Thermal impact on spiking properties in Hodgkin–Huxley neuron with synaptic stimulus

SHENBING KUANG[1,*], JIAFU WANG[1,2], TING ZENG[1] and AIYIN CAO[1]

[1]Department of Physical Science and Technology, Wuhan University of Technology, Wuhan, 430070, China
[2]State Key Laboratory of Advanced Technology for Materials Synthesis and Processing, Wuhan, 430070, China
*Corresponding author. E-mail: whutjoey@hotmail.com

Abstract. The effect of environmental temperature on neuronal spiking behaviors is investigated by numerically simulating the temperature dependence of spiking threshold of the Hodgkin–Huxley neuron subject to synaptic stimulus. We find that the spiking threshold exhibits a global minimum in a specific temperature range where spike initiation needs weakest synaptic strength, which form the engineering perspective indicates the occurrence of optimal use of synaptic transmission in the nervous system. We further explore the biophysical origin of this phenomenon associated with ion channel gating kinetics and also discuss its possible biological relevance in information processing in neuronal systems.

Keywords. Thermal impact; spiking threshold; ion channel kinetics; synaptic transmission.

PACS Nos 87.17.Aa; 87.19.La; 87.10.+e

1. Introduction

Neuronal spiking is the basis of communication and coding in nervous systems and has been studied for decades [1–3]. Spiking behaviors of a neuron come from the activation and inactivation of various ion channels, which may vary due to the influence of environmental factors [4,5]. Temperature is one of the most important regulators to neuronal activities [6–9]. Electrophysiological experiments on neural spiking activities are mostly conducted either at room temperature *in vitro* or at body temperature *in vivo*. Thus our knowledge about how a neuron behaves in a continuously changing temperature environment is usually fragmental. Variation in temperature leads to two main impacts in the spiking dynamics of excitable neurons: one is on the maximum ion channel conductances [10,11] and the other is on ion channel gating kinetics [12–14], thus altering the shape and amplitude of action potentials [15] and the generation [16,17] and propagation [18] of spikes.

Neuronal spiking activities can be described by means of firing properties, such as firing rates [19], the precise timing of spikes [20–22], or the spiking threshold properties [23–26]. The temperature dependence of spiking threshold of giant squid axons under current injection has been investigated experimentally [23,24,27] and numerically [28,29]. More realistically, in fact, neurons communicate with each other via synaptic connections and respond to synaptic stimuli by firing spikes, so as to detect, process, and transmit the neuronal information. How the environmental temperature affects the spiking properties of a neuron stimulated by realistic synaptic input is an interesting question.

This study is to approach the above topic by examining the temperature dependence of spiking threshold of a neuron subject to synaptic stimulus, based on the widely accepted Hodgkin–Huxley (HH) neuron model, as an example, which was originally proposed to account for the exciting properties of giant squid axons [12] and is now regarded to be a useful paradigm that accounts naturally for the spiking behaviors of real neurons. Our results reveal that there is an environmental temperature range where the spiking threshold shows a global minimum, from an engineering point of view, implying that the optimal use of synaptic transmission occurs in the nervous systems. The biophysical origin, with respect to ion channel gating dynamics, of this interesting phenomenon together with its biological relevance is also investigated and discussed.

2. Model description

The dynamics of the HH model with synaptic stimulus is described by the following coupled differential equations [12]:

$$\begin{aligned}
\mathrm{d}V/\mathrm{d}t &= (I_{\mathrm{syn}} - I_{\mathrm{ion}})/C, \\
\mathrm{d}m/\mathrm{d}t &= [m_\infty(V) - m]/\tau_m(V,T), \\
\mathrm{d}h/\mathrm{d}t &= [h_\infty(V) - h]/\tau_h(V,T), \\
\mathrm{d}n/\mathrm{d}t &= [n_\infty(V) - n]/\tau_n(V,T),
\end{aligned} \tag{1}$$

with V being the membrane potential, C the membrane capacity, T the environmental temperature, n the activation variable of potassium channel, and m and h the activation and inactivation variables of sodium channel. m_∞, h_∞, n_∞ and τ_m, τ_h, τ_n represent the saturated values and the time constants of the gating variables. The ionic current I_{ion} includes the usual sodium, potassium, and leak currents:

$$I_{\mathrm{ion}} = G_{\mathrm{Na}}(T)m^3h(V - V_{\mathrm{Na}}) + G_{\mathrm{K}}(T)n^4(V - V_{\mathrm{K}}) + G_{\mathrm{L}}(T)(V - V_{\mathrm{L}}), \tag{2}$$

where V_{Na}, V_{K}, V_{L} are the reversal potentials for the channel currents.

Generally, as temperature T increases, the ionic conductance increases and the channel gating kinetic speeds up, i.e., the time constant of gating variable decreases with increasing temperature. Usually, to take into account the effects of environmental temperature on the neuronal activities, a mathematical quantity, Q_{10} factor, is often introduced. The Q_{10} factor is defined as below:

$$Q_{10}(T,a) = a^{(T-T_0)/10}, \tag{3}$$

where T_0 denotes the reference temperature at which the original electrophysiological experiment for model construction is done. ($T_0 = 6.3°$C in this study for the HH system, see ref. [4]). To mimic these two effects of temperature on the HH system, the time constants of gating variables, τs, in eqs (1) are divided by a Q_{10} factor of $a = 3$, whereas the maximum channel conductances, Gs, are multiplied by a Q_{10} factor of $a = 1$–1.5 (suggested in ref. [4]).

The synaptic input is modeled by $I_{\text{syn}} = g_{\text{syn}}(t)(V - V_{\text{syn}})$ with V_{syn} being the synaptic reversal potential and $g_{\text{syn}}(t)$ the time-dependent post-synaptic conductance, $g_{\text{syn}}(t) = G_{\text{syn}}\alpha(t - t_0)$, where t_0 represents the onset time of the synapse, G_{syn} determines the peak of synaptic conductance and $\alpha(t) = (t/\tau_{\text{syn}})\exp(1 - t/\tau_{\text{syn}})$, $t > 0$, with τ_{syn} determining the characteristic time of the synaptic interaction. In this study we choose $\tau_{\text{syn}} = 2$ ms, and $V_{\text{syn}} = 0$ mV to mimic excitatory synapse input in neural system [25,30]. The other values of parameters can be found in ref. [12]. The spiking threshold here is characterized as the critical value of G_{syn}, by which the membrane potential of the stimulated neuron exceeds a voltage threshold V_{th} (chosen as $V_{\text{th}} = -20$ mV here).

3. Thermal impact on spiking threshold

Our investigation begins with the question how environmental temperature affects the spiking threshold of HH neuron stimulated by synaptic input. An example of thermal impacts on the spiking activities could be found in figure 1, where the HH neuron is subjected to the same single excitatory post-synaptic conductance (EPSG) at three different environmental temperatures. When $T = 6.3°$C, a suprathreshold EPSG can initiate an action potential in the HH neuron (solid line). As T increases, the same EPSG turns into a sub-threshold one, as no spike appears in the outputs of the HH neuron (both dashed line and dotted line). This illustration shows that the spiking thresholds of neurons have critical dependence on the environmental temperature. To quantify this dependence, we systematically calculate the spike thresholds in a variety of environmental temperatures within the physiological range, as shown in figure 2. One may find that the spiking threshold undergoes a U-shaped dependence on the environmental temperature, i.e., there is a global minimum spiking threshold in a temperature range. We refer to this temperature range as 'comfortable temperature' one for the neuron, though the specific temperature range may not be quantitatively accurate with realistic situations. Nevertheless, the qualitative relationship of dependence of spiking thresholds on environmental temperature should be of some functional indications. In these ranges of environmental temperature the neuron needs weakest synaptic stimulus to fire spikes; from the engineering perspective this facilitates the extraction, transmission and processing of information in neuronal systems. Our result suggests that environmental temperature can make the neurons communicate easier with each other by maximizing the utility of synaptic transmitters. The optimal use of synaptic stimulus in nervous system is of great biological significance for real neurons.
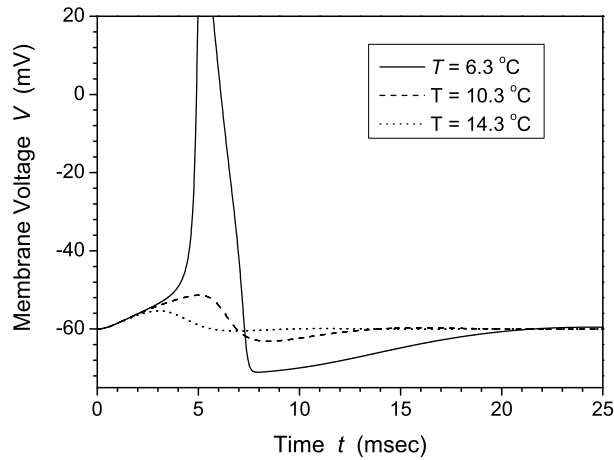
Figure 1. The time course of membrane potential in the output of the HH neuron under the identical single EPSG at three environmental temperatures, i.e., $T = 6.3°C$ (solid line), $10.3°C$ (dashed line) and $14.3°C$ (dotted line). As T increases, the same synaptic input turns, from a supra-threshold stimulus, into a sub-threshold one. Q_{10} factors of $a = 1.25$ and $a = 3$ are employed for the maximum ion conductances (the Gs in eq. (2)) and the gating time constants of ion channels (the τs in eqs (1)), respectively.
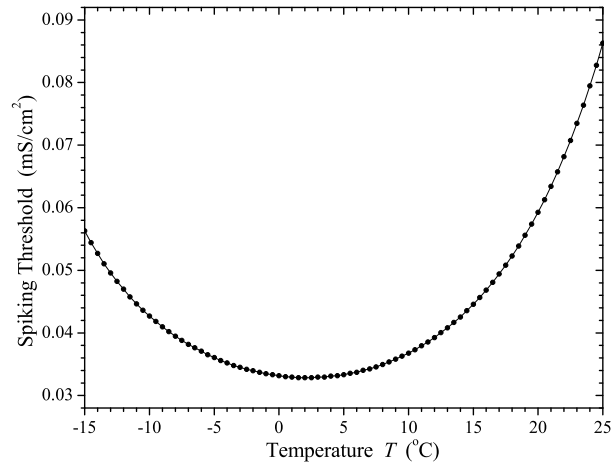

Figure 2. The dependence of spiking threshold of an HH neuron subject to synaptic stimulus on environmental temperature. Q_{10} factors of $a = 1.25$ and $a = 3$ are employed for the maximum ion conductances (the Gs in eq. (2)) and the gating time constants of ion channels (the τs in eqs (1)), respectively.

Theoretically, a U-shaped dependence of a characteristic physical quantity may result from the competition of (at least) two contrary factors/aspects. In a neuronal system, environmental temperature influences the maximum ion conductances and the channel gating rates, as demonstrated by experimental observations [4] and
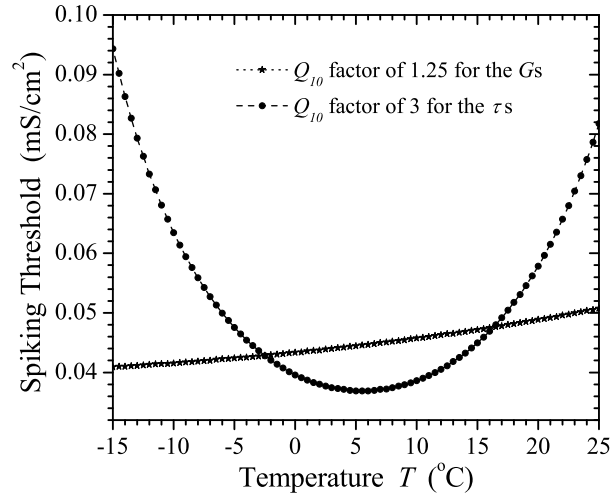
Figure 3. The influence of temperature on the spiking threshold via maximum channel conductances and channel gating kinetics, respectively. Dots: only the maximum ion channel conductances (the Gs in eq. (2)) are multiplied by a Q_{10} factor of $a = 1.25$. Stars: only the time constants of gating variables (the τs in eqs (1)) are divided by a Q_{10} factor of $a = 3$.

explicitly included in our model simulation. To find out what factors account for this U-shaped dependence phenomenon, we make a comparative examination. The effects of temperature regulation on spiking threshold through the maximum ion conductances and through the gating time constants of channel variables (see figure 3) are investigated respectively. If only the influence of temperature on the maximum ion conductances is considered, the spiking threshold increases monotonously with temperature. In direct contrast, the sole temperature effect via gating kinetics of ion channels gives rise to a temperature dependence of spiking threshold that almost resemble the control result in figure 2. Thus one can conclude that it is the dominant role of temperature on the gating kinetics of ion channels that yields the phenomenon of optimal use of synapse transmission in neuronal system, though changes in maximum channel conductances simultaneously contribute slightly to the elevation of spiking threshold with increasing environmental temperature.

So far we have been aware that the occurrence of optimal use of synaptic transmission attributes mainly to the thermal impacts on the gating kinetics of ion channels. However, the direct link between the two still lacks: why does a monotonous dependence of gating time constants on temperature result in a non-monotonous temperature dependence of spiking threshold in neuronal systems? As is well known, the activation of sodium ion channel depolarizes the membrane potential and forms the rise course of an action potential; on the contrary, the activation of potassium ion channel along with the inactivation of sodium ion channel forms the decay course of an action potential. Is it the competition of the gating behaviours between these two types of channels that yields the U-shaped temperature dependence of spiking threshold? The answer to this question is unfortunately negative (simulation
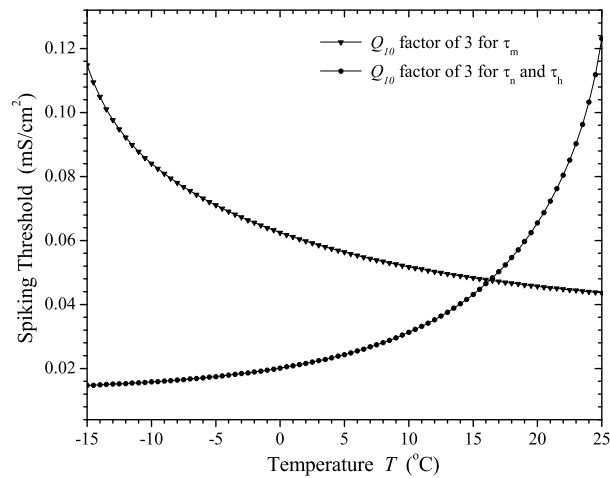
Figure 4. The influence of temperature on the spiking threshold via the thermal regulations on the activation/inactivation variables. If only the time constant of sodium channel activation variable m is regulated with a reciprocal Q_{10} factor of $a = 3$, the spiking threshold decreases with increasing temperature (triangles); if only the time constants of sodium channel inactivation variable h and potassium channel activation variable n are divided by a Q_{10} factor of $a = 3$, spiking threshold increases with temperature (dots).

results are not shown here). Thus we divide the three gating variables of ion channels into two categories: one is the sodium ion channel activation variable m, which is beneficial for a neuron to initiate spikes, and the other includes the sodium ion channel inactivation variable h and the potassium ion channel activation variable n, which serve to terminate action potentials. We speculate that it is the interaction between these two contrary (competitive) aspects that lead to the temperature dependence of the neuron's spiking threshold. To confirm our interpretation, we design further comparative explorations. In figure 4 one can find contrasting dependencies of spiking threshold on environmental temperature between the thermal impact via activation kinetic of sodium ion channel alone and that via the inactivation of sodium ion channel together with the activation kinetics of potassium ion channel. These results are in good agreement with our speculation.

In the above, simulation results for the temperature dependence of spiking threshold are obtained by choosing the specific Q_{10} factors of $a = 3$ for time constants of channel gating variables and $a = 1.25$ for the maximum ion conductances. Although other Q_{10} factors might also be used for the neuronal system [4,31], they are not expected to yield essential difference and the U-shaped temperature dependence still occurs. Examples for the HH neuron are shown in figure 5, where one can see that temperature dependencies of spiking threshold are very similar to the control case (see figure 2). The characteristic time τ_{syn} of synaptic interaction may also vary with environmental temperature, but again it does not lead to any essentially different result against our conclusions. In fact, the elegance of optimal use of synaptic transmission in a range of environmental temperature in giant squid axons
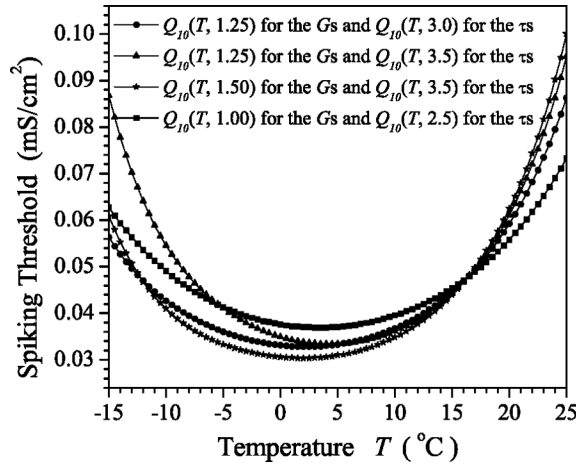
Figure 5. The temperature dependencies of spiking threshold of the HH neuron in a variety of Q_{10} factors for maximum ion conductances (the Gs in eq. (2)) and the gating time constants of channel variables (the τs in eqs (1)). The Q_{10} factors are chosen within the physiologically suitable range.

can be further generalized to other nervous systems, such as the cochlear nucleus neuron in auditory system [32]. Presumably, this subcellular mechanism of thermal impacts on the neuronal spiking via ion channel kinetic behaviours can serve as the base for the psychophysical evidence that various animals live optimally in a specific range of environmental temperature.

4. Conclusions

In summary, we have investigated the effects of environmental temperature on the spiking behaviours of a neuron subject to synaptic stimulus. Our results reveal that the spiking threshold shows a global minimum in a specific temperature range, which from engineering perspective implies the occurrence of optimal use of synaptic transmission in neuronal system. It seems that the nervous systems are naturally designed/tuned to optimize the signal processing capacities. We further illustrate that the emergence of this phenomenon attributes mainly to the combined competition of the temperature-dependent gating kinetics of ion channel activation/inactivation variables. The optimal use of synaptic transmission in neuronal system may largely facilitate the extraction, processing and transmission of neuronal information in neurons.

Acknowledgments

References

[1] M I Rabinovich, P Varona, A I Selverston and H D I Abarbanel, *Rev. Mod. Phys.* **78**, 1213 (2006)

[2] J Feng and H C Tuckwell, *Phys. Rev. Lett.* **91**, 018101 (2003)

[3] V A Makarov, V I Nekorkin and M G Velarde, *Phys. Rev. Lett.* **86**, 003431 (2001)

[4] A L Hodgkin, A F Huxley and B Katz, *J. Physiol.* **116**, 424 (1952)

[5] J S Schweitzer, H Wang, Z Xiong and J L Stringer, *J. Neurophysiol.* **84**, 927 (2000)

[6] V Y Vasilenko, E M Belyavskii and V N Gurin, *Neurophysiol.* **21**, 259 (1989)

[7] J D Miller, V H Cao and H C Heller, *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **266**, 1259 (1994)

[8] H Xu and R M Robertson, *J. Comp. Physiol.* **A175**, 193 (1994)

[9] M Radmilovich, A Fernández and O Trujillo-Cenóz, *J. Exp. Biol.* **206**, 3085 (2003)

[10] J W Moore, *Fed. Proc.* **17**, 113 (1958)

[11] X Cao and D Oertel, *J. Neurophysiol.* **94**, 821 (2005)

[12] A L Hodgkin and A F Huxley, *J. Physiol.* **117**, 500 (1952)

[13] F Bezanilla and R E Taylor, *Biophys. J.* **23**, 479 (1978)

[14] Y Zhao and J A Boulant, *J. Physiol.* **564**, 245 (2005)

[15] A L Hodgkin and B Katz, *J. Physiol.* **108**, 37 (1949)

[16] J J C Rosenthal and F Bezanilla, *J. Exp. Biol.* **205**, 1819 (2002)

[17] M Volgushev, T R Vidyasagar, M Chistiakova, T Yousef and U T Eysel, *J. Physiol.* **522**, 59 (2000)

[18] A F Huxley, *Ann. New York Acad. Sci.* **81**, 221 (1959)

[19] F Rieke, D Warland, R R Steveninck and W Bialek, *Spikes: Exploring the neural code* (MIT Press, 1997), p. 395

[20] A V Holden, *Nature (London)* **428**, 382 (2004)

[21] M J Chacron, B Lindner and A Longtin, *Phys. Rev. Lett.* **92**, 080601 (2004)

[22] R VanRullen, R Guyonneau and S J Thorpe, *Trends Neurosci.* **28**, 1 (2005)

[23] R A Sjodin and L J Mullins, *J. Gen. Physiol.* **42**, 39 (1958)

[24] R Guttman and B Sandler, *J. Gen. Physiol.* **46**, 257 (1962)

[25] Y Yu, W Wang, J Wang and F Liu, *Phys. Rev.* **E63**, 021907 (2001).

[26] S Kuang, J Wang and T Zeng, *Chin. Phys. Lett.* **23**, 3380 (2006)

[27] R Guttman and R Barnhill, *J. Gen. Physiol.* **49**, 1007 (1966)

[28] R FitzHugh, *Biophys. J.* **2**, 11 (1962)

[29] R FitzHugh, *J. Gen. Physiol.* **49**, 989 (1966)

[30] C Koch, *Biophysics of computation: Information processing in single neurons* (Oxford University Press, 1999), p. 562

[31] J S Rothman and P B Manis, *J. Neurophysiol.* **89**, 3097 (2003)

[32] T Zeng, J Wang and S Kuang, *Influence of temperature on neuronal excitability in cochlear nucleus*, submitted to *Phys. Lett. A* (also available on arXiv:q-bio/0702013)