Effects of internal noise on the spiking regularity of a clustered Hodgkin–Huxley neuronal network

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Abstract Spiking regularity in a clustered Hodgkin–Huxley (HH) neuronal network has been studied in this letter. A stochastic HH neuronal model with channel blocks has been applied as local neuronal model. Effects of the internal channel noise on the spiking regularity are discussed by changing the membrane patch size. We find that when there is no channel blocks in potassium channels, there exist some intermediate membrane patch sizes at which the spiking regularity could reach to a higher level. Spiking regularity increases with the membrane patch size when sodium channels are not blocked. Namely, depending on different channel blocking states, internal channel noise tuned by membrane patch size could have different influence on the spiking regularity of neuronal networks.

Keywords spiking regularity, internal noise, clustered neuronal network, Hodgkin–Huxley neuron

Random fluctuations have been found widely in biological systems.1,2 Especially, in neuronal systems, neurons are living in a noisy environment. This randomness origins from random ion flow across the plasma membrane (channel noise)3 or the stochastic activities of other neurons (synaptic noise).4 Previous experimental works have indicated that both channel noise5,6 and synaptic noise7 could give important influence on neuronal behaviors.

In dynamical studies, it is also revealed that these two types of noise could have great impacts on various nonlinear dynamics of neuronal systems. For example, it is found that channel noise could either increase or decrease the spontaneous spiking regularity of both single neuron8 and neuronal network9–11 by potassium channel noise or sodium channel noise. And channel noise could also influence information processing,12 stochastic resonance,13 pattern formation,14–16 action potential initiation and propagation.17,18 Moreover, synaptic noise could improve detection of subthreshold signals,19 ensure unlagged neuronal responses to high-frequency inputs,20 etc.

As we know, neuronal system (e.g., brain cortex) contains billions of neurons with each neuron connecting to nearly 10^4 other neurons through synapses, and forms a huge complex network. More and more researches has revealed that this huge complex network exhibits some typical characteristics.21–23 It has been revealed that the neuronal system is an efficient small-world network.21 It has hubs22 and exhibits hierarchical and modular (or clustered) structures.23 In the past years, researchers mainly focused on investigating neuronal dynamics in single neuronal models or single neuronal networks. As we just mentioned, neuronal system exhibits hierarchy
and clustered structure characteristic. Thus, it may be more interesting and attractive to study neuronal dynamics in hierarchy or clustered neuronal networks.

In the present paper, we consider the influence of channel noise, which could be considered as internal noise, on a clustered neuronal network’s spiking regularity with a stochastic Hodgkin–Huxley (HH)\(^{24,25}\) as the building block. In clustered network, it contains several small subnetworks with dense connections inside subnetwork and sparse connections between them. Spiking regularity measures the regularity of spiking times of the neuronal systems. Thus, the variability of spiking regularity could have important effects on neuronal information transmission.

Internal channel noises’s influences on spiking regularity of the HH clustered neuronal network are studied by tuning the membrane patch size for various ratios of working sodium or potassium ion channels. The mathematical model and the network topology we used in this letter are subsequently demonstrated. Finally, we present the main results and give a summary of this letter.

We describe the dynamics of the studied neuronal network using equations as follows

\[
C \frac{dV_{i,j}}{dt} = -G_{Na}(m_{i,j}, h_{i,j})(V_{i,j} - V_{Na}) - G_{K}(n_{i,j})(V_{i,j} - V_{K}) - G_{L}(V_{i,j} - V_{L}) + 
\]

\[
\epsilon_{\text{intra}} \sum_{j} A_{I}(i,j)(V_{i,j} - V_{i}) + \epsilon_{\text{inter}} \sum_{j} B_{I,J}(i,j)(V_{j,j} - V_{i}),
\]

(1)

\[
\frac{dm_{i,j}}{dt} = \alpha_{m_{i,j}}(V_{i,j})(1 - m_{i,j}) - \beta_{m_{i,j}}(V_{i,j})m_{i,j} + \xi_{m_{i,j}}(t),
\]

(2)

\[
\frac{dh_{i,j}}{dt} = \alpha_{h_{i,j}}(V_{i,j})(1 - h_{i,j}) - \beta_{h_{i,j}}(V_{i,j})h_{i,j} + \xi_{h_{i,j}}(t),
\]

(3)

\[
\frac{dn_{i,j}}{dt} = \alpha_{n_{i,j}}(V_{i,j})(1 - n_{i,j}) - \beta_{n_{i,j}}(V_{i,j})n_{i,j} + \xi_{n_{i,j}}(t).
\]

(4)

In Eq. (1), \(V_{i,j}\) is the membrane potential and \(h_{i,j}, n_{i,j}\) and \(m_{i,j}\) are the gating variables representing the sodium channel inactivation, fractions of potassium and sodium channel activations, respectively. \(C = 1 \mu F \cdot cm^{-2}\) denotes the cell membrane capacity. Reversal potentials for the potassium, leakage currents, and sodium are \(V_{K} = -77 \text{mV}, V_{L} = -54.4 \text{mV},\) and \(V_{Na} = 50.0 \text{mV},\) respectively. As \(G_{L}\) as the leakage conductance is presumed to be constant 0.3 \(\text{mS} \cdot \text{cm}^{-2},\) the sodium and potassium conductance read as

\[
G_{K}(n_{i,j}) = g_{K}^{\text{max}} x_{K} n_{i,j}^{3}, \quad G_{Na}(m_{i,j}, h_{i,j}) = g_{Na}^{\text{max}} x_{Na} m_{i,j}^{3} h_{i,j},
\]

(5)

where \(g_{K}^{\text{max}} = 36 \text{mS} \cdot \text{cm}^{-2}, \quad g_{Na}^{\text{max}} = 120 \text{mS} \cdot \text{cm}^{-2}\) are the maximal conductance (with every channel open) and \(x_{K}, x_{Na}\) represent the fractions of working. \(\epsilon_{\text{intra}}\) and \(\epsilon_{\text{inter}}\) present the electrically coupled neurons’ coupling strength inside a subnetwork and the electrically coupled neurons’ coupling strength between different subnetworks, respectively. Here, the inter-coupling and intra-coupling strength \(\epsilon_{\text{inter}}, \epsilon_{\text{intra}}\) are set equally as 0.1. The subscript pairs \((i,i)\) represent the \(i\)-th neuron in the \(I\)-th cluster with \(1 \leq i \leq n (n\) is the size of the subnetwork) and \(1 \leq I \leq M (M\) represents the number of the clusters inside the whole system). The matrix \(A_{I} = (A_{I}(i,j))\) is a connectivity matrix for neurons inside the \(I\)-th cluster and the elements satisfy: \(A_{I}(i,j) = 1\) if neuron \(i\) is connected to neuron \(j; A_{I}(i,j) = 0\) otherwise; \(A_{I}(i,i) = 0\). The matrix \(B_{I,J} = (B_{I,J}(i,j))\)
(I ≠ J) is also a connectivity matrix, however this matrix denotes the connections between neurons which belong to different clusters. The elements of \( B_{1,J} \) satisfy: \( B_{1,J}(i, j) = 1 \) if the \( i \)-th neuron in the \( I \)-th cluster is connected to the \( j \)-th neuron in the \( J \)-th cluster; \( B_{1,J}(i, j) = 0 \) otherwise.

In this letter, we consider that each subnetwork has equal number of nodes \( n \), which is independent of the index \( I \). Nodes in each subnetwork are arranged along a ring, and each node is connected to its 2\( k \) nearest neighbors. Here, \( k \) is set to be 2. Especially, we assume that \( M \) subnetworks are also arranged on a ring, and neurons in each subnetwork just connect to the neurons from its two nearest subnetworks. The interconnections between different subnetworks exist randomly with the probability \( p \). In our case, the parameter \( p \) represents the fraction of total links in the network devoted to the connections between different subnetworks, and is taken as 0.05 in the whole letter.

In Eqs. (2)–(4), \( \alpha_{mI}(V_{I,i}) \) and \( \beta_{mI}(V_{I,i}) \) \((mI, hI, nI,i)\) represent the transition rates which is subjected to voltage and they are described as\(^{26}\)

\[
\alpha_{mI}(V_{I,i}) = 0.1(V_{I,i} + 40)/\{1 - \exp[-(V_{I,i} + 40)/10]\},
\]
\[
\beta_{mI}(V_{I,i}) = 4.0\exp[-(V_{I,i} + 65)/18],
\]
\[
\alpha_{hI}(V_{I,i}) = 0.07\exp[-(V_{I,i} + 65)/20],
\]
\[
\beta_{hI}(V_{I,i}) = \{1 + \exp[-(V_{I,i} + 35)/10]\}^{-1},
\]
\[
\alpha_{nI}(V_{I,i}) = 0.01(V_{I,i} + 55)/\{1 - \exp[-(V_{I,i} + 55)/10]\},
\]
\[
\beta_{nI}(V_{I,i}) = 0.125\exp[-(V_{I,i} + 65)/80],
\]

and \( \xi_{mI}(t), \xi_{hI}(t), \xi_{nI}(t) \) denote the channel noises. They are assumed to be independent, and their statistical properties act like those of Gaussian white noise. We set the first-order moments \( \langle \xi_{mI}(t) \rangle, \langle \xi_{hI}(t) \rangle, \langle \xi_{nI}(t) \rangle \) to be 0 and express the noise correlations as

\[
\langle \xi_{mI}(t)\xi_{mI}(t') \rangle = \frac{2}{N_{Na}\times Na} \frac{\alpha_{mI}(V_{I,i})\beta_{mI}(V_{I,i})}{\alpha_{mI}(V_{I,i}) + \beta_{mI}(V_{I,i})} \delta(t - t'),
\]
\[
\langle \xi_{hI}(t)\xi_{hI}(t') \rangle = \frac{2}{N_{Na}\times Na} \frac{\alpha_{hI}(V_{I,i})\beta_{hI}(V_{I,i})}{\alpha_{hI}(V_{I,i}) + \beta_{hI}(V_{I,i})} \delta(t - t'),
\]
\[
\langle \xi_{nI}(t)\xi_{nI}(t') \rangle = \frac{2}{N_{K}\times K} \frac{\alpha_{nI}(V_{I,i})\beta_{nI}(V_{I,i})}{\alpha_{nI}(V_{I,i}) + \beta_{nI}(V_{I,i})} \delta(t - t').
\]

In the above equations, numbers of potassium ion channel and sodium ion channel are denoted as \( N_{K} \) and \( N_{Na} \) on an excitable membrane patch. \( \rho_{K} = 18 \mu m^{-2}, \rho_{Na} = 60 \mu m^{-2} \) are ion channel densities and assumed homogeneously. The numbers \( N_{K} \) and \( N_{Na} \) are expressed as \( N_{K} = \rho_{K}S \) and \( N_{Na} = \rho_{Na}S \), in which \( S \) is the membrane patch size. The factors \( x_{Na} (0 \leq x_{Na} \leq 1) \) and \( x_{K} (0 \leq x_{K} \leq 1) \) denote the ratios of working (non-blocked) ion channels versus the total numbers of sodium and potassium ion channels.\(^{24}\) For all the neurons, \( x_{Na} \) and \( x_{K} \) are presumed to be equal, i.e., neurons have the same amount of non-blocked ion channels for sodium and potassium.

To quantify the spiking regularity of the neuronal network, we introduce the inverse of the coefficient of variation \( R_{i} \), which could quantify the regularity of spike timing in a neuron, and be
represented as

\[ R_i = \frac{\langle T_{i,k} \rangle}{\sqrt{\langle T_{i,k}^2 \rangle - \langle T_{i,k} \rangle^2}}. \]  

(10)

Here \( T_{i,k} = t_{i,k+1} - t_{i,k} \) represents the inter-spike interval with \( t_{i,k} \) denoting the \( k \)-th spike’s time of the \( i \)-th neuron. Meanwhile, \( \langle T_{i,k}^2 \rangle \) and \( \langle T_{i,k} \rangle \) are the mean squared and mean inter-spike intervals. Using the upward crossing of \( V \) (the membrane potential) past a certain value \( V_{th} \) (here \( V_{th} \) is taken as \(-20 \text{ mV}\)), we can define spiking times. Note that without altering the results, the threshold value can change over a wide range. With the aid of definition of \( R_i \), we can define spiking regularity of the whole network as an average factor of \( R_i \) by the following formula

\[ R = \frac{1}{N} \sum_{i=1}^{N} R_i, \]  

(11)

where \( N = 120 \) denotes the number of neurons inside the considered clustered network. Larger \( R \) means better spiking regularity of the whole neuronal network. In the followings, we take \( S \) (the membrane patch size) as control parameter to investigate the internal channel noise’s effects on the spiking regularity of the considered clustered neuronal network.

The impact of internal channel noise on the spiking regularity of the clustered network is studied using the membrane patch size. First, we investigate how \( R \) changes with \( S \) for various \( x_{Na} \) by fixing \( x_{K} = 1.00 \). Namely, we assume that sodium channels are partially blocked, the ratio of working sodium channels is represented by \( x_{Na} \); while all the potassium channels are non-blocked at first. Obtained results are showed in Fig. 1. For all values of \( x_{Na} \) considered in Fig. 1, \( R \) increases to some higher levels and then decreases with the increasing of \( S \). This means that there exist some intermediate membrane patch sizes, at which the spiking times of the neurons inside the neuronal network are most regular. At this case, internal channel noise could induce coherence resonance in the clustered neuronal network.

Next, we fix \( x_{Na} = 1.00 \), i.e., all sodium channels are at working states. And we discuss the dependence of \( R \) on \( S \) by just blocking some potassium channels. Different from the above obtained results, it is found that spiking regularity of the system increases with \( S \) (except \( x_{K} = 1.00 \)) when all sodium channels are open, as shown in Fig. 2.

It is worth mentioning that the increasing of \( S \) decreases both the sodium and potassium internal channel noise level. And the different blocking state of sodium and potassium channels results in different dependence of spiking regularity on \( S \). When all potassium channels are at working state and blocking some sodium channels, reductions of internal noise level could induce coherence resonance behavior against spiking regularity. However, when all sodium channels are working and some potassium channels are blocked, reduction of internal noise level can increase the spiking regularity. As reported in Refs. 8–11, decreasing of working sodium channels (decreasing of \( x_{Na} \)) diminishes the collective spiking regularity, while decreasing of working potassium channels (decreasing of \( x_{K} \)) enhances it by a fixed membrane patch size for a single neuron and neuronal network. Furthermore, it is revealed that compared to potassium, sodium channel noise may play a prominent role in neuronal behaviors.11 With these previous results, we give some illustrations on our obtained results here. Increasing \( S \) could decrease sodium and potassium
Fig. 1. The dependence of the spiking regularity $R$ on the membrane patch size $S$ for various sodium channel non-blocked fraction $x_{Na}$ by fixing $x_{K} = 1.00$.

Fig. 2. The dependence of the spiking regularity $R$ on the membrane patch size $S$ for various sodium channel non-blocked fraction $x_{K}$ by fixing $x_{Na} = 1.00$. 
channel noise level. Reduction in sodium channel noise could increase the spiking regularity of the neuronal system, while reduction in potassium channel noise may decrease it. As shown in Fig. 2, spiking regularity $R$ increases with $S$ for various of $x_K$ when all sodium channels are at working state. It indicates that sodium channel noise dominantly influence the spiking regularity regardless of potassium channel noise. While for $x_K = 1.00$ (i.e., all potassium channels are working), it is found that with reduction of both sodium channel noise and potassium channel noise, dominant channel noise changes from sodium one to potassium one. Thus, we can observe some intermediate membrane patch size at which spiking regularity becomes higher.

In summary, it is exhibited that we can resonantly enhance the regularity of spiking activity by fine-tuning of the membrane patch size $S$ when all potassium channels are at working states. When all sodium channels are working, sodium channel noise plays a dominant role when $S$ is small (approximately $S < 3.0$) and makes the spiking regularity increases at first. With $S$ increases further, the dominant channel noise has changed from sodium channel noise to potassium channel noise, which leads to the reduction of spiking regularity when $S$ is larger. Considering the importance of spiking regularity, we hope that our results could give some implications on understanding the role of internal noise on neuronal information transmission.

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