Physica D 239 (2010) 327–334

Contents lists available at ScienceDirect

Physica D

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

Suprathreshold stochastic resonance induced by ion channel fluctuation

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ARTICLE INFO

Article history:
Received 19 May 2009
Received in revised form
31 October 2009
Accepted 1 December 2009
Available online 11 December 2009
Communicated by S. Coombes

Keywords:
Noise
Stochastic resonance
Neuronal modeling
Ion channel
Population coding
Information theory

ABSTRACT

In this study, we examine the signal detection ability of an array of neurons with intrinsic channel fluctuation. Numerical simulations show that estimation of the input signal from the output spiking activity of the neuronal array is most accurate if a proper amount of channel noise exists. Theoretical calculation of the mutual and Fisher information confirms the effect of the noise-aided information transfer in the array, or the presence of suprathreshold stochastic resonance. These results indicate that the channel noise, which induces response variability, may play an essential role in population coding.

1. Introduction

One of the most prominent features of the central nervous system is the remarkably high variability in spiking patterns [1–3]. From trial to trial, a neuron shows different firing activity against the same stimulus while the behavior of the animal is much more robust. Investigating the mechanisms enabling reliable information processing through these unreliable neuronal elements is a central challenge in neuroscience. Population coding, where information is encoded in the ensemble response of neurons, has been suggested to be a mechanism for solving this problem [4–6]. In the framework of population coding, a neuronal group involved in specific information processing shows robust and reproducible activities whereas the discharge pattern of each neuron is not necessarily identical or similar in every trial.

Neuronal variability may arise from several noise sources, such as thermal agitation, stochastic ion channel opening and random background synaptic activity [7,8]. Of these three, noise of synaptic origin has been assumed to be dominant [9] and studied most intensively [10–12]. However, "channel noise", or the fluctuation in ionic current through the membrane induced by stochastic opening and closing of ion channels, is receiving increasing attention [8,13], because recent experimental studies have revealed that channel noise may significantly change the real neuron activity [14,15]. Development of the patch clamp technique has revealed the detailed properties of ion channels and shown that a change in membrane potential does not directly alter the open–closed state but rather the open–close probability of voltage gated ion channels [16,17]. The macroscopic ionic current through the membrane is not fixed but fluctuates around the level determined by the voltage dependence of the channel. If the number of channels on the membrane patch is large enough, ion channel stochasticity is averaged out and the total ionic current can be regarded as deterministic and continuous. However, when the number of channels recruited in a process decreases, microscopic channel fluctuation increases and thus the macroscopic behavior of the membrane may become different from the prediction of the noiseless model [18–23].

One of the most important findings on interactions between nonlinear systems and noise is the phenomenon called stochastic resonance (SR) [24,25]. In the last quarter century, SR, or the noise-aided information transfer, was found in various types of physical and biological fields including the nervous system [10,11,26–30]. Collective properties of noisy ion channels in terms of SR have also been receiving increasing attention [31–34]. Conventional studies on SR focus mainly on the enhancement of weak (or subthreshold) signals by noise. However, recent studies have revealed that noise can facilitate information transfer through a parallel array of threshold devices receiving large (or suprathreshold) signals [35–37]. This phenomenon is called

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doi:10.1016/j.physd.2009.12.002

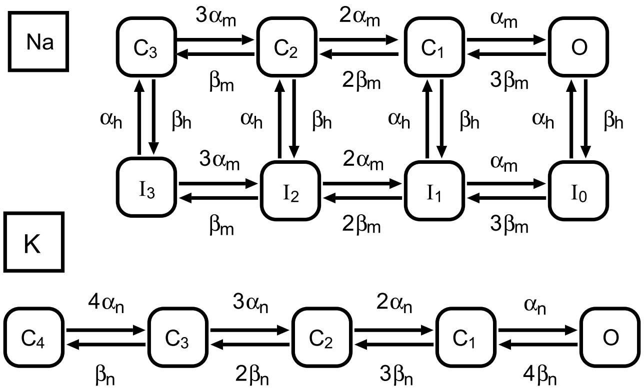

Fig. 1. Markov diagrams of sodium (Na) and potassium (K) channels. A Na channel in the Hodgkin–Huxley model takes eight states and a K channel takes five states. The state labeled "O" denotes the open state in which the channel is permeable to ions. "C_x" ($x = 1, 2, 3, 4$) and "I_x" ($x = 0, 1, 2, 3$) are closed and inactivated states, respectively.

Table 1
Transition probability functions.

$\alpha_m = \phi\ \frac{0.1\ (25-V)}{\exp((25-V)/10)-1}$,	$\beta_m = \phi \cdot 4.0\ \exp\left(-\frac{V}{18}\right)$
$\alpha_h = \phi \cdot 0.07\ \exp\left(-\frac{V}{20}\right)$,	$\beta_h = \phi\ \frac{1}{\exp((30-V)/10)+1}$
$\alpha_n = \phi\ \frac{0.01\ (10-V)}{\exp((10-V)/10)-1}$,	$\beta_n = \phi \cdot 0.125\ \exp\left(-\frac{V}{80}\right)$
$\phi = Q_{10}^{(T-23)/10}$	

suprathreshold stochastic resonance (SSR). The existence of noise leads to diversity in the response of the threshold devices, each of which shows identical response to inputs without noise, and thus the global response pattern of the array becomes more diverse and efficient.

In this paper, we examine the effect of SSR in a neuronal array having intrinsic channel noise. Signal transmission capability, measured by input estimation error, becomes optimal if a proper amount of channel fluctuation exists. This simulational result is confirmed by theoretical calculation of the mutual and Fisher information. These results, connecting SSR with the ion channel-based modeling, indicate the potential importance of channel noise in population coding.

2. Modeling

In order to investigate the effect of channel noise in signal detection, we use the deterministic Hodgkin–Huxley neuron model of the neuronal membrane [38] and the corresponding stochastic Markov channel model (see [20,22] for detailed modeling procedures).

In the conventional Hodgkin–Huxley model:

$$C_m \frac{\mathrm{d}V}{\mathrm{d}t} = I_{\mathrm{Na}} + I_{\mathrm{K}} + I_{\mathrm{leak}} + I_{\mathrm{ext}},$$
$$I_{\mathrm{Na}} = g_{\mathrm{Na}} \cdot (E_{\mathrm{Na}} - V),$$
$$I_{\mathrm{K}} = g_{\mathrm{K}} \cdot (E_{\mathrm{K}} - V),$$
$$I_{\mathrm{leak}} = g_{\mathrm{leak}} \cdot (E_{\mathrm{leak}} - V),$$

each ionic current is described as a product of the ionic conductance and the driving voltage. The ionic conductances g_{Na} and g_{K} are continuous variables written as $g_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} \cdot m^3 h$ and $g_{\mathrm{K}} = \bar{g}_{\mathrm{K}} \cdot n^4$ where $\bar{g}_{\mathrm{Na}}$ and $\bar{g}_{\mathrm{K}}$ are the maximum conductance densities and $m^3 h$ and n^4 corresponds to the fraction of "open" channels. Temporal evolution of the variables $x = m, h, n$ is described as $\mathrm{d}x/\mathrm{d}t = \alpha_x \cdot (1 - x) - \beta_x \cdot x$, where α_x and β_x are experimentally determined functions which correspond to the voltage dependence of the channel [17,38] (Table 1). In this description, once the input to the model neuron I_{ext} is fixed, the output response calculated through the equations is deterministic.

Table 2
Parameters used in the simulation.

C_m	Membrane capacitance	1 (μF/cm^2)
σ_{Na}	Na channel density	100 (channels/μm^2)
σ_{K}	K channel density	18 (channels/μm^2)
γ_{Na}	Na channel conductance	6 (pS/channel)
γ_{K}	K channel conductance	20 (pS/channel)
g_{leak}	Leak conductance	3.66 (pS/μm^2)
E_{Na}	Na reversal potential	+ 50.0 (mV)
E_{K}	K reversal potential	−75.0 (mV)
E_{leak}	Leak reversal potential	−60.0 (mV)
T	Temperature	20.0 (°C)
Q_{10}	Temperature dependence	2.0

In contrast to the conventional Hodgkin–Huxley description, the microscopic behavior of the ion channel is modeled as a Markov process of finite states (Fig. 1) and a single channel conductance takes discrete values [16,17]. When this ion channel behavior is combined with the Hodgkin–Huxley description, the conductance densities $g_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} \cdot m^3 h$ and $g_{\mathrm{K}} = \bar{g}_{\mathrm{K}} \cdot n^4$ are replaced with

$$g_{\mathrm{Na}} = \gamma_{\mathrm{Na}} \sigma_{\mathrm{Na}} \frac{M_{\mathrm{Na}}^{\mathrm{open}}}{M_{\mathrm{Na}}} \quad \text{and} \quad g_{\mathrm{K}} = \gamma_{\mathrm{K}} \sigma_{\mathrm{K}} \frac{M_{\mathrm{K}}^{\mathrm{open}}}{M_{\mathrm{K}}},$$

where γ_{Na} and γ_{K} denote the single channel conductances, σ_{Na} and σ_{K} denote the number of channels per unit area, M_{Na} and M_{K} denote the total numbers of ionic channels on the membrane, and $M_{\mathrm{Na}}^{\mathrm{open}}$ and $M_{\mathrm{K}}^{\mathrm{open}}$ denote the numbers of open ionic channels on the membrane. Parameter values used in our simulation are summarized in Table 2.

To calculate the membrane potential numerically, we used the forward Euler methods with a time increment of 0.5 μs. At each time step, the state of each ion channel changes according to the transition probability functions α_x and β_x (Table 1), and the resulting ionic currents and the membrane potential are calculated according to the equations above.

In all the simulations below, we control the number of channels on the isopotential membrane by changing the membrane patch area S [20,22]. The amplitude of the intrinsic fluctuation, which is defined as the standard deviation of the membrane potential around the resting state, is inversely proportional to $\sqrt{S}$ (Fig. 2), just as predicted by the central limit theorem. In small membrane patches, fluctuation size is above the $1/\sqrt{S}$ line because spontaneous action potentials occur without external inputs [18,21].

3. Response of single neuron

We changed external inputs to the model neuron and calculated the firing probability (Fig. 3). External input is modeled by a so-called alpha function $I_{\mathrm{ext}}(t) = s \cdot (t/\tau) \exp(1 - t/\tau)$ where s is the peak height and τ (fixed to 0.3 ms in our simulation) is the time constant. In the conventional noiseless Hodgkin–Huxley model, the neuron never fires with subthreshold inputs and always fires with suprathreshold inputs (Fig. 3, inset). In the stochastic channel-based model, however, a neuron does not have a definite threshold. Rather, the firing probability increases continuously with the input size. The slope of this input–output curve depends on the membrane patch area, or the number of channels of the membrane. The response of the stochastic neuron with a sufficient number of channels is similar to that of the noiseless model, and as the number of channels decreases, the slope becomes more linear (Fig. 3). The s-shaped response curves were fitted by the integrated Gaussian function with parameters μ and σ:

$$f(x) = \int_{-\infty}^{x} \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(\xi - \mu)^2}{2\sigma^2}\right) \mathrm{d}\xi$$
$$= \frac{1}{2}\left(1 + \mathrm{erf}\left(\frac{x - \mu}{\sqrt{2}\sigma}\right)\right),$$