]. \quad (23)$$

Below, by five steps we provide an analytic proof of inequality (23), and in the meantime, explain how the inequality implies a stochastic mechanism of signal propagation in a brain structural network.

The first step is to explain that in regard to the signal propagation, the right side of inequality (23) is close to 1. Let

$$Q = n((\ell-1)N+L+1)\left[\exp\left(-\frac{N-N^{2\lambda}}{4}\right)+4\exp\left(-2N^{\theta}\right)\right],$$

and write the right side of inequality (23) by $1-Q$. Six of the nine parameters used in this paper, which are n, ℓ, N, L, λ and θ, appear in the quantity Q. The other three parameters are τ, b and δ.

We let $\tau = 10^{-6}$ s, i.e., the unit of a timescale where RRF in every individual neuron (i) occur is 1 μs. Then we let $N = 10^3$ so that the very first synaptic delay $N\tau$ is 1 ms. Here we use $N = 10^3$ to represent a gap between the timescale of μs (microsecond) where RRF in every individual neuron occur and the timescale of ms (millisecond) where signals propagate.

Parameters n, ℓ and L appear in Q and nowhere else. To have a conservative estimate of how $1-Q$ is close to 1, we let the three parameters take values as reasonably large as possible: $n = 10^{12}$, a upper bound of the average number of neurons in the brain; $\ell = 10$, a upper bound for the total number of synaptic delays in the signal propagation (this is equivalent to say that the number of neurons in any signaling pathway is not greater than 10 which is true according the anatomy of the brain); and $L = 10^5$ such that $L\tau = 10^{-1}$ s, i.e., the length of a signal is 10^{-1} s.

Parameter b introduced in inequality (15) is used in a bound for deviations in increments of every individual neuron (i) during the signal propagation, i.e. $\left|(x_{k\tau}^{(i)}-x_{(k-1)\tau}^{(i)})-(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}])\right| \le b\tau, i = 1, \ldots, n$ and $k = 1, \ldots, (\ell N+L)$. Such deviations were observed and reported by Fatt and Katz (1950): When such deviations accumulate over time in membrane potential of neuron (i) and the accumulation approaches 1 mV, an unexpected physiological response by neuron (i) may occur. Based on this, we let $b = 10^3$ so that $b\tau = 10^3 \times 10^{-6} = 10^{-3}$ mV. It means that in every 1 μs, the actual increment $(x_{k\tau}^{(i)}-x_{(k-1)\tau}^{(i)})$ always is within $(\mathbb{E}[x_{k\tau}^{(i)}]-\mathbb{E}[x_{(k-1)\tau}^{(i)}]) \pm 1$ μV. Notice that this includes the case where deviations may accumulate to approach 1 mV in milliseconds.

Having assigned values to parameters τ, N and b, we can decide a value for parameter θ as below. Recall that parameter δ represents a bound of deviations in neuronal membrane potentials

tolerable in the signal propagation (see definition of event $\mathcal{E}(\phi)$). Parameter θ appears in $\delta = 4bN^{\theta}\tau$ which is one of the two conditions for inequality (23), and at the same time, θ appears in the conclusion of inequality (23), i.e. in the estimate of $1-Q$ for $\mathbb{P}\{\mathcal{E}(\phi)\}$. Therefore, θ describes a trade-off between the accuracy characterized by $\delta = 4bN^{\theta}\tau$ and the reliability characterized by $1-Q$. Hence θ can take any value in $(0,1)$. To have a meaningful trade-off, we let θ=0.466 such that δ=0.100 mV. This assignment is based on the result by Fatt and Katz (1950), which means that after the very first synaptic delay $N\tau = 1$ ms, in every 1 μs, an observed value $x_{k\tau}^{(i)}(\omega)$ of membrane potential of neuron (i) should be within $\mathbb{E}[x_{k\tau}^{(i)}] \pm 0.100$ mV. It should be noted that, in general, if two patterns of the dynamics of membrane potentials of a neuron agree with each other within ± 0.100 mV in every 1 μs, then the two patterns can be treated as the same.

Once values are assigned to parameters $\tau, N, n, \ell, L, b, \theta$ and δ as described above, we consider a relation between Q and λ.

In what follows, by the term "the typical scenario" we mean that the parameters are taking values as described earlier. In the typical scenario, the signal propagation is observed at the timescale with 1 μs being the unit, and the observation starts in 1 ms after the signals originate. The values assigned to the nine parameters reflect a meaningful trade-off between the accuracy and the reliability of the signal propagation. In what follows, we use the typical scenario to numerically describe our results. Meanwhile, we still use the symbols assigned to the nine parameters to facilitate our analysis. Notice that in the typical scenario, condition (17), $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\} \geq \exp\left(-\frac{N^{2\lambda}}{4}\right), \lambda \in [0, 0.48]$, means that probability $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$ may take any value between $\exp\left(-\frac{10^{3\times 2\times 0.48}}{4}\right) = 4.35 \times 10^{-83}$ and $\exp\left(-\frac{10^{3\times 2\times 0}}{4}\right) = 1$, i.e., $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$ may be anywhere in $[4.35 \times 10^{-83}, 1]$.

The second step is to prove that, in a single trial, for each $1 \leq i \leq n$ and each $N \leq k \leq (\ell N + L)$, probability of observing an altered version of some sequence (21) is at least $1 - \exp\left(-\frac{N-N^{2\lambda}}{4}\right)$ as long as $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\} \geq \exp\left(-\frac{N^{2\lambda}}{4}\right)$ (which means $\mathbb{P}\{\mathcal{E}_{i,k}^{net}(\phi)\}$ may be anywhere in $[4.35 \times 10^{-83}, 1]$ as mentioned above). Take a strictly increasing sequence of positive numbers, $h_e, e = 1, 2, \ldots$, with $\lim_{e\to\infty} h_e = \frac{1}{2}$, and for each h_e, define

$$\mathcal{J}_{i,k}^{h_e}(\phi) = \left\{\omega \in \Omega : \min_{\tilde{\omega} \in \mathcal{E}_{i,k}^{net}(\phi)} \left|\left\{q \in [1,k] : m_q^{(i)}(\tilde{\omega}) \neq m_q^{(i)}(\omega)\right\}\right| \leq k^{h_e + 1/2}\right\}.$$

Here $\left|\left\{q \in [1,k] : m_q^{(i)}(\omega) \neq m_q^{(i)}(\tilde{\omega})\right\}\right|$ is the number of indices q from 1 to k where $m_q^{(i)}(\omega) \neq m_q^{(i)}(\tilde{\omega})$ indicate that a sequence (21) is altered by RRF in neuron (i) in some time intervals $[(q-1)\tau, q\tau]$. Supported by the underlying synaptic connection, any sequence (21) may physically take place, and hence, so does any altered version of a sequence (21). By event $\mathcal{J}_{i,k}^{h_e}(\phi)$ we consider such an altered version, which is a result by altering some sequence (21) such that the number of alterations is not greater than $k^{h_e + (1/2)}$ and is minimal when all possible alterations on all sequences (21) are considered. Then, by applying Talagrand's concentration inequality (Talagrand, 1995), we estimate probability of observing such an altered version:

$$\mathbb{P}\left\{\mathcal{J}_{i,k}^{h_e}(\phi)\right\} \geq 1 - \exp\left(-\frac{k^{2h_e} - N^{2\lambda}}{4}\right) \geq 1 - \exp\left(-\frac{N^{2h_e} - N^{2\lambda}}{4}\right). \tag{24}$$

A proof for inequality (24) is in Appendix B. Define $\mathcal{J}_{i,k}(\phi) = \bigcup_{e=1}^{\infty} \mathcal{J}_{i,k}^{h_e}(\phi)$, and let $h_e \to \frac{1}{2}$ in inequality (24). Then we have

$$\mathbb{P}\{\mathcal{J}_{i,k}(\phi)\} \geq 1 - \exp\left(-\frac{N - N^{2\lambda}}{4}\right). \tag{25}$$

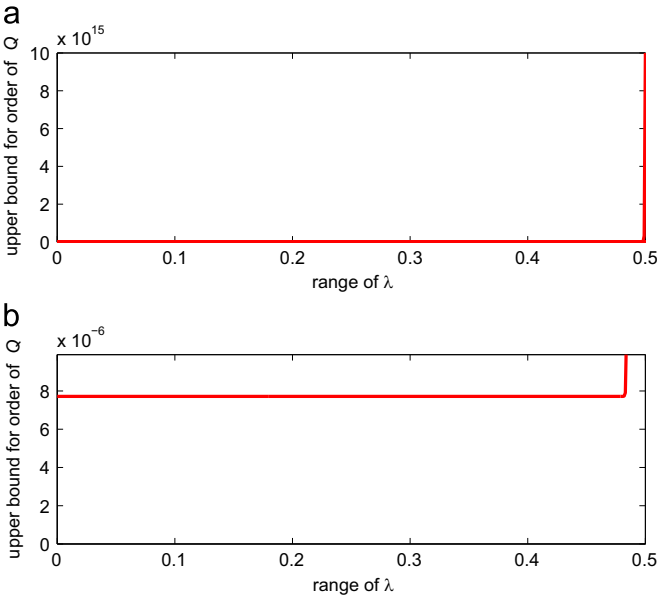

Fig. 2. (a) As shown by the red curve, Q is near zero for most $\lambda \in [0, 0.5]$. Q drastically increases when λ gets close to 0.5 and reaches about 10^{17} when λ=0.5. (b) For $\lambda \in [0, 0.48]$, Q has a constant upper bound 8.36×10^{-5}, and the drastic increase of Q takes place when λ is in $(0.48, 0.5]$. It shows that the right side of inequality (23) is $1 - 8.36 \times 10^{-5}$ for all $\lambda \in [0, 0.48]$ (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.).

It implies in the typical scenario,

$$\mathbb{P}\{\mathcal{J}_{i,k}(\phi)\} \geq 1 - \exp\left(-\frac{N - N^{2\lambda}}{4}\right) \geq 1 - 6.137 \times 10^{-27}. \tag{26}$$

The second step is crucial. For neuron (i), at time $t = k\tau$ the underlying synaptic connection ensures any sequence (21) to physically take place; but the insurance comes with probability that may be as small as 4.35×10^{-83} as shown in Fig. 2. How can the signal propagation proceed? By inequality (26) the signal propagation can almost surely proceed with an altered version of some sequence (21).

The third step is to synthesize what was proved in the second step. Event $\bigcap_{i=1}^{n} \bigcap_{k=N}^{\ell N+L} \mathcal{J}_{i,k}(\phi)$ states that, in a single trial, for each neuron $(i), i = 1, \ldots, n$, at each time $t = k\tau, k = N, \ldots, (\ell N + L)$, an altered version of some sequence (21) is observed. Note that it may well be the case that for neuron (i), at different times $k_1\tau$ and $k_2\tau$, two observed altered versions are from two disparate sequences (21), respectively. But, if each of such two altered versions occurs with high probability then the two altered versions may both occur in a single trial. Since events $\mathcal{J}_{i,k}(\phi), i = 1, \ldots, n$ and $k = N, \ldots, (\ell N + L)$, are related in regard to the signal propagation, we use the complementary event $\overline{\bigcap_{i=1}^{n} \bigcap_{k=N}^{\ell N+L} \mathcal{J}_{i,k}(\phi)}$ to estimate $\mathbb{P}\left\{\bigcap_{i=1}^{n} \bigcap_{k=N}^{\ell N+L} \mathcal{J}_{i,k}(\phi)\right\}$. We have $\mathbb{P}\left\{\overline{\bigcap_{i=1}^{n} \bigcap_{k=N}^{\ell N+L} \mathcal{J}_{i,k}(\phi)}\right\} \leq \sum_{i=1}^{n} \sum_{k=N}^{\ell N+L} \mathbb{P}\left\{\overline{\mathcal{J}_{i,k}(\phi)}\right\}$, which together with inequality (25) yields

$$\mathbb{P}\left\{\bigcap_{i=1}^{n} \bigcap_{k=N}^{\ell N+L} \mathcal{J}_{i,k}(\phi)\right\} \geq 1 - n((\ell - 1)N + L + 1)\exp\left(-\frac{N - N^{2\lambda}}{4}\right). \tag{27}$$

It implies in the typical scenario,

$$\mathbb{P}\left\{\bigcap_{i=1}^{n} \bigcap_{k=N}^{\ell N+L} \mathcal{J}_{i,k}(\phi)\right\} \geq 1 - 6.689 \times 10^{-10}. \tag{28}$$

The fourth step is to prove that, in every τ seconds (which is 10^{-6} s) after the very first synaptic delay $N\tau$ (which is 10^{-3} s), what may possibly be observed in a single trial so highly concentrate that they are close to each other at the timescale with τ being the unit. For neuron (i), two possibly observed sequences of

membrane potentials in a single trial are $\left\{x_{k\tau}^{(i)}(\omega_1): k=N,\ldots,(\ell N+L)\right\}$ and $\left\{x_{k\tau}^{(i)}(\omega_2): k=N,\ldots,(\ell N+L)\right\}$. By Hoeffding's inequality (Hoeffding, 1963), we have for $\omega_1,\omega_2\in\Omega$ and for $\theta\in(0,1)$,

$$\mathbb{P}\left\{\max_{1\le i\le n \text{ and } N\le k\le((\ell-1)N+L)}\left(\left|x_{k\tau}^{(i)}(\omega_1)-x_{k\tau}^{(i)}(\omega_2)\right|\right)\le 2bN^{\theta}\tau\right\}$$
$$\ge 1-4n((\ell-1)N+L+1)\exp\left(-2N^{\theta}\right). \tag{29}$$

A proof for inequality (29) is in Appendix C.

The fifth step is to put what were proved from the second to the fourth step together. Let

$$\mathcal{G}(\phi)=\left\{\omega\in\Omega:\ \exists\tilde{\omega}\in\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{net}(\phi)\right.$$
$$\left.\left[\max_{1\le i\le n \text{ and } N\le k\le((\ell-1)N+L)}\left(\left|x_{k\tau}^{(i)}(\omega)-x_{k\tau}^{(i)}(\tilde{\omega})\right|\right)\le 2bN^{\theta}\tau\right]\right\}.$$

By inequality (29) we have

$$\mathbb{P}\{\mathcal{G}(\phi)\}\ge 1-4n((\ell-1)N+L+1)\exp\left(-2N^{\theta}\right). \tag{30}$$

It implies in the typical scenario,

$$\mathbb{P}\{\mathcal{G}(\phi)\}\ge 1-8.352\times10^{-5}. \tag{31}$$

For $\omega\in\left(\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{J}_{i,k}(\phi)\right)\bigcap\mathcal{G}(\phi)$, a sequence

$$\left\{X_{k\tau}(\omega)=(x_{k\tau}^{(1)}(\omega)\ldots x_{k\tau}^{(i)}(\omega)\ldots x_{k\tau}^{(n)}(\omega)): k=N,\ldots,(\ell N+L)\right\} \tag{32}$$

describes that for each neuron $(i), i=1,\ldots,n$, at each time $t=k\tau, k=N,\ldots,(\ell N+L)$, an altered version of some sequence (21) is observed. And at the same time, a sequence (32) is close to a sequence supported by the underlying synaptic connection, i.e.

$$\left\{X_{k\tau}(\tilde{\omega})=(x_{k\tau}^{(1)}(\tilde{\omega})\ldots x_{k\tau}^{(i)}(\tilde{\omega})\ldots x_{k\tau}^{(n)}(\tilde{\omega})): k=N,\ldots,(\ell N+L)\right\},$$

with $\tilde{\omega}\in\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{net}(\phi)$. By definition we have

$$\mathcal{E}(\phi)\supseteq\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{E}_{i,k}^{noise}(\phi)\supseteq\left(\bigcap_{i=1}^{n}\bigcap_{k=N}^{\ell N+L}\mathcal{J}_{i,k}(\phi)\right)\bigcap\mathcal{G}(\phi). \tag{33}$$

Putting inequalities (27) and (30) and inclusion (33) together, we complete a proof for inequality (23). And putting inequalities (28) and (31) and inclusion (33) together, we have that in the typical scenario,

$$\mathbb{P}\{\mathcal{E}(\phi)\}\ge 1-n((\ell-1)N+L+1)\left[\exp\left(-\frac{N-N^{2\lambda}}{4}\right)+4\exp\left(-2N^{\theta}\right)\right]$$
$$\ge 1-\left(6.689\times10^{-10}+8.352\times10^{-5}\right)\ge 1-8.36\times10^{-5}, \tag{34}$$

as shown in Fig. 2.

Based on the analysis presented in the above five steps, we below describe a stochastic mechanism of signal propagation in a brain structural network. The stochastic mechanism follows the principle of causality for dynamic systems: For a dynamic system, when the input is given over a time interval, the output is determined over the same time interval. Consider a brain structural network that may contain up to $n=10^{12}$ neurons. At time marked as $t=0$, signals going to propagate in the brain structural network originate. The propagation of the signals is over time $t\in[0,(\ell N+L)\tau]$ where $(\ell N+L)\tau$ is about 10^{-1} s. In regard to the signal propagation, the input consists of the signals and the source that causes RRF in each individual neuron $(i), i=1,\ldots,n$, in the brain structural network over time $t\in[0,(\ell N+L)\tau]$. The output–a stochastic process over time $t\in[0,(\ell N+L)\tau]$–is determined as the unique strong solution of an SDE (4). The analysis presented in the above five steps implies such a stochastic process should reflect the following two characteristics of the signal propagation.

- The underlying synaptic connection is a very flexible framework that guides signals to propagate but does not guarantee success of the signal propagation.
- A portion of the energy consumed by RRF in each neuron $(i), i=1,\ldots,n$, is utilized for the signal propagation; especially with the energy consumed during the very first synaptic delay $N\tau$–a time delay of 1 ms, RRF in each neuron (i) can cause a lasting effect, i.e. the alter-and-concentrate effect, on the signal propagation.

The first characteristic is necessary for the stability of the signal propagation, i.e., membrane potentials of each individual neuron should be close to their expectations during the signal propagation (ref. Section 2.3). Experimental and theoretical studies have shown that activity in a brain structural network *in vivo* is generated through a dynamic balance of excitations and inhibitions received by each individual neuron in the network; see Shu et al. (2003), Haider et al. (2006) and references therein. An individual neuron in a brain structural network is connected by thousands of its presynaptic neurons, each of which gives the neuron input with certain randomness. Moreover, no changes in the underlying synaptic connection of a brain structural network can be made at a small timescale (of 10^{-3} s) at which signals propagate in the network. Hence, the underlying synaptic connection can hardly keep membrane potentials of each individual neuron close to their expectations with high probability all the time. Therefore the underlying synaptic connection needs to be flexible. Using condition (17) we formulate the flexibility: During the signal propagation, a period of $(\ell N+L)\tau\approx10^{-1}$ s, the underlying synaptic connection ensures events $\mathcal{E}_{i,k}^{net}(\phi), i=1,\ldots,n and k=N,\ldots,(\ell N+L)$. This, as shown in our analysis, means that during the signal propagation, in every 1 μs the underlying synaptic connection ensures sequence (21) to take place with a probability that may take any value in $[4.35\times10^{-83},1]$, and such a probability may vary in every 1 μs, i.e., it may take different values in $[4.35\times10^{-83},1]$ from time to time. Because 4.35×10^{-83} is so small, the underlying synaptic connection merely needs to ensure every neuron $(i), i=1,\ldots,n$, to remain being connected in the network during the signal propagation. To this extent, the underlying synaptic connection is a very flexible framework that guides signals to propagate but does not guarantee success of the signal propagation.

The second characteristic answers the question of how the stability of the signal propagation can establish under a very flexible framework provided by the underlying synaptic connection. As shown in our analysis, the very first synaptic delay $N\tau$–a time delay of 1 ms–is critical. After the time delay, in every 1 μs, for each neuron $(i), i=1,\ldots,n$, membrane potential $x_{k\tau}^{(i)}(\omega)$ which may be observed in a single trial is the sum of a sequence (20) (ref. expressions (18) and (19)). And, because of the time delay, the length k of a sequence (20) is large, $k\ge N=10^3$. This makes it possible for RRF in each neuron (i) to make the alter-and-concentrate effect. Indeed, as shown by inequalities (25) and (26), during the signal propagation, in every 1 μs, with probability not less than $1-6.137\times10^{-27}$ membrane potential $x_{k\tau}^{(i)}(\omega)$ which may be observed in a single trial is the sum of such a sequence (20) that is an altered version of some sequence (21), as long as the underlying synaptic connection provides a very flexible framework as described in the previous paragraph. The fact that $1-6.137\times10^{-27}$ is so close to 1 gives a basis for the concentration to take place (ref. inequalities (33) and (34)). This shows that a portion of the energy consumed by RRF in each neuron $(i), i=1,\ldots,n$, is for the stability of the signal propagation under a very flexible framework provided by the underlying synaptic connection. Especially, with the energy consumed during the very first synaptic delay $N\tau$–a time delay of 1 ms, RRF in each neuron $(i), i=1,\ldots,n$, can cause the alter-and-concentrate effect which, with probability

close to 1, forces membrane potentials of neuron (i) to be close their expectations during the signal propagation.

Thus, inequality (23) quantitatively summarizes a stochastic mechanism of signal propagation in a brain structural network in a general setting: The network, the signals to propagate in the network and the source that causes RRF in every individual neuron in the network together determine the outcome of the signal propagation in a single trial which consists of the expectations of membrane potential of each individual neuron in the network. In contrast to most human-engineered networks, the underlying synaptic connection–an analogy of the hard-wiring in a human-engineered network–is not rigid circuit, rather a very flexible framework. In such a framework, with the very first synaptic delay, RRF in each neuron force membrane potentials of each neuron to be close what determined by the network, the signals to propagate in the network and the source that causes RRF in every individual neuron in the network.

4. Discussion

Forces caused by random fluctuations of a classical or a quantum nature are named Casimir forces in the literature. For a Casimir force to occur, a system must be in a critical state; see Balibar (2008). In contrast, the force caused by RRF in every individual neuron in a brain structural network–that may be an analogue of Casimir force–occurs under general conditions. RRF in every individual neuron only need to fit a general characterization in which knowledge of probability distributions of RRF is not required. In the characterization, independence (12) is a mathematical formulation of the resilience of neuronal membrane, and inequality (15) follows from the fact that RRF in an individual neuron always are bounded. RRF in every individual neuron in a brain structural network are present at a timescale of 10^{-6} s so that the alter-and-concentrate effect takes place over all frequencies that may appear in signal propagation in a brain structural network.

An implication of inequality (23) is that a brain functional network may occur in a brain structural network which ensures the occurrence of the brain functional network merely with probability not greater than 4.35×10^{-83}. This may provide a physical basis to explain how the rich functionality can arise from a relatively fixed structure in the brain, which is one of the most important open questions in neuroscience (see Park and Friston, 2013).

The energy consumption by the brain may be the physical evidence for the existence of the force caused by RRF in every individual neuron. A considerable portion of the energy consumed by the brain was found for functions unaccounted for (Raichle and Mintun, 2006), which was termed “the brain's dark energy” by Raichle (2006). Strong evidence suggested a relation between disease and the brain's dark energy (Zhang and Raichle, 2010). RRF in every individual neuron consume energy that appears to be for functions unaccounted for. By the results of this paper, the energy consumed by RRF in every individual neuron in a brain structural network is for signal propagation in the network. The energy consumed by RRF in individual neurons resides at about 1 MHz in the energy spectrum of membrane potentials of neurons in the brain. It appears to be technically challenging to obtain the energy spectrum. However, analysis of the energy spectrum–a proper decomposition of the energy spectrum–would reveal characteristics of RRF in every individual neuron. For such an analysis, ideas of theorems in Meyer et al. (1999) and methods in Hong et al. (2014) might be applicable. Results from such an analysis may potentially have applications in neurology, e.g., to explain differences in capability of neuronal information processing among subjects whose brain structural networks are not that different.

A brain structural network is organized as modules in a hierarchy with each module being responsible for processing a specific aspect of information. Integration of these aspects of information is by coupling synchronized activities in the modules involved in processing the information (Martin, 2007). According to the free-energy principle (Friston, 2010), such activities in the modules may be represented by the expectations of membrane potentials of neurons in the modules (Friston, 2013). In a time delay of 1 ms after (external or internal) signals originate, the alter-and-concentrate effect caused by RRF in every individual neuron in a brain structural network can almost surely force the membrane potentials of every neuron in the network to be close to their expectations for a time period of at least 10^{-1} s, under a very flexible framework provided by the underlying synaptic connection. This suggests that neuronal information processing is carried out in a very flexible framework rather than a rigid circuit. In our view, the stochastic dynamics in such a very flexible framework may be modeled and analyzed by the approach in Stroock (2000), and obtained results would provide a basis for theoretical models of neuronal information processing that underlies cognition.

Conflict of interest

None declared.

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Appendix A. The stability of signal propagation in repeated trials

For the same brain structural network and the same signal, patterns of propagation of the signal in the network never duplicate in repeated trials and yet these patterns can all be reliable; see Fellous et al. (2004) and references therein. How can these patterns as different responses to the same signal in the same brain structural network all be reliable? Let us, without loss of generality, consider the following case. Over time $t\in[0,(\ell N+L)\tau]$, a pattern of success of the signal propagation is observed in a single trial. Over time $t\in[t_0,t_0+(\ell N+L)\tau]$, another pattern of success of the signal propagation is observed in the second single trial where the signal re-originates at time $t=t_0$. Such two single trials can be modeled by the same SDE (4), i.e., the same $dX_t=f(t,X_t)dt+\sigma(t,X_t)dB_t$ over time $t\in[0,(\ell N+L)\tau]$ and $t\in[t_0,t_0+(\ell N+L)\tau]$, respectively. Two Brownian motions respectively model the source that causes RRF in every individual neuron in the same brain structural network in the two single trials: $\left\{B_t=(B_t^{(1)}\dots B_t^{(r)}\dots B_t^{(\alpha)}):t\in[0,(\ell N+L)\tau]\right\}$ for the first single trial; and $\left\{\tilde{B}_t=(\tilde{B}_t^{(1)}\dots\tilde{B}_t^{(r)}\dots\tilde{B}_t^{(\alpha)}):t\in[t_0,t_0+(\ell N+L)\tau]\right\}$ for the second single trial.

The dimension α of the Brownian motion B_t as well as $\tilde{B}_t$ is huge such that as many as necessary random factors, each of which is modeled by a 1-dimensional Brownian motion, are taken into account. In this way, B_t and $\tilde{B}_t$ represent random disturbance in synaptic input to each individual neuron and in converting the synaptic input to membrane potential of each individual neuron, over two time intervals $[0,(\ell N+L)\tau]$ and $[t_0,t_0+(\ell N+L)\tau]$ respectively. Random factors, e.g., those represent random disturbance in diffusion of neurotransmitters, in the second single trial may drift away from their counterparts in the first single trial. Consequently, we have $\tilde{B}_t^{(r)}=B_t^{(r)}+h_r(t)$ for each $1\le r\le\alpha$, where $h_r(t)$ describes how the random factor modeled by $\tilde{B}_t^{(r)}$ in the second single trial may drift away from its counterpart modeled by $B_t^{(r)}$ in the first single trial. The Brownian motion B_t is with respect to probability measure $\mathbb{P}$. The Brownian motion $\tilde{B}_t$ is with respect to probability measure $\mathbb{Q}$ obtained by a Girsanov transform on $\mathbb{P}$ using the drift terms $h_r(t), r=1\ldots\alpha$. $\mathbb{P}$ and $\mathbb{Q}$ yield two weak solutions of the same SDE (4). Thus there are two sets of expectations: for the first single trial, $\left\{\mathbb{E}_{\mathbb{P}}[x_{k\tau}^{(i)}]: k=N,\ldots,(\ell N+L),\ i=1,\ldots,n\right\}$, and for the second single trial, $\left\{\mathbb{E}_{\mathbb{Q}}[x_{k\tau}^{(i)}]: k=N,\ldots,(\ell N+L),\ i=1,\ldots,n\right\}$. Here $\mathbb{E}_{\mathbb{P}}$ and $\mathbb{E}_{\mathbb{Q}}$ specify expectations with respect to probability measures $\mathbb{P}$ and $\mathbb{Q}$, respectively. Because of the drift terms, we have $\mathbb{E}_{\mathbb{P}}[x_{k\tau}^{(i)}]\neq\mathbb{E}_{\mathbb{Q}}[x_{k\tau}^{(i)}]$ at least for some i and k. By the stability of signal propagation in a brain structural network in a single trial (which is proved by results of this paper), two different patterns of success of the signal propagation are observed. But, to the brain structural network, the same input, which consists of the same signal and a Brownian motion that models the source that causes RRF in every individual neuron in the network, is supplied in the two single trials. This gives a basis on which different responses to the same signal in the same brain structural network may be reliable in the two single trials.

In a view of modeling, by using weak solutions of the same SDE (4), one can systemically generate infinitely many different patterns of success of the signal propagation as different responses to the same signals in the same brain structural network.

Appendix B. A proof for inequality (24)

Recall that we denote by $(\Omega,\mathcal{F},\mathbb{P})$ the underlying probability space of an SDE (5). Now we construct a probability space $(H^{(i)}(\Omega),\mathcal{H}^{(i)},\mu^{(i)})$ based on $(\Omega,\mathcal{F},\mathbb{P}), 1\le i\le n$. Denote a vector $(\xi_1^{(i)}\ldots\xi_q^{(i)}\ldots\xi_{\ell N+L}^{(i)})\in\mathbb{R}^{\ell N+L}$ by $\Xi^{(i)}$. For an event $\mathcal{E}\in\mathcal{F}$, we define a subset of $\mathbb{R}^{\ell N+L}$,

$$H^{(i)}(\mathcal{E})=\left\{\Xi^{(i)}\in\mathbb{R}^{\ell N+L}:\ \exists\ \omega\in\mathcal{E}\ \forall\ 1\le q\le(\ell N+L)\left(\xi_q^{(i)}=m_q^{(i)}(\omega)\right)\right\},$$

where $m_q^{(i)}(\omega)$ is the same shorthand notation used in Section 3.1, i.e.

$$m_q^{(i)}(\omega)=\left((x_{q\tau}^{(i)}(\omega)-x_{(q-1)\tau}^{(i)}(\omega))-(E[x_{q\tau}^{(i)}]-E[x_{(q-1)\tau}^{(i)}])\right). \tag{B.1}$$

We say $H^{(i)}(\mathcal{E})$ is induced by $\mathcal{E}$. Different events in $\mathcal{F}$ may induce the same subset of $\mathbb{R}^{\ell N+L}$. We always regard $\mathcal{E}$ as the union of all events that induce the same $H^{(i)}(\mathcal{E})$. Such a union can be thought measurable with respect to $(\Omega,\mathcal{F},\mathbb{P})$, since $x_t^{(i)}$ represents values of membrane potential of neuron (i) observed in experiments. The following can be verified: All $H^{(i)}(\mathcal{E})$ form a sub σ-algebra $\mathcal{H}^{(i)}$ of the Borel σ-algebra of $\mathbb{R}^{\ell N+L}$; and by using the one-to-one correspondence $H^{(i)}(\mathcal{E})\leftrightarrow\mathcal{E}$ and letting $\mu^{(i)}\{H^{(i)}(\mathcal{E})\}=\mathbb{P}\{\mathcal{E}\}$, we have a probability space $(H^{(i)}(\Omega),\mathcal{H}^{(i)},\mu^{(i)})$ where

$$H^{(i)}(\Omega)=\left\{\Xi^{(i)}\in\mathbb{R}^{\ell N+L}:\ \exists\ \omega\in\Omega\ \forall 1\le q\le(\ell N+L)\left(\xi_q^{(i)}=m_q^{(i)}(\omega)\right)\right\}.$$

By independence (12), it can be verified that $(H^{(i)}(\Omega),\mathcal{H}^{(i)},\mu^{(i)})$ is a $(\ell N+L)$-dimensional product probability space.

For each $1\le i\le n$ and each $N\le k\le(\ell N+L)$, we have

$$H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))=\left\{\tilde{\Xi}^{(i)}\in H^{(i)}(\Omega):\ \exists\ \tilde{\omega}\in\mathcal{E}_{i,k}^{net}(\phi)\quad\forall 1\le q\le(\ell N+L)\left(\tilde{\xi}_q^{(i)}=m_q^{(i)}(\tilde{\omega})\right)\right\}.$$

Here we use the notation $\tilde{\Xi}^{(i)}=(\tilde{\xi}_1^{(i)}\ldots\tilde{\xi}_q^{(i)}\ldots\tilde{\xi}_{\ell N+L}^{(i)})$ to indicate that vector $\tilde{\Xi}^{(i)}$ is induced by a basic event $\tilde{\omega}$ in $\mathcal{E}_{i,k}^{net}(\phi)$. According to condition (17), we have

$$\mu^{(i)}\{H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))\}\ge\mathbb{P}\left\{\mathcal{E}_{i,k}^{net}(\phi)\right\}\ge\exp(-N^{2\lambda}/4),\quad\lambda\in[0,0.48]. \tag{B.2}$$

Recall events $\mathcal{J}_{i,k}^{h_e}(\phi)$ are defined as

$$\mathcal{J}_{i,k}^{h_e}(\phi)=\left\{\omega\in\Omega:\min_{\tilde{\omega}\in\mathcal{E}_{i,k}^{net}(\phi)}\left|\left\{q\in[1,k]:m_q^{(i)}(\omega)\neq m_q^{(i)}(\tilde{\omega})\right\}\right|\le k^{h_e+1/2}\right\},$$

where $h_e, e=1,2,\ldots$, is a strictly increasing sequence of positive numbers with $\lim_{e\to\infty}h_e=\frac{1}{2}$. We have

$$H^{(i)}(\mathcal{J}_{i,k}^{h_e}(\phi))=\left\{\Xi^{(i)}\in H^{(i)}(\Omega):\min_{\tilde{\Xi}^{(i)}\in H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))}\left|\left\{q\in[1,k]:\xi_q^{(i)}\neq\tilde{\xi}_q^{(i)}\right\}\right|\le k^{h_e+(1/2)}\right\}.$$

Denote by $d_{\mathcal{T}}(\Xi^{(i)},H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi)))$ Talagrand's convex distance between $\Xi^{(i)}\in H^{(i)}(\Omega)$ and $H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))$, which can be written as

$$d_{\mathcal{T}}(\Xi^{(i)},H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi)))=\sup_{\beta\in\mathbb{R}^{\ell N+L}}\left\{\Delta_\beta=\inf_{\tilde{\Xi}^{(i)}\in H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))}\left\{\sum_{q=1}^{\ell N+L}(\beta_q\times\mathrm{I}(\xi_q^{(i)}\neq\tilde{\xi}_q^{(i)}))\text{ and }\sum_{q=1}^{\ell N+L}\beta_q^2\le 1\right\}\right\} \tag{B.3}$$

where $\beta=(\beta_1\ldots\beta_{\ell N+L})$ and $\mathrm{I}(\cdot)$ is the indicator,

$$\mathrm{I}(\xi_q^{(i)}\neq\tilde{\xi}_q^{(i)})=\begin{cases}1 & \text{if}\ \xi_q^{(i)}\neq\tilde{\xi}_q^{(i)}\\ 0 & \text{otherwise}\end{cases},\quad q=1,\ldots,(\ell N+L);$$

see, e.g., Steele (1997). As $(H^{(i)}(\Omega),\mathcal{H}^{(i)},\mu^{(i)})$ is a product probability space, by Theorem 4.2.1 in Talagrand (1995), often called Talagrand's concentration inequality, we have

$$\int_{H^{(i)}(\Omega)}\exp\left(\frac{\left(d_{\mathcal{T}}(\Xi^{(i)},H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))\right)^2}{4}\right)d\mu^{(i)}(\Xi^{(i)})\le\frac{1}{\mu^{(i)}\left\{H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))\right\}},$$

and consequently for $\gamma>0$,

$$\mu^{(i)}\left\{d_{\mathcal{T}}(\Xi^{(i)},H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi)))>\gamma\right\}\le\frac{\exp\left(-\frac{\gamma^2}{4}\right)}{\mu^{(i)}\left\{H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))\right\}}. \tag{B.4}$$

Proposition 1. *For h_e, we have*

$$\mu^{(i)}\left\{H^{(i)}(\mathcal{J}_{i,k}^{h_e}(\phi))\right\}\ge 1-\frac{\exp\left(-\frac{k^{2h_e}}{4}\right)}{\mu^{(i)}\left\{H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi))\right\}}.$$

Proof. By (B.4), it suffices to show $d_{\mathcal{T}}(\Xi^{(i)},H^{(i)}(\mathcal{E}_{i,k}^{net}(\phi)))>k^{h_e}$ for $\Xi^{(i)}\in H^{(i)}(\Omega)\backslash H^{(i)}(\mathcal{J}_{i,k}^{h_e}(\phi))$. In (B.3) we take a vector $\beta(\Xi^{(i)})$ in accordance with $\Xi^{(i)}$ as follows:

$$\beta(\Xi^{(i)})=(\beta_1(\Xi^{(i)})\ldots\beta_k(\Xi^{(i)})\ldots\beta_{\ell N+L}(\Xi^{(i)}))$$

$$\text{with}\quad\beta_q(\Xi^{(i)})=\begin{cases}\frac{1}{\sqrt{k}} & 1\le q\le k\\ 0 & k<q\le(\ell N+L).\end{cases}$$

Since $\Xi^{(i)} \in H^{(i)}(\Omega)\backslash H^{(i)}(\mathcal{J}^{h_e}_{i,k}(\phi))$, we have

$$\Delta_{\beta(\Xi^{(i)})} \geq k^{h_e} + \frac{\varepsilon(\Xi^{(i)})}{\sqrt{k}} \text{ for some} \varepsilon(\Xi^{(i)}) > 0,$$

which implies $d_{\mathcal{T}}(\Xi^{(i)}, H^{(i)}(\mathcal{E}^{net}_{i,k}(\phi))) > k^{h_e}$. □

$\mathcal{J}^{h_e}_{i,k}(\phi)$ is defined by a set of sequences $\left\{x^{(i)}_{k\tau}(\omega) : k = 0, \ldots, (\ell N+L)\right\}$, for each of which there is a sequence $\left\{x^{(i)}_{k\tau}(\tilde{\omega}) : k = 0, \ldots, (\ell N+L)\right\}, \tilde{\omega} \in \mathcal{E}^{net}_{i,k}(\phi)$, such that the two sequences have some disagreements, i.e. $m^{(i)}_q(\omega) \neq m^{(i)}_q(\tilde{\omega})$. For any sequence $\left\{x^{(i)}_{k\tau}(\omega') : k = 0, \ldots, (\ell N+L)\right\}$ that has the same disagreements, i.e. $m^{(i)}_q(\omega') \neq m^{(i)}_q(\tilde{\omega})$, we have $\omega' \in \mathcal{J}^{h_e}_{i,k}(\phi)$. Thus, $\mathcal{J}^{h_e}_{i,k}(\phi)$ is the union of events induce the same event in $\mathcal{H}^{(i)}$. Hence we have

$$\mu_i\left\{H^{(i)}(\mathcal{J}^{h_e}_{i,k}(\phi))\right\} = \mathbb{P}\left\{\mathcal{J}^{h_e}_{i,k}(\phi)\right\}. \tag{B.5}$$

Putting (B.2), Proposition 1 and (B.5) together, we complete a proof for inequality (24).

Appendix C. A proof for inequality (29)

Recall that since the initial network state $X_0 = (x^{(1)}_0 \ldots x^{(i)}_0 \ldots x^{(n)}_0)$ is deterministic in a single trial, for each $1 \leq i \leq n$ and each $N \leq k \leq (\ell N+L)$, we have

$$(x^{(i)}_{k\tau}(\omega) - E[x^{(i)}_{k\tau}]) = \sum_{q=1}^{k}\left((x^{(i)}_{q\tau}(\omega) - x^{(i)}_{(q-1)\tau}(\omega)) - (E[x^{(i)}_{q\tau}] - E[x^{(i)}_{(q-1)\tau}])\right)$$
$$\text{almost every} \omega \in \Omega. \tag{C.1}$$

By independence (12) and inequality (15), the right side of (C.1) is the sum of a sample of k bounded independent random variables,

$$\left((x^{(i)}_{q\tau} - x^{(i)}_{(q-1)\tau}) - (E[x^{(i)}_{q\tau}] - E[x^{(i)}_{(q-1)\tau}])\right), \quad q = 1, \ldots, k.$$

Each of these random variables has zero mean. We use the same shorthand notation as in (B.1), i.e.

$$m^{(i)}_q(\omega) = \left((x^{(i)}_{q\tau}(\omega) - x^{(i)}_{(q-1)\tau}(\omega)) - (E[x^{(i)}_{q\tau}] - E[x^{(i)}_{(q-1)\tau}])\right),$$

$1 \leq i \leq n, 1 \leq q \leq (\ell N+L)$ and $\omega \in \Omega$.

Take $\omega_1, \omega_2 \in \Omega$. Let $1 \leq q_1 < \ldots < q_h < \ldots < q_p \leq k$ denote the indices such that $m^{(i)}_{q_h}(\omega_1) \neq m^{(i)}_{q_h}(\omega_2), h = 1, \ldots, p$. We have

$$\left|x^{(i)}_{k\tau}(\omega_1) - x^{(i)}_{k\tau}(\omega_2)\right| \leq \left|\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_1)\right| + \left|\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_2)\right|. \tag{C.2}$$

On the right side of (C.2), $\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_1)$ as well as $\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_2)$ is the sum of a sample of p bounded independent random variables, $m^{(i)}_{q_h}, h = 1, \ldots, p$, each of which has zero mean. Using the parameter θ, we consider two cases as below. Notice that $k \geq N > N^{\theta}$ since $\theta \in (0, 1)$.

Case 1. $1 \leq p \leq N^{\theta}$. By inequality (15), we have for almost every $\omega \in \Omega$,

$$\left|\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_j)\right| \leq N^{\theta} b_1 \tau, \quad j = 1, 2. \tag{C.3}$$

Case 2. $N^{\theta} < p \leq k$. By independence (12) and inequality (15), we apply Hoeffding's inequality (Hoeffding, 1963), which yields for any $\varepsilon > 0$,

$$\mathbb{P}\left\{\left|\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_j)\right| \leq \varepsilon\right\} \geq 1 - 2\exp\left(-\frac{2\varepsilon^2}{p b_1^2 \tau^2}\right)$$
$$> 1 - 2\exp\left(-\frac{2\varepsilon^2}{N^{\theta} b_1^2 \tau^2}\right), \quad j = 1, 2.$$

Then, letting $\varepsilon = b_1 N^{\theta} \tau$ we have

$$\mathbb{P}\left\{\left|\sum_{h=1}^{p} m^{(i)}_{q_h}(\omega_j)\right| \leq b_1 N^{\theta} \tau\right\} > 1 - 2\exp\left(-2N^{\theta}\right), \quad j = 1, 2. \tag{C.4}$$

Putting (C.2)–(C.4) together, we have

Proposition 2. *For $\omega_1, \omega_2 \in \Omega$ and for each $1 \leq i \leq n$ and each $N \leq k \leq (\ell N+L)$,*

$$\mathbb{P}\left\{\left|x^{(i)}_{k\tau}(\omega_1) - x^{(i)}_{k\tau}(\omega_2)\right| \leq 2b_1 N^{\theta} \tau\right\} > 1 - 4\exp\left(-2N^{\theta}\right). \square$$

As a consequence, we have

Corollary 1. *For $\omega_1, \omega_2 \in \Omega$,*

$$\mathbb{P}\left\{\max_{1 \leq i \leq n \text{ and } N \leq k \leq ((\ell-1)N+L)}\left(\left|x^{(i)}_{k\tau}(\omega_1) - x^{(i)}_{k\tau}(\omega_2)\right|\right) \leq 2b_1 N^{\theta} \tau\right\}$$
$$\geq 1 - n((\ell-1)N + L + 1)4\exp\left(-2N^{\theta}\right). \square$$

This proves inequality (29).

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