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Research Article

Impact of the Variations in the Temperature on the First Spike Latency of a Hodgkin-Huxley Neuron Model

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Abstract

For stimuli just beyond threshold and certain noise strength, the Hodgkin–Huxley (HH) neuron model shows sensitivity to noise with respect to latency to first spike after stimulus onset. This effect has been called "noise delayed decay" (NDD). Here we investigate how the NDD is affected by the variation in temperature using a HH model that includes stochastic ion channels. We show that the NDD effect increases and emerges for smaller noise strengths (or larger cell sizes) as the temperature increases. We also show that the potassium channel noise plays a key role on the appearance of the NDD effect.

Keywords: First spike, Temperature effect, Hodgkin-Huxley neuron model

1. Introduction

Over the years, a large body of research has been directed at understanding of neuronal spiking and information coding within the nervous systems (Rabinovich et al. 2006, Feng and Tuckwell 2003, Makarov et al. 2001). The spiking activity of a neuron is a collective property of voltage-gated ion channels, embedded in membranes, whose behaviors may change due to the different factors such as temperature (Hodgkin et al. 1949), magnetic or electromagnetic fields (Hallet 2007) etc. The variations in environmental temperature affect the spiking dynamics of neurons through gating kinetics of ion channels (Hodgkin and Huxley 1952, Zao and Boulant 2005, Bezanilla and Taylor 1978), leading to a change in the form and amplitute of action potentials (Hodgkin and Katz 1949) and generation (Rosenthal and Bezanilla 2002) and propagation (Hodgkin 1959) of spikes.

Neurons transmit information about their inputs by transforming them into the spike trains, and coding may be in timing of the spikes (temporal coding) (Abeles 1991, Abeles et al. 1999, Mackie and Zhao 1999) or in the average rate of firing (rate coding) (Adrian 1926, de Ruyter van Steveninck and Bialek 1988). In the context of temporal coding, it has been reported that the first-spike timing or latency carry a considerable amount of information than other spikes (VanRullen et al. 2005). Pankratova et al. (2005) recently analyzed the influence of external noise on the first-spike latency of two different neuronal models driven by a suprathreshold periodic forcing, and obtained non-monotonic behavior for the mean latency at the input frequency boundaries where latency first dramatically increases, then reaches a maximum, and finally decreases as a function of the noise strength. The authors suggested that their results demonstrated the first example of NDD, a phenomenon called noise delay decay (NDD), in a neuronal model.

Ozer and Graham (2008) also examined the NDD effect on activity of a network with varying the membrane time constant. Their results show that NDD effect increases as the network activity increases (a smaller time constant) and thus, constrains the neuronal coding for suprathreshold stimulus. In another study, Ozer and Uzuntarla (2008) studied the effects of connection topology of the network and coupling strength on the NDD, and showed that the NDD effect decreases with the increasing number of random shortcuts. Recently, Uzuntarla et al. (2012) examined response time of a single HH neuron model subject to both a suprathreshold periodic forcing and synaptic background activity. Their results show that first-spike latency of a neuron can be regulated via unreliable synapses.

In this paper, our aim is to investigate how the NDD is affected by the variation in temperature using a more biophysically realistic HH model which relates the membrane area or cell size (and thus the level of intrinsic noise) to the firing characteristics in a manner that more closely mimics actual conditions.

2. Models and Methods

In the H-H model (Hodgkin and Huxley 1952), the time evolution of the membrane potential is given by

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$$C_m \frac{dV}{dt} + G_{Na}(V - E_{Na}) + G_K(V - E_K) + G_L(V - E_L) = I_{ext} \quad (1)$$

where V is the deviation of membrane potential from its equilibrium value, $C_m = 1\mu F cm^{-2}$ is the membrane capacity and I_{ext} is an externally applied current; $I_{ext}(t) = A\sin(\omega t + \varphi)$, where A and f denote the amplitude and frequency of the sinusoidal forcing current, respectively. G_{Na}, G_K and G_L represent sodium, potassium and leakage conductances, respectively. $E_{Na} = 115mV$, $E_K = -12mV$ and $E_L = 10.6mV$ are the reversal potentials for the sodium, potassium and leakage channels, respectively. In the model, the leakage conductance is assumed to be constant, $G_L = 0.3mScm^{-2}$ while the sodium and potassium conductances dynamically change according to the following equation:

$$G_{Na} = g_{Na}^{\max} m^3 h, \quad G_K = g_K^{\max} n^4 \quad (2)$$

where $g_{Na}^{\max} = 120mScm^{-2}$ and $g_K^{\max} = 36mScm^{-2}$ are the maximal sodium and potassium conductances, respectively. m and h denotes activation and inactivation gating variables for the sodium channel, respectively. The potassium channel includes an activation gating variable, n.

In the H-H model, activation and inactivation gating variables m, n and h change over time in response to the membrane potential following first-order differential equations. The effects of the channel noise have been modeled by using different computational algorithms (Mino et al. 2002). Here, we follow the approach put forward by Fox (Fox 1997) by expressing the gating variable dynamics with the corresponding Langevin generalization:

$$\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x + \xi_x(t), \quad x = m, n, h \quad (3)$$

where α_x and β_x are rate functions for the gating variable x. The parameters of the rate functions are same with those used in (Pankratova et al 2005, Schneidman et al. 1998) as follows:

$$\alpha_n = \frac{0.01\phi(T)(V_m + 55)}{1 - \exp[-(V_m + 55)/10]}$$

$$\beta_n = 0.125\phi(T)\exp[-(V_m + 65)/80]$$

$$\alpha_m = \frac{0.1\phi(T)(V_m + 40)}{1 - \exp[-(V_m + 40)/10]} \quad (4)$$

$$\beta_m = 4\phi(T)\exp[-(V_m + 65)/18]$$

$$\alpha_h = 4\phi(T)\exp[-(V_m + 65)/20]$$

$$\beta_h = \frac{\phi(T)}{1 - \exp[-(V_m + 35)/10]}$$

where

$$\phi(T) = Q_{10}^{\frac{(T-6.3^0C)}{10^0C}} \quad (5)$$

where α_n and β_n the opening and closing rates of potassium channel, α_m and β_m are the opening and closing rates for the activation gates of sodium channel, α_h and β_h and are the opening and closing rates for the inactivation gates of sodium channel. $\phi(T)$ is a temperature function and the value of Q_{10} is 3 for ion channels.

The probabilistic nature of the channels appears as a noise source in Eq. (3), $\xi_x(t)$, which is an independent zero mean Gaussian white noise source whose autocorrelation function is given as follows (Fox 1997):

$$\langle \xi_m(t)\xi_m(t') \rangle = \frac{2\alpha_m\beta_m}{N_{Na}(\alpha_m + \beta_m)} \delta(t-t'),$$

$$\langle \xi_h(t)\xi_h(t') \rangle = \frac{2\alpha_h\beta_h}{N_{Na}(\alpha_h + \beta_h)} \delta(t-t'), \quad (6)$$

$$\langle \xi_n(t)\xi_n(t') \rangle = \frac{2\alpha_n\beta_n}{N_K(\alpha_n + \beta_n)} \delta(t-t').$$

where N_{Na} and N_K denotes total number of sodium and potassium channels, respectively. Given the assumption of homogeneous sodium and potassium ion channel densities, channel numbers are calculated by $N_{Na} = \rho_{Na}S$, $N_K = \rho_K S$, where $\rho_{Na} = 60\mu m^{-2}$ *and* $\rho_K = 18\mu m^{-2}$ are the sodium and potassium channel densities, respectively, and S represents total membrane area (Fox 1997). Eqs. (1)-(6) constitute the stochastic H-H model, where the membrane area S globally determines the intrinsic noise level. In the simulations presented here, the amplitude of the forcing input is set to 4 $\mu A/cm^2$ as by Pankratova et al. (2005b). We define the latency to the first spike as the time of the first upward crossing of the membrane potential past a detection threshold of 20mV. We obtain the mean latency of an ensemble of first spikes by averaging their latencies over N realizations as follows:

$$\langle t \rangle = \frac{1}{N}\sum_{i=1}^{N} t_i \quad (9)$$

where t_i is the response time for ith realization. In order to calculate the mean latency, we averaged the first spike latencies over $N = 1000$ realizations. The numerical integration of the stochastic H-H model is computed by the standard stochastic Euler algorithm with a step size of 10 μs.

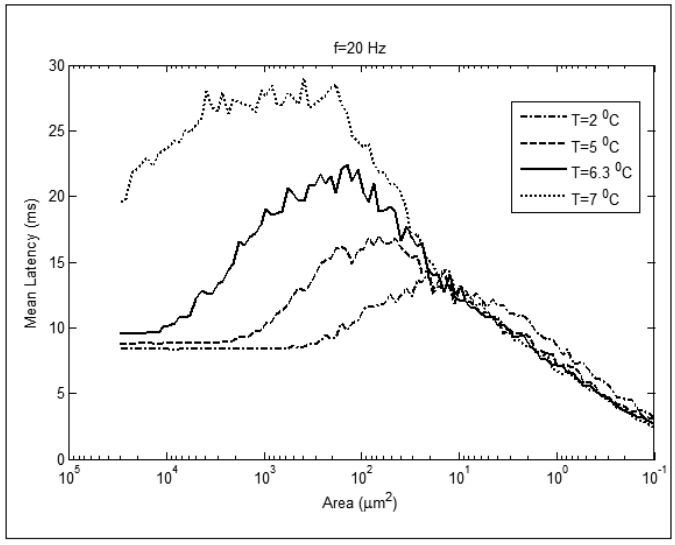

Figure 1. The change of the mean latency with temperature versus membrane area (f=20Hz).

3. Results and Discussion

In the case of sinusoidal current input to the H-H neuron, current threshold changes in a frequency-dependent manner (Tuckwell 2005, Ozer and Graham 2008, Ozer and Uzuntarla 2008) and thus for a given fixed magnitude the input is suprathreshold over a certain range of frequencies. In the model considered in this study, a sinusoidal input with a magnitude of 4 $\mu A/cm^2$ is suprathreshold for frequencies between 17 and 144 Hz. Since the NDD effect is the most prominent near the threshold (Pankratova et al. 2005b, Tuckwell 2005) we first studied the NDD effect for different temperatures in response to a suprathreshold stimulus as a function of membrane area, thus the channel noise. We conducted simulations for the temperature range between 2^0C and 7^0C and computed the mean latency of the first-spiking times for a large range of membrane areas (0.1 to 30.000 μm2; Figure 1). As shown in Figure

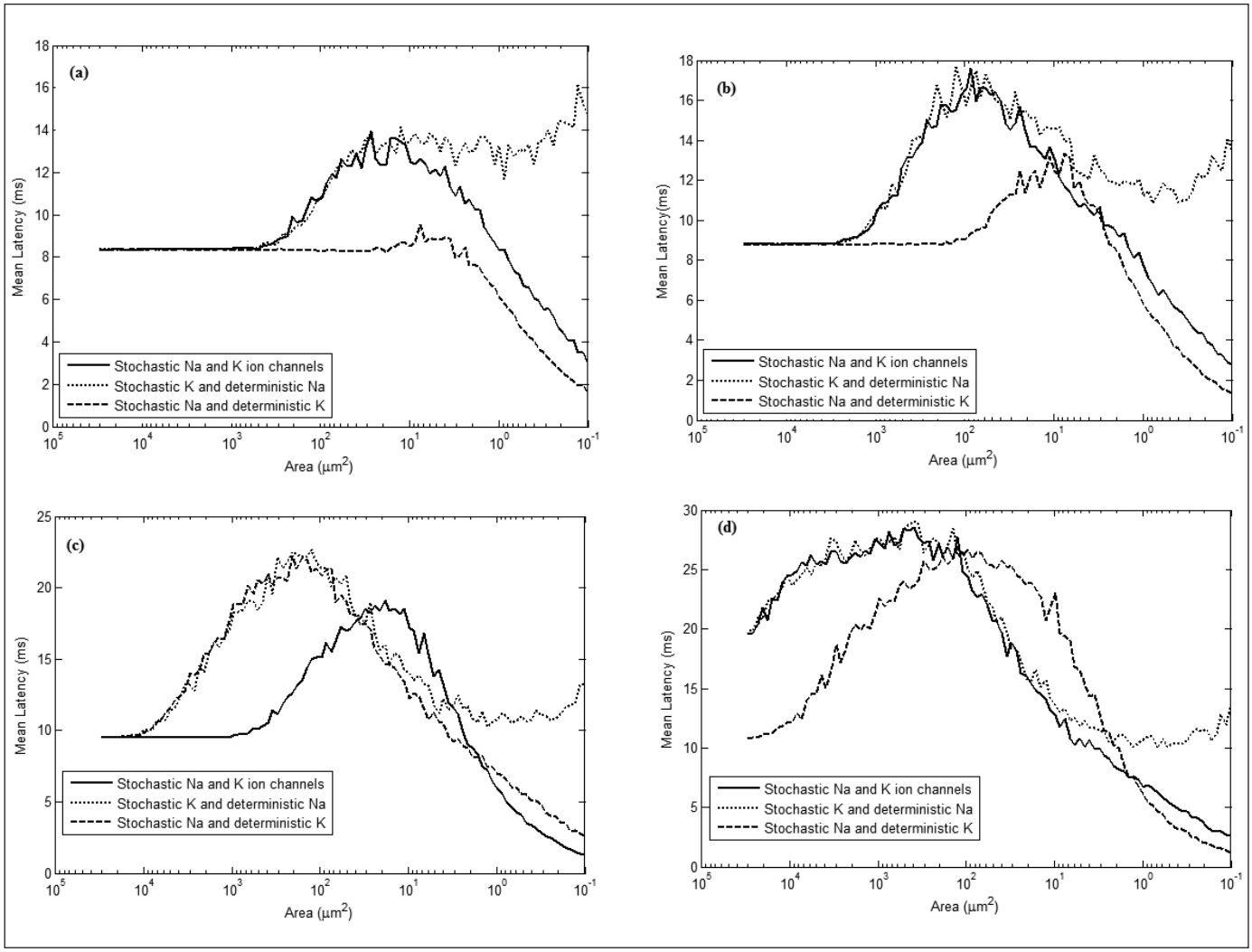

Figure 2. Individual channel noise contributions to the latency statistics, the mean latency versus membrane area (f=20Hz): **A)** T=2^0C, **B)** T=5^0C, **C)**T=6.3^{0}C, **D)**T=7^0C.

1, for all temperatures the mean latency first increase as the membrane area decreases (or, equivalently, as the channel noise increases), reaching a maximum and then decreasing. The stronger NDD effect emerges for higher temperature. The NDD effect also shifts to larger cell size (or smaller noise strengths) as the temperature increases.

We next investigated the relative contributions of the potassium and sodium channel noise to the NDD effect for different temperatures, by substituting deterministic versions of one channel type or the other (Figure 2). Figure 2 shows that potassium channel noise alone can account for the NDD mediated increase on spike latency for all patch sizes. Other than for a limited range of areas, sodium channel noise alone gives a latency increase which is smaller than either the control case with both stochastic channel types or for that of stochastic potassium channels alone. This effect of sodium channel is clearly visible with increasing the temperature. On the other hand, stochastic sodium channels are entirely responsible for a decreased latency seen in small patches, where the spike latency of the potassium-only stochastic model is larger than the deterministic value for smaller temperature but similar to the deterministic value for higher temperature.

In summary, a NDD latency increase for intermediate noise values is caused by potassium channels, while a decrease of the latency with large noise is due to sodium channel noise for all temperatures.

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