Collective firing regularity of a scale-free Hodgkin–Huxley neuronal network in response to a subthreshold signal

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A B S T R A C T

We consider a scale-free network of stochastic HH neurons driven by a subthreshold periodic stimulus and investigate how the collective spiking regularity or the collective temporal coherence changes with the stimulus frequency, the intrinsic noise (or the cell size), the network average degree and the coupling strength. We show that the best temporal coherence is obtained for a certain level of the intrinsic noise when the frequencies of the external stimulus and the subthreshold oscillations of the network elements match. We also find that the collective regularity exhibits a resonance-like behavior depending on both the coupling strength and the network average degree at the optimal values of the stimulus frequency and the cell size, indicating that the best temporal coherence also requires an optimal coupling strength and an optimal average degree of the connectivity.

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1. Introduction

In the last decade, the great attention has been dedicated to research complex system dynamics by using different network topologies [1–3]. The scale-free (SF) and the small-world (SW) network topologies have been widely used due to their capability of modeling many real networks. Recently, dynamics of biological neuronal networks has been examined by adapting these topologies [4–8]. In the field of computational neuroscience, understanding the weak signal detection and the coding within the nervous system of noisy components is of great importance. In this context, collective spiking regularity or temporal coherence of the neuronal networks has been extensively investigated for the SW network topology. Ozer et al. [9] examined the collective firing regularity of HH neurons in an SW network and showed that an optimal number of randomly added shortcuts and a certain level of noise intensity warrant the maximal temporal coherence both in presence and absence of a subthreshold periodic current. Gong et al. [10] investigated spatial synchronization and temporal coherence of an SW network driven by a subthreshold periodic current and found that synchronization and coherence can be enhanced by small-world network topology. Li and Gao [11] studied regularity of the spiking oscillation of the Fitz-Hugh–Nagumo neurons induced by colored noise and proposed that the regularity of spike train in the SW networks is higher than those in a regular network at an intermediate noise level.

Although the SW network topology provides more insight into the neuronal information processing, Barabasi and Albert [12] evidently showed that most of the real networks exhibit neither small-world nor random topology, but they display the SF topological features. The real networks such as web pages [13], the electric distribution system [14], the pattern of citations of scientific articles [15] and the movie actors taking the role at the same film [12] have been shown to be constructed through the SF topology. Moreover, the findings from the voxel based resting state connectivity analyses confirmed the modeling possibility with the SF topology of intra-regional connectivity in the functional brain regions [16]. In addition, Eguiluz et al. [17] reported that a scale-free architecture of functionally connected brain regions has been observed at a voxel scale during the performance of a number of motor and auditory tasks.

A literature survey leaves us with the impression that the collective spiking regularity of neuronal networks has not been investigated in any detail using the SF topology. Therefore, in this study, our aim is to examine the collective spiking regularity of the SF Hodgkin–Huxley (HH) neuronal network driven by a subthreshold periodic stimulus. In addition, we use a biologically more realistic model for the stochastic behavior of the voltage-gated ion channels embedded in the membrane patch, where the channel noise intensity depends on the membrane patch area or the cell size. We examine the collective regularity depending on both the stimulus frequency and the cell size. We also investigate how the network

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average degree and coupling strength affect the collective regularity.

2. Model

In a scale-free network of HH neurons, membrane potential dynamics is described by the following equation:

$$C_m \frac{dV_i}{dt} = -g_{Na}^{max} m^3 h(V_i - V_{Na}) - g_K^{max} n^4 (V_i - V_K)$$
$$- g_L^{max}(V_i - V_L) + \sum_j \varepsilon_{ij}[V_j(t) - V_i(t)] + I_{ext},$$
$$i = 1, 2, \ldots, N \tag{1}$$

where $g_{Na}^{max} = 120$ mS/cm^2, $g_K^{max} = 36$ mS/cm^2 and $g_L^{max} = 0.3$ mS/cm^2 denote the maximal sodium, the maximal potassium and the leakage conductance, respectively. N is the number of neurons within the network, $C_m = 1$ μF/cm^2 is the membrane capacitance. $V_{Na} = 50$ mV, $V_K = -77$ mV and $V_L = -54.4$ mV are the reversal potential of sodium, potassium and leakage currents respectively. $I_{ext} = A\sin(\omega t)$ is externally applied subthreshold sinusoidal stimulus, where A is the amplitude of the stimulus and set to 1 μA/cm^2. ε_{ij} denotes the coupling strength between neurons i and j. If neurons i and j are connected then $\varepsilon_{ij} = \varepsilon$, otherwise equal to zero. m and n represent the open probabilities for the sodium and potassium activation gating variables, respectively; and h represents the open probability for the sodium inactivation gating variable. The factors m^3h and n^4 are the mean portions of open sodium and potassium channels within the membrane patch, respectively.

In the HH model, dynamics of gating variables change over time in response to membrane potential [18]. However, if the number of ion channels is finite, the stochastic behavior of the ion channels may have remarkable effects on the neuronal dynamics. To consider the channel stochasticity, we use Fox's algorithm [19] due to its widespread use and computational efficiency [9,20–22]. In Fox's algorithm, the gating dynamics is described by the Langevin generalization as follows [19]:

$$\frac{dx_i}{dt} = \alpha_{x_i}(1 - x_i) - \beta_{x_i} + \zeta_{x_i}(t), \quad x_i = m, n, h \tag{2}$$

where α_x and β_x are the voltage-dependent rate functions for the gating variable x_i. ζ_{x_i} denotes the independent zero mean Gaussian white noise whose autocorrelation functions are given as follows [19]:

$$\langle \zeta_m(t)\zeta_m(t')\rangle = \frac{2\alpha_m\beta_m}{N_{Na}(\alpha_m + \beta_m)}\delta(t - t'), \tag{3a}$$

$$\langle \zeta_h(t)\zeta_h(t')\rangle = \frac{2\alpha_h\beta_h}{N_{Na}(\alpha_h + \beta_h)}\delta(t - t'), \tag{3b}$$

$$\langle \zeta_n(t)\zeta_n(t')\rangle = \frac{2\alpha_n\beta_n}{N_K(\alpha_n + \beta_n)}\delta(t - t') \tag{3c}$$

where N_{Na} and N_K represent the total numbers of sodium and potassium channels in a given membrane patch area, respectively. The total channel numbers are calculated as $N_{Na} = \rho_{Na}S$ and $N_K = \rho_K S$, where S represents the membrane patch area or the cell size. $\rho_{Na} = 60$ μm^{-2} and $\rho_K = 18$ μm^{-2} are sodium and potassium channel densities, respectively [9,20–22]. The strength of ion channel noise in Eq. (3) is inversely proportional to the cell size S.

Following the procedure in [12], we construct the scale-free neuronal network, using $N = 200$ neurons with different average degree of connectivity, k_{avg}. To quantify the collective firing regularity or the network temporal coherence, we use the inverse

of coefficient of variation (CV) of the inter-spike intervals (ISIs) [9,10,22]:

$$\lambda = \frac{1}{CV} = \frac{\langle T \rangle}{\sqrt{\langle T^2 \rangle - \langle T \rangle^2}} \tag{4}$$

where $\langle T \rangle^2$ and $\langle T^2 \rangle$ denote the mean and mean-squared ISIs, respectively. Spike times are defined by the upward crossing of the average membrane potential of the network, $V_{avg}(t) = 1/N \sum_{i=1}^N V_i(t)$, past a detection threshold of 0 mV. Notably, a larger λ corresponds to a stronger temporal coherence. The numerical integration of the stochastic model is performed by using the standard Euler algorithm with a step size of 10 μs. To ensure the statistical consistency, all results are calculated over 20 different network realizations.

3. Results

In what follows, we systematically analyze how the collective firing regularity of the scale-free HH neuronal network driven by a subthreshold periodic stimulus changes with the stimulus frequency, the cell size, the coupling strength and the network average degree. Therefore, we first investigated how the collective firing regularity of the network changes with the stimulus frequency. We computed λ during 100 second simulations for seven different cell sizes ranging from 1 to 32 μm^2, in each case for nine different angular frequencies ranging between $\omega = 0.1$–0.9 ms^{-1} (Fig. 1). We found a clear optimal island of λ in the S–ω parameter space, with an optimal frequency of $\omega = 0.3$ ms^{-1} and an optimal cell size of $S = 6$ μm^2, suggesting a double-stochastic resonance. We also found a second and third smaller peaks for the same cell of $S = 6$ μm^2 size at $\omega = 0.6$ ms^{-1} and 0.9 ms^{-1}, which are the second and third harmonics of $\omega = 0.3$ ms^{-1}. This is very clear as shown in an inset of Fig. 1. Yu et al. [23] showed that the HH neuron shows a subthreshold oscillations with an angular frequency of $\omega = 0.3$ ms^{-1}. Ozer et al. [9] also obtained inter-spike interval histograms (ISIHs) of an undriven HH neuron, and showed that the ISIH is very broad with a distinct peak near the mean of distribution (21 ms), corresponding to the period of the subthreshold oscillations, $\omega = 0.3$ ms^{-1}. Both findings indicate that the optimal frequency of $\omega = 0.3$ ms^{-1} for the network corresponds to the frequency of intrinsic subthreshold oscillations of the HH neurons [9,23]. Therefore, we suggest that the best temporal coherence of the network is obtained if the frequency of the subthreshold stimulus matches that of the intrinsic oscillations of the network elements.

To provide a clear picture of the dependence of the collective regularity on the cell size, we obtained the change of the regularity with the cell size for the network without external stimulus, $I_{ext} = 0$, and driven by an external subthreshold stimulus with three values of ω mentioned above (Fig. 2). The collective regularity exhibits a resonance-like behavior depending on the cell size regardless of an external stimulus, where a cell size of $S = 6$ μm^2 leads to the maximum coherence, suggesting that the best temporal coherence requires an optimal cell size or an optimal level of the noise. Our results are consistent with the results of Gong et al. [10] and Ozer et al. [9] for an SW HH neuronal network.

To gain more insight into the dependence of the best temporal coherence on the cell size, we obtained ISIHs computed from 10 000 ISIs for the network spikes driven by an external stimulus, $I_{ext} = \sin(0.3t)$, for three values of the cell size, as shown in Fig. 3. For the network with $S = 6$ μm^2, the ISIH has a single sharp peak at the stimulus period, indicating a high degree of phase locking (increasing the network output, i.e., the mean firing frequency), whereas for the network with larger cell sizes, the ISIHs exhibit relatively wider multiple peaks at harmonics of